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Considering Risk Factors for the Development of Complications With Perforations of the Esophagus

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Abstract: The main factors in the formation of esophageal suture failure were: the etiological factor of esophageal perforations (p=0.031), the duration of the period between esophageal perforation and surgery (p=0.047), the severity of the general condition (p=0.016), and the presence of purulent-infectious complications during hospitalization ($0.002 \leq p \leq 0.026$). The duration of the period from receiving perforation of the esophagus to the start of the operation is of great power (more than 24 hours increases the risk by 3.62 times, right-sided colitomy - by 3.72 times, perforation of the esophagus by foreign bodies - by 2.95 times, the presence of mediastinitis at admission - by 4.18 times, localization of perforations of the esophagus in the lower thoracic region - by 2.68 times, hypertensive disease, diabetes mellitus and coronary artery disease - by almost 2. These risk factors should be considered when planning the tactics of managing patients with esophageal perforations.

Keywords: esophageal perforations, risk factors.

Introduction

Injuries of the esophagus (EA) are a rather rare pathology, however, it is very dangerous and has a large number of clinical symptoms, which complicates timely diagnosis, causes many intra- and postoperative complications, and often leads to patient mortality [10].

Until now, there are disputes in the literature about the choice of tactics for managing PP, many authors state errors in the choice of tactics, however, there is still no consensus and standard for managing such patients, which leads to a high incidence of complications and mortality among such patients [5].

The success of PP treatment relies, as in many other cases, on the timeliness of diagnosis and the accuracy of differential diagnosis, so when surgical intervention is performed a day after PP, it leads to a 2.5-fold increase in the incidence of postoperative complications and doubles the mortality of patients [7].

However, the relative rarity of the occurrence of PP, especially penetrating PP, is extremely rare for most surgeons, which increases the number of complications and mortality in such patients, sometimes up to 67% [1], but most authors give figures of 29-35% [6].

The effectiveness of PP treatment is due to the localization and isolation of PP, etiology, the duration of the period from receiving PP to the start of surgery, complications on admission, and the comorbid background of the patient [9]. Comorbidity is of great importance, since these pathologies affect both wound healing, the development of complications, and the body's response to medications, and hence the favorable outcome [11]. A significant role is also played by the duration of the period from receiving PP to the start of surgical intervention [8].

This clearly proves the undoubted relevance of improving the effectiveness of PP treatment in patients of surgical departments, which is based on the assessment of risk factors for the development of postoperative complications of PP, which served as a prerequisite for the present study.

The purpose of the study is to identify and determine the strength of the influence of various factors in the development of complications of esophageal perforations in the prognostic matrix and to determine the risk groups of patients with PP in accordance with the strength of the influence of each factor and the sum of their influences.

Material and research methods

The total random sample was 320 patients. In accordance with the specified criteria, the patients were divided into the following groups: comparison group 2005-2017. - 201 patients (62.8%) and the main group 2018-2022. - 119 patients (37.2%).

Among the studied patients, people of young working age (19-44 years) predominated, there were no gender differences among patients, the average age of our patients was 34.6±2.4 years, the average age of women was 36.1±2.8 years, men – 32.8±2.4 years (Fig. 1).

In the diagnosis of PP, we used anamnestic, clinical, endoscopic, X-ray contrast research methods, esophagogastroduodenofibroscopy (EGDFS), the international specialized questionnaire GIQLI (Gastrointestinal Quality of Life Index), the GSRS questionnaire (Gastrointestinal Symptom Rating Scale), the scale of the overall clinical impression (Clinical Global Impression - CGI) in order to objectify the assessment of the patient's condition by the doctor before (CGI-s) and after (CGI-i) treatment, which completely satisfied us in the diagnosis.

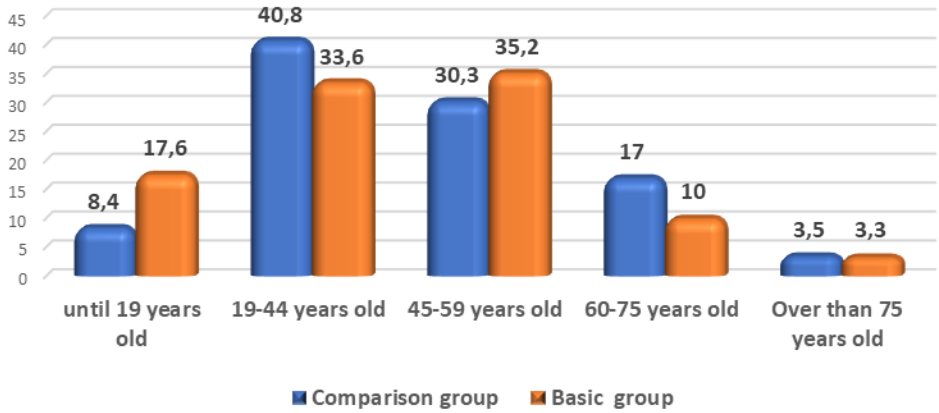

Figure 1. The diagnosis of PP

Statistical processing of the results of this study was carried out by the methods of variational statistics in the Microsoft Office software package by the Excel-2019 program by determining the standard deviation and the arithmetic mean by the method of moments (M ± m), standard deviation (□).

To determine the statistical significance of the obtained measurements, parametric criteria for the significance of Student's differences (t) were used, non-parametric criteria were determined by the Mann-Whitney method, and the $\chi 2$ method was used for qualitative characteristics.

The occurrence of the trait in the analyzed groups was determined by nonparametric frequency analysis with the calculation of the Fisher criterion, $\chi 2$ with the Yates correction [3].

Correlation relationships of the studied indicators were calculated using the Spearman linear correlation coefficient (r) with parametric data distribution and the Spearman rank correlation coefficient (r) with nonparametric distribution of indicators with the determination of the levels of statistical significance of each by correlation matrices, cluster and logistic regression analysis [2, 3 , 4].

Non-parametric data were evaluated by the non-parametric Mann-Whitney U-test, parametric data were evaluated by Pearson's test. A correlation greater than 0.7 was considered strong, 0.3-0.7 - medium, less than 0.3 - weak [2].

A predictive model characterizing the dependence of a quantitative variable on factors was developed using the linear regression method [3, 4].

Comparison of independent groups was carried out according to Student's t-test with a normal distribution of a trait and Mann-Whitney with a distribution other than normal, comparison of dependent groups with a normal distribution of a trait was carried out according to Student's t-test, with a distribution other than normal, by the Wilcoxon test. Differences were considered significant at 95% confidence interval ($P \leq 0.05$).

The statistical significance of comparing the results of the study of significance (P) according to the Student's test of significance (t) with a 95% confidence interval in our work had 4 levels: "high - $P<0.001$, medium - $P<0.01$, low (marginal) - $P<0.05$, insignificant (insignificant) – $P>0.05$" [3].

Results and Discussion

The most common complaint of the studied patients was chest pain - it was stated in all patients of both groups, 272 (85%) patients of both groups complained of general weakness, soft tissue emphysema - in 253 (79.06%) patients of both groups, vomiting (in including those with an admixture of blood) - in 210 (65.63%) patients, and all these complaints were distributed identically within the groups, almost in equal proportions. Complaints of nausea were in 214 (66.88%) patients, and in the CG - in 118 (58.71%), and in the MG - in 96 (80.67%), an increase in body temperature was noted in 75 (45.31%) %) of patients in both groups, with 30 (14.93%) in the HC and 45 (37.82%) in the MG, which is most likely due to the etiological factor of PP in these patients (Fig. 4).

The most common comorbid diseases in the studied patients with PP were coronary heart disease (CHD) (66 (20.63%) patients) and essential hypertension (AH) (62 (19.38%) patients).

In both groups, the most common cause of PP was foreign bodies - 45.31% of patients (in the CG - 89 (44.28%) and in the MG - 56 (47.06%) patients, respectively), the next most common etiological cause of PP was iatrogenic damage (38.81% and 33.61%, respectively, in groups). Injuries of the neck and chest caused PP in 42 (13.13%) patients, with chest injuries predominating in the CG (7.96%). The rarest cause of PP in our study was found to be spontaneous ruptures of the esophagus - 4.69% (3.48% and 6.72%, respectively, in groups).

The most common foreign bodies were meat bones - 38 (11.88%) patients and dentures - 31 (9.69%) patients, and the rarest were coins and buttons - 8 (2.5%), respectively.

Most often, PP occurred on the left wall of the esophagus - 33.1%, the most rarely damaged wall in our study was the anterior wall - 18.62%

The most common iatrogenic causes of PN were bougienage of the esophagus - 33.9%, and the rarest - intraoperative PN - 6.78%. It should be noted that most of the iatrogenic PPs (66.1%) were found in the GS, while only 33.9% of such PPs were recorded in the MG.

Most often, iatrogenic PP occurred on the right wall of the esophagus - 31.36%, in second place - the posterior wall - 22.88%, with almost the same frequency, PP was found on the left wall - 21.19%, and the most rarely damaged wall in our The study included the anterior wall - 9.32% and

its angles with the left and right walls - 7.63% each. In an intragroup comparison in both groups, it is stated that it is completely identical to the overall picture of PP.

As in the case of iatrogenic SP, traumatic SP due to a neck injury prevailed in the SG - 61.11% versus 38.89% in the MG. The most common cause of neck injuries and PP caused by them was blunt neck trauma - 55.56%, and the rarest - a suicide attempt in the form of hanging - 5.56%, the difference between them is 1 order.

Among the traumatic PP of the cervical region, injuries of the anterior-left wall of the esophagus prevailed - 44.44%, the least common was complete dissection of the esophagus - 16.67%.

Most patients with PP of various etiologies, with the exception of iatrogenic PP, went to the hospital within 6 hours (iatrogenic - within the first 3 hours), and a slightly larger proportion of patients with chest injuries, spontaneous ruptures of the esophagus and foreign bodies of the esophagus sought qualified medical care within 3-6 hours, a slightly smaller proportion of patients with PP of this etiology - up to 3 hours from the moment of PP.

The longest period before seeking medical help is characteristic of PP due to spontaneous rupture of the esophagus and foreign bodies - 20.0% and 8.28%, respectively, of such patients postpone contacting a specialist for more than a day.

The most common complication of PP of any etiology is esophagitis. Mediastinitis, as a very formidable complication of PP, was stated in our study in 27.5% of patients (29.35% in the HC and 24.37% in the MG, $p>0.05$), pleural empyema, damage to the trachea and bronchi and bronchitis was stated in approximately equal proportions (10-11% each), the rarest complication of PP was peritonitis - 1.88% of patients.

The presence of mediastinitis has a direct correlation with the duration of the period before hospitalization for foreign bodies and spontaneous ruptures of the esophagus ($r=0.58$ and $r=0.52$, respectively).

The mean VAS score for pain on admission in patients with AFL who were admitted to the hospital was 6.48±1.23 points, with iatrogenic etiology of PP, the pain was on average 6.16±1.19 points, which is quite explainable by the amount of injuries and conditions of the patient's stay.

The mean Overall GIQLI in all our patients before surgery was 79.12±20.02 points; CI = 97.10-101.13), i.e. the level of QOL in patients before surgery reached only 54.86% of the possible maximum. The maximum value of QoL was observed in the component "Symptom" 43.98±10.32; CI = 52.94-55.02) with a minimum in the "Social function" component 12.41±2.87; CI = 11.12-11.70), of course, subject to the exclusion of the "Medical treatment" component, taking into account the fact that patients were only admitted to the hospital. The minimum and maximum QOL (Overall GIQLI) before surgery were 33 and 91 points.

In patients of both groups, according to the GSRS questionnaire, moderately severe disorders predominate (36.32% and 37.82%), and mild and severe disorders account for approximately the same number of patients (22.89% and 22.39% in the GS, respectively, and 21 .85% in OG).

According to the CGI-s subscale assessed by the doctor, the condition of the patients was somewhat different - in both groups moderately severe disorders predominated, then severe and severe disorders were in 2nd and 3rd place - 32.34%, 25.87% and 14.43% in the GS respectively, and in the OG - 31.93%, 25.12% and 15.13%, respectively.

The total severity of the patients with PP examined by us was 15.0 according to the GSRS questionnaire [9.0; 18.0] scores for Me [25%; 75%], and for ranked scores – 3.0 [2.0; 3.0] and CGI-s subscale 3.0 [2.0; 4.0].

The correlation of scores on the GSRS questionnaire and the CGI-s scale is quite high and strong in many respects, so moderate and severe conditions have a strong direct correlation - $r=0.76$

and r=0.79, respectively (p≤0.001), which can be perceived as a very reliable relationship of the questionnaire GSRS with CGI-s scale. Mild and severe conditions correlate more moderately in our study, but have a direct relationship - r=0.48 and r=0.54, respectively (p≤0.005).

Determining and assessing the impact of clinical symptoms on the prognosis of complications after surgery to eliminate esophageal defects is extremely important for a full understanding of the patient by the doctor. The study of risks and their assessment, based on prognostic factors, determines the choice of optimal diagnostic measures and tactics for the treatment of patients with PP.

To fulfill the objectives of the study, we needed to develop a prognostic matrix, for which we applied a modified probabilistic Bayesian method - the technique of "normalized intensive indicators (NIP)" [4] with the calculation of all necessary indices and parameters. The weight and power of influence of all potential factors was determined by relative risks (relative risk - RR), calculated as the product of NIP and the "weight" of the factor. Really influencing weighty factors are selected as significant by RR = c/d, where c is the maximum and d is the minimum of the intensity of each individual factor [4].

Irrelevant factors are equal to 1, the larger the RR, the greater the influence of the factor on the risk of complications after PN surgery.

The NIP indicator was calculated by the formula: "N = r/M, where: N is the NIP, r is the intensive indicator of the development of complications per 100 examined, M is the normalizing indicator" [4].

Table 1. Prognostic matrix for a comprehensive assessment of the risk of complications after PP

Risk factors	Gradation of factors	(r) intense complication rate	M, normalizing indicator for 249 patients	NIP	RR	X, integrated indicator
Admission deadline	Up to 24 hours	16	26,5	0,603		2,19
	Later 24 hours	58	67,5	2,188	1,42	7,94
Localization of PP	Cervical	72,2	73,8	1,0		0,91
	Upper and middle chest	27,8	26,3	1,1	0,93	0,98
	lower thoracic	88,9	78,8	1,1		2,44
	Abdominal	11,1	21,3	0,5	2,16	1,13
PP suturing	Later 24 hours	81,5	72,5	1,1	1,67	1,88
	Up to 24 hours	18,5	27,5	0,7		1,12
colitomy	right-sided	90,7	72,5	1,3	3,72	4,65
	left-sided	9,3	27,5	0,3		1,25
Imposition of a gastrostomy according to Stam-Sen-Kader	There is	63,0	48,8	1,3		2,31
	No	37,0	51,3	0,7	1,79	1,29
Application of "Systems for Decompression and Nutrition"	No	63,0	56,3	1,1		1,48
	There is	37,0	43,8	0,8	1,32	1,12
Subtotal and total	There is	64,8	73,8	0,9	1,53	2,04

rupture of the esophagus	No	35,2	26,3	1,3		1,34
hypertonic disease	There is	83,3	71,3	1,2		2,36
	No	16,7	28,8	0,6	2,02	1,17
cardiac ischemia	There is	88,9	82,5	1,1		1,83
	No	11,1	17,5	0,6	1,70	1,08
DS	There is	87,0	80,0	1,1		1,83
	No	13,0	20,0	0,6	1,68	1,09
Foreign bodies	There is	31,5	28,8	1,1		3,25
	No	68,5	71,3	1,0	1,14	1,10
Mediastinitis on admission	There is	79,6	81,3	1,0		5,14
	No	20,4	18,8	1,1	4,17	1,23
VAS score at admission	Over 6.5	68,5	73,8	0,9		1,55
	Less than 6.5	31,5	26,3	1,2	1,29	1,20
Overall GIQLI scores at admission	Less than 80	72,2	63,8	1,1		1,67
	80 and over	27,8	36,3	0,8	1,48	1,13
GSRS scores at admission	17 and over	53,7	41,3	1,3		2,15
	Less than 17	46,3	58,8	0,8	1,65	1,30
CGI-s score at admission	4 or more	83,3	71,3	1,2		2,36
	Less than 4	16,7	28,8	0,6	2,02	1,17

For example, in patients hospitalized with penetrating PP up to 24 hours after the formation of a defect in the esophagus, the incidence of mediastenitis (r) was 16%, and in the period 24-48 hours after the formation of a defect in the esophagus - 58%. This indicator among all 249 patients is 26.5%, this is M. Thus, in those hospitalized with a prescription of PN up to 24 hours, NIP1 = 16/26.5 = 0.603, and with a prescription of 24-48 hours - NIP2 = 58/26.5 = 2.188. RR=2.188/0.603=3.628.

We identically calculated the NIP for all other risk factors and formed a matrix for an integrated assessment of the risk of complications after RA suturing operations. After calculating RR and NIP, we calculated the strength of the influence of each factor - the prognostic coefficient X according to the formula: “X = R*N, where X is the risk indicator for the influence of the factor strength, N is the IIP of complications, RR is the relative risk” [4].

In our example, the RR of prescription of PP was 3.628, NIP1 - 0.603, NIP2 - 2.188, then the prognostic coefficient X = 3.628 * 0.603 = 2.188, with hospitalization up to 24 hours with PP and 3.628 * 2.188 = 7.941, with hospitalization later than 24 hours with PP.

According to the calculated prognostic coefficients of PP complications, we carried out a step-by-step selection in a logistic regression analysis according to the following parameters: the timing of admission, the location of the esophageal defect, right-sided colitomy, suturing of the PP upon admission of the patient 24 hours after the injury, the use of laser irradiation, the imposition of a gastrostomy according to Stam-Sen- Kaderu, the use of the "System for decompression and nutrition", subtotal and total rupture of the esophagus with subsequent closure tightly, the presence of coronary artery disease, hypertension and diabetes, the etiological factor of PP, the development of mediastinitis, peritonitis, Overall GIQLI and GSRS scores, VAS and CGI-s scale (Table 1).

After that, according to the compiled prognostic matrix (Table 1), we calculated the risk ranges for a combination of significant risk factors by analyzing the minimum initial sum of all X and the maximum sum. Minimum sum of all X: 2.19+0.91+1.13+1.12+1.25+1.29+1.12+1.34 +1.17+1.08+1.09+1 ,10+1.23+1.24+1.13+1.33=20.9. The initial risk is 20.9 points.

Maximum sum of all X: 7.94+0.98+2.44+1.88+4.65+2.31+1.48+2.04 +2.36+1.83+1.83+3 .25+5.14+1.55+1.67+2.15+2.36=45.9.

Table 2. Values of subranges and groups of individual prediction of the risk of complications after operations for PP

Subrange	Subband size	Risk group
Weak Probability	20,9-28,4	Favorable prognosis
Average probability	28,5-36,0	Attention
High probability	36,1-45,9	Unfavorable prognosis

The maximum possible risk is 45.9 points. The risk range is 20.9-45.9 points. It is logical that the greater the amount of risk a patient with PP gains, the higher his risk of developing complications and a more unfavorable prognosis. We divided the entire risk range into subranges and determined the thresholds for X sums as critical for the likelihood of complications of PP (Table 2).

Let us consider an example of calculating the individual risk of PP complications.

Patient E., 42 years old, was admitted after 29 hours (this period corresponds to a coefficient of 7.94), RA in the cervical region (0.91), he underwent an attempt to suture the RA (1.88) during left-sided colitomy (1.25), gastrostomy according to Stam-Sen-Kader (2.31), without the use of the "System for decompression and nutrition" (1.48), esophagus without subtotal and total rupture (1.34), AH is absent (1.17), CAD is absent (1.08), DM is present (1.83), PP is caused by a foreign body – bone (3.25), mediastinitis was diagnosed at admission (5.14), VAS score at admission 7 (1.55), overall GIQLI score at admission 59 (1.67), GSRS score at admission 19 (2.15), CGI-s score at admission 4 (2.36). The risk of complications and death after operations for PP was 37.3.

In this case, the prognosis is unfavorable and the risk of complications is high. the result obtained is in the range of 36.1-45.9.

Individual prediction of the development of complications makes it possible to predict the outcome after operations for PP, to develop therapeutic, prophylactic and rehabilitation measures.

Individual forecasting can be used in hospitals for treatment, while obtaining a reasonable forecast for the development of complications in the early postoperative period after surgery for PP. Also, with the help of individual forecasting, it is possible to develop a targeted scheme for the rehabilitation of patients who have undergone surgery for PP.

In order to test the prognostic matrix for a comprehensive assessment of the risk of complications, we analyzed the data of 91 patients with OH who underwent surgery for PP.

The predictors of possible postoperative complications of interventions for the elimination of PN were determined, the duration of the period from receiving PN to the start of the operation is very strong (more than 24 hours increases the risk by 3.62 times, right-sided colitomy - by 3.72 times, PN by foreign bodies - by 2, 95 times, the presence of mediastinitis at admission - 4.18 times, localization of PP in the lower thoracic region - 2.68 times, hypertension, diabetes mellitus and coronary artery disease - almost twice. These risk factors should be taken into account when planning the management of patients with PP.

Using regression stepwise analysis, we calculated a statistical model for assessing the risk of a negative prognosis for all factors (Table 3).

When evaluating the specificity, sensitivity, and accuracy of the proposed predictive risk factors, we used subranges of the probability of complications of PP.

Table 3. Regression variables of the original model for predicting complications after surgery for PP

Forecast predictors	Coefficient	Wald	P	OSH

		statistics		(95% DI)
Admission deadline	6,42	26,4	0,011	1,7
Localization of PP	2,16	12,6	0,001	2,8
PP suturing	1,67	8,2	0,004	9,4
Right-sided colitis	3,72	7,4	0,0047	1,3
Imposition of a gastrostomy according to Stam-Sen-Kader	1,79	7,4	0,006	2,2
Application of "Systems for Decompression and Nutrition"	1,32	7,3	0,001	2,7
Subtotal and total rupture of the esophagus	1,53	6,5	0,007	2,5
hypertonic disease	2,02	11,2	0,002	3,2
cardiac ischemia	1,70	10,2	0,01	4,1
diagnostic sensitivity	1,68	9,8	0,003	3,9
Foreign bodies	1,44	3,6	0,002	2,8
Mediastinitis on admission	4,17	18,6	0,001	8,5
VAS score at admission	1,29	3,5	0,005	2,3
Overall GIQLI scores at admission	1,48	14,2	0,001	5,9
Defeated more than 2-X KA	1,65	5,4	0,001	6,5
GSRS scores at admission	6,3	28,2	0,001	

The diagnostic value of the prognosis assessment model was assessed according to standard characteristics: “diagnostic specificity (DS), diagnostic efficacy (DE), diagnostic sensitivity (DS), negative predictive value (PCVR), positive predictive value (PCPR) according to the formulas DS=d/ (d+b)×100%, DE=(DC+DS%)/2, DC=a/(a+s)×100%, PCR=d/(c+d)×100%, PCR=a/ (a + b) × 100%, where a is a true positive result, b is a false positive result, c is a false negative result, d is a true negative result” [4].

Thus, in the MG, when calculating the size of the subranges, out of 91 patients with penetrating PP, 32 (35.16%) were assigned to the group with a favorable prognosis, 31 (34.07%) - to the attention group, and 28 (30.77%) - to the group with a poor prognosis.

In the dynamics of observation in the group with a favorable prognosis, complications developed in 5 patients (15.63%) - a false negative result, in 27 patients postoperative complications were not observed (84.37%) - a true negative result; in the group of patients with an unfavorable prognosis, 3 patients (10.71%) did not develop postoperative complications - a false positive result, 25 (89.28%) patients developed some kind of early complications after surgery for PP - a true positive result (Table . 4).

Table 4. Diagnostic value of the proposed risk factors for predicting early complications after PN surgery

Operating characteristics	Indicators
DS=d/(d+b)×100%	27/(3+27)×100%=90%
DS=a/(a+c)×100%	25/(25+5) ×100%=83,3%
DE=(DCH+DS%)/2	(83,3+90)/2=86,65%

PSOR=d/(c+d)×100% PSPR=a/(a+b)×100%	27/(5+27)×100%=84,37% 25/(25+3)×100%=89,28%

According to the data obtained, shown in Table 4, DS was 90%, PM - 83.3%, and DE - 86.65%. An important step in the development of any diagnostic tool is validation.

Conclusions

The prognostic matrix developed by us will make it possible to determine the likelihood of developing complications of PP in each patient individually, and it will not be difficult to do this in practical surgery, since we have identified and determined the strength of each factor with a high degree of sensitivity and specificity. In addition, according to the totality of X scores, it will be possible to classify each patient into risk groups for developing complications of PP and, based on this, optimize the tactics of treating the patient.

The predictors of possible postoperative complications of interventions for the elimination of PN were determined, the duration of the period from receiving PN to the start of the operation is very strong (more than 24 hours increases the risk by 3.62 times, right-sided colitomy - by 3.72 times, PN by foreign bodies - by 2, 95 times, the presence of mediastinitis at admission - 4.18 times, localization of PP in the lower thoracic region - 2.68 times, hypertension, diabetes mellitus and coronary artery disease - almost two times.These risk factors must be taken into account when planning the tactics of managing patients with PP.

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