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Original article

Evolution of management of esophageal atresia with or without tracheoesophageal fistula (EA/TEF) across five decades at a single academic medical center

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Abstract

Background: Despite improved survival in esophageal atresia with or without tracheoesophageal fistula (EA/TEF), complications remain common. We evaluated surgical outcomes at our institution over time and compared them to published benchmarks.

Methods: We performed a retrospective single-center review of patients with EA/TEF treated between 2008 and 2023, comparing outcomes to a prior institutional cohort from 1975 to 1995. Patients were identified using ICD and CPT codes.

Results: A total of 132 patients were included across both cohorts. Patient characteristics were similar between groups. Operative repair increased from 84% to 100% ($p = 0.001$). Stricture (40% vs. 37%) and TEF recurrence (7% vs. 10%) rates remained stable and comparable to benchmarks. Leak rate decreased from 19% to 12%, lower than benchmark reports. Overall mortality dropped significantly from 22% to 6% ($p = 0.012$). Among high-risk Waterston C infants, survival improved markedly from 38% to 79% ($p = 0.015$).

Conclusion: EA/TEF survival has significantly improved, especially among high-risk infants with low birth weight and cardiac disease. While stricture and recurrence rates remain unchanged, leak rates have improved. These findings reflect evolving surgical practices and improved neonatal care.

Keywords

Esophageal atresia, tracheoesophageal fistula, surgical procedures, operative, postoperative complications, infant, newborn, treatment outcome.

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Introduction

Esophageal atresia with or without tracheo-esophageal fistula (EA/TEF) affects 1 in 2,000 to 1 in 4,000 live births, and it is a commonly treated surgical congenital anomaly at major pediatric surgical centers [1]. There has been a dramatic improvement in the survival of infants born with EA/TEF over the last 5 decades, ranging from 36% in the pre-1950 era to over 90% in more recent reviews [2-8]. Improvements in survival are largely attributable to early detection of complex genetic malformations *in utero*, improvements in intensive care management of neonates, especially very low and extremely low birth weight infants, early correction of cardiac defects, and advances in anesthetic management and surgical techniques [9-11].

Despite improvements in survival, the morbidity associated with repair of these anomalies remains high, with leak rates varying from 7-36%, stricture rates varying from 8-37% and recurrent TEF rates ranging from 3-12% [2-4, 12-20]. The wide range of reported complications and their rates is likely attributed to method of diagnosis, variability in surgical techniques, surgical experience, intra-operative protocols, postoperative management and follow-up times [21]. Given the multifactorial nature of these outcomes, comparability across studies describing patients with this rare condition is limited. As such, the current era has led to developments of pediatric surgery consortiums that are interested in collaborative, multi-institutional clinical research to improve clinical outcomes in pediatric surgical care such as the Eastern Pediatric Surgery Network (EPSN) and the Midwest Pediatric Surgery Research Consortium (MWPSC). Both consortia have looked at multicenter EA/TEF outcomes in order to develop uniform pathways for management of EA/TEF patients [22, 23]. The present study aims to examine surgical outcomes for a contemporary cohort of EA/TEF patients treated at our institution, comparing it to a previously published cohort of EA/TEF patients from the same institution between 1975 and 1995 in order to examine changes in care patterns and clinical outcomes over time [24].

Methods

In this single center retrospective cohort study of patients with EA/TEF, chart review was performed for all patients who underwent primary repair at NewYork-Presbyterian/Weill Cornell Medical Center (NYP/WCM) between 1975 and 2023. Our study includes 2 cohorts: period 1, from 1975 to 1995, and period 2, from 2008 to 2023.

The Institutional Review Board (IRB 22-05024774) at NYP/WCM approved this study. To identify charts for review, our institution's i2b2 database was used to query charts for patients < 18 years of age at the time of initial encounter with specific International Classification of Diseases (ICD) 9 and 10 and Current Procedural Code (CPT) codes as follows. The following ICD 10 codes were used: Q 39.1 (EA with TEF), Q 39.2 (congenital TEF without EA), Q 39.0 (EA without TEF). The following ICD 9 codes were used: 530.84 (TEF) and 750.3 (congenital TEF, EA and stenosis). We also captured patients based on CPT codes: 43314 (congenital TEF, EA and stenosis); 43300, 43305 (esophagoplasty [plastic repair or reconstruction], cervical approach); 43310, 43312 (esophagoplasty [plastic repair or reconstruction], thoracic approach); 44313, 43314 (esophagoplasty for congenital defect [plastic repair or reconstruction], thoracic approach). Clinical data were used to classify each patient according to Waterston [25] and Spitz [26] classifications. Operative notes and/or diagnostic esophagram reports were used to classify EA/TEF subtype. Long-gap EA/TEF was defined as > 2 vertebral bodies or > 3 centimeters (cm). Operative repair was classified as primary, delayed primary, or staged. Primary repair was defined as any procedure which restored esophageal continuity at the index procedure. Delayed primary repair was defined by

TEF division and esophageal anastomosis beyond 48 hours. Staged repairs are cases where a total repair was attempted but not feasible, and had to be completed at a later interval.

Associated congenital anomalies were documented from the chart, and only patients with cardiac anomalies that required operative intervention were entered in the cardiac category. For comorbidities, tracheomalacia cases that required intervention, including diagnostic laryngoscopy and bronchoscopy, were counted as significant. Surgical cases of tracheomalacia were those that required tracheopexy or tracheostomy. Complications of esophageal stricture were deemed clinically significant if an intervention was required.

We used a previously published data set [24] from 1975 to 1995 of 81 patients with EA/TEF treated at NYP/WCM and used descriptive statistics to compare this to the data from 1995 to 2022. Cases done from 2008 to 2023 were performed by 5 surgeons; whereas between 1975 and 1995 cases were performed by 2 surgeons. All EA/TEF patients are cared for in a dedicated level IV Neonatal Intensive Care Unit (NICU).

Fisher's exact test for Count Data with simulated p-value (based on 2,000 replicates) was used for comparative statistical analysis with a significance level of $p < 0.05$.

Results

In the historical/period 1 cohort (1975-1995) 81 patients were diagnosed with EA/TEF. Of those patients, 43% (35) were female (**Tab. 1**). The mean gestational age (GA) was 37 weeks (range 28-42), with a mean birth weight (BW) of 2,443 grams (g) (range 915-4,035). Rates of Waterston classes A, B and C were 30% (24), 38% (31) and 32% (26), respectively [24].

For our current/period 2 cohort (2008-2023) 51 patients were diagnosed with EA/TEF. Of those patients, 39% (20) were female (**Tab. 1**). The mean GA was 37 weeks (range 29-41), with a mean BW of 2,400 g (range 670-4,980). Rates of Waterston classes A, B and C were 39% (20), 33% (17), and 27% (14). Most infants from 2008 to 2023 were Spitz class 1 (33, 65%). There were no significant differences in baseline characteristics between periods 1 and 2.

In the period 1 cohort, 30% of patients had cardiac anomalies (24). Seventeen percent (14) of patients had associated gastrointestinal (GI) anomalies and 11% (9) of patients had associated renal anomalies. Two patients had trisomy 18, and 7 (9%) had chromosomal anomalies overall; however the number of patients with VACTERL (vertebral, anal, cardiac, tracheo-esophageal, renal, and limb) defects was not specified. Most patients had type C EA/TEF (67, 83%) with type A and H being the next most common (7, 9% and 5, 6%, respectively). Most patients had a short gap length (69, 85%).

Table 1. Baseline clinical characteristics of esophageal atresia with or without tracheoesophageal fistula (EA/TEF) patients treated in period 1 (1975-1995) and period 2 (2008-2023).

		Period 1 (1975-1995) [a]	Period 2 (2008-2023)
Total patients (n)		81	51
Gender	**Male**	46 (57%)	31 (61%)
	Female	35 (43%)	20 (39%)
Birth data	**Mean GA, weeks (range)**	37 (28-42)	37 (29-41)
	Mean BW, grams (range)	2,443 (915-4,035)	2,400 (670-4,980)
Apgar	**Mean Apgar 1 minute [b] (range)**	7	7 (1-9)
	Mean Apgar 5 minutes [b] (range)	5	8 (3-10)
Waterston classification	**A**	24 (30%)	20 (39%)
	B	31 (38%)	17 (33%)
	C	26 (32%)	14 (27%)
Spitz classification	**1**	Unknown	33 (65%)
	2	Unknown	13 (25%)
	3	Unknown	5 (10%)
Associated congenital anomalies	**Major cardiac anomalies**	24 (30%)	13 (25%)
	Chromosomal anomalies	7 (9%)	2 (4%)
	VACTERL anomalies	Unknown	15 (29%)
	GI anomalies	14 (17%)	14 (27%)
	Renal anomalies	9 (11%)	8 (16%)
EA type, Gross classification	**A**	7 (9%)	0 (0%)
	B	1 (1%)	0 (0%)
	C	67 (83%)	48 (94%)
	D	1 (1%)	1 (2%)
	E (H-type)	5 (6%)	2 (4%)
Gap length	**Short**	69 (85%)	43 (84%)
	Long	12 (15%)	6 (12%)

Data are presented as n (%) if not otherwise indicated. There were no significant differences in baseline characteristics between periods 1 and 2.
[a] Data is abstracted from Tsai et al. [24]; [b] period 2 has APGAR data for 43 of 51 patients.
BW: birth weight; EA: esophageal atresia; GA: gestational age; GI: gastrointestinal; VACTERL: vertebral, anal, cardiac, tracheo-esophageal, renal, and limb.

In the period 2 cohort, 25% of patients had cardiac anomalies (13). Of these major anomalies, 6 patients had a right sided aortic arch (12%), 1 patient had pulmonic stenosis (2%), 1 patient had a hypoplastic left heart (2%), 2 patients had tetralogy of fallot (4%), 2 patients had aortic coarctation (4%). Twenty-seven percent (14) of patients had associated GI anomalies and 16% (8) of patients had associated renal anomalies. Twenty-nine percent of patients (15) had VACTERL defects. One patient had trisomy 18. Most patients had type C EA/TEF (48, 94%) with H being the next most common (2, 4%). Most patients had a short gap length (43, 84%).

Of all 132 patients, 90% (119) underwent operative intervention, and the rate of surgical intervention increased significantly with time, from 84% (68) in the period 1 cohort, to 100% (51) in period 2 (p = 0.001, **Tab. 2**). In the period 2 cohort, half (3/6, 50%) of the EA/TEF repairs that were started thoracoscopically were converted to open. All 3 cases were converted to open due to concern for tension on the esophageal-esophageal anastomosis and inability to approximate the esophagus without tearing through the esophageal tissue with suture. All cases that were attempted thoracoscopically were either Spitz 2 or Spitz 3. In period 2 all patients who underwent intervention had restoration of esophageal continuity except for 2 patients who had TEF ligation only due to hemodynamic instability. Use of delayed primary repair decreased over time from 9% (7) to 4% (2) and no interposition grafts were performed in period 2, whereas esophageal replacement was performed in 8 patients from period 1.

Regarding major complications (**Tab. 2**, **Fig. 1**), the overall leak rate was 16% (18), with a decrease leak rate from period 1 of 19% (12) to 12% (6)

Table 2. Outcomes of esophageal atresia with or without tracheoesophageal fistula (EA/TEF) patients treated in period 1 (1975-1995) and period 2 (2008-2023).

			Period 1 (1975-1995) [a]	Period 2 (2008-2023)	p-value
Total patients (n)			81	51	-
Operative repair type	**Primary repair**		49 (60%)	45 (88%)	0.099
	Delayed primary repair		7 (9%)	2 (4%)	
	Staged repair	**Total**	12 (15%)	4 (8%)	
		Primary esophageal anastomosis	2/12 (17%)	2/4 (50%)	
		Esophageal replacement	8/12 (67%)	0	
		Extrathoracic esophageal lengthening	2/12 (17%)	0	
Operative repair characteristics	**Total patients who underwent operative intervention**		68 (84%)	51 (100%)	**0.001**
	Total number of anastamoses		62 (77%)	49 (96%)	**0.003**
Leak	**Overall**		12/62 (19%)	6/49 (12%)	0.313
	Esophageal-esophageal anastomosis		6/12 (50%)	6/6 (100%)	
	Esophageal-colonic anastomosis		6/12 (50%)	None in series	
Stricture	**Overall**		25/62 (40%)	18/49 (37%)	0.7
	Management type	Managed with dilation	22/25 (88%)	17/18 (94%)	0.473
		Required anastomotic revision	3/25 (12%)	1/18 (6%)	
	Mean number of dilations (range)		2 (1-9)	3 (1-12)	-
Tracheomalacia	**Total**		9 (11%)	9 (18%)	0.287
	Management type	Non-op management	2/9 (22%)	5/9 (55%)	0.147
		Surgical intervention	7/9 (78%)	4/9 (44%)	
Recurrent TEF	**Overall**		6 (7%)	5 (10%)	0.628
Mortality	**Overall**		18 (22%)	3 (6%)	**0.012**
	Death timing	**Death before definitive repair**	7 (9%)	2 (4%)	0.368
		Death after surgical repair	11 (14%)	1 (2%)	
	Death rates by Waterston criteria [b]	**Waterston A**	0/24 (0%)	0/20 (0%)	1.000
		Waterston B	2/31 (6%)	0/17 (0%)	0.412
		Waterston C	16/26 (62%)	3/14 (21%)	**0.015**

Data are presented as n (%) if not otherwise indicated.
[a] Data is abstracted from Tsai et al. [24]; [b] patient distribution by Waterston classification is reported in **Tab. 1**.
Non-op: non-operative; TEF: tracheoesophageal fistula.

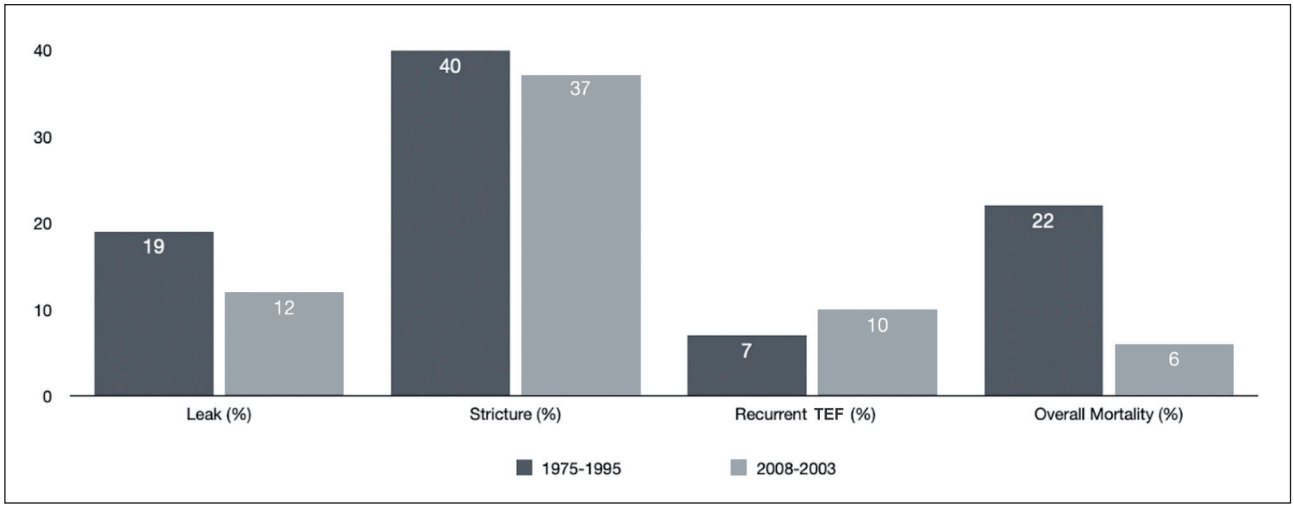

Figure 1. Surgical outcomes of esophageal atresia with or without tracheoesophageal fistula (EA/TEF) infants treated in period 1 (1975-1995) [a] and period 2 (2008-2023) based on Waterston Classification.
[a] Data is abstracted from Tsai et al. [24].
TEF: tracheoesophageal fistula.

in period 2. The stricture rate across all cohorts was 39% (43) and did not change with time (40% in period 1, 37% in period 2). The majority of strictures (91%) were managed with dilation; out of the patients with strictures, only 3 (12%) patients in period 1 and 1 (6%) patient in period 2 underwent anastomotic revision. A total of 14% (18) of patients developed tracheomalacia: in period 2, 4 of those patients required operative management which included tracheostomy or tracheopexy. Of all 132 patients, 11 (8%) experienced recurrent TEF, with 6 (7%) in period 1 and 5 (10%) in period 2.

In a subgroup analysis based off Gross type, in period 1, anastomotic leak rates were substantially higher in patients undergoing staged repair – primarily for long-gap type C and type A EA – compared with those receiving primary or delayed primary repair (6/11 [54%] vs. 6/51 [11%]). In period 2 all 6 leaks occurred in patients with type C EA/TEF, of which only 1 involved a long-gap defect. Three patients with leaks developed strictures, each successfully managed non-operatively; 1 leak was associated with recurrent TEF and treated surgically.

Recurrent TEF timing and management also varied by period. In period 1, 6 patients were diagnosed between 10 days and 4 years post-repair, confirmed by upper GI series and bronchoscopy [24]. Three underwent re-operation with TEF division and pleural flap interposition, 1 was observed for a pinpoint TEF, and 2 had undocumented follow-up. In period 2, 5 recurrent TEFs were identified – 4 with type C and 1 with type D EA/TEF – between 2 and 2.5 months postoperatively.

The overall mortality rate was 16% (21) with 7% (9) of infants dying prior to definitive repair and 9% (12) of infants dying after surgical repair. Mortality rates decreased over time from 22% (18) to 6% (3) in the 2 cohorts (p = 0.012). Survival based on Waterston criteria also improved over time, with the most dramatic increase in survival seen for Waterston C infants – from 38% in 1975-1995 to 79% in 2008-2023 (p = 0.015) (**Fig. 2**).

Follow-up duration varied between eras. In period 1, follow-up ranged from 2 weeks to 9 years, reflecting variability in historical documentation and post-discharge practices. In period 2, follow-up was more consistently recorded, with a median duration of 24 months (IQR 10-49.5) and a median of 3 clinic visits (IQR 2-5.75). The shortest follow-up in this cohort was 1 month and the longest nearly 12 years (140 months). Two patients in the contemporary cohort were lost to follow-up. These follow-up intervals provide the context for the capture and interpretation of postoperative complications in both periods.

Of the 18 deaths from 1975 to 1995, 6 deaths were from cardiac anomalies, 2 deaths were from intracranial hemorrhage, 1 was from hyaline membrane disease, another from hypoplastic lungs, 2 from biliary atresia, 1 was from renal failure, 2 deaths were a result of trisomy 18, 2 deaths had an unknown cause and a singular death was caused by recurrent aspiration caused by a missed TEF (**Tab. 3**). In this cohort of the 11 deaths prior to definitive surgical repair, 4 died after staging procedures and 7 died prior to any surgical intervention (**Tab. 2**).

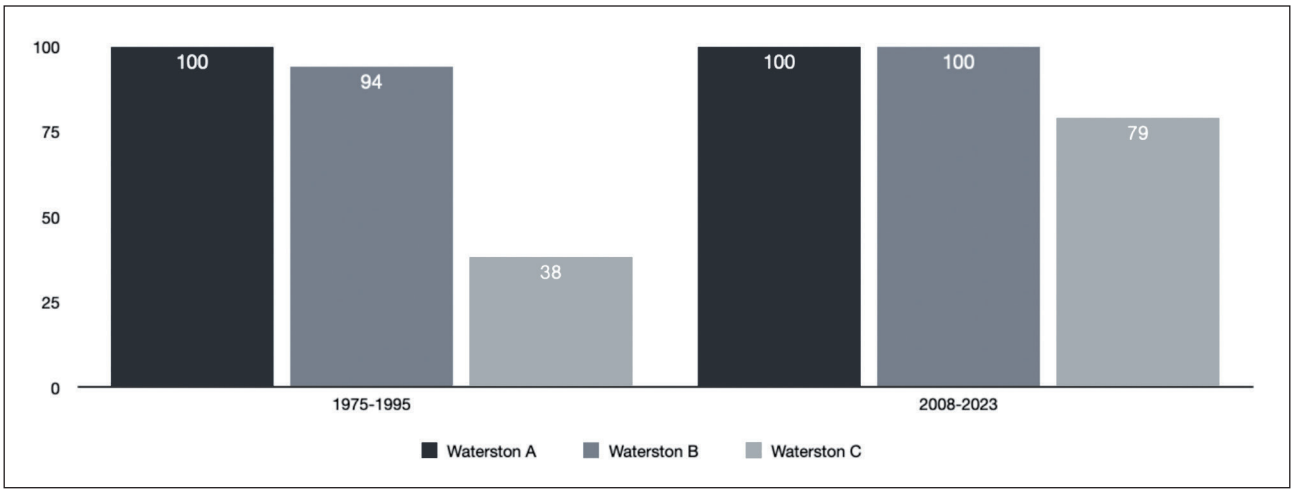

Figure 2. Survival of esophageal atresia with or without tracheoesophageal fistula (EA/TEF) infants treated in period 1 (1975-1995) [a] and period 2 (2008-2023) based on Waterston Classification.
Data are presented as percentages.
[a] Data is abstracted from Tsai et al. [24].

Table 3. Causes of death among infants with esophageal atresia with or without tracheoesophageal fistula (EA/TEF) treated in period 1 (1975-1995) and period 2 (2008-2023).

	Period 1 (1975-1995) [a] (n = 18)	Period 1 (2008-2023) (n = 3)	Total (n = 21)
Cardiovascular	6 (33%)	2 (67%)	8 (38%)
Lung disease of prematurity	2 (11%)	0	2 (10%)
Frasier syndrome/ renal failure	1 (6%)	0	1 (5%)
Trisomy 18	2 (11%)	1 (33%)	3 (14%)
Intracranial bleed	2 (11%)	0	2 (10%)
Biliary atresia	2 (11%)	0	2 (10%)
Aspiration from missed TEF	1 (6%)	0	1 (5%)
Unknown	2 (11%)	0	2 (10%)

Data are presented as n (%).
[a] Data is abstracted from Tsai et al. [24].
TEF: tracheoesophageal fistula.

Discussion

Our data demonstrate a clear improvement in mortality to an overall mortality of 6% from 2008 to 2023, including the sickest infants in Waterston class C. Moreover, only in the 1975-1995 cohort were there any pre-operative deaths before any attempt at TEF repair was made (7). This is consistent with previous literature which has demonstrated that EA/TEF patients with very low BW (VLBW) and patients in Spitz class 1 and 2 have improved over time. More recently the MWPSC conducted a multicenter retrospective study of 282 type C EA/TEF patients at 11 centers from 2009 to 2014, and their mortality rate was similar to ours at 6% [23]. Improved survival for Waterston C infants and in overall survival can be attributed to the fact that we are performing earlier definitive primary repairs in low BW (LBW) infants, as LBW is no longer a contraindication for performing primary repair as was originally advocated for by Waterston and colleagues in 1962 [25]. More importantly, early detection of complex genetic and chromosomal malformations *in utero* as a result of more comprehensive antenatal testing and counseling, early correction of cardiac defects as well as improved management of LBW infants in the NICU including improved and standardized NICU care across the United States, innovations in ventilator strategies and management of lung disease of prematurity have contributed to improved survival [27-35]. Over the long-time period of this study, strides in NICU care have been tremendous and while trends in outcomes provide insight into evolving clinical practice, we acknowledge that improved survival and evolving surgical outcomes are in large part due to improved neonatal care.

Nonetheless, children in highest-risk categories have higher rates of postoperative complications, which was also seen in our study [36-39]. The 2008-2023 patient cohort was classified into the amended EA/TEF classification system based on a review by Spitz et al. of 372 cases of EA/TEF treated between 1980 and 1992 which demonstrated that BW and cardiac disease were major determinants of survival [26]. Of note with this classification a Spitz class 3 infant is more tenuous than a Waterston C infant – with a Spitz class 3 infant weighing less than 1,500

g and having a major cardiac anomaly, whereas Waterston C encompasses infants weighing less than 1,800 g and having a severe pneumonia or a major cardiac anomaly.

Of our 5 Spitz class 3 infants in the contemporary cohort, 3 died. One infant was 670 g with severe VACTERL anomalies including atrial septal defects, ventricular septal defects (VSD) and pulmonic stenosis as well as anorectal atresia requiring a colostomy on day of life 1. This infant suffered from a preoperative perforation of the hypopharynx from Repogle placement and required a perioperative gastrostomy tube for gastric decompression. The infant was taken to the Operating Room for worsening respiratory status and the TEF was ligated with the esophagus left in discontinuity due to hemodynamic instability. The infant died at 3 months of life from multisystem organ failure. The second mortality was a 1,300 gram infant also with severe VACTERL anomalies including a persistent ductus arteriosus, hypoplastic left heart, aortic coarctation, left superior vena cava, duodenal atresia, and choanal atresia. After cardiac surgery this infant was planned for EA/TEF repair but this was also ultimately aborted due to hemodynamic instability and the TEF was clipped with the esophagus left in discontinuity. This patient also died at 3 months of life, at that time autopsy showed cause of death as left ventricular hypoplasia resulting in single ventricle physiology as well as total parenteral nutrition-induced liver injury. The final death occurred in a 1,000 gram infant with trisomy 18 with associated atrioventricular canal, VSD, congestive heart failure and severe chronic lung diseases. This infant's EA/TEF was successfully repaired; however, the infant died at 4 months of life from respiratory complications unrelated to EA/TEF repair. All 3 deaths occurred in VLBW infants with severe cardiac anomalies and none of the deaths were directly related to the patients' EA/TEF (**Tab. 3**).

Our data also demonstrated a shift in operative management, with more infants undergoing any operative repair and primary rather than delayed repairs, and none with esophageal replacement procedures, in more recent years. This is consistent with multiple small cohort studies [40, 41].

Our study demonstrated a dramatic reduction in anastomotic leak rate, 12% from 19%. The benchmark leak rate from the MWPSC is 18% [23]. We attribute this to fewer delayed or staged procedures in the modern era as surgeons are more comfortable operating on sicker, smaller premature infants as NICU care has improved. Moreover with each operation there is an incredible attention to adequate focus on adequate mobilization of the pouch and a tension free repair.

In our study, the recurrent TEF rate from 2008 to 2023 was 10%, while the benchmark set by the MWPSC of 5%. As mentioned above, our leak rate from 2008 to 2023 (12%), however, is lower than the 18% reported by the MWPSC; though, our sample size is much smaller [23]. Our stricture rate from 2008 to 2023 (36%) was similar to that of the MWPSC – which was 43%. Our data shows that management of these complications shifted from an emphasis on surgical correction to medical and minimally invasive approaches. This is consistent with an international survey of 170 surgeons from 31 countries conducted in 2012, which found 77% of surgeons had no limit on the number of esophageal dilations for stricture until operative management was considered. In our study, in the 2008-2023 patient cohort, only 1 stricture required surgical intervention.

Strengths and limitations

A strength of this study is its longitudinal review of outcomes and practice patterns, with a controlled comparison given their origin from a single institution. Furthermore, characteristics of both groups were comparable. However, limitations of the present study include the limited generalizability given the patients were all treated at a single institution and the inability to use statistical tests for hypothesis testing across groups given the lack of raw data from the earlier time periods.

Conclusions

Future efforts at our center are focused on strengthening multidisciplinary collaboration across pediatric surgery, neonatology, cardiology, gastroenterology and other sub-specialties to further optimize management of EA/TEF patients. Standardized protocols have now been implemented for prenatal counseling, NICU hand-offs, safety checks, sedation and endotracheal tube management for prevention of inadvertent extubations, consistent use of proton pump inhibitors, feeding pathways, as well as for long-term follow-up with an aerodigestive clinic. In parallel we plan to incorporate patient and family reported outcomes into follow-up to provide a more comprehensive understanding of long-term quality of life as well as functional status. We are

closely monitoring multicenter data on posterior tracheopexy, a relatively newer surgical technique that aims to prospectively minimize the morbidity of tracheomalacia, and to eliminate the risk of recurrent TEF. We also aim to expand participation in regional and national pediatric surgery consortia to facilitate multicenter data sharing, improve statistical power, and support the development of standardized care pathways for EA/TEF [42]. Despite improved survival for EA/TEF infants, continued research is needed to identify risk factors for and ways to mitigate risk of postoperative complications after EA/TEF repair.

Declaration of interest

The Authors have no conflicts to report. The Authors did not receive support from any organization for the submitted work. The Authors have no relevant financial or non-financial interests to disclose.

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