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Original Article

Surgical Outcomes in Esophageal Atresia and Tracheoesophageal Fistula: A Comparison between Primary and Delayed Repair

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ABSTRACT

Background: The purpose of this study was to investigate outcomes of surgical repair of esophageal atresia (EA) or tracheoesophageal fistula (TEF) in newborns, with respect to incidence of death and other complications in early or late operations.

Methods: Charts of all 80 infants with EA/TEF, operated in Alzahra hospital (A tertiary hospital of Isfahan University of Medical Sciences) from 2002 to 2004 were reviewed. Patients were designed in two groups as, primary and delayed repair groups. Patients demographics, frequency of associated anomalies, and details of management and outcomes were studied.

Results: There were 48 male and 32 female patients with a frequency of 28(35%) preterm infant and mean birth weight of 2473±595 g. Overall survival rate was 71.2%. Mortality rate in delayed repair group was significantly higher than the other one (22.5% vs. 6.3%) but with matching, according to full term/preterm proportion, the significant differences were failed. Female sex and being preterm were the most powerful predictors of death (nearly odds ratio=7 for both).

Conclusion: in this study mortality and complications rates are higher in delayed repair than early one, although our data proposed that in absence of sever life threatening anomalies the most important factor for death is gestational age and female sex, and primary repair is opposed to it. Although mortality rate and complications are equal in two strategies, with matching cases for being preterm, but primary repair stays the better choice due to economic considerations.

Keywords: tracheoesophageal fistula, esophageal atresia, delayed repair, primary repair, outcome

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Esophageal atresia is the epitome of modern surgery[1]. The survival of infants born with esophageal atresia (EA), tracheoesophageal fistula (TEF), or both has improved dramatically since Cameron Haight's first successful repair in 1941[2]. Improvements in survival are largely attributable to refinements in neonatal intensive care, anesthetic management, ventilatory support, and surgical techniques. Survival may now be achieved in infants with low birth weight [3] and mortality is limited to those patients who have severe life-threatening anomalies[4]. The "ideal" management of EA/TEF is division of the fistula and primary esophageal repair performed in a single operation during the newborn period of life. This approach is successful in most patients born with EA and distal TEF, today[5, 6]. The premature infants with significant respiratory distress syndrome (RDS) or the newborns with associated congenital anomalies, specifically cardiac lesions, for whom it is difficult to provide effective support with mechanical ventilation, may not tolerate the lung retraction or operative time necessary for complete repair during a single setting. Early surgical repair (transpleural or extrapleural) is done for those babies with adequate arterial

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blood gases, adequate weight and no significant associated anomalies and delayed repair (gastrostomy first) is used for all other patients. Since 1962, the Waterston classification has been used to stratify neonates who have EA/TEF into prognostic categories based on birth weight, the presence of pneumonia, and the identification of other congenital anomalies[12] which surgical management (staged or delayed vs. primary repair) differed according to this classification. As neonatal care continued to improve and more effective ventilators became available, many of the criteria outlined by Waterston et al became less significant[15] and some evidences found that primary repair can be performed in all patient [6,7,16,17] and premature infants weighing even less than 1500 gr$_s$ tolerate a major thoracotomy well with correction of an esophageal anomaly with no differences in complication rate and overall mortality[7], but some other evidences oppose it traditionally, low birth weight infants underwent gastrostomy and fistula ligation followed by repair after a period of weight gain[7, 18, 19].

Repair consists of muscle-sparing thoracotomy, closure of TEF, and primary anastomosis[7] but surgical approaches and techniques vary according to surgeons' preferences. There is an evidence that the risk profile of children born with oesophageal atresia (which is the expression or incidence of these risk factors) has changed over time[8]. This study had 2 goals: (1) to compare delayed (staged) repair and primary repair for main complications and mortality rate and (2) to assess which of the major known risk factors is most predictive for mortality.

Subjects and Methods

In a historical cohort study, the case records of operated infants with oesophageal atresia and/or tracheoesophageal fistula, which were admitted to the Alzahra hospital (A tertiary hospital of Isfahan University of Medical Sciences) from November 2002 to December 2004, were reviewed based on two main management strategy (primary and delayed repairs) in equal groups(n=40). It was calculated that 80 subjects would be required to detect and difference in mortality rate of these two methods (10 to 30 percent in other studies) with 80% power at the 2-tailed 0.025 level of significance. Cases were selected with simple random sampling. Data were collected retrospectively from hospital and office records. Mean of follow-up days was 28, ranging from 3 to 62 days. Patients who had expired before operation were excluded. These infants usually are patients who suffer from severe anomalies or patients with severe respiratory distress due to delayed diagnosis or transportation. After presence of clinical signs the diagnoses were confirmed with CXR and visit of coiled nasogastric NG, tube. Primary repair included fistula division and end-to-end esophagoesophageal anastomosis within the first 48 hours of life. Delayed primary repair included fistula division and esophageal anastomosis after 48 hours (median time, 9 days) after an initial gastrostomy. This type of repair was performed in patients with severe pneumonia or other anomalies that prohibited an immediate definitive operation. Four surgeons managed cases, some of them had tendency to delayed (staged) repair in infants who could tolerate primary repair and others preferred primary repair. Primary repairs were performed by a retropleural approach whenever possible. A single layer end-to-end esophageal anastomosis was constructed using interrupted 5-0 silk sutures in both of strategies. Recorded data included birth weight, sex, duration of pregnancy, presence of cardiac defects and other associated anomalies, respiratory failure before and after operation (defined as need to mechanical ventilation), multi organ failure (defined as presence of at least two of these: Acute Tubular Necrosis, septic shock, coagulopathies, respiratory failure**)**, surgical interventions, complications (leakage and narrowing), duration and recurrence of hospitalization, and outcome. There were no routine para clinic surveys for associated anomalies (VACTERL) but para clinics were done, each time there was any clinical doubt. Leakage were diagnosed in patients with good condition till 5-6th day of post

op that involved in fever, leukocytosis, purulent discharge of chest tube, respiratory distress and it was confirmed with esophagogeram and gastrogeraphy. Narrowing as a late complication with poor feeding was confirmed with endoscopy. All cases were classified based on their anatomic anomaly types (type A-D, plus H-type TEF) according to the gross observation [9] during surgical operation. The most common variant was EA with a distal TEF (type C). Statistical analysis was performed using SPSS ver.9. Categorical data were compared using chi-square analysis, and continuous data were compared using student t-test and Mann-Whitney test as a nonparametric variant of it, when t-test assumptions were violated (to compare duration of hospitalization). Statistical significance was achieved at $P<0.05$. Logistic Regression was used as a complementary analysis to find risk factors of infants with EA/TEF induced death. Sensitivity and specificity of model were achieved from SPSS output.

Results

Over a period of 2 years, 80 infants [48(60%) boys and 32(40%) girls] with EA/TEF were operated in the Alzahra hospital, Isfahan, with one of two main strategy. Twenty eight (35%) infant were preterm and 52(65%) were full term. The average birth weight was 2473±595 gr_s (Mean±SD, ranges from, 1200 to 3500 gr_s) and 6(7.5%) infants have weight<1500g. Average of hospitalization duration was 17.4 (SD=11) days [45 patients (56.3%) less than two weeks]. Recurrences of hospitalization in 19(23.8%) cases were more than one time.

Being preterm, death, multi organ failure, hospitalization duration more than two weeks, and overall associated anomalies are significantly more frequent in delayed repair group. Table 1 shows details of important characteristics and main outcomes of two main strategies. Because stenosis is a late complication and early death may lead to loose some differences, we reanalyzed this complication in two groups with omitting expired infants, but no changes happened in non significant differences. Patients' weight were significantly more in primary repair group (2631.2±86 gr_s vs. 2315±95 gr_s, Mean±SE), t=2.45, P=0.017). Relative Risk for death (primary/delayed) was 0.27(95% confidence interval, 0.11 to 0.67). Mann-Whitney test showed more duration of hospitalization in patients with delayed repair (Median=17 vs. 12days in early repair group, Mean Rank=46 vs 34, U=569.5, P=0.026).When we deleted 24 full term cases from primary repair group to obtain the same distribution of gestational age as delayed repair group (as a post matching strategy in analysis), all significant differences failed except duration of hospitalization (Median=17 vs. 12days in early repair group, Mean Rank=30 vs. 22, U=224.5, P=0.048).

Only 6 factors of all above data (demographics, conditions, and complications), obtained from these infants, can significantly be accepted in logistic regression equation to predict odds of death as main outcome. These factors are showed in table 2. Sensitivity, specificity and accuracy of this model are 73.91%, 92.98% and 87.5%, respectively.

Additive analysis was performed with deleting cases who must traditionally undergo delayed repair (respiratory failure, or body weight<1500g) from delayed repair group and equal number of cases in primary group with opposed characteristics. Sixteen cases were found in each group met this criteria. Differences in duration of hospitalization (Median=16 vs. 12days in early repair group, Mean Rank=40 vs. 27, U=298.5, P=0.012), respiratory failure before operation (7 cases in primary group vs. zero in another group, due to our type of omitting cases) and associated anomalies (7 cases in delayed group vs. zero in another group) remain significant after deleting these 16 cases and there was not any significant difference in complications or death rates. Table 3 shows the details. No significant differences were found between 16 cases with respiratory failure or body weight<1500gr_s and similar 8 cases in early repair group, not even in duration of hospitalization.

Table 1. Frequencies of complications and other characteristics in two main strategies.

Characteristics	Primary repair N (%)	Delayed repair N (%)	Total N (%)	P- value
sex(female)	19(47.5)	13(32.5)	32(40)	0.171
preterm *	8(20)	20(50)	28(35)	0.005
death *	5(12.5)	18(45)	23(28.8)	0.001
anastomotic leaks	5(12.5)	5(12.5)	10(12.5)	1.000
narrowing	6(15)	9(22.5)	15(18.8)	0.360
respiratory failure before operation	7(17.5)	12(30)	19(23.8)	0.189
respiratory failure after operation	21(52.5)	27(67.5)	48(60)	0.171
multi organ failure * (MDF)	2(5)	10(25)	12(15)	0.012
associated anomalies *	4(10)	10(25)	14(17.5)	0.077
hospitalization duration > two weeks *	11(27.5)	24(60)	35(43.8)	0.003
recurrences of hospitalization > one time	12(30)	7(17.5)	19(23.8)	0.189
total	40(100)	40(100)		

* P-value < 0.05

Table 2. Logistic regression analysis of death risk factors after surgical repair (only significant factors have been showed).

Risk factors	β	SE*	wald	p-valve	OR**
female sex	1.95	0.89	4.79	0.028	7.03
preterm	1.95	0.79	6.10	0.013	7.06
primary repair	-2.11	0.89	5.58	0.018	0.12
no MOF	-2.65	1.15	5.22	0.022	0.07
duration of hospitalization	-0.08	0.03	6.17	0.012	0.91
no respiratory failure after repair	-2.51	1.03	5.93	0.014	0.08
constant	2.49	1.29	3.77	0.05	

* standard error, ** Odds ratio

Table 3. Frequencies of complications and other characteristics in two main strategies after omitting [a] 16 cases of each group.

Characteristics	Primary repair N (%)	Delayed repair N (%)	Total N (%)	P-value
sex(female)	13(54.2)	7(29.2)	20(41.7)	0.079
preterm	8(33.3)	10(41.7)	18(37.5)	0.551
death	4(16.7)	7(29.2)	11(22.9)	0.303
anastomotic leaks	2(8.3)	3(12.5)	5(10.4)	1.000 **
narrowing	5(21.7)	4(16.7)	9(19.1)	0.724 **
respiratory failure before operation *	7(29.2)	0(0)	7(14.6)	0.009 **
respiratory failure after operation	15(62.5)	13(54.2)	28(58.3)	0.558
multi organ failure	2(8.3)	4(16.7)	6(12.5)	0.666 **
associated anomalies *	0(0)	7(29.2)	7(14.6)	0.009 **
hospitalization duration > two weeks *	6(25)	15(62.5)	21(43.8)	0.009
recurrences of hospitalization > one time	7(29.2)	5(20.8)	12(25)	0.505
Total	24(100)	24(100)		

* P-value < 0.05 ** Fisher's Exact test

[a] cases with weight<1500g or respiratory failure in delayed group and cases with none of them in primary group.

Discussion

Preoperative prognostic classification systems are important to provide for a realistic prognosis for children clinicians and parents and to compare results among institutions. In 1962, Waterston et al devised one of the first classification systems for EA/TEF. They compared the results based on preoperative stratification of cases by severity and expected outcome. Risk factors that Waterston included were low birth weight, pneumonia, and associated congenital anomalies (Waterston Classification[13]: A: Birth wt>2500 g and well; B: Birth wt 1800 to 2500 g and well or Birth wt>2500 g, but moderate pneumonia and other congenital anomaly; C: Birth wt<1800 or Birth wt>1800 with severe pneumonia, and severe congenital anomaly). He concluded that delayed definitive repair should be done for patients in groups B and C. With advances in anesthetic, surgical, nutritional, and intensive care management leading to improved outcomes, the validity of the Waterston classification has been questioned.[3, 4, 10] A number of new classification systems have been proposed which include major cardiac anomalies, preoperative pulmonary status, or physiological status.[3,4,10,11] Poenaru et al[3] (1993), from Montreal, proposed that birth weight was not a significant factor for mortality, but the need for preoperative ventilation was a significant one. Spitz et al[11] (1994) proposed that birth weight and major congenital heart disease were the major factors associated with mortality. Yagyu et al[10] (2000) proposed the Bremen classification, which modifies Spitz's classification to include preoperative pulmonary status. Limited evaluation has been published comparing these classification systems.[12] Although the purpose of this investigation was not to examine these classification systems our study is consistent with recent research and emphasis on the role of being preterm (Odds ratio for death: 7). On the other hand, several risk factors are well established for adverse outcome after correction for esophageal atresia, including birth weight and the presence of associated anomalies[11,12, 13]. There is some evidence that the risk profile of children born with oesophageal atresia (which is, the expression or incidence of these risk factors) has changed over time[8]. Deruloo et al reported a decrease in mean gestational age and birth weight of patients born with esophageal atresia over the last 5 decades [14]. Our patients treated nowadays are born earlier and have less weight than those treated 30 years ago [8] but according to our logistic regression analysis, weight is not a risk factor for death in these patients. Our results were consistent with previous published reports on EA/TEF in regard to anatomic types, male-to-female ratio, associated congenital anomalies, and complications of treatment [3, 4, 11, 12]. The mortality rate in patients, which was studied, was higher than other studies. In this study mortality rate (6.3% vs. 22.5%) and complications rate (7.6% vs. 11.4%) are higher in delayed repair group than the other one, although our data proposed that in absence of sever life threatening anomalies the most important death predictors are gestational age and female sex (OR: 7 for both), and primary repair is opposed to it (OR: 0.12). According to the fact that unique duration of hospitalization is the difference which remains significant after matching, the utility of primary repair may be acceptable even in presence of preterm delivery. On the other hand, when we selected infants who could tolerate primary repair in delayed repair group and compared them with a matched primary repair group (omitting some full term and high weight infants), no significant differences were detected in mortality and complications rates. Though, because of economic considerations, nosocomial infections risk and less residing in hospitals in primary repair and similarity of complications and death rates in high risk patients in both strategies and improvements in intensive care management and surgical skills; this strategy is propounded as a better choice.

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