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SURVIVAL ANALYSIS OF NEWBORN WITH ESOPHAGEAL ATRESIA DEPENDING ON SURGICAL TREATMENT

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Abstract. In this article, mortality and one-week, 30-day, and 60-day survival rates of infants born with esophageal atresia (EA) were analyzed depending on the operation performed. Out of 167 infants presented with EA, the control group included 63 infants who underwent conventional examinations, and 104 infants who underwent advanced esophagoplasty were included in the main group. In the main group, the fatal outcome was 12.%, and in the control group, it was 33.3%, that is, a 2.5-fold reduction in mortality was achieved. Absolute viability was 79.6%. 7-day survival was 1.8% (3 of 167 patients), while 30-day survival was observed in 58.7% (98 of 167 patients). By the 60th day, the probability of survival of the infants of the main group compared to the control group increased by almost 20.8% or 1.5 times. By this period, the lethality in the control group was 33.3%, while in the main group, this indicator decreased to 12.5%. The probability of survival was 66.7% (95%CI: 33.02-45.84) and 87.5% (95%CI: 51.95-61.98) in the high statistical confidence level, respectively.

Keywords. Esophageal atresia, infants, viability, lethality index.

Introduction

The trachea and esophagus are formed by the division of a single tube composed of the foregut endoderm [1] and the surrounding mesenchyme [2, 3, 4, 5, 6]. Their disruption causes disruption of anterior intestinal compartmentation, and in turn, tracheo-esophageal malformations [7, 8, 9, 10, 11, 12]. Disruption of these processes leads to the development of congenital defects such as esophageal atresia (AAT) [13, 14, 15, 16] and tracheoesophageal fistula [17, 18]. These defects prevent the baby from swallowing and breathing, requiring timely diagnosis [19] and surgical intervention [20]. According to the information of a large number of CIS countries and foreign authors on the treatment of esophageal atresia in babies, despite the many achievements, many problems in this regard, as well as problems related to technical aspects, have not been solved [21, 22], and the mortality rate due to this pathology is 40-60 % [22, 24].

In the field of neonatology, significant positive results are being achieved in infant surgery. However, neonatal surgical care in developing countries remains a challenge for the treatment of esophageal atresia, especially in the emergency setting [25]. International data on the survival of infants born with esophageal atresia are somewhat limited, and these data are mainly based on separate registries from Europe and the United States [26, 27, 28]. In addition, there is little scientific information on this problem from these countries, and there are almost no scientific publications on esophageal atresia from Central Asian countries [29]. In developing countries, the mortality rate from esophageal atresia is still 30% to 80%, and this indicator requires a radical improvement of medical care measures for this category of patients [30, 31].

The aim of the study.

The study of weekly, 30-day and 60-day survival and mortality of newborns operated for esophageal atresia.

Materials and methods. During 2015-2019, 167 babies brought to the Neonatal Surgery Department of the Republican Neonatal Surgery Training-Treatment-Methodological Center and the Andijan Regional Multidisciplinary Medical Center were selected for the study. During the study, methodological approaches changed according to the possibility of complications and the possibilities of intensive care in the diagnosis and treatment tactics of infants diagnosed with EA. Because of this, all clinical materials were studied in two groups. The control group included 63 babies diagnosed with EA and who were examined in the traditional way in 2015-2016, and 104 babies diagnosed with EA who were treated during 2017-2019 were included in the main group. One-week, 30-day, and 60-day survival and lethality rates of infants operated on EA in 2015-2019 were analyzed depending on the surgical tactics alone, excluding factors affecting survival.

Statistical analysis of the obtained numerical results was carried out in Windows 10 software using IBM SPSS Statistics Base (https://www.ibm.com/spss) version 23.0 with a proprietary license (2020). One-week, 30-day, and 60-day survival and lethality of infants operated for EA were analyzed using Kaplan-Meier curve and Mantel-Cox logarithmic classification. The level of significance of differences in study groups was performed at 95% confidence intervals (CI) using the Clopper-Pearson binomial "exact" method based on the β-distribution. The relative risk (RR) index was used to estimate the effect of a particular factor. In order to determine the relationship between the qualitative signs, the tetrachoric coefficient of the qualitative signs coherence (Pearson's $\chi 2$-criterion) was calculated using a four-field table. The Yates continuity correction is used to clarify the results obtained using the table.

Results. 28 (44.4%) of the babies in the control group were boys, 35 (55.6%) were girls, and the proportion of full-term babies (57; 90.5%) was higher than premature babies (6; 9, It turned out to be 5%). By the time of birth, the average gestational age of the babies was 38.2 weeks (from 30 to 41 weeks), and the average body weight was 2792 grams (1222±4000 gr.). According to the anatomical form of the defect, distal tracheo-esophageal fistula (type C) – 59 (93.6%); upper tracheo-esophageal tracheal fistula (type V) – 2 (3.17%); double (upper and lower) tracheo-oesophageal fistula (type D) – 2 (3.17%) babies were found.

104 infants with EA in the main group were boys, 48 (46.1%) were girls, and the proportion of full-term infants (76; 73.1%) was higher than that of premature infants (28 It was found that 26.9%). By the time of birth, the average gestational age of the babies was 37.3 weeks (from 25 to 43 weeks), and the average body weight was 2760 grams (1190±4480 gr.). According to the anatomical form of the defect, distal tracheo-esophageal fistula (type C) – 99 (95.2%); upper tracheo-esophageal tracheal fistula (type V) – 4 (3.8%); double (upper and lower) tracheo-esophageal fistula (type D) was found in 1 (0.96%) baby.

During the study period, a total of 167 babies were operated on, 34 of them (20.3%) had a fatal outcome from 2 to 51 days after the operation. The analysis of lethal consequences by years showed that in 2015-2016, post-operative death was observed in 21 (12.6%) infants, while in 2017-2019, this indicator was observed in 13 (7.7%) infants, which means that post-operative lethal outcomes are increasing. decreased by 2 times (Fig. 1).

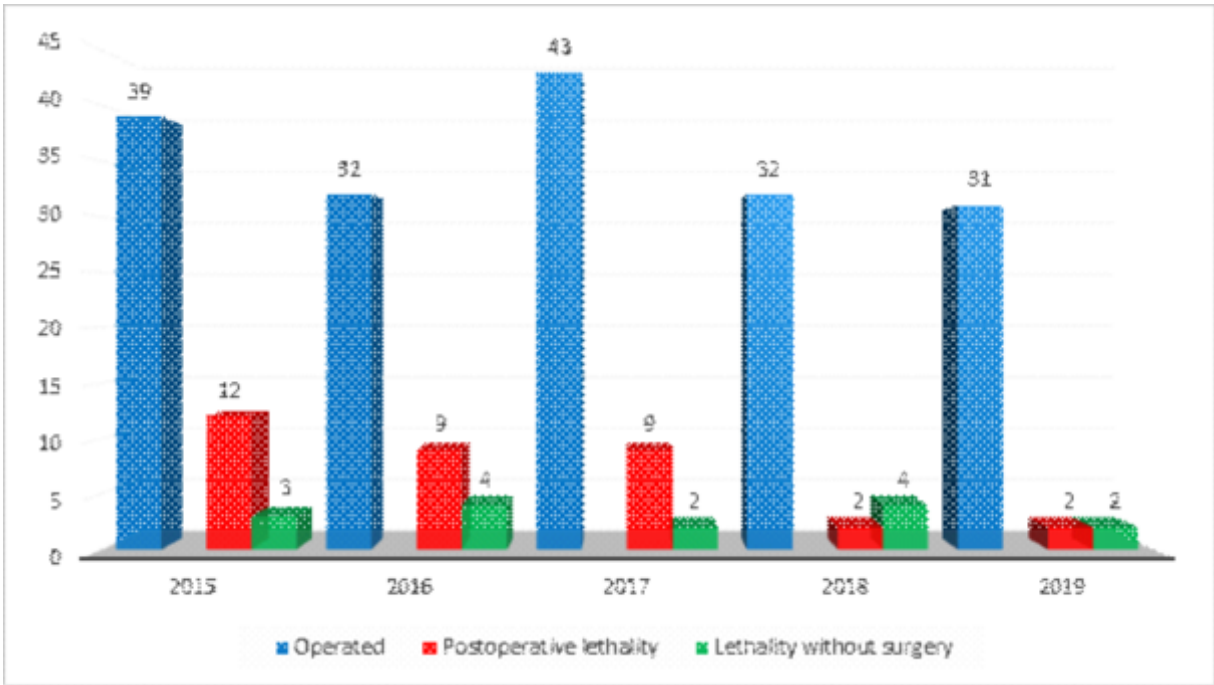


Fig. 1 . Mortality rate of infants operated with EA during the study period

The comparative analysis of the lethality rate in the cross-section of the research groups showed that the lethal consequences in the main group were 12.%, and in the control group, 33.3%, that is, a 2.5-fold reduction in the mortality rate was achieved, in turn, the proportion of positive results was 66.6%. increased from to 87.5%.

It is known that such factors as premature birth, low birth weight, late diagnosis, prolonged period of pre-operative preparation and the development of infectious diseases during this period, accompanying birth defects, diastasis distance of the ends of the esophagus affect the survival of babies. At the same time, according to the authors, the change in surgical tactics has almost no effect on the outcome of the disease due to the presence of concomitant and background diseases. It is also recognized that the development of intensive care and neonatal resuscitation plays a significant role in the survival of infants diagnosed with EA [32]. In order to verify this scientific point of view in our study, excluding the factors affecting the viability, the one-week, 30-day and 60-day survival rate and lethality index of the babies who were operated on EA only depending on the surgical tactics, Kaplan-Meier curve and Mantel-Cox logarithmic classification was analyzed using [33, 34, 35] (Table 1).

Table 1.

7, 30, 60-day survival rate of infants with a lethal outcome in the study groups, depending on the surgical strategy

Groups	Days	Lethal consequence		Survived		Total		M ± m	95% CI	Log-rank* ch 2	P
		abs	%	abs	%	abs	%				
Control group	7	8	88.8	1	11.1	9	14.3	4.33±0.44	3.46-5.20	0.042 a 6,889 p 8,869 c	>0.05 a <0.05 p <0.001 c
	30	19	38.8	30	61.2	49	77.7	22.18 ± 1.48	19.29-25.08		
	60	21	33,3 –	42	66.7	63	100	39.43 ± 3.27	33.02-45.84		
Main group	7	11	84.7	2	15.4	13	12.5	3.77 ±0.69	2.41-5.13		
	30	12	15.0	68	85.0	80	76.9	26.08 ± 1.05	24.02-28.14		
	60	13	12.5	91	87.5	104	100	56.96 ± 2.56	51.95-61.98		
Total	60	34	20.3	133	79.6	167	100	26.57±0.99	24.63-28.51		

Note: * - according to Mantel-Cox's logarithmic classification ch 2 -criterion: Log-rank test on the 7th day in a-research groups; Log-rank test on the 30th day in b-research groups; Log-rank test at day 60 in s-study groups. P -statistical reliability coefficient

As can be seen from Table 1, the absolute survival rate during the total study period (2015-2019) was 79.6%, that is, 133 of 167 patients survived within 60 days after surgery. Also, 7-day survival was 1.8% (3 of 167 patients) in all study groups, while 30-day survival was observed in 58.7% (98 of 167 patients) of patients.

7, 30 and 60-day Kaplan-Meier survival of infants operated with EA is shown in Figures 2-4.

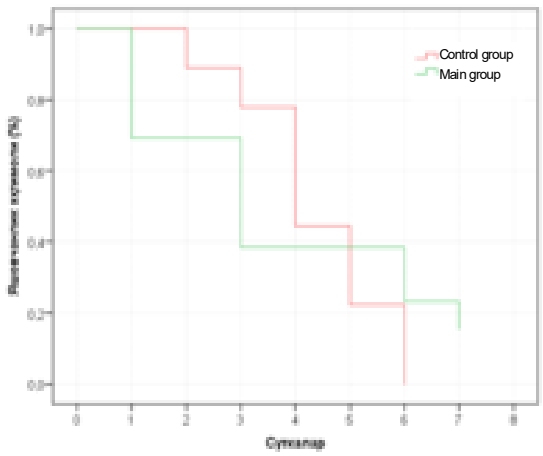


Fig.2. Kaplan-Meier 7-day survival curve in study groups

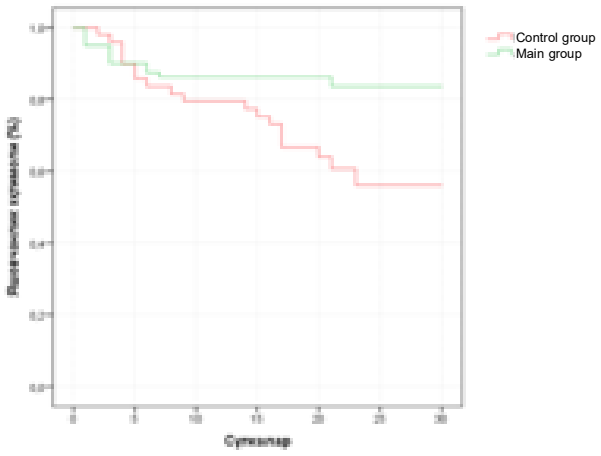


Fig.3. Kaplan-Meier 30-day survival curve in study groups

Kaplan-Meier analysis of survival at day 7 showed that none of the patients in the control group survived this period, but up to day 5, lethal outcome was observed earlier in the infants of the main group than in the control group. The overall postoperative mortality rate was 88.8% (95%CI: 3.46-5.20) in the control group and 84.7% (95%CI: 2.41-5.13) in the control group, which was not statistically significant. (Mantel-Cox test, $\chi 2$ – 0.042; r>0.05).

As shown in the chart data, compared to the control group (61.2%; 95%CI: 19.29-25.08), the 30-day survival probability was found to be statistically significantly higher in the main group according to the Kaplan-Meier method, and 85.0% (95%CI: 24.02-28.14) (Mantel-Cox test, $\chi 2$ – 6.889; r<0.05). The probability of 60-day survival of infants operated with EA was also studied (Figure 4).

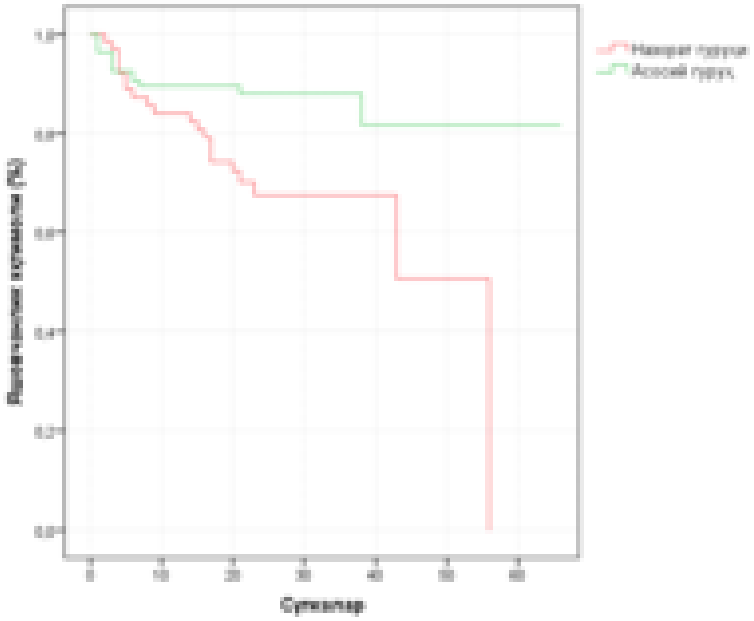
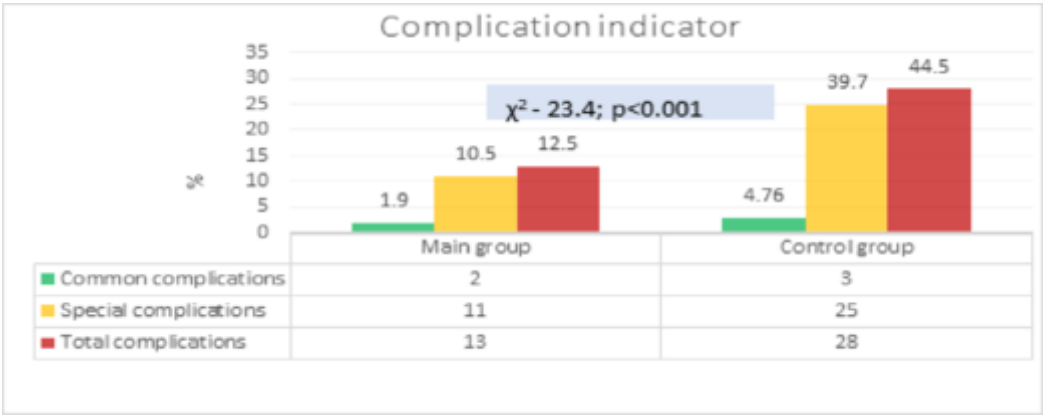


Fig.4. Kaplan-Meier 60-day survival curve in study groups

As can be seen from the data of Figure 4, in the early postoperative period, the probability of survival of infants in the main group by day 60 increased by almost 20.8% or 1.5 times compared to the control group. By this period, the lethality in the control group was 33.3%, while in the main group, this indicator decreased to 12.5%. The probability of survival was 66.7% (95%CI: 33.02-45.84) and 87.5% (95%CI: 51.95-61.98), respectively (Mantel-Cox test, χ^2 – 8.869; r<0.001).

In conclusion, it can be noted that the survival rate of babies who underwent EA surgery, excluding factors that aggravate the course of the disease (congenital defects, congenital heart defects, etc.), has increased significantly in recent years, which is due to the surgical technique and tactics used in this category of patients, as well as postoperative proves the effectiveness of intensive therapy methods. We also studied the postoperative mortality rate in relation to surgical complications and concomitant somatic diseases (Fig. 5).



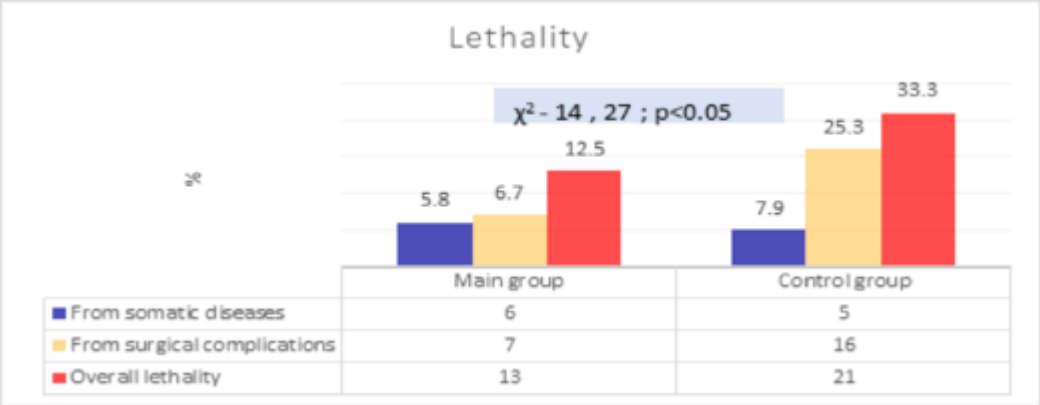


Fig.5. Postoperative complication and mortality rate in study groups

As can be seen from the diagram, the mortality rate due to surgical complications was statistically significantly reduced by 2.1 times, that is, from 76.1% (16/21) in the control group to 53.8% (7/13) in the main group compared to the total mortality. .

In our opinion, adequate pre-operative preparation and adequate intensive treatment and care taking into account concomitant birth defects and somatic diseases and their complications during the postoperative period led to a radical improvement of treatment results in babies diagnosed with EA. The improvement of operative treatment technique significantly increased its quality and allowed to reduce the mortality rate by 2.5 times (from 33.3% to 12.5%) during the research period.

It is important to note that surgical treatment of the underlying problem cannot guarantee complete recovery of babies born with EA. Concomitant diseases cause a complicated course of treatment and, in turn, an increase in hospital length of treatment (Fig. 6).

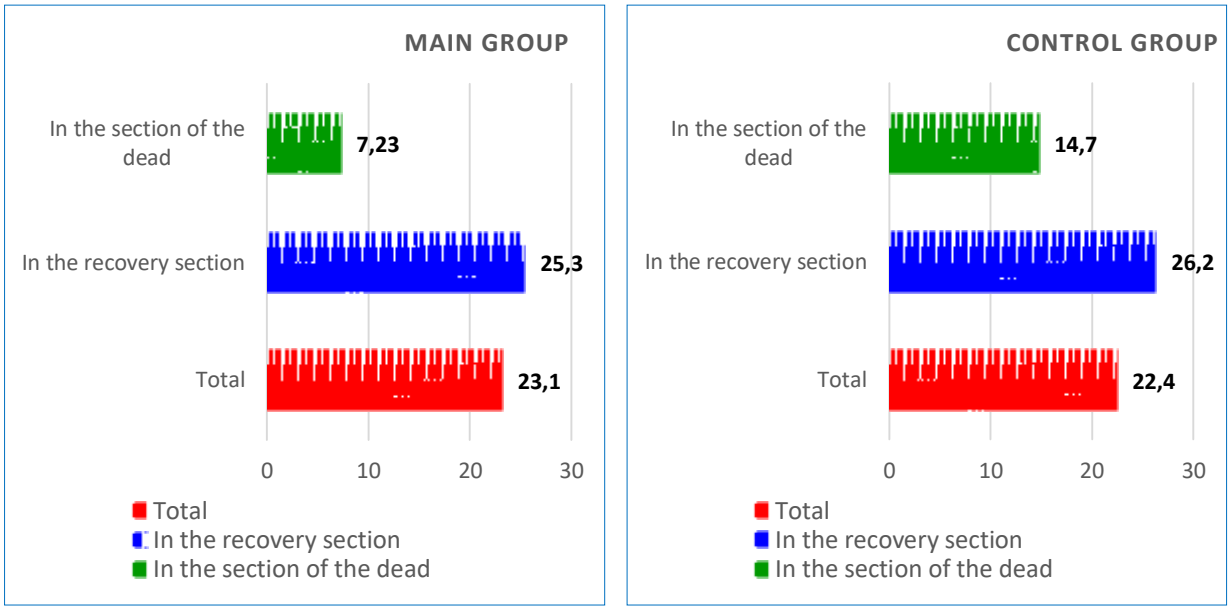


Fig.6. Average duration of hospital treatment (days)

At the same time, it is somewhat difficult to evaluate the cost-effectiveness of treatment by the proposed method in terms of hospital length of stay, because the length of stay in the hospital often depends on concomitant defects and somatic diseases, their complications (aspiration pneumonia, septic complications, DVS-syndrome, bleeding

into the cerebral ventricles, heart, brain, congenital kidney defects) are determined by costs associated with elimination.

Conclusion. Thus, the analysis of the results of surgical treatment in infants diagnosed with esophageal atresia showed that the proposed tactical and technical approaches provide an opportunity to reduce early postoperative complications and operative mortality.

Adequate pre-operative preparation, taking into account concomitant birth defects and somatic diseases and their complications, taking into account adequate intensive treatment and care measures in infants diagnosed with EA will not only improve the treatment results, but also cause a significant reduction in lethal outcomes.

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