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## Clinical outcomes in the surgical treatment of pyoinflammatory diseases of pelvic organs: the possibility of predication

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### Abstract

Among inflammatory processes of female genital more than 80% account for the pathology of uterine appendages and the share of complicated forms of purulent inflammatory diseases accounts 4 - 10%. Diagnosis and prediction of PID are based on clinical, laboratory, biochemical, immunological parameters and data of instrumental research methods which are often cumbersome and not always available in most surgical hospitals. **The objective:** to identify significant predictors of clinical outcomes in the surgical treatment of pyoinflammatory diseases of the pelvic organs. 108 women of fertile age with PID were examined. 73 of them were treated conservatively (group I, comparison). Group II (main) consisted of 35 women who underwent surgery according to vital indications. **Results.** The main group patients were operated on with laparotomy access, adnexectomies (right-sided - 27.8%, left-sided - 22.2%) constituted a considerable number. In 22.2% of cases, total hysterectomy was performed, and the same number of patients abdominal cavities were drained in the postoperative period. A telephone survey conducted showed that the overall response rate decreased in proportion to the time elapsed since discharge from the hospital, e.g. in three years only 13.2% of the former patients had been in contact. **Conclusion.** The highest

predictive value in the operative treatment of pyoinflammatory diseases of the pelvic organs has TNF and procalcitonin (PPV = 0.77 and 0.81, respectively).

**Key words: inflammatory process of female genital, outcome of surgical treatment, TNF, procalcitonin.**

**Introduction.** Inflammatory processes of female genital occupy one of the leading places in the structure of gynecological diseases [1-3, 7, 9]. Among these diseases, about 80-82% account for the pathology of the uterine appendages, and the share of complicated forms of purulent inflammatory diseases accounts, according to different authors, from 4 to 10% [4, 5].

Pelvic inflammatory disease (PID) is characterized by various manifestations, depending on the level of damage and the strength of the inflammatory reaction. The disease occurs as a result of pathogens (enterococci, bacteroides, chlamydia, mycoplasmas, ureaplasma, trichomonads) penetration into the genital tract in the presence of favorable conditions for their development and reproduction [3, 7].

Existing natural defense mechanisms, such as anatomical features, functional state of local immunity, acidic environment of vaginal contents, absence of endocrine disorders or serious extragenital diseases, are able in most cases to prevent the development of genital infection. On the invasion of a particular microorganism there is a systemic inflammatory response of varying intensity [1, 2, 8].

One of the leading factors in PID's semiotics formation is the resistance of microorganisms to the antibiotic therapy used, which causes high virulence of nosocomial infection, a change in the etiological structure, the transformation of clinical symptoms towards eroded forms and atypical course. This, in turn, leads to a belated diagnosis and a worsening of the clinical prognosis [9]. Difficulties in diagnosing and selecting the optimal treatment program for patients are largely due to the variety of clinical symptomatology, late or non-core hospitalization of patients, the lack of a unified classification and a systematic approach to assessing the severity of PID course [3, 8, 9].

In recent years, scientific research has been actively conducted for significant predictors of purulent-inflammatory diseases search. Significant progress in the development of the problem of optimizing the diagnosis and treatment of PID patients was achieved after the implementation of the recommendations of the III International Consensus of the definitions of sepsis and septic shock [10]. As a rule, diagnosis and prediction of PID are based on a number of clinical, laboratory, biochemical, immunological parameters and data of instrumental research methods combined into

the so-called integral scales of assessment and prognosis (Ranson, Osborne, APACHE-2, SAPS, MEWS, etc.) which are often cumbersome and not always available in most surgical hospitals. Using existing evaluation systems it is difficult to correctly predict the dynamics of the pathological state [6, 8, 9].

**The objective:** to identify significant predictors of clinical outcomes in the surgical treatment of pyoinflammatory diseases of the pelvic organs.

**Material and methods.** The study was carried out on the basis of State Clinical Hospital No.1 (Odessa) in 2013-2018. 108 women of fertile age with PID participated in it. 73 women were treated conservatively - they made up group I (comparison). The main group (II) consisted of 35 women who underwent surgery according to vital indications.

Clinical management of patients was conducted according to the current orders of Ukrainian Ministry of Health Care.

All women underwent a bimanual gynecological examination, a study of general clinical and biochemical indices, an ultrasound study of pelvic organs (Siemens Acuson X150, Germany) with the use of standard methods. All patients signed an agreement to participate in the study in accordance with the bioethical requirements of Helsinki Declaration. The follow-up period was 36 months. The original questionnaire in the format of a telephone interview was applied.

The cases of PID relapses, the features of the fertile function realization, the presence of chronic pelvic pain manifestations were taken into account. The content of cytokines TNF and IL-6 was evaluated by ELISA methods, the content of procalcitonin - by ECLIA. The level of blood lactate was determined spectrophotometrically.

The statistical processing was carried out by methods of dispersion and correlation analysis using the software Statistica 13.0

**Results.** The main group patients mean age was  $37.0 \pm 0.7$  years. The patients were in hospital from 4 to 14 days, on average -  $10.5 \pm 0.5$  days. An aggravated gynecological anamnesis was defined in 56.7% of the patients.

Upon admission to the hospital, all patients complained of pain in abdomen. Only 9 (12.0%) patients had normal body temperature, others had subfebrile symptoms or hyperpyrexia. In 45.3% of the patients, the body temperature did not exceed  $37.5^{\circ}\text{C}$ , and the temperature was above  $39.0^{\circ}\text{C}$  only in 6 (8.0%) patients. The average temperature was  $37.3 \pm 0.04^{\circ}\text{C}$ . Against the background of fever, tachycardia was observed, heart rate averaged  $93.2 \pm 1.6$  bpm. There was a tachypnea (BR –  $24.3 \pm 0.3$ ) with spO<sub>2</sub> of  $96.9 \pm 0.8\%$ .

Practically all patients at the time of admission had signs of irritation of the peritoneum: in 72 (96.0%) - a positive symptom of Blumberg, in 14.7% - soreness of the posterior vaginal fornix. Each fifth woman experienced hyperesthesia of the anterior abdominal wall. In 6.7% of cases there was no muscle defensiveness. 93.3% of the patients had vaginal discharge, including purulent - in 4.0% of cases. In 96.7% of the women under examination menstrual irregularities occurred.

Signs of severe vaginal dysbiosis were observed in 72.0% of patients, with multicomponent microbial associations (Staphylococcus spp., E. coli, Chlamidia trachomatis, Prevotella spp., etc) in 44.0% of cases, microbiocenosis formed only by Staphylococci spp. and E. coli was defined in 54.5% of cases.

The hemograms obtained in the main group patients under their admission to the hospital are of considerable interest. A part of the patients showed moderate anemia (red cells content -  $3.44 \pm 0.09 \cdot 10^{12} / l$ , Hb -  $113.5 \pm 3.2 \text{ g} / l$ ), hypovolemia (hematocrit  $0.48 \pm 0.09$ ). The average platelet content was  $153.7 \pm 22 \cdot 10^9 / l$ . Characteristic phenomena were leukocytosis (total number of leukocytes -  $9.86 \pm 0.9 \cdot 10^9 / l$ ) with a left shift, relative monocytopenia and ESR accelerated to  $31.3 \pm 3.4 \text{ mm} / \text{hr}$ .

The cytokine profile was  $24.4 \pm 1.1 \text{ pg} / \text{ml}$  for IL-6, and  $15.5 \pm 0.9 \text{ pg} / \text{ml}$  for TNF, that is, there was a significant activation of pro-inflammatory cytokines. At the same time, the degree of cytokines levels growth closely correlated with the severity of symptoms of irritation of the peritoneum and general intoxication.

When comparing the indices obtained in patients operated on for PID and treated conservatively (Table 1), it was found that the level of the main markers of inflammation was higher in the II group, but the statistical significance was high only for the indicators of TNF and procalcitonin ( $p < 0.05$ ).

Table 1

**DYNAMICS OF INDICES OF THE MAIN MARKERS OF INFLAMMATION  
IN THE GROUPS OF COMPARISON**

Index	Unit of measure	Group I, n=73	Group II, n=35
IL-6	pg/ml	$24.4 \pm 1.1$	$25.9 \pm 1.4$
TNF	pg/ml	$15.5 \pm 1.1$	$19.1 \pm 0.7^*$
Procalcitonin	ng/l	$1.14 \pm 0.3$	$3.67 \pm 0.6^*$
Lactate	mmol/l	$1.9 \pm 0.2$	$1.9 \pm 0.2$

\* -  $p < 0.05$

Important are the results of procalcitonin level study in the patients of different groups. In conservative treatment patients, the level of procalcitonin was  $1.14 \pm 0.3$  ng / l, whereas in patients operated on according to vital signs it was  $3.67 \pm 0.6$  ng / l ( $p < 0.05$ ). The concentration of lactate in the clinical groups did not differ and amounted to  $1.9 \pm 0.2$  mmol / l.

In 53.3% of cases SAPS index did not exceed 4 points, which corresponds to a favorable forecast for perioperative risk. In the rest of 46.7% patients, SAPS index was 5 - 7 points.

Subsequent analysis showed that the main risk factors for the clinical course of purulent-inflammatory diseases of the uterine appendages determining the severity of the clinical course are promiscuity (OR = 2.4), urogenital infections (OR = 2.5), endocrine disorders (OR = 2.2). The severity of the systemic inflammatory response correlated with the severity of the syndrome of endogenous intoxication ( $r = 0.83$ ).

The highest predictive value has TNF and procalcitonin (PPV = 0.77 and 0.81, respectively).

Purulent tubo-ovarian inflammatory formations, such as mono- and bilateral tumors (9 cases or 25.7%) and pirosalpinx with perforation (5 cases or 14.3%) prevailed in PID structure, detected in the patients of the main group. Abscesses of the small pelvis (4 cases or 11.4%), cyst ruptures (2 cases or 5.7%) were registered less frequently.

The main group patients were operated on with laparotomy access, adnexectomies (right-sided - 27.8%, left-sided - 22.2%) constituted a considerable number. In 22.2% of cases, total hysterectomy was performed, and the same number of patients abdominal cavities were drained in the postoperative period.

A telephone survey conducted during the follow-up period showed that the overall response rate decreased in proportion to the time elapsed since discharge from the hospital. If at the end of the first year of observation it was possible to establish contact with 65.3% of patients, at the end of the second year it was established with 34.7% of patients, and in three years only 13.2% of the former patients had been in contact with us.

The most common symptoms in patients who underwent surgery were chronic pelvic pain (24.4% in 12 months after treatment, 69.2% - in 24 months, and 80.0% - in 36 months). In the patients of the main group 4 (11.4%) cases of ectopic pregnancy were registered, while 5 (14.3%) had repeated episodes of PID. Pregnancy occurred in 7 (9.6%) patients of the first group and 5 (14.3%) patients of the second group. Given that a significant proportion of late reproductive age women have no reproductive intentions, this is a satisfactory result.

**Discussion.** PID encapsulate a significant problem for women's health. These diseases have both serious short-term and potentially destructive long-term complications. PID women are at risk of infertility, ectopic pregnancy and chronic pelvic pain.

Unfortunately, most of the clinical and laboratory criteria traditionally used to assess the clinical severity of acute PID are unreliable in assessing the future individual risk.

According to our data, the main factors that caused the development of long-term consequences of PID were the severity of the disease, the presence of concomitant gynecological, urological or gastroenterological pathology, delay in initiating therapy and re-infection. Thus, timely diagnosis and initiation of treatment of PID patients are an essential element of the secondary prevention of long-term effects, including infertility, ectopic pregnancy, chronic pelvic pain and occasional PID.

The complex of clinical, clinical and laboratory and ultrasound methods for diagnosis of acute inflammatory diseases of the uterine appendages is of the top diagnostic value.

We believe that the reasons of PID progression are primarily in the features of a woman's immune system. Due to the influence of exogenous and endogenous factors against the background of immunosuppression, the ability to resist decreases or a body's response to the presence of an inflammatory focus reduces.

Humoral and cellular factors play an important role in the formation of adhesions in the inflammatory focus, including immunocompetent cells, proteins, inflammatory mediators and some biologically active substances. Cytokines' contribution to the induction of inflammation is the most significant. These factors of intercellular interaction not only activate the inflammatory process (pro-inflammatory cytokines), recruiting leukocytes from circulating blood to the inflammation focus, but they are powerful stimulators of growth, proliferation and differentiation of new cells, which leads to vascular remodeling and the formation of adhesions, and, accordingly, to the reduction of fertility potential.

### **Conclusions.**

1. The patients who underwent operative treatment for PID most often had the signs of chronic pelvic pain (in 24.4% of cases in 12 months; 69.2% in 24 months and 80.0% of cases in 36 months after treatment)
2. The main group patients had 4 (11.4%) cases of ectopic pregnancy, and 5 (14.3%) had PID occasional episodes.
3. . Restoration of fertile function occurred in 14.3% of the main group patients.

4. The highest predictive value in the operative treatment of pyoinflammatory diseases of the pelvic organs has TNF and procalcitonin (PPV = 0.77 and 0.81, respectively).

5. With the combined use of clinical, clinical and laboratory and ultrasound methods for diagnosing acute inflammatory diseases of the uterine appendages, the accuracy of the predictions increases.

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