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Peritoneal Laser Doppler Flowmetry in Predicting and Diagnosing Tertiary Peritonitis

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RELEVANCE The article is devoted to one of the most difficult and controversial problems in the treatment of intra-abdominal infection, the prediction and diagnosis of tertiary peritonitis. The technique of peritoneal laser Doppler flowmetry (PLDF) makes it possible to assess the degree of visceral microcirculation disorders in various diseases of the abdominal organs.

AIM OF STUDY To identify early, trigger indicators of peritoneal microcirculation in tertiary peritonitis, obtained by the PLDF method.

MATERIAL AND METHODS A retrospective analysis of the results of treatment of 48 patients operated on for secondary diffuse purulent peritonitis in the clinic of general surgery of the Astrakhan State Medical University in the period from 2015 to 2019 was carried out. All patients were divided into two equal groups: the main group with subsequently developed tertiary peritonitis, and the comparison group with arrested peritonitis. The study of peritoneal microcirculation was performed at the time of laparotomy, after debridement, 24 and 48 hours later. A total of 768 scans were performed. Evaluation was carried out using the APACHE II scales , abdominal index and SOFA scale. Spearman's rank correlation test was one of the main statistical methods.

RESULTS Twenty-four hours after the primary operation, the values of the percentage of microcirculation, standard deviation and coefficient of variation showed a direct correlation with the development of tertiary peritonitis. According to Spearman's criterion, the closeness of the relationship according to these indicators was: r=0.71, r=0.55, r=0.63, respectively, at p≤0.05. After 48 hours, all the studied values of microcirculation made it possible to diagnose tertiary peritonitis. The data obtained correlated with the data obtained by the systems for assessing the severity of the patient's condition.

CONCLUSION 1. The generally accepted scales for assessing the severity of patients' condition (APACHE II, abdominal index and SOFA) used in patients with diffuse purulent peritonitis do not allow predicting the risk of tertiary peritonitis 24 hours after surgery. The data obtained as a result of the scoring on the above scales becomes representative 48 hours after the initial intervention. 2. The percentage of microcirculation, standard deviation and coefficient of variation can be used as early screening indicators of peritonetal laser Doppler flowmetry to predict tertiary peritonitis 24 hours after primary surgery. 3. The whole range of indicators of peritoneal laser Doppler flowmetry allows the degree of impairment of the tissue microcirculation in patients with peritonitis to be objectively assessed even 48 hours after the initial operation and to be diagnostic criteria of tertiary peritonitis.

Keywords: tertiary peritonitis, peritoneal laser Doppler flowmetry , prognosis of tertiary peritonitis, diagnosis of tertiary peritonitis, peritoneal microcirculation; diagnostic criteria for tertiary peritonitis, monitoring of peritoneal microcirculation

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ACI - abdominal cavity index
IME - index of microcirculation efficiency
NT - neurogenic tone
ICU - Intensive Care Unit
MT - myogenic tone
p.u. - perfusion units
PLDF - Peritoneal Laser Doppler Flowmetry
PM - percentage of microcirculation
SP - shunting percentage
SD - standard deviation
TP - tertiary peritonitis
APACHE II — disease severity classification system
Kv — the coefficient of variation
SOFA — organ dysfunction scale

INTRODUCTION

One of the most difficult and controversial problems in the treatment of intra-abdominal infection is the diagnosis and treatment of tertiary peritonitis (TP). The term was proposed by O.D. Rotstein in 1986. Until now, there is no generally accepted definition of TP. TP is understood as "an inflammatory process in the abdominal cavity that develops after an episode of "secondary peritonitis", which has its own microflora, different from the secondary, characterized by an inability to localize the process and the absence of a direct focus" (J.L. Meakins, 2002). In domestic surgery, TP is defined as “a recurrent and persistent form of peritonitis; develops in critically ill patients with damage to the mechanisms of anti-infectious defense with secondary immunodeficiency and multi-resistant microorganisms "(National clinical guidelines,"Abdominal infection and sepsis", 2017). The difficulty and ambiguity of this problem is evidenced by the fact that this complication has many synonyms - "recurrent peritonitis", "persistent peritonitis", "peritonitis without a source", "sluggish peritonitis", etc. [1–4].

TP is characterized by a scanty and blurred clinical picture in the presence of pronounced morphological changes, which, unfortunately, are sometimes detected only during surgery or during sectional examination. One of the permanent manifestations of TP is the syndrome of systemic anti-inflammatory response, which is expressed in a state of immunoparalysis. According to some authors, due to its microbiological etiology, TP is most often associated with community-acquired endogenous, autochthonous (i.e., raised in its own intestinal biocenosis) polymicrobial aerobic and anaerobic microflora. The main reasons for the occurrence of TP, according to some studies, are inadequate sanitation of the abdominal cavity, translocation of pathogens from the gastrointestinal tract, nosocomial infection, etc. [5–7].

Postoperative monitoring and the choice of treatment tactics for the patient are problematic, in connection with which unnecessary diagnostic laparotomies and open drainage operations are often performed, which, in turn, increases the frequency of pyoinflammatory complications and leads to an increase in mortality [8].

Undoubtedly, the most important and urgent problem in the treatment of TP is the possibility of its prediction and timely diagnosis. Currently, there are no clear and objective both prognostic and diagnostic criteria for TP. Monitoring of peritoneal microcirculation, in our opinion, can help in predicting and early diagnosis of TP. The existing method of monitoring the microcirculation – capillary resistometry is low-informative and does not give a complete picture of violations, and the biopsy method is invasive and hardly applicable in the clinic [9, 10]. In domestic and foreign scientific literature, there are works devoted to peritoneal laser Doppler flowmetry (PLDF) for intestinal obstruction, ischemic intestinal damage and peritonitis [11–18]. The lack of works devoted to the prediction and diagnosis of TP using PLDF served as the basis for this study.

Purpose of the study — to evaluate the prognostic and diagnostic capabilities of PLDF in TP. To identify early, trigger indicators of peritoneal microcirculation obtained by the PLDF method in the development of TP.

MATERIAL AND RESEARCH METHODS

The object of the study was 48 patients operated on for secondary diffuse fibrinous-purulent peritonitis in the general surgery clinic of the Astrakhan State Medical University in the period from 2015 to 2019. Primary surgeries were performed for a destructive disease or damage to the abdominal organs during trauma. The duration of the disease ranged from 23 to 78 hours. The age of the patients averaged 56 ± 4.2 years, there were 27 men, 21 women. Inclusion criteria for the study: treatment with the open abdomen method with passive drainage of the abdominal cavity and the implementation of program sanitation; abdominal cavity index (ACI) (according to V.S. Saveliev) ≥14 points; severity of the condition according to APACHE II ≥10 points; SOFA ≥8 points. Exclusion criteria: peritonitis caused by impaired mesenteric circulation; peritonitis, accompanied by persistent arterial hypotension associated with extra-abdominal causes (myocardial infarction, acute cerebrovascular accident, etc.); decompensated septic shock; peritonitis against the background of stage IV malignant neoplasms and carcinomatosis. The programmed readjustments were carried out at intervals of 24 hours. All patients were divided into two equal groups (24 patients each): the main group – with subsequent TP, and comparison – with relapsing peritonitis. At the start of treatment, the groups were comparable in terms of sex, age, and severity of pathology. The criteria for the diagnosis of TP were: no signs of relief of peritonitis after the third sanation; UPS ≥14 points, APACHE II ≥10 points, SOFA ≥8 points – 48 hours after the primary sanitation of the abdominal cavity; presence of microbial associations with opportunistic pathogens and / or fungal superinfection. All patients after laparotomy underwent PLDF analysis of microcirculation and microlymph flow using the Lazma MC-1 apparatus (Russia), which was repeated after removal of the source of infection and sanitation, as well as 24 and 48 hours after surgery (Fig. 1).

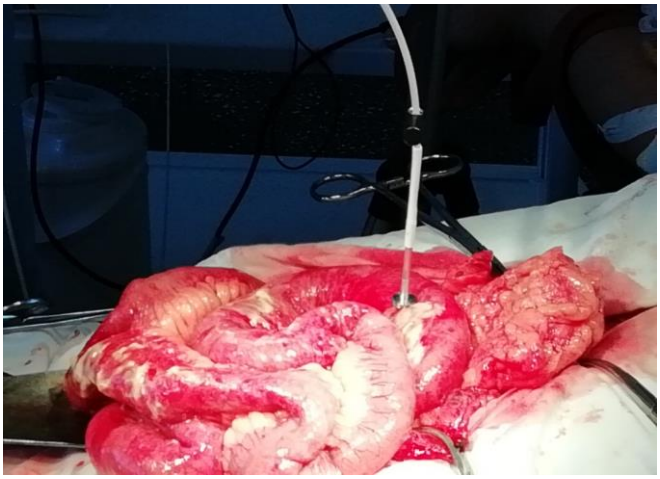

Fig. 1. Peritoneal laser Doppler flowmetry. Jejunum scanning. Intraoperative photo.

For the purpose of objectification, the indicators were taken within 2 minutes from 4 points: parietal peritoneum in the area of the focus; parietal peritoneum as distant as possible from the focus; jejunum (40 cm from Treitz's ligament); colon (middle third of the transverse colon). Thus, 768 scans were performed in both groups. We investigated: the percentage of microcirculation (PM) (perfusion units - p.u.), which is a function of the concentration of erythrocytes in the probed tissue volume and their average velocity; standard deviation (RMS) (o', p.u.), i.e. average fluctuations in perfusion relative to the average PM value, which characterizes the temporal variability of perfusion and reflects the average variability of blood flow in all frequency ranges, as well as the coefficient of variation (Kv) (%) – characterizes the relationship between variability of perfusion with the average level of perfusion in the probed area, that is, reflects vasomotor activity of blood vessels. The indicators obtained as a result of wavelet transformation were also analyzed – neurogenic tone (NT), myogenic tone (MT), shunting percentage (PS) and index of microcirculation efficiency (IEM). The data were compared with the reference PM values obtained during planned operations for non-inflammatory diseases of the abdominal organs (12 patients).

Statistical relationships between indicators were assessed using the correlation module "Basic Statistics and Tables STATISTICA 6.0", regression analysis, analysis of variance and multivariate statistics methods. In order to determine the significance of p differences between the groups, Student's t test and univariate analysis of variance with the calculation of Fisher's F test were used. The significance of differences in the data in the groups was assessed using the criterion of paired comparisons of the Mann – Whitney U-test. The relationship of indicators was determined using the Spearman's rank correlation coefficient. Differences were considered statistically significant at $p \leq 0.05$.

RESULTS OF THE STUDY

On admission, the microcirculation indices obtained with PLDF in both groups were characterized by pronounced disorders of pre- and postcapillary resistance and tissue perfusion disorders and did not differ statistically. After 24 hours, the microcirculation indices in the groups had their own differences. In the main group, the values of PM, standard deviation and Kv remained significantly lower in the comparison group ($p \leq 0.05$); MT and NT of peritoneal vessels, as well as IEM in the main group were comparatively lower. В то же время ПШ в основной группе повышался ($p \geq 0,05$). After 48 hours, more distinct changes were noted in the microcirculation indices. In the main group, microcirculation disorders progressed, which was confirmed by a decrease in PM, RMS, Kv, MT, NT and IEM ($p \leq 0.05$). At the same time, the PS in the vessels of the parietal and visceral peritoneum increased ($p \leq 0.05$) (Table. 1).

Table 1

Indicators of peritoneal microcirculation in studied groups

Groups	Indicators	Reference values (n =12)	Before lavage	After lavage	24 hours	48 hours
Comparison (n = 24)	MP (p.u.)	32.23 ± 1.22	17.9 ± 1.54	18.45 ± 1.33	24.9 ± 1.34 *	26.34 ± 1.88 *
	SD (p.u.))	5.43 ± 0.36	2.34 ± 0.23	2.88 ± 0.34	3.43 ± 0.22 *	3.45 ± 0.20 *
	Kv (%)	12.61 ± 1.55	6.82 ± 3.88	7.21 ± 0.81	8.76 ± 1.41 *	11.72 ± 4.31 *
	NT (p.u.)	0.61 ± 0.07	0.78 ± 0.03	0.74 ± 0.02	0.59 ± 0.04	0.60 ± 0.05
	MT (p.u.)	0.58 ± 0.03	0.74 ± 0.04	0.85 ± 0.08	0.62 ± 0.05	0.60 ± 0.03
	BP (p.u.)	1.17 ± 0.08	1.33 ± 0.04	1.30 ± 0.05	1.20 ± 0.02	1.19 ± 0.03
	MEI	1.24 ± 0.05	1.04 ± 0.12	1.11 ± 0.09	1.19 ± - .08	1.28 ± 0.11
Main (n = 24)	MP (p.u.)	32.23 ± 1.22	18.45 ± 2.11	19.22 ± 2.11	20.11 ± 1.88 *	17.37 ± 1.45 *
	SD (p.u.)	5.43 ± 0.36	2.20 ± 0.34	2.31 ± 0.67	2.48 ± 0.23 *	2.16 ± 0.24 *
	Kv (%)	12.61 ± 1.55	7.33 ± 0.94	7.88 ± 0.92	8.22 ± 1.07 *	7.91 ± 1.12 *
	NT (p.u.)	0.61 ± 0.07	0.78 ± 0.03	0.55 ± 0.02	0.48 ± 0.04	0.30 ± 0.03 *
	MT (p.u.)	0.58 ± 0.03	0.77 ± 0.04	0.80 ± 0.08	0.44 ± 0.05	0.28 ± 0.03 *
	BP (p.u.)	1.17 ± 0.08	1.34 ± 0.06	1.32 ± 0.07	1.44 ± 0.04	2.05 ± 0.07 *
	MEI	1.24 ± 0.05	1.04 ± 0.12	1.02 ± 0.11	0.88 ± 0.08	0.62 ± 0.09 *

Notes: * – indicators with the value of changes $p \leq 0.05$; BP – bypass percentage; Kv – coefficient of variation; MEI – microcirculation efficiency index; MT – myogenic tone; MP – microcirculation percentage; NT – neurogenic tone; p.u. – perfusion units; SD – standard deviation

In order to identify and assess the tightness of the relationship between the two series of compared quantitative indicators of microcirculation (PM, RMS and Kv) in the study groups, the Spearman rank correlation coefficient was calculated, which allows you to check the heteroscedasticity of random errors in the regression model. In the study of PM, there was a direct correlation with a high closeness of connection in the study groups ($r = 0.71$ at $p \leq 0.05$). When carrying out the relationship in terms of Kv, data were obtained indicating a moderate direct correlation in the study groups ($r = 0.63$ at $p \leq 0.05$). The study of the correlation relationship in terms of RMS in the study groups revealed a direct relationship with a moderate closeness of the relationship ($r = 0.55$ at $p \leq 0.05$) (Fig. 2-4).

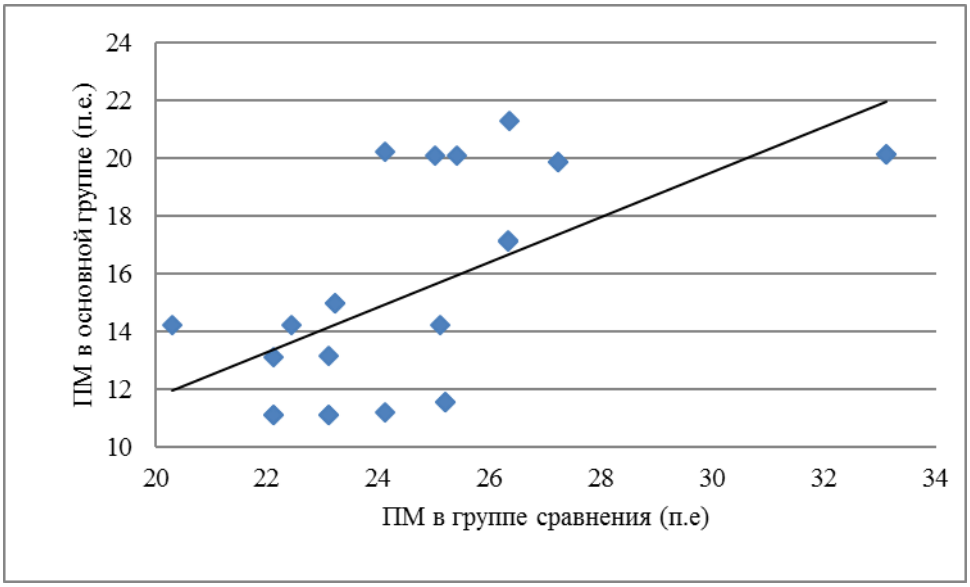

Fig. 2. Spearman ‘s rank correlation coefficient for the parameter “percentage of microcirculation” (PM) in studied groups (r=0.71 at p≤0.05)

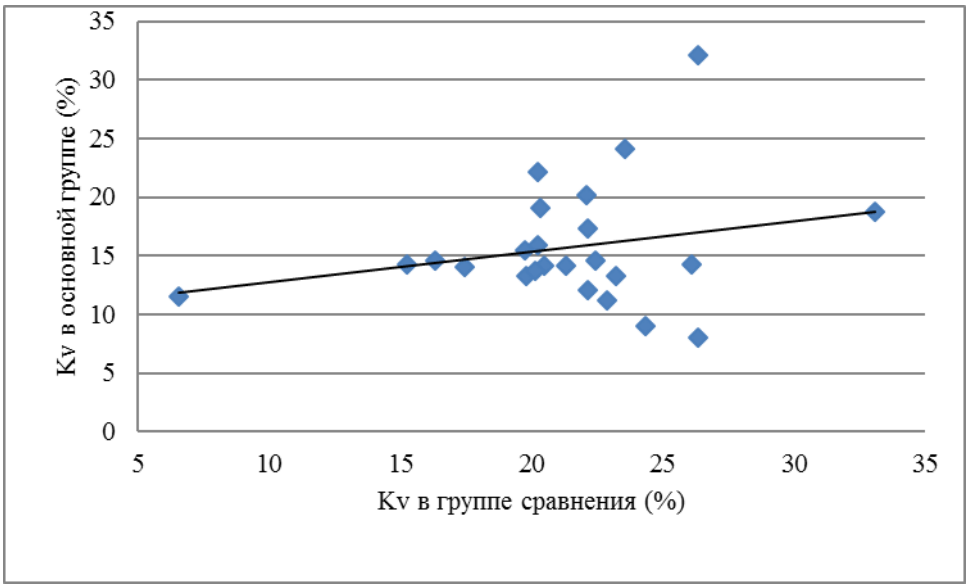

Fig. 3. Spearman ‘s rank correlation coefficient for the parameter “coefficient of variation” (Kv) in studied groups (r=0.63 at p≤0.05)

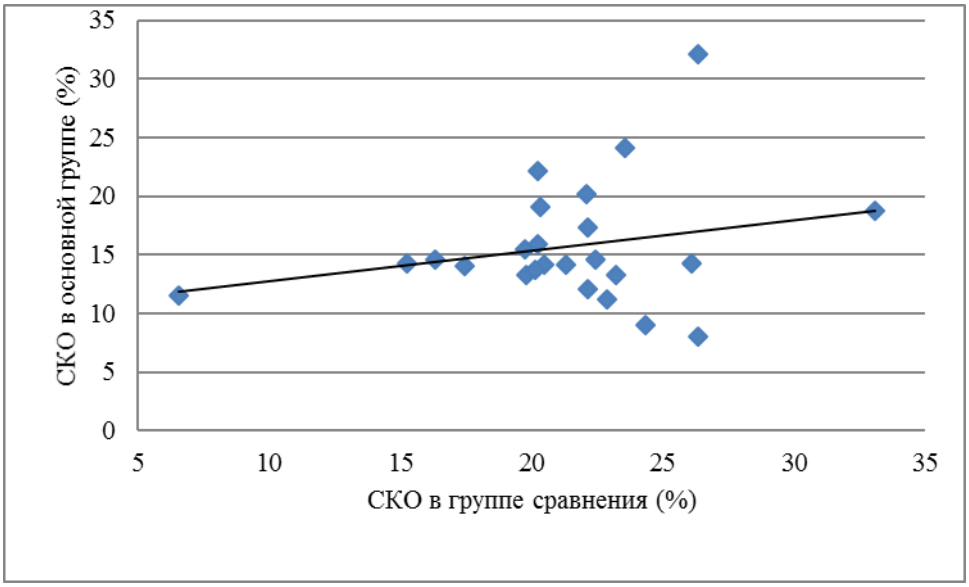

Fig. 4. The coefficient of rank correlation Spearman the parameter standard deviation in studied groups (r=0.55 with p≤0.05)

In a dynamic study of the severity of the patient's condition using the APACHE II, IBP and SOFA scales, it turned out that at the start of treatment and 24 hours after the first operation, the sum of points in the study groups was high, which indicated the serious condition of patients and multiple organ dysfunction, but it was not statistically differed (p≥0.05). After 48 hours, in the group of patients with LT, the values of the integral scales for assessing the severity of the patient's condition were significantly lower in the comparison group (p≤0.05) (Table 2).

Table 2
Treatment results in studied groups

Indicators	Main group (n = 24)			Comparison group (n = 24)		
	Upon admission	After 24 hours	After 48 hours	Upon admission	After 24 hours	After 48 hours
Abdominal index	23.0 ± 0.3	18.8 ± 0.4	15.5 ± 0.5 *	22.8 ± 0.4	16.8 ± 0.4	12.6 ± 0.5 *
APACHE II	24.5 ± 0.3	22.7 ± 0.2	16.7 ± 0.3 *	24.3 ± 0.2	15.3 ± 0.4	10.5 ± 0.4 *
SOFA	8.2 ± 0.1	9.4 ± 0.3	12.4 ± 0.5	8.3 ± 0.1	7.8 ± 0.2	7.5 ± 0.2 *
Average number of lavage procedures	4.5			3.2		
Mortality	6 (25%)			3 (12.5%)		

Note: * - indicators with the value of changes p≤0.05

Mortality in the comparison group was 12.5%, in the main group - 25%.

DISCUSSION

The generally accepted scales for assessing the severity of the condition of patients with diffuse peritonitis are universal and quite sensitive, which has been confirmed by many clinical meta-analyzes. However, integral scales do not include many “specific” criteria necessary for assessing TP: local, microbiological, immunological, etc. [19]. Thus, the study showed that statistically significant changes in the indices of integral scales during TP can be "lagging". The mean scores in the main and comparison groups 24 hours after the primary surgery did not have a statistical difference. This fact can create an illusion of well-being in the surgeon and direct him to the wrong therapeutic path. Given the complexity of the TP problem, the most important thing is to identify early trigger markers that would make it possible to predict its development in a timely manner and, therefore, to promptly correct the treatment. Timely implementation of additional operational technologies into the complex of treatment of patients with diffuse purulent peritonitis, correction of antimicrobial chemotherapy with the inclusion of antifungal drugs in the complex, immunocorrective therapy, etc. will undoubtedly reduce the risk of developing TP. It is also important to designate clear diagnostic criteria for already developed TP.

Experimental and clinical studies conducted earlier by various authors on the study of peritoneal microcirculation in peritonitis showed significant disorders, which were expressed in changes in pre- and postcapillary resistance, which ultimately leads to perfusion disorders of the

intestinal wall and peritoneum. The works emphasize: these violations are especially pronounced in patients who receive treatment according to the "open abdomen" method and require multiple sanitization. [20]. The study showed that PLDF can be a screening method for the early detection of trigger markers of TP, which makes it possible to predict its development within 24 hours after the primary operation and correct treatment. The indicators of PM, RMSD and Kv, as it turned out, can be them. After 48 hours, all the studied parameters obtained with PLDF can be diagnostic criteria, as well as an indicator of the effectiveness of treatment.

Currently, surgeons have a need for more portable, accurate instruments that will quickly and non-invasively determine the degree of microcirculation disturbance in the abdominal cavity. Conducting multicenter studies on PLDF will allow an even deeper assessment of its prognostic and diagnostic value in surgery.

CONCLUSION

A retrospective analysis of the results of treatment of patients with diffuse peritonitis showed that the generally accepted scales for the study of the severity of the patient's condition (APACHE II, IBD and SOFA) demonstrated their statistically significant effectiveness in the diagnosis of TP only 48 hours after the primary operation. The study proved that the PLDF technique allows to fairly objectively assess the degree of tissue microcirculation disturbance in patients with diffuse purulent peritonitis. Dynamic research and analysis of PLDF indicators (PM, RMS, Kv) 24 hours after the primary surgery confirmed the presence of a direct correlation with a high and moderate closeness of communication in the study groups, which allows predicting the development of TP. The PLDF data obtained as a result of the wavelet analysis, along with the above, as well as the APACHE II, IBP and SOFA scales, can serve as diagnostic criteria for TP 48 hours after the primary operation, as well as criteria for the effectiveness of treatment.

FINDINGS

1. The generally accepted scales for assessing the severity of the condition (APACHE II, abdominal index and SOFA) used in patients with diffuse purulent peritonitis do not allow predicting the risk of tertiary peritonitis 24 hours after surgery. The data obtained as a result of the scoring on the above scales becomes representative 48 hours after the initial intervention.

2. As early screening indicators of peritonetal laser Doppler flowmetry to predict tertiary peritonitis 24 hours after primary surgery, the percentage of microcirculation, standard deviation and coefficient of variation can be used.

3. The whole range of indices of peritonetal laser Doppler flowmetry allows to objectively assess the degree of tissue microcirculation disturbance in patients with peritonitis in 48 hours after primary surgery and serve as diagnostic criteria for the development of tertiary peritonitis.

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