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9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანე-ლის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა,მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა,რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შე-ჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

PROGNOSTIC MODEL OF POSTOPERATIVE ADHESIVE INTESTINAL OBSRUCTION RISK IN CHILDREN

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Abstract.

Objective: to develop a prognostic model of the postoperative adhesive intestinal obstruction risk in children by the use of multivariate statistics.

Materials and methods: To create a model for the prediction of the postoperative adhesive intestinal obstruction by using the method of binary logistic regression, a retrospective analysis of the features of the acute inflammatory disease of the abdominal cavity organs and treatment strategy in 119 children.

Results: The level of significance of clinical and anamnestic signs in children with appendicular peritonitis and the postoperative adhesive intestinal obstruction was determined using Pearson's test χ^2. The main factors (leukopenia at hospitalization) (p=0.033) pronounced stigmatization with signs of connective tissue dysplasia (p=0.013) and duration of surgery (p=0.0002) were highlighted, which indicate the postoperative adhesive intestinal obstruction risk. The logistic regression method was used to create a prognostic model for calculating the postoperative adhesive intestinal obstruction risk, which was assessed as "very good" by ROC analysis (test sensitivity – 77%; specificity – 72%): AUC = 0.796.

Conclusions: The application of the proposed prognostic model of the postoperative adhesive intestinal obstruction risk in children with acute inflammatory diseases of the abdominal organs allows to make decision as for the extent of surgery and optimization of treatment strategy at all stages of rendering care.

Key words. Prognostic model, risk, postoperative adhesive intestinal obstruction, children.

Introduction.

Determining the risk of intra-abdominal adhesions in children with acute abdominal pathology helps to optimize the treatment of such patients and prevent the development of postoperative adhesive intestinal obstruction (PAIO), which occurs in 62% of cases [1-4]. Since peritoneal adhesiogenesis is multifactorial, the use of individual clinical and anamnestic factors or their set without considering the total effect for a concrete patient does not allow to reliably predict the development of adhesions [2,5,6]. The best way to diagnose the PAIO risk in children, in our opinion, is to develop a prognostic model by using multivariate statistics to identify the mutual influence of predictors to optimize preventive measures.

Materials and methods.

To create a method for predicting PAIO by the way of the binary logistic regression, a retrospective analysis of the clinical course of acute inflammatory disease of the abdominal organs (AO) and treatment strategy was performed in 119 children who were treated at the surgical departments of the Regional Children's Clinical Hospital in Odessa. The first group (A) consisted of 59 children with adhesive intestinal obstruction (AIO) occurred

after surgical treatment of appendicular peritonitis (AP). The second group (B) included 60 children with AP who had no signs of AIO during the postoperative follow-up period.

To determine the logistic regression parameters, the selection of predictors with the known AIO in both groups of children was conducted. The logistic function looks like this:

$$f(z) = \frac{1}{1 + e^{-z}}$$

$$z(x) = \beta_0 + \beta_1 x_1 + \ldots + \beta_n x_n$$

where: f–gets the value between 0 и 1; $\beta 0, \ldots, \beta n$ – logistic regression parameters. $x_1, \ldots, x_n$ – signs determination.

This equation allows us to estimate the probability of the event (in our case PAIO) in each study participant with an individual set of predictors. For significant assessment of the diagnostic test, the area under the characteristic curve (AUC) is determined, which reflects the optimal value of sensitivity and specificity of each feature [7-10]. Statistical processing of the study results was performed using MedCalc 9.03 packages: Statistica 8.0 and SPSS 11.01.

Results.

The first step in creating a diagnostic model was to identify statistically significant factors having influence on the PAIO risk. With this purpose, we analyzed the diagnostic value of 47 signs, which were considered by potential predictors: demographic and individual factors of the patient, clinical and anamnestic signs, laboratory parameters, intraoperative data and extent of surgery, features of the postoperative period course, the presence and severity of undifferentiated connective tissue dysplasia (UCTD). In addition, the acetylation genotype was studied by determining point mutations in the N-acetyltransferase 2 (NAT2) gene using polymerase chain reaction and restriction fragment length analysis. The list of features that were analyzed is shown in table 1.

Relevant features were identified by filtering low-frequency features. In our case, the features that in 90% or more cases take the same value were excluded, because they do not improve the prognostic ability of the model. At that stage, 12 binary features were excluded.

The next step for the remained signs a statistical significance to assess the risk of PAIO by using Pearson's criterion χ^2 and ANOVA variance analysis was calculated. Empirically, the features with the lowest p-value were selected to create a logistic model. Simultaneously the factors were identified that demonstrated a statistically significant relationship with the PAIO development: leukopenia at the time of hospitalization (p = 0.033), pronounced stigmatization of NCTD signs (p = 0.013), duration of surgery (p = 0.0002).

Table 1. *Potential predictors of the adhesive intestinal obstruction risk.*

Demographic/ individual	age, sex; place of residence (city/countryside); belonging to socially and economically disadvantaged groups; *NAT2* acetylation genotype; presence and degree of NCTD; functional disorders of the digestive tract in the anamnesis
Clinical and anamnestic signs	The duration of the disease at the time of treatment; general condition at hospitalization; degree of exsiccosis; localization and nature of pain, defense, peritoneal signs; the nature of vomiting; violation of defecation and gas discharge; fever; rectal examination data.
Laboratory indicators	The presence of hyperleukocytosis; the presence of leukopenia; total number of leukocytes, leukocyte shift; hematocrit; C-reactive protein; fibrinogen; dyselectrolytemia; acid-base condition; serum glucose.
Intraoperative data and scope of intervention	Type of operational access; type of peritonitis; position of the appendix; the presence and nature of effusion; the presence of fibrin in the abdominal cavity; technical difficulties; omentectomy; intestinal deserosation; drainage; duration of intervention.
Features of the postoperative period	The presence of complications (intra-abdominal / from the wound); relaparotomy; restoration of peristalsis / independent defecation; removal of nasogastric probe; the beginning of enteral nutrition (a day); prokinetics stimulation; duration of stay at the intensive care unit and inpatient treatment

Table 2. *Logistic Regression Equation Predictors.*

	Predictors	β Coefficient
x_1	pronounced stigmas of NCTD	1.031
x_2	midline laparotomy	0.710
x_3	leukopenia at hospitalization	0.697
x_4	intra-abdominal complications at the early postoperative period	0.475
x_5	duration of intervention, min	0.027
x_6	local unrestricted peritonitis	-0.516
x_7	no vomiting	-0.755
x_8	medial position of the appendix	-1.004

According to the results of the analysis, surgical treatment of peritonitis is one of the most important risk factors for adhesions. The performance of omentectomy and the total intervention time are the factors that showed the lowest p-value, and accordingly have a significant impact on the postoperative adhesion process. In particular, among children with AIO, omentectomy was performed in 21 (35.6%) cases, in group B in 41 (68.3%) cases. Pearson's criterion χ^2 is 12.78; p<0.001. These indicators also correlate with our observations as for intraoperative data in the surgical treatment of AIO, because in a significant number of cases the cause of obstruction is joints involving a strand of a large omentum or the omentum itself, soldered to the postoperative scar. In addition, omentitis, intra-abdominal infiltrates and omental abscesses are the main causes of relaparotomy at the early postoperative period of peritonitis treatment in children, which are independent predictors of excessive adhesions risk.

The duration of surgery has a significant impact on the PAIO risk. For children from the main group, this figure averaged (77.7 ± 23.99) minutes, in the control group – (64.0 ± 13.74) minutes. It should be noted that this indicator is integral and depends, for example, both on the experience of the surgeon and the clinical situation, including the location of the inflammatory focus, technical difficulties, the occurrence of intraoperative complications, the spreading of intra-abdominal inflammation etc.

The last step is to analyze all possible combinations of selected features. For each combination, logistic regression was studied and evaluated by cross-checking using AUC ROC analysis, as this indicator reflects the combination of sensitivity and specificity of the proposed predicting model [8-10].

The obtained logistic regression equation includes 8 predictors and corresponding coefficients (Table 2).

The value of the free member of the equation β0 was (-1.5193).

So, a probability of PAIO development, namely the value (*z*) in the logistic regression equation is calculated as follows:

$z(x) = -1.5193 + 1.031x_1 + 0.810x_2 + 0.697x_3 + \ldots - 1.004x_8$

As this formula demonstrates, the negative value of the coefficient means the protective effect of the sign on PAIO development. Calculation of the PAIO developing probability – *f(z)* according to this formula, classifies the child's belonging to the PAIO risk group. With the purpose of automatical calculation of this indicator using the mathematical or statistical analysis program, we have created an appropriate algorithm in Microsoft Office Excel.

The quality assessment of the prognostic model was performed by cross-checking using AUC ROC-analysis. Figure 1 shows the characteristic curve by values *f(z)*. The optimal dividing point corresponds to the value 0.0.
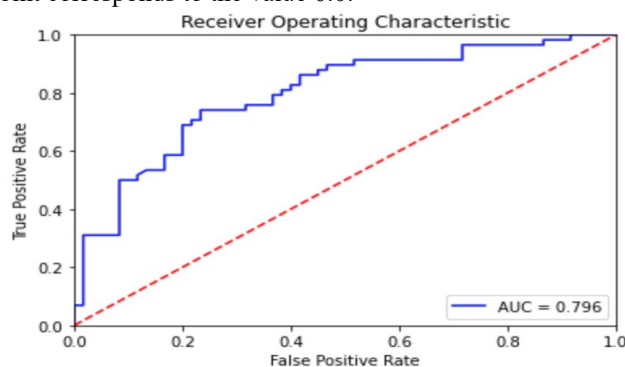

Figure.1. *Characteristic curve of the prognostic model ROC-analysis (Sp = 77%, Se = 72%).*
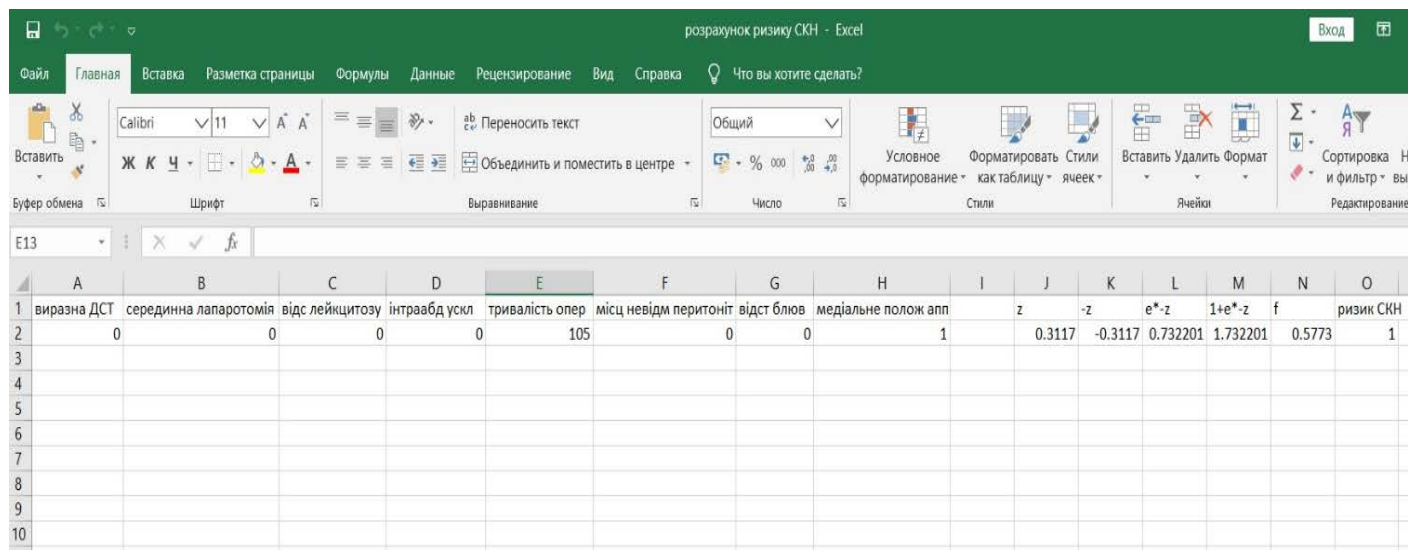
Figure. 2. *Example of calculating the PAIO risk using MO Excel.*

If the patient has $f(z) \geq 0.5$, the model is considered positive for the risk of PAIO developing according to certain predictors. The area under the ROC curve was AUC 0.796, which indicated a "very good" operation of the prognostic model.

The prognostic specificity of this model is (Sp) = 77%, sensitivity (Se) = 72%. The probability of intraperitoneal adhesions is 72% (test sensitivity). The statistical estimation of the area under the ROC curve is quite high ($p = 0.0001$), so developed on the basis of the logistic regression, the proposed model can be used to prognosis of the PAIO risk in children with acute inflammatory diseases and choice of an adequate treatment strategy.

Here is an example of calculating the PAIO risk developing in a child T. of 7 years old with appendicular peritonitis (Medical card No 90548. Postoperative diagnosis: Gangrenous-perforated appendicitis, widespread peritonitis) based on the results of entering the values of the corresponding predictors in Figure 2.

According to the calculations of the logistic regression equation, the child belongs to the PAIO risk group, because $f(z) = 0.5773$, i.e., $f(z)$ is closure to 1. In 11 months after the initial intervention, the child was hospitalized with signs of acute intestinal obstruction. During the operation, an extensive adhesion process in the abdominal cavity, multiple viscero-parietal and viscero-visceral adhesions with the formation of "double-barrels" were determined. Obstruction was caused by a cord-like adhesion between the loop of the small intestine and the anterior abdominal wall, which caused strangulation of the adjacent loop of the intestine.

So, the prognostic model of the PAIO risk by logistic regression showed a good result, and the predictor that showed the greatest connection with the development of AIO is the duration of abdominal surgery. The application of the proposed prognostic model of the PAIO risk by logistic regression method of selected signs at the stage of clinical history and intraoperative data allowed to make a decision as for the extent of surgical treatment and postoperative management in children with appendicular peritonitis.

Discussion.

Abdominal operations in children cause postoperative AIO in the unpleasantly high part of cases, with variations depending on the type of initial operation and its clinical peculiarities. According to the modern concept of adhesions pathogenesis development, intraperitoneal inflammation plays an important role in this process [1,2,5]. This correlates with our data [11], indicating that peritonitis is the key condition followed by adhesions formation. It is important to consider as many aspects and variables as feasible to develop clinically relevant and practical predictors. In the present study, we first developed a logistic regression model for adhesive small bowel obstruction prognosis based on the data of a retrospective cohort of 119 pediatric patients.

We also identified, for the first time, the impact of several variables on the possibility of postoperative adhesive intestinal obstruction in patients with appendicular peritonitis using a logistic regression ROC-analysis. These data delineate several key risk factors, associated with adhesions-related sequelae such as type of peritonitis, time spent for the first intervention, incision type, signs of connective tissue dysplasia, leucopenia at the admission, intraabdominal postoperative complications. The absence of vomiting and typical position of the appendix have shown a protective impact.

Understanding which features of operations carry a greater risk of subsequent PAIO will be helpful to prevent acute intestinal obstruction events, as readmission or further surgical interventions. Moreover, our predictive model provides a useful tool for detecting the group of patients that has high chances for adhesion formation and respectively require preventive strategies application on every stage of treatment. The specificity and sensitivity of the developed predictive model account for 77 % and 72 % respectively.

The follow-up evaluation showed that patients who belong to the adhesive obstruction risk group had a considerably higher rate of readmission and requirement for surgical treatment.

Moreover, this cohort of patients has an advanced intraabdominal adhesive process. Our experiences support the active preventive measures in high-risk patients using intraoperative prophylaxis and enhanced recovery after surgery.

Conclusion.

1. Retrospective analysis of 119 case histories determined the level of significance of potential predictors (demographic and individual patient factors, clinical and anamnestic features, laboratory parameters, intraoperative data and volume of surgery, features of the postoperative period course) in children with appendicular peritonitis and PAIO by Pearson's criterion χ^2. The main factors (leukopenia at hospitalization) (p = 0.033) pronounced stigmatization with signs of connective tissue dysplasia (p = 0.013) and duration of surgery (p = 0.0002) indicated the possibility of the PAIO risk.

2. The method of logistic regression created a prognostic model for calculating the risk of PAIO, which ROC-analysis (test sensitivity – 77%; specificity – 72%) was assessed as "very good": AUC = 0.796.

3. The proposed prognostic model of the PAIO risk in children with acute inflammatory diseases of the abdominal cavity can be used to optimize treatment strategy at all stages of medical care.

Conflict of interest.

The authors did not find any conflict of interest.

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ПРОГНОСТИЧЕСКАЯ МОДЕЛЬ РИСКА ПОСЛЕОПЕРАЦИОННОЙ СПАЕЧНОЙ НЕПРОХОДИМОСТИ КИШЕЧНИКА У ДЕТЕЙ

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Резюме.

Цель: разработка прогностической модели риска послеоперационной спаечной непроходимости кишечника (ПСНК) у детей путем использования многомерной статистики.

Материалы и методы. Для создания модели прогнозирования ПСНК путем использования метода бинарной логистической регрессии был проведен ретроспективный анализ особенностей течения острых воспалительных заболеваний органов брюшной полости и *лечебной* тактики у 119 детей.

Результаты. Был определен уровень значимости клинико-анамнестических признаков у детей с апендикулярним перитонитом и ПСНК, используя критерий Пирсона χ^2. Выделены основные факторы (лейкопения при госпитализации (p = 0,033), выраженная стигматизация признаков соединительнотканной дисплазии (p = 0,013) и продолжительность оперативного вмешательства (p = 0,0002)), указывающие на возможность риска ПСНК. Методом логистической регрессии создана прогностическая модель для расчета риска ПСНК, которая ROC-анализом (чувствительность теста – 77%; специфичность - 72%) оценивается как «очень хорошая»: AUC = 0,796.

Выводы. Применение предложенной прогностической модели риска ПСНК у детей с острыми воспалительными заболеваниями органов брюшной полости позволяет скорее принять решение относительно объема хирургического лечения и оптимизации лечебной тактики на всех этапах оказания помощи.

Ключевые слова: прогностическая модель, риск, послеоперационная спаечная непроходимость кишечника, дети.