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The 30-day outcome of neonates operated for esophageal atresia

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KEYWORDS

Esophageal atresia, Surgical outcomes, Tracheoesophageal fistula, Resource restricted

ABSTRACT

Background: Despite great advances in the overall management of neonates with esophageal atresia (EA), many complications leading to morbidity still occurs. Most complications can be treated conservatively, but effective management is needed to reduce long-term morbidity.

Methods: A retrospective cohort study was performed on neonates treated for EA with/without a tracheoesophageal fistula (TEF) between 2001 and 2020. Data were collected from patient records, discharge summaries, and surgical notes. The information recorded included: maternal and neonatal demographics, information regarding the diagnosis, and details surrounding the surgery.

Results: During the 19-year study period, 53 neonates with a mean gestational age of 36.7 weeks were included for analysis. Forty-nine percent presented with an associated anomaly (most commonly, complex cardiac lesions). The majority (83%) had a primary repair on a median of day 3 of life. Nineteen neonates had a surgical complication 30 days post-repair: 7 minor (contained leaks and a chylothorax) and 12 major complications including anastomotic strictures, major anastomotic breakdowns, a recurrent TEF, and 5 surgery-related mortalities.

Conclusion: This study showed less morbidity and mortality of neonates born with EA, despite a high incidence of associated anomalies, in a resource-restricted hospital. It is important to highlight that even with limited resources, centers in low- or middle-income countries can have good outcomes.

INTRODUCTION

Esophageal atresia (EA) is a rare and potentially life-threatening congenital disease with the incidence being approximately 1 in 2500-3000 live births.[1-4] Although there are many different types of esophageal atresia described, approximately 90% are associated with a distal tracheoesophageal fistula (TEF).[1]

In 1941 Cameron Haight performed the first successful EA with a distal TEF repair. Currently, the survival improved as surgical strategies combined with neonatal anesthesia and intensive care improved.[4-8] Despite improved survival, we still see high mortality rates in certain countries around the globe including the Middle East and Asia.[1,7] Mortality usually occurs secondary to prematurity and cardiac abnormalities.[2] Spitz's revised prognostic classification of babies with EA with/without TEF published in 1994, includes 2 determinants for prognosis: birth weight and the presence of cardiac anomalies. [2] Although this classification is partially outdated, it is still used as a reference for prognosis today.

The morbidity includes anastomotic leakage, anastomotic stricture, gastroesophageal reflux disease, and recurrent TEF.[1,2] Most of these complications can be treated conservatively, especially if detected early.[3] It is, therefore, essential to managing these early complications effectively in order to reduce long-term morbidity. [4]

We present a retrospective review of the 30-day surgical outcome of neonates born with EA with or without a TEF.

METHODS

Data collection: A retrospective descriptive cohort study was performed that included all neonates treated for EA with/without a TEF between 2001 and 2020, at our tertiary unit.

Inclusion criteria: Neonates with esophageal atresia with and without tracheoesophageal fistula operated with esophageal anastomosis (primary or delayed) in our unit were included in this study. Those in whom esophagostomy and gastrostomy performed as initial surgery and planned for esophageal replacement at a later age was not included.

Data were collected from patient records, discharge summaries, and surgical notes. The information recorded included: maternal demographics (maternal age and antenatal history), neonatal demographics (gestational age, sex, birth weight, multiple pregnancy and place of delivery (born at or transfer to center)), and information regarding the diagnosis (date, type of EA and presence of associated anomalies). Details about the surgery and 30-days post-repair complications and mortality included: duration of ICU stay, post-repair ventilation, hospital stay, and information on the feeds.

Ethical and statistical considerations: Descriptive statistical analysis was performed including means and standard deviation, frequency and percentage, as appropriate. All the data were anonymized. Ethics approval was obtained.

RESULTS

Demography: During the 19-year study period, 63 neonates were presented with different types of EA. Ten neonates did not meet the inclusion criteria and were excluded (Table 1). The remaining 53 neonates were included for analysis.

Table 1: Neonates excluded from the surgical data analysis

Exclusion criteria	Number of neonates excluded
Neonates that died prior to any surgery	2
Neonates that had no EA/TEF repair and esophageal replacement planned for an older age (they only received a gastrostomy +/- esophagostomy +/- fistula ligation at initial procedure)	5
H-type TEF without EA	3

The mean gestational age was 36.7 ± 2.6 weeks, and the mean birth weight was 2480 ± 735 grams. Four (8%) neonates were twins. Seventeen (32%) neonates were in-born, while 51% were transferred from referring units (this information was not documented for the remaining 9 neonates). Further demographic data are summarized in Table 2.

Diagnosis and associated anomalies: The postnatal diagnosis of an EA with/without a TEF was made at a mean age of 1.4 ± 1.3 days. Fifty (94%) neonates presented with an EA and a distal TEF (Gross Type C), while the remaining three (6%) presented with isolated esophageal atresia (Gross Type A) [5] Six neonates (11%) presented with a long gap EA, defined by the surgeon on a contrast study (pre-operative or in the theater) or at the time of surgery, as a gap of more than 3 cm or 2 vertebral bodies. [6] Two (4%) neonates with long-gap had isolated EA. Different surgical strategies were used for the neonates born with a long gap EA (Fig. 1).

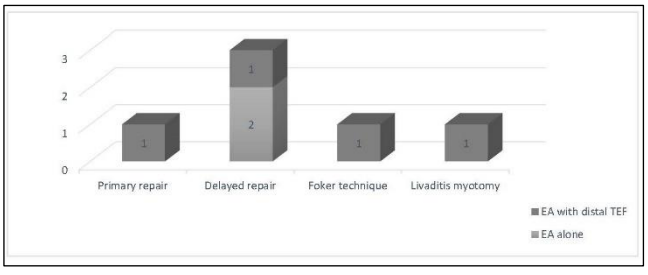

Figure 1: Summary of surgical strategies for neonates born with a long gap EA with/without a TEF

Almost half of the neonates (n=26 (49%)) presented with an associated anomaly, including twenty-two patients with VACTERL anomalies (the most common being complex cardiac lesions (n=16)), three with chromosomal abnormalities (Trisomy 18 (n=1), Trisomy 21 (n=1), and CHARGE syndrome (n=1)) and one neonate with duodenal atresia.

Table 2: Summary of the demographic data

Demographic data	Results (n=53)
Male: Female	32:21
Premature (GA <37 weeks), n (%)	17 (32)
Very low birth weight (birth weight <1500 g), n (%)	4 (8)
Mothers that had a documented antenatal ultrasound at any time during the pregnancy (independent of the findings), n (%)	28 (53)
Mothers that had an antenatal ultrasound with polyhydramnios at any stage during pregnancy, n (%)	9 (17)
Maternal age (years), mean ± SD	28 ± 6
Retroviral disease positive mothers*, n (%)	4 (8)
VDRL positive mothers, n (%)	3 (6)

*All neonates of retroviral positive mothers, had a negative PCR at 6 weeks
VDRL: venereal disease research laboratory test; GA: gestational age; PCR: polymerase chain reaction

Seventeen (32%) neonates presented with a complex cardiac lesion which included atrio-ventral septal defect (AVSD) (n=6), AVSD with tricuspid atresia (n=1), ventricular septal defect (VSD)/patent ductus arteriosus (PDA) (n=3), atrial septal defect (ASD)/PDA (n=2), ASD (n=1), PDA needing surgical repair (n=1), atrial stenosis (n=1), tricuspid atresia (n=1) and a double aortic arch (n=1). Neonates with uncomplicated patent ductus arteriosus (PDA's) alone, were not included as complex cardiac lesions.

Surgical outcome: Neonates born with EA with/without a TEF had their surgery on a median of 3 days (IQR 2-5 days) after birth. Forty-four (83%) neonates had a primary EA and TEF repair, while 7 (13%) had a delayed repair with/without a fistula ligation at initial surgery. Two (4%) neonates had an attempted repair (one of which was a Foker procedure), but both demised prior to definitive repair.

Table 3: Summary of feeding post repair

Feeds post repair	Results
NGT feeds started (days), mean ± SD	2.2 ± 2.1
Oral feeds started (days), mean ± SD	10.6 ± 6.2
Full oral feeds (days), mean ± SD	17.0 ± 12.6
Neonates that received gastrostomies before or after the repair, n (%)	12 (23)

The neonates were extubated on a mean day of 7.6 ± 9.2 post-repair. They stayed in NICU for a mean of 16.6 ± 14.0 days and were discharged on a mean of 31.5 ±29.5 days. The post-repair feeding history is summarized in Table 3. Thirty (57%) neonates had a contrast swallow on a mean of 10.5 ± 5.2 days post-repair. Contrast study was normal in 19 cases. The remaining 11 included a minor contained leak (n=7), major anastomotic breakdown (n=2), anastomotic stricture (n=1) and recurrent TEF (n=1).

Thirty-day post-surgery complications were classified according to the classification of surgical complications published in the Annals of surgery 2004 (Table 4). [7] Nineteen (36%) neonates had a surgical complication 30-days post-primary or delayed repair (Table 4): 7 (13%) minor and 12 (23%) major complications. Five (9%) neonates died due to surgery-related complications (30-days post-repair) with one death being on the operating table secondary to bleeding and a tension pneumothorax.

Table 4: Surgical complications 30 days post-repair according to the post-surgical complication's classification.[7]

Grade	Description	Complication	Total (n=19)
I	Any deviation from the normal post-operative course, with no need for pharmacological treatment, surgical or radiological interventions (with some allowances).	Contained anastomotic leak	6 (32%)
II	Pharmacological treatment not allowed in Grade I, the need for blood transfusion or TPN.	Chylothorax	1 (5%)
III	Any surgical/endoscopic/radiological intervention.		
IIIb	GA needed.	Anastomotic strictures needing dilatation Recurrent TEF Major leak needing redo-surgery and ± gastrostomy	4 (21%) 1 (5%) 2 (11%)
V	Death.	Major anastomotic disruption needing redo-surgery, leading to sepsis and later death Sepsis, persistent acidosis leading to multi-organ failure and death 30-day post-op Attempted repair only (demised prior to definitive repair) On-table death	1 (5%) 1 (5%) 2 (11%) 1 (5%)

On further follow-up, fourteen (26%) neonates were diagnosed with symptomatic tracheomalacia, of which 11 (21%) were confirmed on bronchoscopy. Only 3 of these neonates required an anterior aortopexy, the remainder improved with conservative management. Eight (15%) neonates required a Nissen fundoplication for severe gastroesophageal reflux disease at a mean age of 10.4 ± 8.5 months and five (9%) neonates required an esophageal replacement at a mean age of 17.0 ± 8.5 months.

DISCUSSION

Surgical outcomes of neonates born with esophageal atresia (EA) with/without a TEF have improved in recent years due to improvements in surgical technique, anesthetic care, and neonatal intensive care. [3]

There appears to be a slight male predominance in most studies. In the Global PedSurg Research Collaboration, a multicenter, international study, 56%

of patients with EA/TEF were male. [9] This is in keeping with our results where 60% of neonates were male. In the Global PedSurg Research Collaboration, the median weight at presentation was 2500g with a median gestational age of 37 weeks. Similarly, in our study, we found that most of the neonates were close to term, with a mean gestational age of 36.7 weeks and a mean birth weight of 2480g. Historically, weight is a prognostic factor and should be considered when planning a repair in neonates born with an EA with/without a TEF.

EA with/without TEF can occur in isolation or can be associated with various anomalies, most commonly VACTERL syndrome. [10-13] Other anomalies include CHARGE syndrome, complex cardiac lesions, and other chromosomal abnormalities such as Trisomy 13, 18, and 21. Wang et al. performed a nationwide (USA) analysis of the clinical outcome of 4168 neonates born with EA with/without a TEF in 2014. [13] The most common associated congenital anomaly in their cohort was cardiac abnormalities, with the most common non-cardiac anomaly being renal. This was similar to the Global PedSurg Research Collaboration study (2021) with similar rates occurring in middle-income countries (47%). [9] In a Ghanian study (2016), 33% of patients presented with associated congenital anomalies with 6 patients having two or more associated anomalies. [14] Our results are similar to the international literature, with 49% of all neonates presenting with an associated congenital anomaly.

The Global PedSurg Research Collaboration found that 69% of patients in middle-income countries received a primary anastomosis, as compared to 78% in high-income countries. [9] This was similar in our study, where 83% underwent a primary repair. They also found that the primary procedure was performed at a median of 2 days after arrival at the referring hospital which was similar to our study. [9] This is much different in Ghana, where surgery was performed at a mean age of 10.3 ± 6.2 days of life. [14] They did however include both primary repair and staged repair in their study.

Eighty-five percent of patients included in the Global PedSurg Research Collaboration were ventilated for 5 ± 6 days after surgery with a hospital stay of 18 ± 18 days. [9] They did include all types of EA surgery in their data and most of these results were similar in both high-income countries and middle-income countries with a big difference in low-income countries. In our study we ventilated the patients for over 7 days on average after surgery with a longer hospital stay.i

In the Global PedSurg Collaboration, the median time to first enteral feed was 6 ± 6 days, to first oral feed was 7 ± 6 days and full oral feeds were achieved on a median day 14 ± 12 post-surgery. [9] Full feeds were established on a median of 5 days postoperatively for the 120 patients included in the review article by Roberts, et al.[1]

As seen in different studies, there is still no consensus among surgeons regarding the need and duration of postoperative ventilation, when to start enteral feeds, and whether to start enteral feeds via a nasogastric tube or orally. We prefer to keep our neonates intubated and ventilated post-repair for at least 24 – 48 hours, but due to other factors like congenital abnormalities (e.g., complex cardiac lesions) they stay ventilated for longer. Our main reasons for postoperative ventilation are small and/or premature neonates, a long surgical procedure, and mostly to protect our repair from a potential traumatic re-intubation if needed in the middle of the night by an inexperienced registrar on call. The ERNICA consensus statement for patients born with EA and TEF in 2018 recommended that postoperative ventilation should not be routinely done and only reserved for selected patients. [15] They also recommended that feeding may routinely be started via a trans-anastomotic tube 24 hours post-surgery and that oral feeding may be initiated any time after 24 hours postoperatively. In contrast to this consensus statement, neonates in our unit are routinely first fed via nasogastric tube and oral feeds are mostly started after a contrast study had been performed post-repair.

Okata, et al., (2016), evaluated the risk factors for anastomotic complications and reported an incidence of 3 – 9% for anastomotic leaks and 21 - 57% for anastomotic strictures. [16] They found tension on the anastomosis to be a significant intraoperative predictor for the development of anastomotic complications. Teague et al., similar to Okata et al., found that the most common early postoperative complications of EA surgery with the greatest impact on medium and long-term outcomes were anastomotic leaks (3 - 20 %), anastomotic strictures (39 - 57%), and a recurrent TEF (3 - 7%). [17]

The Midwest Pediatric Surgery Consortium, in their large, multicenter study, reported a complication rate of 62% in 292 babies. [18] Anastomotic strictures requiring intervention occurred most (43%), followed by anastomotic leaks (18%) and recurrent fistulae (16%). Esophageal dehiscence occurred in 5% of their patients and they had an overall mortality of 6%. They reported that placement of a trans-anastomotic tube was associated with an increase in anastomotic strictures in their experience. In our study, the stricture rate 30 days post-repair was low (only 8%), possibly due to the routine placement of a trans-anastomotic tube that we found both protects the anastomosis and assists with early enteral feeding. We would postulate that other factors e.g., the tension

on the anastomosis, delayed surgery, and surgical technique might be bigger risk factors for strictures than a trans-anastomotic tube alone.

Recurrent fistulae are a less common postoperative complication but have increased morbidity. Teague et al. cited incidences of 3 - 7% and confirm that this complication can present with recurrent chest infections, acute life-threatening events and are often difficult to diagnose. [17] The Midwest Pediatric Surgery Consortium reported 15 infants (5%) who developed recurrent fistulae with a long gap EA. [18]

Our overall 30-day post-surgery complication rate (36%) is similar to international data. Four (8%) neonates developed esophageal strictures that required dilatation before discharge from the hospital which is much lower than reported in the literature (21 – 57%). [16–18] We do not routinely dilate patients post-repair, even if the contrast study shows a narrowing. Routine follow-up with parental counseling is done after discharge and dilatation is done only if symptoms of dysphagia develop.

Seven of our neonates developed minor leaks with another three that had major anastomotic breakdowns (suspected clinically and/or diagnosed on contrast study) requiring surgical intervention. Our overall anastomotic leak rate (of 19%) is again comparable to those reported in the literature (3 - 20%). [16–18] We had only one patient that developed a recurrent TEF within the first 30-days post-primary repair, which is much lower than reported in the literature we reviewed (2% vs 3-16%). [17,18] We would suggest special care should be taken when it comes to the division of the fistula, closer to the trachea without leaving too much of a stump behind.

Our mortality rate 30-day post-repair was 15% of which only 5 (9%) deaths could be attributed to surgical complications and is comparable to the 7% mortality rate from high-income countries. [9] The remaining 3 mortalities were due to medical and congenital complications that included: bronchopneumonia (n=1), problems with ventilation and re-intubation (n=1), and congenital abnormalities (Trisomy 18, n=1). The mortality rate of the Midwest Pediatric Surgery Consortium was 6% with a significant association between mortality and congenital heart disease. [18] The national cohort from France reported a similar rate of 5% in the first year of life. [12] They found EA with a distal TEF, prematurity, and associated anomalies to have strong associations with mortality. The large multicenter study by the Global PedSurg Research Collaborators reported an overall 30-day mortality rate of 25%. [9] The majority of these (86%), however, were in low-income countries, followed by middle-income countries (29%), and only 7% in high-income countries.

Our results show that it is possible for middle-income countries to achieve similar results as in high-income countries and high-volume centers, specifically when it comes to the 30-day post-surgical outcome. Our 30-day surgical complications are similar to those discussed in the literature and include anastomotic leaks (minor and major), strictures, recurrent TEF and tracheomalacia.

The limitation of this study is that it is only a single-center study and future directives can include multicenter outcome studies for neonates born with EA with or without a TEF.

CONCLUSION

Decades after the first esophageal atresia was described in the 17th century, this congenital disease remains unique with continued improvement in the outcome, especially in high volume centers and high-income countries. This study shows low morbidity and mortality of neonates born with EA with/without a TEF, despite a high incidence of associated anomalies, in a resource-restricted hospital.

It is important to highlight that even with limited resources, centers in low- or middle-income countries can have good outcomes. A good multidisciplinary team approach for early diagnosis, appropriate surgery, post-operative care, and long-term follow-up constitutes the future in the management of this unique group of patients.

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Author Contributions: Author(s) declared to fulfil authorship criteria as devised by ICMJE and approved the final version.

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