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Original Article

Post-Operative Prognosis of the Patients with Esophageal Atresia: The 22-Year Experience of a Reference Hospital

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Abstract

Introduction: To investigate the post-operative prognosis of newborns with esophageal atresia (EA). ***Methods:*** Patients operated for EA were classified according to their gestational age, birth-weight, gender, and study period (1996-2006 & 2007-2017), type of atresia, accompanying additional anomaly and Waterston risk categories. ***Results:*** Of the 87 cases, 87.4% had EA + distal tracheoesophageal fistula, 11.5% had isolated EA and 1.1% had isolated tracheoesophageal fistula. While 36.8% patients developed post-operative complications, 37% patients died. There was a statistically significant difference between full-term and preterm newborns in terms of mortality rate ($p<0.05$). Most of dead cases had low birth-weight of <2500 g (n=28/55). Mortality rates of the patients with EA according to two study periods were 57% and 22%, respectively. Main causes of mortality were sepsis (n=17), pneumonia (n=9), and respiratory failure (n=6). Mortality rate among those had accompanying additional anomaly was 84.4% ($p<0.05$). There was a significant difference between Waterston's risk classification (Groups C and B) and post-operative complication, and mortality rates ($p<0.05$). In those surviving cases, the most common long-term complication was dysphagia (83%). ***Conclusion:*** Morbidity and mortality rates of patients with EA in developing countries like to our study are still high. Low birth-weight, accompanying additional anomaly, Waterston Groups C and B, and post-operative complications are the most important causes of mortality. Waterston's risk classification is a good predictor of the prognosis in patients with EA.

Key words *Classification; Esophageal atresia; Mortality; Prognosis; Surgery; Tracheoesophageal fistula*

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Introduction

Esophageal atresia (EA), which is the most important congenital anomaly of esophagus, presents with many different anatomical forms; however, the proximal EA and distal tracheoesophageal fistula (TEF) is most frequently encountered type of EA.[1-3] EA was firstly described by William Durston in 1670 and included in the medical literature. It occurs in one of every 2500 live births.[2,4] This congenital anomaly previously was 100% fatal; however, 90% of these newborns recently have a chance to survive.[1] Although it has not a genetic trait, some familial cases with EA/TEF have been reported. In 30-50% of the cases, EA might be associated with VACTERL (**V**ertebral defects, **A**nal atresia, **C**ardiac defects, **T**racheoesophageal fistula, **R**enal anomalies, and **L**imb abnormalities). Accompanying additional anomalies have impact on the prognosis of EA. In 6.6% of newborns with EA, chromosomal anomalies,

such as trisomy 13 and trisomy 18, have been identified.[4-6]

Despite progress in surgical techniques and neonatal care, short-term and long-term complications like anastomosis leakage, stricture and recurrence of TEF, and mortality rate of these patients are still high.[1,7,8] However, there are no enough published studies on post-operative prognosis. Therefore, the present study was aimed to investigate the post-operative prognosis of newborns with EA.

Methods

After approval was obtained from the ethics committee of our faculty (Decision No: 13, Date: 22.09.2011), the demographic and clinical data of 87 patients who operated for EA between January 1996 and December 2017 was retrospectively analysed. In order to compare the mortality rates by periods, the overall study period was divided to years of 1996-2006 & 2007-2017. All patients with EA/TEF were included in study and there was no any exclusion criterion from the study.

All patients were cared in a level III neonatal intensive care unit (NICU) and operated under elective conditions as soon as their clinical condition permitted for surgery. Primary anastomosis was performed to patients those had EA + TEF (single-staged procedure). But, gastrostomy was firstly opened in patients with isolated EA while later colonic transposition was performed at three months of postnatal age (staged procedures). During postoperative period, all patients were mechanically ventilated about for at least two days. The patients were given total parenteral nutrition about for seven days, and then enteral feeding was started. The patients were operated after treatment of pre-operative complications if present. In post-operative period, the care of them was provided by both experienced neonatologists and paediatric surgeons.

Postnatal age, gender, birth-weight, gestational age; type of delivery, clinical and radiological findings, age at surgery, duration of mechanical ventilation and hospital stay, presence of accompanying additional anomaly such as cardiac defects, Waterston risk categories,[9] type of surgery, post-operative complications, and causes for mortality were investigated from patients' medical files. According to their birth-weight, the patients were divided into three groups which were 1000-1799 g, 1800-2499 g and ≥2500 g. The patients were also grouped according to Waterston's risk classification and then intergroup comparisons were made. Patients with or without accompanying additional anomaly, and preterm and full-term newborns were compared in terms of post-operative complications and mortality rate.

Statistical Analysis

Statistical analyses were performed using the SPSS 17.0 for Windows software pocket program (SPSS Inc., Chicago, IL, USA). The demographic and clinical characteristics of the patients were compared using the Chi-square testing. The data were expressed as mean ± standard deviation. A p value <0.05 was considered as significant.

Results

Of the 10458 newborns admitted to NICU during study period, 87 had EA (0.83%). Study population consisted of 51 male and 36 female patients with a male/female ratio of 1.42. The mean birth-weight of the patients was 2255.26 ± 600.27 g (1150-3600 g). Demographic and clinical characteristics of the patients with EA were summarised in Table 1. Of the 33 patients with a hospital admission age of more than 2 days, while postoperative complications were observed in 20 patients (74.1%), remaining 13 patients (48.1%) were died. A significant difference was found between day of admission, post-operative complications and mortality rates ($p<0.05$).

The incidence of post-operative complication was significantly lower in newborns with ≥2500 g birth-weight ($p<0.05$). Distribution of post-operative complications according to birth-weight, gestational age and Waterston's risk classification was shown in Table 2. Mortality rate was significantly higher in low birth-weight newborns. Most of died cases had <2500 g birth-weight (n=28/55). A statistically significant difference was found in mortality rate among groups with respect to birth-weight ($p<0.05$). Distribution of mortality rates according to birth-weight and study periods was given in Table 3 and Table 4, respectively.

According to gestational age, a statistically significant difference was found between full-term and preterm newborns with respect to incidence of post-operative complications ($p<0.05$). Distribution of post-operative complications in full-term and preterm newborns was shown in Table 2. Overall, 24 preterm and 8 full-term newborns died (75% *vs* 25%). Hence, there was a statistically significant difference between full-term and

preterm newborns with respect to mortality rates ($p<0.05$).

Accompanying additional anomaly associated with EA was detected in a total of 38 patients; distribution of these anomalies was demonstrated in Table 5. Of them, cardiovascular system anomaly was detected in 15 patients (17.2%), and of them, 9 were associated with VACTERL. These cardiovascular system anomalies were ventricular septal defect (n=5), ventricular septal defect + atrial septal defect (n=3), atrial septal defect (n=2), atrial septal defect + patent foramen ovale (n=2), pulmonary stenosis (n=2), and dextrocardia (n=1).

Main causes of mortality were sepsis (n=17), pneumonia (n=9), and respiratory failure (n=6). Mortality rate among those with and without accompanying additional anomaly was 84.3% and 15.7%, respectively ($p<0.05$). According to Waterston's risk classification, 27 patients were Group A (31%), 26 patients were in Group B (29.9%) and 34 patients were in Group C (39.1%). There was a significant difference between Waterston's risk classification and post-operative complication and mortality rates ($p<0.05$) (Table 2 and Table 6). Higher mortality rate were detected in patients with post-operative complications (75% *vs* 3.9%) ($p<0.05$).

Table 1 Demographic and clinical characteristics of the patients with EA

Characteristic	Number of patients n (%)
Gender (M/F)	51/36 (59/41)
Gestational age (full-term/preterm)	50/37 (58/42)
Birth-weight	
1000-1799 g	21 (24)
1800-2499 g	34 (39)
≥2500 g	32 (37)
Type of anomaly	
EA + distal TEF	76 (87)
Isolated EA	10 (12)
Isolated TEF	1 (1)
Complication	
Pneumonia	21 (66)
Anastomosis leakage	6 (18)
Atelectasis	5 (16)
Total	32 (100)
Mortality	
EA + distal TEF	24 (75)
Isolated	8 (25)
Total	32 (100)

M: Male; F: Female; EA: Esophageal atresia; TEF: Tracheoesophageal fistula

Table 2 Distribution of post-operative complications according to birth-weight, gestational age and Waterston's risk classification

Postoperative complication	Birth-weight (g) 1000-1779 (n)	1800-2449 (n)	≥2500 (n)	Preterm newborns n (%)	Full-term newborns n (%)	Group A (n)	B (n)	C (n)	Total n (%)
Atelectasis	4	0	1	4 (18)	1 (10)	0	1	4	5 (16)
Pneumonia	5	12	4	15 (68)	6 (60)	3	8	10	21 (66)
Anastomosis leakage	3	3	0	3 (14)	3 (30)	0	2	4	6 (18)
Total	12	15	5	22 (100)	10 (100)	3	11	18	32 (100)

Table 3 Mortality rates of the patients with EA according to their birth-weight

Birth-weight (g)	Survival n (%)	Mortality n (%)	Total (n)
1000-1779	4 (19)	17 (81)	21
1800-2449	23 (68)	11 (32)	34
≥2500	28 (88)	4 (13)	32
Total n (%)	55 (64)	32 (36)	87

EA: Esophageal atresia

In addition, long-term complications in surviving patients were mainly dysphagia (n=46) and recurrent pulmonary infections (n=37) (83.6% and 67.3%, respectively). But, there was no any case with recurrent fistula. Major long-term complications seen in 55 patients (63%) were demonstrated in Table 7. Of them, 1 patient with gastroesophageal reflux underwent anti-reflux surgery and remaining was given medical treatment.

Discussion

Types of anomalies in our patients were mainly EA + distal TEF (87%), isolated EA (12%) and isolated TEF (1%). Absence of cases with EA + proximal TEF, and EA + distal and proximal TEF in our study was thought to related to rarity of these types of atresia / TEF and relatively limited number of our study population. However, because there is not enough data in the literature regarding the early postoperative prognosis of the patients with EA, our study would provide important contributions to this field. It also confirms the importance of the Waterston's risk classification. Based on classification system proposed by Holder and Ashcraft,[3] the following incidence rates have been reported in 1964: EA + distal TEF 85.8%, isolated EA 7.8%, isolated TEF 4.2%, EA + proximal TEF 0.8% and EA + distal proximal TEF 1.4%.[10] Types of atresia in our patients were similar to those reported by Celayir et al[11] who conducted a study on 231 patients between the years of 1978 and 2000, and reported the following incidence rates: EA + distal TEF 84.4%, isolated EA 6.1%, isolated TEF 2.5%, EA + distal and proximal TEF 2.2%, EA + proximal TEF 1.3%, and others 3.5%.

Birth-weight is a most important parameter in the Waterston's risk classification. Hence, according to Waterston's risk classification, one our patient died in Waterston Group A, six in Group B and 25 in Group C. Patients with birth-weight <1800 g and with accompanying

Table 4 Mortality rates of the patients with EA according to study periods

Periods	Survival n (%)	Mortality n (%)	Total (n)
1996-2006	16 (43)	21 (57)	37
2007-2007	39 (78)	11 (22)	50
Overall	55 (63)	32 (37)	87

EA: Esophageal atresia

Table 5 Distribution of accompanying additional anomalies among patients with EA

Accompanying additional anomalies	Number of patients n (%)
Gastrointestinal system	10 (26)
Cardiovascular system	15 (39)
Genitourinary system	4 (11)
VACTERL	9 (24)
Total	38 (100)

EA: Esophageal atresia; VACTERL: **V**ertebral defects, **A**nal atresia, **C**ardiac defects, **T**racheoesophageal fistula, **R**enal anomalies, and **L**imb abnormalities

Table 6 Mortality rates according to Waterston's risk classification

Waterston Group	Survival n (%)	Mortality n (%)	Total (n)
A	26 (96)	1 (4)	27
B	20 (77)	6 (23)	26
C	9 (26)	25 (74)	34
Total	55 (63)	32 (37)	87

Table 7 Long-term complications in survivors of the children with EA

Long-term complication	Number of patients* n (%)
Gastroesophageal reflux	13 (23)
Recurrent pulmonary infections	37 (67)
Dysphagia	46 (83)
Anastomotic stricture	11 (20)
Growth retardation**	2 (4)

EA: Esophageal atresia

* Some long-term complications were overlapping

** Having a height of less than 3% at end of first year

additional anomaly was included in Waterston Group C. According to the results of study conducted by Spitz et al[12] between the years of 1980 and 1990, survival rates of newborns based on Waterston's risk classification were 99% in Waterston Group A, 95% in Group B and 71% in Group C. However, according to a new classification system in the same study, mortality rate in those patients with birth-weight <1500 g and/or cardiac anomaly was 22%. In a study conducted by Bal et al[13] in India, survival rates of these patients operated for EA according to Waterston's risk classification were 100% in Waterston Group A, 89% in Group B, and 60% in Group C. Similarly survival rates were reported by Tandon et al[14] which were 100% in Waterston Group A, 83% in Group B and 22% in Group C. In our study, survival rates in each Waterston risk categories were found to be 96.3%, 76.9% and 26.5%, respectively. Our mortality rates in Waterston Group A and Group B were parallel to those studies published in the literature. Though, survival rate of our patients in Waterston Group C were comparatively low, it were concordant to those reported by Spitz et al[15] who used a new classification system. That classification modified by Okamotomato has shown that low and very low birth weighted children have better survivals and the most effective parameter on survival is cardiac anomalies.[15-17]

During the post-operative period, complications were detected in 32 patients. They were seen in 23 patients with EA + distal TEF, eight patients with isolated EA, and one patient with TEF. There wasn't a statistically significant difference between the type of atresia and post-operative complication rate. Among died cases, 24 had EA + distal TEF, and eight had isolated EA. There was a statistically significant difference between the type of atresia and mortality rate. So, eight of 10 cases with isolated EA died. We think that this high mortality rates resulted from low birth-weight and having major cardiac anomalies of these newborns. The complications were observed in 22 preterm and 10 full-term newborns. A statistically significant difference was found between full-term and preterm newborns regarding the complication rate. A total of 24 preterm and eight full-term newborns died. Hence, a statistically significant difference was found between gestational age and mortality rate. Because most of the preterm newborns had low birth-weight, the prematurity has an apparent impact on mortality rate.

In present study, patients who admitted from out centres after postnatal age of two days had higher complication and mortality rates. Because of their inability to swallow his/her saliva, the risk of aspiration increases among patients with EA. Major cardiac anomalies, serious pulmonary dysfunction and preoperative positive ventilation need were shown to be the most important risk factors. Therefore, early post-operative complications and mortality rate increase with late admission. Hence, we think that newborns with EA should be delivered in an appropriate centre where their management is possible.

In newborns with EA, the incidence of accompanying additional anomaly ranges between 30% and 60%. Although it is lowest in cases with isolated TEF, it is highest in cases with isolated EA.[1] Different rates of accompanying cardiovascular system anomalies were reported by Spitz et al,[12] Mortell et al,[16] and Okamoto et al,[17] which were 29%, 30.5%, and 30.5%, respectively. Although accompanying additional anomaly was present in our 26 of 32 died patients, there was no any significant difference between this accompanying additional anomaly and post-operative complication rate. But, the impact of additional anomaly on mortality rates was statistically significant. Hence, the major cardiac anomalies were among the important cause of mortality in cases with EA.

In our study, the main post-operative complications were pneumonia, anastomosis leakage and atelectasis (24.1%, 6.9% and 5.7%, respectively). Different rates of anastomosis leakage have been reported by Celayir et al[11] and Mortell et al[16] which were 9.1% and 3-5%, respectively. Van der Zee et al[18] reported anastomosis leakage in 18% of patients with EA who later underwent to thoracoscopic interventions. In our study, complications were observed in 10 survived (10/55, 18.2%) and 22 died patients (22/32, 68.8%). Hence, a statistically significant difference was found between complication and mortality rates.

Mortality rate in our study was 36.8% (32/87). The main causes of mortality were respiratory failure (6.9%), pneumonia (10.3%), and sepsis (19.5%). Our mortality rate was higher than those developed countries. However, the gap length was not assessed in our study which was a limiting factor. Okamoto et al[17] conducted a study on 121 patients between the years of 1980 and 2005 and reported a mortality rate of 16.5%. Teich et al[9] reported a mortality rate of 12.7% among their 94 patients. However, we have found that our mortality rate was in parallel to those of other studies which conducted in our country. Celayir et al[11] conducted a study between the years of 1978 and 2000 and reported a mortality rate of 59.7% (138/231). Similarly, Bilirim et al[19] reported the mortality rates of 76%, 45% and 56% for their Group 1, 2 and 3 patients, respectively. High mortality rates were reported by Sharma et al[20] and Krishna et al[21] in the past years in India, whereas low mortality rate was reported by Bal et al[13] in the recent years in same country, which shows an improvement by years. In

our study, survival rates were far from being satisfactory which might be related to low level of health care services, type of atresia (e.g. isolated EA) and referral of only high risk cases with major (e.g. cardiac and pulmonary) anomalies.

The postoperative care which is the most important factor in predicting the prognosis is done in NICU by neonatology specialists and paediatric surgeons. In parallel to development in intensive care units, anesthesia, mechanical ventilation strategies, cardiac surgery and total parenteral nutrition, the mortality rates have been decreased by years. Recently, presence of accompanying additional anomalies are more common cause of mortality.[22,23]

In conclusion, morbidity and mortality rates of patients with EA in developing countries like to our study are still high. Among the patients with EA, mortality rate is significantly high in isolated EA. Low birth-weight, additional anomaly, Waterston Groups C and B and post-operative complications are the most important causes of mortality. Waterston's risk classification is a good predictor of the prognosis in patients with EA. Besides, the long-term complications and hospital visits are common in surviving cases.

Authors Contributions

UB and FE designed the study; UB, TT, MA and MS collected and analysed data; UB, MA, M.S. and TT wrote the manuscript; FE, MA, MS, TT, AO and AK gave technical support and conceptual advice. All authors read and approved the final manuscript.

Declaration of Conflicting Interest

The authors declare that they have no any conflict of interest.

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Ethical Approval

The local ethics committee approved this study (Decision No: 13, Date: 22.09.2011).

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