Esophageal atresia with tracheoesophageal fistula and early postoperative mortality

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Summary

Background: **Several recent reports showed that associated anomalies represent the main cause of postoperative mortality in infants born with esophageal atresia (EA) and/ or tracheoesophageal fistula (TEF). Our observations present additional causes of mortality to the above mentioned. The aim of this study is to identify the major causes of early postoperative mortality in cases of EA and/or TEF in our setup. The ongoing preoperative classifications predicting mortality will be also used for comparison.**

Patients and methods: **We reviewed 101 charts of all cases with EA and/or TEF in a period of 11 years from 1990 to 2000. Morbidity and causes of postoperative mortality during the first admissions were identified. The factors predicting mortality were documented. Patients were classified according to Waterston, Montreal and Spitz classifications.**

Results: **Thirty-one patients (30.7%) died. Two main groups of post operative mortality were identified. The first group included the possibly avoidable causes of mortality which were primary sepsis (n=10, 32.3%), technical problems (n=8,25.8%) and severe pneumonia (n=5,16.1%). The unavoidable causes of mortality included major congenital anomalies (n=6, 19.3%) and anomalies incompatible with life (n=2, 6.5%).**

Conclusion: **Primary sepsis and sepsis due to technical problems were the main causes of mortality in our series. Factors predicting mortality were pneumonia at presentation, sepsis at presentation or that acquired during hospitalization, major or life threatening anomalies, long gaps and major leaks. The Waterston classification was statistically the best applicable in this study.**

Key-words: ***Esophageal atresia, Tracheosopheal fistula, Mortality, Risk factors - congenital anomalies, Sepsis.***

Résumé

Introduction: Des rapports diverses récents avaient indiqués que les anormalies liées représentent la cause principale de la mortalite postopératoire chez des enfants nés atteints d'atresie oesophage (AO) et / ou fistule tracheoesophage (FTO) Nos observations donnent des causes supplementaires de la mortalité en plus des causes citées ci-dessus. L'objet de cette étude est d'identifier les causes principales de la mortalite postopératoire dans les cas de AO et / ou FTO dans notre programme. On va également utiliser cette classification préopératoire qui prédit le taux de la mortalité de faire la comparaison nécessaire.

Patients et méthodes: Nous avons fait le bilan de 101 graphiques de tous les cas atteints de AO et / ou FTO d'une durée de 11 ans de 1990 au 2000. Mobidité et causes de la mortalité postopératoire pendant la première admission ont été identifiés. Des facteurs qui prédéterminent la mortalité ont été documentés. Les patients ont été groupés selon les classification de Waterton, Montreal et Spitz.

Résultat: Trente et un patients soit 30,7% étaient morts. On avait identifié deux groupes majeurs de la mortalité post opératoire. Le premier groupe comprend les causes possible de la mortalité évitable qui étaient le sepsis premaire (n = 10, 32, 3%), problème techniques (n = 8,25,8%) et pneumonie grave (n = 5, 16, 1%). Les causes inèvitables de la mortalité comprend des anormalies congénitales principales, (n = 6, 19,3%) et anormalies incompatibles avec la vie (n = 2,6,5%).

Conclusion: Sepsis primaire et sepsis provoqué par des problèmes techniques étaient les causes principales de la mortalité dans nos séries. Des facteurs qui prédéterminent la mortalité était la pneumonie et présentation, septicité au cours de la présentation ou bien septicite acquise pendant l'hôpitalization, majeur ou bien des anormalies qui menacent la vie, un écart long et des fuites principales statisquement, la classification de Waterston était la meilleur utilisée dans cette étude.

Introduction

Improved survival rates were noted after operations for EA and/or TEF irrespective of Waterston classification[1], which now seems to be outdated in the opinion of some authors[2]. In Montreal classification reference, birth weight was not found to independently influence mortality. In the latter, only severe pulmonary dysfunction with preoperative ventilator dependence and major associated anomalies had bad prognostic influence[3]. In a study done by Spitz et al in 1994, major associated cardiac anomalies and low birth weight were found to be the two risk factors for mortality[4], the latter classification has been modified by adding respiratory distress syndrome and pneumonia to the risk factors[5].

The objectives of the present study are to identify the main causes of early postoperative mortality, the risk factors predicting mortality and to compare the usefulness of the different risk classifications.

Patients and methods

Charts of 101 newborns with EA and/or TEF admitted to the pediatric Surgery Department at Asir Central Hospital, Abha, Saudi Arabia between January 1990 and December 2000 were reviewed using a special format. Data related to place of delivery; age at presentation (in days), weight (in Kg) and gestational age (in weeks) were gathered. Also history of feeding before referral, preoperative dye esophagogram and history of polyhydramnios were also obtained. Septic work-up was done for all cases upon admission to the nursery. Clinical sepsis was suspected at presentation according to Siegel and McCracky[6]. This was

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further supported by the presence of thrombocytopenia, leucopenia or leucocytosis. Patients were examined for any dysmorphic features or any associated anomalies. The latter were subdivided according to severity into: minor, major and life threatening anomalies[3]. A major cardiac anomaly was defined according to Spitz et al[4]. The pulmonary dysfunction was classified upon admission into: none or mild and moderate or severe[3]. Preoperative abdomino-pelvic sonography and echocardiography were done only whenever renal or cardiac anomalies were suspected. Patients were classified according to Waterston, Montreal and Spitz classifications.

Primary or delayed primary repair was tried whenever possible. A long gap was defined as a gap length of more than 2cm, measured between the two pouches during surgery[7], and if the anatomosis was under tension. To transfix the fistula at its take off from the trachea, silk 3/0 or 2/0 was always used. Before the year 1990, 4/0 silk was used for repair of the EA. However, it was replaced by prolene 5/0 thereafter. An intercostal tube and a transanastomotic tube were always used.

Postoperatively, all patients were mechanically ventilated. Abdominal sonography as well as barium swallow and meal were done on the seventh to twelfth postoperative day. Postoperative morbidity and mortality were determined. A minor leak was diagnosed by barium swallow and treated conservatively. A major leak was diagnosed clinically and treated by early surgical intervention. Anastomotic stricture was treated by esophageal dilatation under general anesthesia using esophageal bougies or filiform urethral dilators over followers. Gastro-esophageal reflux (GER) was treated conservatively. However, an antireflux surgery was undertaken if conservative measures failed or a life threatening complication developed. Esophageal dysmotility was defined during barium study as a peristalsis, antiperistalsis or uncoordinated contractions. The dysmotility was considered major if the transient time for the barium to go to the stomach was greater than five minutes. Early morbidity and mortality were defined as those occurring during the postoperative period during the first admissions.

Statistical methodology

Comparison between survivors and deceased was done using Student's t-test for independent groups. The χ^2 test and Fisher's exact test were used for comparison between two distributions of qualitative variables, whenever applicable. The χ^2 for trend was used for comparison of mortality status among ordinal variables. The full model logistic regression was used, as a multivariate statistical technique, to predict the mortality status from a set of independent variables. Kendall tau-b is a non-parametric measure of association for mortality in the present study and each of Waterston, Montreal and Spitz classifications.

Results

There were 89 patients with EA and distal TEF, 11 had pure EA and one had isolated H-type fistula. Characteristics of the patients are shown in table 1.

Females had insignificantly higher mortality rate than males. Eleven patients (10.9%) were delivered at home and received feeding. Preoperative contrast study was performed for seven patients (6.9%). Polyhydramnios was documented only in 32 (31.6%) mothers. The last three variables were not statistically significant regarding mortality. The mean age at presentation was higher among deceased neonates than that of survivors ($p < 0.0003$). Significantly, lower gestational age and birth weight were found among the deceased in comparison to survivors ($p = 0.003$ & 0.007 respectively). Preoperative ventilation was required in nine patients (29%) of those who died and in six patients (8.6%) of those who lived ($p = 0.008$). Similarly, 12 patients (38.7%) of those who died compared to only eight patients (11.4%) of those who lived had sepsis at presentation ($p = 0.002$). Table 2 shows how severe or moderate pneumonia at presentation was significantly higher among deceased than among survivors.

Patients were classified according to Waterston, Montreal and Spitz groups (Fig 1). The causes of mortality are shown in table 3. Before the year 1990, three patients of those who died were allocated in Waterston group A and all had major leaks. All of them died eventually due to sepsis as proven by blood culture. There were six deaths among the

Table 1 Comparison of the studied cases according to survival and each of sex, age at presentation, gestational age and weight

Variables	Deaths n = 31	Survivals n = 70	Total	Significance
Sex				
M	14 45.2%	44 62.9%	58 (57.4%)	$\chi^2_1 = 2.752$
F	17 54.8%	26 37.1%	43 (42.6%)	NS
Age at presentation (days)				
Min - Max	1 - 13	1 - 7	1 - 13	t = 3.0817
$\xi \pm s$	3.03 ± 3.14	1.71 ± 1.17	2.12 ± 2.07	p < 0.003
GA (weeks)				
Min - Max	28 - 37	32 - 38	28 - 38	t = 3.235
$\xi \pm s$	34.42 ± 2. 93	36.21 ± 1.47	35.7 ± 2.18	p = 0.003
Weight (kg)				
Min - Max	1.05 - 3.70	1.29 - 3.80	1.05 - 3.80	t = 2.746
$\xi \pm s$	2.11 ± 0.61	2.43 ± 0.49	2.33 ± 0.55	p = 0.007

Table 2 Distribution of the studied cases according to survival and pneumonia at presentation

Pneumonia at presentation	Deaths		Survivals		Total	
	n	%	n	%	n	%
None/mild	15	48.4	68	97.1	83	72.2
Moderate/severe	16	51.6	2	2.9	18	17.8
Total	31	100	70	100	101	100

$\chi^2_{(1)} = 34.87$ $p < 0.001$

Table 3 Direct causes of mortality

Causes of death	n	%
I. Avoidable causes		
• Primary sepsis	10	32.3
• Technical problems	8	25.8
• Severe pneumonia	5	16.0
II Unavoidable causes		
• Major congenital anomaly	6	19.3
• Bilateral renal agenesis	2	6.5

Table 4 Organisms recovered from blood at death (n = 23)

Single organism	n	%	Combined infection	n	%
Klebsiella spp	5	21.7	Klebsiella spp & MRSA	1	4.3
P. aeruginosa	5	21.7	Klebsiella spp & P. aeruginosa	1	4.3
Serratia spp	4	17.4	Candida & P. aeruginosa	1	4.3
Enterobacter spp	1	4.3	Klebsiella spp & Serratia spp	1	4.3
Staph epidermidis	1	4.3			
Salmonella spp	1	43			
Citrobacter spp	1	4.3			
Staph aureus	1	4.3			
Total	19	82.6		4	17.4

Table 5 Full model logistic regression analysis for factors predicting mortality of the studied neonates

The linear combination (Z) = -0.1049 constant	
+1.1117	if the associated anomaly is either major or incompatible
- 3.9397	if no pneumonia
- 4.8554	if mild pneumonia
+1.7205	if there is major leakage
+1.8545	if there is sepsis at presentation
+3.5070	if there is acquired sepsis
+1.7333	if the gap is long

Associated anomaly is coded (0) for none or minor and (1) for major or incompatible. Leakage by barium is coded (0) for no major leakage and (1) for major leakage. Sepsis at presentation and acquired sepsis are coded (0) for no and (1) for yes. The gap is coded (0) for short and (1) for long gap.

44 neonates (13.6%) in risk group B. All cases died due to verified sepsis, proven by blood cultures. Four cases died due to secondary sepsis, three of them were due to major leaks. The remaining one was due to inadvertent division of a bronchus. Twenty-two patients (71%) died among 31 neonates in group C. Two patients (6.5%) died due to bilateral renal agenesis. Six patients (19.3%) died due to major associated anomalies. Eight patients (25.8%) died due to primary sepsis. One patient (3.2%) died because of secondary sepsis due to peritonitis after jejunal perforation. Five patients (16.1%) died as a result of severe pneumonia. Twenty-three patients (74.2%) of those who died had positive blood

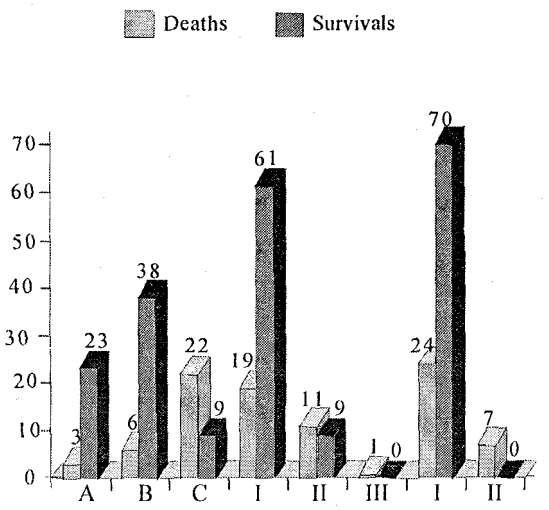

Fig. 1 ***Distributions of the studied cases and the different groups of classification.***

cultures. The different types of organisms recovered are shown in table 4. Waterston C patients had 71% mortality rate which is significantly higher ($p < 0.05$) than each of Waterston A (11.5%) and Waterston B (13.6%). The mortality rates for Montreal-II patients were statistically greater than Montreal-I (100% vs. 25.5%). Similarly, the mortality rates for class 3 (100%) in Spitz et al' classification were significantly higher ($p < 0.05$) than each of class 1 (23.8%) and class 2 (55%).

Table 5 shows the logistic regression equation for factors significantly predicting mortality of the studied neonates. From the equation, it is noted that the predictors increasing the probability of mortality were the presence of major or incompatible associated anomalies, sepsis at presentation or that acquired during hospitalization, if the gap was long, and if there was major leakage as shown by the different values of the estimated coefficient. On the other hand, compared to severe pneumonia, none and mild pneumonia are associated with decreased log odds of mortality. This equation of full model logistic regression is statistically significant, where the model χ^2_7=69.795 ($p<0.0001$). This model explained about 70.8% of the variation in the occurrence of mortality.

The equation succeeded in 91% to correctly classify the studied cases, being better in classifying survivors (94.2%) than deaths (83.9%).

Regarding correlation between mortality in the present study and other prognostic classifications, it was found that Kendall's tau-b value is the highest for the Waterston (0.479), followed by Montreal (0.410), then that of Spitz (0.297). This means that Waterston classification is the most applicable in our group of patients.

Discussion

The factors predicting early postoperative mortality could be divided into preoperative, operative and postoperative. The preoperative factors are sepsis at presentation, severe pneumonia and major or life threatening anomalies. Sepsis at presentation may be due to perinatal factors, maternal (e.g. premature rupture of membranes) or neonatal factors (e.g. impaired host defense) or due to delayed diagnosis. Although, the incidence of clinically proven sepsis in the neonate is only one to five per 1000 live birth, the mortality rate remains high at 30% to 59%[8]. The low rate of appreciation of polyhydramnios in this study (31.6%) might be due to lack of health awareness among pregnant mothers. The delay in diagnosis leads to preoperative feeding, aspiration and increased incidence of pneumonia. Those who died were significantly older at presentation than those who survived. The study showed that those who presented late had higher incidence of pneumonia. Both low gestational age and low birth weight were significantly higher among deceased neonates ($p <0.03$ & 0.007 respectively). However, gestational age and birth weight were not critical variables when factors were analyzed using the logistic regression.

Eight patients died due to major and life threatening associated anomalies. We think that preoperative abdominopelvic ultra sonography (U. S) and echocardiogram should be the minimum investigation prior to EA repair[9]. This study showed an agreement with Saing et al[10] that the multiplicity of the systems involved significantly increased mortality ($p = 0.0009$). Historically, the overall survival rate in EA with CHD has improved from 3% between 1948 and 1962 to 43% between 1963 and 1977 then to 69% between 1978 and 1988[11]. In this study, the overall survival rate in patients with CHD and EA was 52%.

Long gaps were important intraoperative factor that increased mortality in this study. Although, all patients were ventilated post-operatively, long gaps showed high incidence of mortality. Brown and Tam in 1996 used the measurement of gap length as a simple predictor of outcome. Long gaps (greater than 3cm) had higher mortality rate than both intermediate (>1 to ≤3cm) and short gaps (≤1cm)[12].

The postoperative factors predicting mortality were major leakage and sepsis. Postoperative esophageal dysmotility was a prominent feature in this study (36%). This may play a role as a factor for morbidity and mortality. However, this was difficult to evaluate retrospectively and warrants further investigation. The factors causing anastomotic leakage are the use of silk suture material, tension at the anastomotic site, end-to-end anastomosis and interference with the blood supply due excessive mobilization[13-15]. Braided silk was associated with an increased incidence of leakage when compared with polyglycolic acid or polypropylene sutures. The overall reported leakage rate with 5/0 silk ranged from 33% to 36%[13,15]. In this study, silk was associated with 25% leakage rate while prolene was associated with only 9%. The role of the surgeon cannot be ignored as a risk factor for leakage as highlighted by Willis Potts in 1950 and cited by Spitz in 1987[16]. In fact, most of the technical errors in this study were made by less experienced surgeons before the year 1991. the incidence of leakage varies widely from 4% to 36%[17,18]. In this study, there were overall 11 cases (12.6%) out of 87 patients with leaks. It is interesting to know that all but one occurred in groups A and B according to Waterston classification. Probably, early in the course, only full term healthy neonates were offered treatment in this institution.

Primary sepsis was the main cause of mortality in this study (32.3%) followed by secondary sepsis due to major

technical problems (25.8%). Twenty-three patients of the overall mortality (74.2%) proved to have positive blood culture and death. It is worthy to know that eight cases of primary sepsis (25.8%) occurred in Waterston group C patients, two (6.5%) in group B patients and none in group A. Secondary sepsis due to technical problems occurred in three patients (9.7%) in group A and four patients (12.9%) in group B and only one (3.2%) in group C.

In a study done by Spitz et al in 1994[4], there were 357 patients with EA and 15 with H-type in a period between 1980 – 1992. Forty-six patients died. The most common causes were major and life threatening associated anomalies. Some authors reported that none of their patients died due to primary sepsis[19, 20]. In a study done by Yagu et al, 20 patients out of 113 died. Five due to pneumonia (25%) and four due to sepsis (20%). The authors of this study considered pneumonia as an essential preoperative risk factor when therapeutic strategies for EA were selected. So, we proposed a modified Spitz classification by replacing major cardiac anomalies and low birth weight[5], with pneumonia.

Conclusion

The study showed that primary sepsis was the main cause of death followed by sepsis due to technical problems. The risk factors predicting mortality were sepsis at presentation, severe pneumonia, major and life threatening congenital anomalies, long gaps, major leaks and sepsis acquired during hospitalization.

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