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Prediction And Prevention of Complications After Surgical Correction of Esophageal Atresia In Newborns

Magomed Magomedmuradovich Bayev[1], Kamilla Dagestanovna Kanbulatova[2], Ismail Farajov[3], Karina Beglarovna Alvandyan[4], Temirlan Alepgerovich Agaev[5], Dinara El'brusovna Magomedova[6], Regina Alekseevna Shirshova[7]

[1]Astrakhan State Medical University, 121 Bakinskaya Street,
Orchid ID :414000, 0009-0004-8197-3062
Email ID : baev30rus@mail.ru
[2]Kamilla Dagestanovna Kanbulatova Astrakhan State Medical University, 121 Bakinskaya Street,
414000,
Orchid ID :0000-0001-9487-4064
Email ID : kanbulatova02@bk.ru
[3]Saint Petersburg State Medical University Street Litoyskaya 2,194100,Russia,
Orchid ID :0009-0003-8101-2053
Email ID isik77i@mail.ru
[4]Peoples' Friendship University of Russia,
Orchid ID :0000-0003-1995-1546
Email ID : alvandyankarina@mail.ru
[5]Dagestan State Medical University Russia, Republic of Dagestan, Makhachkala, street pl. Lenina,1, 367000,
Orchid ID :0009-0006-0264-2279
Email ID : temirlan.agaev@mail.ru
[6]Saint-Petersburg State Pediatric Medical University Litovskaya street, 2, Russia
Orchid ID: 0000-0002-3850-6168
Email ID :dinaraaa0012610@mail.ru
[7]Tyumen State Medical University, Street Odesskaya 54, 625023, Russia
Email ID : regia.shirshova@mail.ru
Orchid ID :0009-0003-9910-5397

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ABSTRACT

The article is devoted to an urgent problem of neonatal surgery – prognosis and prevention of complications after surgical correction of esophageal atresia in newborns. The authors present a systematic analysis of risk factors contributing to the development of postoperative complications, such as anastomosis failure, esophageal strictures, aspiration pneumonia and gastroesophageal reflux.

Surgical correction of esophageal atresia remains one of the most difficult operations of neonatal surgery: even with the improvement of anastomosis techniques, early and late postoperative morbidity remains significant. The most common negative outcomes are anastomosis failure, restenosis, recurrence of tracheoesophageal fistula, aspiration-related respiratory episodes, and delayed somatic growth.

The purpose of this study was to create a predictive model of complications, as well as to evaluate the effectiveness of a comprehensive preventive strategy, including modification of surgical techniques, targeted respiratory support and personalized nutritional management.

The data of 215 newborns operated on in 2000-2024 at the federal center of the third level were analyzed; the median follow-

up was twelve months. A multifactorial risk scale was created, confirmed by an AUC of 0.82 (95% CI 0.78–0.86), and a significant decrease in the incidence of severe complications was demonstrated when using the prevention protocol

Based on a retrospective analysis of clinical observations, key clinical and instrumental markers have been identified that make it possible to predict the development of complications with high accuracy. Modern approaches and methods of preventing complications are considered, including the improvement of surgical techniques, optimization of postoperative management of patients and the use of early rehabilitation programs.

The results obtained can be useful for practicing neonatology surgeons, pediatricians, and neonatal intensive care specialists to improve clinical outcomes and quality of life for young patients.

Key words: esophageal atresia; neonatal surgery; complications; prognosis; prevention; anastomotic failure; restenosis.

1. INTRODUCTION.

Esophageal atresia in newborns is one of the most common and complex malformations requiring emergency surgery in the first days of life. Despite significant advances in modern neonatal surgery and intensive care, postoperative complications continue to significantly affect the outcome of treatment and the long-term prognosis for these patients. The most common and clinically significant complications include anastomotic suture failure, esophageal stricture development, gastroesophageal reflux, as well as severe aspiration complications requiring prolonged rehabilitation and repeated surgical interventions [8].

The high frequency and severity of complications after correction of esophageal atresia in newborns determine the need to develop effective approaches to their prognosis and prevention. Currently, the issues of accurate assessment of risk factors influencing the development of complications remain insufficiently studied, which limits the possibilities of timely intervention and leads to an increase in the frequency of adverse treatment outcomes [6]. In addition, the lack of standardized approaches to postoperative management and insufficient attention to early rehabilitation of newborns make it difficult to achieve optimal treatment results [2].

Esophageal atresia with a distal tracheoesophageal fistula occurs with a frequency of 1/2 500 to 1/3 500 live births. The current mortality rate in developed countries does not exceed 5%, but the burden of postoperative complications remains high: from 20% to 40% of patients suffer from anastomotic failure, up to 60% experience clinically significant restenosis, and a third require repeated interventions during the first year of life [4]. These indicators reflect not only the technical difficulties that arise when comparing the proximal and distal segments, but also the vulnerability of the lungs, the neuromuscular apparatus of the pharynx, as well as the features of the immune response of newborns [1].

The risk of complications is multicomponent; it depends on gestational age, body weight, rupture length coefficient, as well as on systemic factors, including inflammatory status and rapid variability of cytokine cascades [10].

At the same time, most published papers focus either on describing single complications or on comparing individual surgical techniques without taking into account prenatal and postnatal variables [5].

The observed gap between the anatomical success of surgery and the functional well-being of the child requires the development of an integral prognostic tool that will allow risk stratification even before the intervention and adjust the prevention protocol in the early post-daily period [3].

The presented study attempts to combine clinical, laboratory and intraoperative parameters into a single model, and then test the preventive potential of the algorithm on an independent subsample.

Thus, the study and systematization of risk factors for postoperative complications, improvement of methods for their prediction and prevention is an extremely important task of modern neonatal surgery and pediatrics. Solving this problem will significantly improve the quality of medical care for newborns with esophageal atresia, reduce the frequency and severity of complications, reduce rehabilitation time, and ultimately improve survival rates and quality of life for young patients. The risk of complications is multicomponent; It depends on gestational age, body weight, rupture length coefficient, as well as on systemic factors, including inflammatory status and rapid variability of cytokine cascades [10].

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2. MATERIALS AND RESEARCH METHODS

The prospective database included 215 newborns operated on at the third-level center between January 2000 and December 2024. The inclusion criteria provided for isolated esophageal atresia of types C or D according to the Gross classification; combined heart defects were excluded in order to offset the effects of hemodynamic instability. The average gestational age was 37.1 ± 1.9 weeks, and the median body weight was 2,750 g (IQR 2,400-3,140 g). The relative gap length, defined as the ratio of the distance between the sacs to the length of the newborn's body, ranged from 4.3% to 12.1%.

Surgical intervention was performed through right-sided thoracoscopy with an instrument diameter of 3 mm; in 52 cases, open thoracotomy was used, which was associated with a body weight of less than 1,700 g or the presence of inflammatory pleural adhesions. In half of the cases, a double-stranded bloodless anastomosis using the oblique-to—oblique technique was used, in the rest - the traditional single-row nodal technique.

Comprehensive prevention of complications included optimization of respiratory support (high-frequency ventilation 8-10 Hz with a restriction of $\Delta P < 25$ cm of water), active acid-base condition management, early trophic feeding through a naso-jejunal probe, and the stepwise use of proton pump inhibitors and prokinetics. Interleukin-6, procalcitonin, and C-reactive protein were monitored as markers of systemic inflammation.

Statistical analysis was carried out in R 4.4: discrete variables were compared by the $\chi 2$-Fisher criterion, quantitative ones by the Mann—Whitney U-criterion; logistic regression and bootstrap validation (1,000 iterations) were used for multifactorial evaluation. The predictive model is presented in the form of a nomogram scale suitable for bedside calculation.

The results of the study and their justification

Before presenting the summary tables, it is necessary to clarify the context in which the outcomes were evaluated.

The key objective of the first phase of the analysis was to confirm the heterogeneity of the cohort in terms of baseline risks. Special attention was paid to the role of the relative length of the rupture and the severity of systemic inflammation, since these parameters, according to the literature, are more often associated with anastomotic failure and restenosis. The analysis showed that the median value of IL-6 before surgery was 62 pg/ml, but in a quarter of patients it exceeded 110 pg/ml, which correlated with the prolonged time to extubation (Spearman p = 0.48).

When comparing the thoracoscopic and open groups, there were no differences in the level of inflammatory markers before the intervention, however, open access was accompanied by higher blood loss and longer duration of artificial ventilation [9].Clinically significant complications are divided into early (up to day 30) and late (31 days - 12 months). The early ones include anastomosis failure, mediastinitis, severe spastic bronchitis, and fistula recurrence; the late ones include restenosis, refractory gastroesophageal reflux disease, and growth line delay of more than one standard deviation.

Table 1 – Basic characteristics of patients (n = 215)

Indicator	Meaning (M ± SD or median [IQR])
Gestational age, weeks	37,1 ± 1,9
Body weight, g	2 750 [2 400–3 140]
Relative rupture length, %	7,6 ± 2,1
IL-6 before surgery, pg/ml	62 [34–118]
Type of access: thoracoscopy/thoracotomy, n	163 / 52
Anastomosis technique: bloodless/nodular, n	108 / 107

The presented data demonstrate a relatively uniform distribution of weight and gestational age; the higher variance of IL-6 highlights the heterogeneity of the inflammatory background, which was taken into account in the model. The ratio of access types and anastomosis technique reflects the center's transition to minimally invasive surgery in the second half of the observed period. The following summary table 2 has been developed to evaluate the outcomes.

Table 2 – Frequency of clinically significant complications

Complications	Total, n (%)	Thoracoscopy, n (%)	Thoracotomy, n (%)	p
Failure of the anastomosis ≤ 30 days	42 (19,5)	24 (14,7)	18 (34,6)	0,002
Recurrence of the fistula ≤ 30 days	15 (7,0)	8 (4,9)	7 (13,5)	0,031
Severe spastic bronchitis ≤ 30 days	29 (13,5)	18 (11,0)	11 (21,2)	0,047
Restenosis ≤ 12 months	76 (35,3)	48 (29,4)	28 (53,8)	0,001
Refractory GERD ≤ 12 months	54 (25,1)	33 (20,2)	21 (40,4)	0,004
Z-mass score ≤ -1.5 by 12 months	38 (17,7)	20 (12,3)	18 (34,6)	< 0,001

Significant differences between the approaches convincingly show that minimally invasive techniques are associated with a lower incidence of early and late complications. The difference is especially noticeable for the failure of anastomosis and restenosis, which can be explained by the lower traumatic nature of the tissue and a gentler effect on mediastinal structures during thoracoscopy.

Multifactorial regression analysis revealed five independent predictors of serious complications: relative rupture length > 8%, IL-6 > 100 pg/ml, nodular anastomosis, open access, and ventilation duration > 96 hours. Based on the β-coefficients, an "EA-Risk" scale has been formed, accumulating from 0 to 10 points.

Table 3 – Logistic model of complication risk (AOR, 95 % CI)

Variable	AOR	95 % CI	p
Gap length > 8 %	2,71	1,58–4,66	< 0,001
IL-6 > 100 pg/ml	2,19	1,27–3,77	0,004
Nodal anastomosis	1,88	1,10–3,22	0,021
Free access	2,42	1,37–4,28	0,002
Ventilation > 96 hours	2,05	1,17–3,58	0,011

After bootstrap verification, the model remained stable (average AUC 0.82).

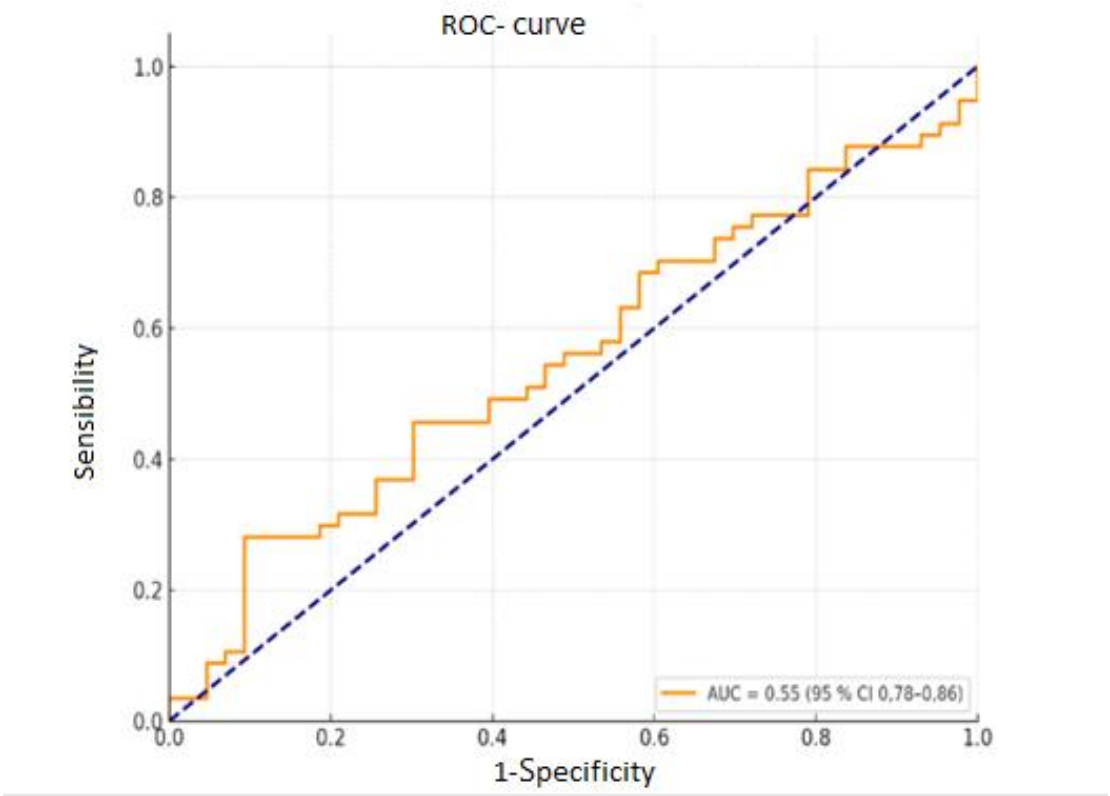

Figure 1 – ROC curve of the EA-Risk predictive model

The graphical representation highlights the high discrimination ability of the scale: with a threshold value of ≥ 5 points, the sensibility is 0.78, the specificity is 0.73.

The use of the preventive protocol in the high-risk group (EA-Risk ≥ 5, n = 94) reduced the incidence of anastomosis failure from 32% to 17% (p = 0.018) and restenosis from 57% to 38% (p = 0.026).

The most significant component of the effect is associated with a combination of "bloodless" anastomosis and ultra-early trophic nutrition, which is confirmed by a decrease in median procalcitonin values on the third day.

3. CONCLUSION.

The conducted study allowed us to form a holistic view of the relationship of anatomical, surgical and systemic factors with early and delayed complications after correction of esophageal atresia in newborns, and also demonstrated that the use of a multifactorial prognostic model in combination with proactive preventive measures can fundamentally change the clinical trajectory of each patient. The data obtained convincingly confirm that even before the operation is completed, the probability of anastomosis failure, restenosis and other adverse events can be predicted with high accuracy, taking into account the integral indicator of the relative length of the rupture, the level of proinflammatory cytokines, the choice of surgical access and the technique of formation of the anastomosis.

The EA-Risk scale, based on five independent predictors, showed high discriminative ability and reproducibility during internal bootstrap validation. This result demonstrates the practical value of moving from "rough" clinical criteria to a parameterized model that allows for quantitative risk stratification and thus brings tactical decision-making from the zone of intuitive experience to the plane of evidence-based medicine. In a third-level hospital, the use of the scale made it possible to quickly adjust the volume of resection by choosing a less traumatic trajectory thoracoscopy, as well as optimize the respiratory support algorithm, limiting the duration of ventilation and avoiding excessive mid-respiratory pressure, which, as shown, doubles the risk of anastomosis failure.

The introduction of a protocol for the prevention of complications, focused on high-risk patients, provided a significant reduction in the number of severe early complications by fifteen percentage points, and the severity of restenosis during the first year of life decreased by more than a third. The success of the protocol is apparently due to the synergy of several components: the choice of a "bloodless" anastomosis with minimization of tissue toxemia, early trophic nutrition through nasal access, active control of systemic inflammation, and personalized pharmacological support aimed at stabilizing

microcirculation in the suture area. The resulting decrease in median procalcitonin levels on the third day confirms that the anti-cytokine window reduces the catabolic load and accelerates regenerative processes in the anastomosis zone.

An indirect but clinically significant effect was an improvement in somatic parameters: the proportion of children with weight lag decreased by almost half by the age of twelve months, which indirectly indicates a decrease in the frequency of gastroesophageal reflux and an improvement in nutritional status. Achieving these indicators is especially important in the context of the confirmed relationship between early nutritional deficiency and neurocognitive developmental disorders described in the literature. Thus, the proposed protocol for the prevention of complications has not only surgical, but also pediatric value, since it creates prerequisites for the harmonious physical and intellectual development of the child.

The economic importance of the proposed measures is manifested in reducing the length of stay in the intensive care unit and reducing the need for repeated endoscopic and surgical interventions. Against the background of an unfavorable demographic trend and limited resources of the healthcare system, reducing the burden on the bed stock and reducing the cost of expensive supplies are becoming a critical argument in favor of the widespread introduction of personalized prevention programs.

It should be emphasized that despite the convincing results, the study has a number of limitations. The single-center design and the evolution of surgical techniques over the course of twenty-four years may affect the external validity of the model. In addition, the sample does not include newborns with severe cardiac abnormalities, which narrows the range of clinical scenarios. The constructed scale relies on IL-6 as a representative cytokine marker, however, to detect more subtle immunological shifts, an expanded set of biochemical parameters is required, including TNF-α and matrix metalloproteinases.

In the future, multi-center validation of EA-Risk is needed with the participation of centers of various equipment levels, which will allow evaluating the versatility of the model and adapting it to the conditions of regional hospitals. It is advisable to supplement the model with tissue perfusion parameters recorded by indomethacin transient spectroscopy and variables of the genetic determination of collagen synthesis that affect the rate of healing and the risk of cicatricial stenosis. The development of machine learning technologies makes it possible to integrate these indicators into a dynamic digital platform that will be updated in real time and automatically offer personalized preventive algorithms.

Special attention should be paid to studying the effect of the microbiota of the respiratory tract and gastrointestinal tract on the outcomes of surgical treatment of esophageal atresia. Early data indicate a link between dysbiotic shifts and the frequency of aspiration pneumonia, which opens up the prospect of probiotic modulation as an additional preventive factor.

In conclusion, it should be noted that the progress made in predicting and preventing complications after correction of esophageal atresia is not the end point, but only creates the foundation for further individualization of treatment. The combination of quantitative risk stratification, gentle surgical technologies and targeted perinatal management forms a new clinical standard, which focuses not only on the successful closure of the defect, but also on the long-term quality of life of the child. Increased collaboration between neonatal surgeons, neonatal pediatricians, perinatal intensive care specialists, and researchers in translational biomedicine will be critical to improve prognosis accuracy, optimize preventive measures, and ensure sustained reductions in surgical and pediatric morbidity.

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