

Prevention and treatment of thromboembolic complications in gynecology

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Objective: to improve the results of the prevention of early thromboembolic complications in gynecological practice.

Material and methods. A review of the literature on the feasibility study after gynecological surgery is presented. The frequency of occurrence of feasibility study and thromboembolism of the pulmonary artery and the percentage of deaths. The classification of patients and their division into 4 groups is given depending on the degree of risk of postoperative venous thrombotic complications in operative gynecology.

Results. Causal and predisposing factors and pathogenesis of pulmonary embolism are described in detail. Particular emphasis in the article is placed on hereditary disorders of the blood coagulation system - thrombophilia. The classic signs of the manifestation of the feasibility study and the diagnostic methods of the feasibility study using modern laboratory (D-dimer, etc.) and instrumental methods, including multi-detector computed tomography are reflected. The methods of treatment (medication and invasive) and prophylaxis (medication, mechanical and combined) of early postoperative feasibility studies in operative gynecology are proposed.

Conclusion The analysis will significantly improve the issues of early diagnosis, the choice of treatment and prevention of early postoperative feasibility studies after gynecological operations

Keywords: thromboembolism, gynecology, complications, treatment, prevention

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Problem of prevention of thrombotic complications for surgical gynecology is very relevant. The overall frequency of thrombo-embolic complications after gynecological interventions is the same as in general surgery, and is about 20%. In recent years, more than 370,000 deaths associated with venous thromboembolic complications have been observed in Europe annually. In European hospitals, in fact, 1 out of 10 people dies from deep vein thrombosis or from pulmo-

nary embolism (PE). The situation is no less alarming in the United States, where more people die every year from PE than from car stanzas, breast cancer, and AIDS combined (American Public Health Association, 2003). Given the emerging trend, it can be expected in the coming years that in the European Union, which unites 25 countries with a population of about 454 million people, mortality from venous thromboembolic complications will reach 500,000 people annually [9, 13, 24].

According to [15], massive PE was detected during autopsy in 7.1% of the deceased in the urological department, 8.3% in the surgical department, and 11.2% in the gynecological department. In gynecological patients, pulmonary embolism is the leading cause of mortality after surgery for malignant neoplasms [37]. Despite the recently increased quality of surgical gynecological care, deep vein thrombosis (DVT) of the lower extremities and the PE generated by it occupy a leading place among postoperative complications and are important problems of modern medicine.

The frequency of DVT after various gynecological operations varies between 11-37% [16]. More than 25% of DVT and PE cases are associated with surgical interventions [21]. Moreover, over the past decades, due to the constant increase in the number of surgical interventions, there has been a tendency to an increase in morbidity and mortality associated with the development of postoperative DVT and its consequences. PE becomes the third cause of sudden death after myocardial infarction and acute cerebrovascular accident. According to statistics, about 100 thousand patients in Russia annually die from sudden PE. With the development of massive pulmonary thromboembolism, mortality is about 5%. DVT in the general population is about 160 annually, with a frequency of fatal PE of 60 per 100,000 population, and these figures tend to be steadily increasing. PE in highly developed countries steadily took the third place in frequency, after ischaemic heart disease and stroke, as the cause of death among cardiovascular diseases [4, 11, 19, 22].

The high prevalence of DVT and its consequences in the postoperative period in gynecology, as well as the associated mortality, disability and enormous economic expenses spent on the treatment of these patients, give the basis to consider DVT of the lower extremities as a disease that has great social importance, and its prevention is extremely important.

Purpose: to improve the results of prophylaxis of early thromboembolic complications in gynecological practice.

Pulmonary embolism - obstruction of the blood flow in the pulmonary artery system

when a blood clot enters it, which leads to spasm of the branches of the pulmonary artery, the development of an acute pulmonary heart, a decrease in cardiac output, a decrease in blood oxygenation and bronchospasm. Thrombotic complications are the formation of fibrin - platelet clots at various levels of blood circulation, leading to malnutrition of organs and tissues. At the same time, thrombosis in the arterial bed is most dangerous, since it contributes to the development of multiple organ failure. At the level of macrocirculation, thrombotic complications are deep vein thrombosis of the lower leg, PE, pneumonia, and myocardial infarction. Thrombosis often occurs at the level of capillaries, contributing to the development of microcirculatory disorders [36, 38].

Deposition of fibrin on the walls of pre- and post-capillaries, leading to disruption of transcapillary metabolism, occurs in any critical condition of the body, including after extensive surgical interventions, which include most gynecological operations. The factors initiating the occurrence of DVT are, first of all, surgical intervention (surgical aggression activates the blood coagulation system), anesthesia (muscle relaxants cause dilatation of the intramuscular veins and slowing the outflow of blood from the lower extremities). Interesting facts are that in half of the cases, DVT begins to form on the operating table (Russian consensus "Prevention of postoperative venous thromboembolic complications", 2000), and the incidence of DVT during epidural anesthesia is lower than with general anesthesia. Exposure of the subendothelial zone is an important mechanism initiating thrombosis. Among the causes are direct damage during the installation of endovascular catheters, intravascular devices (filters, stents, etc.), during vein prosthetics, trauma, and surgery.

Endothelium damage is caused by endotoxins, hypoxia, viruses. Major surgical interventions, severe mechanical trauma, massive blood loss, widespread burns, infectious diseases, and sepsis include a systemic inflammatory response mechanism that involves the production and release of a large number of biologically active compounds (histamine, serotonin) into

the bloodstream, complement fragments, leukotrienes, bradykinin, vessel relaxation factor). A cascade of cytokines activates leukocytes and promotes their adhesion to endothelium. Powerful oxidants secreted by activated leukocytes cause endothelial cell death with subsequent exposure of the subendothelial layer. The likelihood of venous thrombosis increases if the patient has congenital or acquired thrombophilia. The presence of thrombophilia can be associated with many cases of "unexpected" venous thrombosis and PE (in particular, those occurring in young people who do not have serious clinical risk factors).

Thrombosis in patients with thrombophilia can initiate surgical interventions, injuries, pregnancy and childbirth, i.e. those states that are accompanied by tissue damage, a change in the tonus of the vessels and hormonal background [8, 37]. A high risk of phlebothrombosis exists in patients suffering from malignant neoplasms. This pathology is predominantly affected by patients over the age of 40 years, in whom surgical intervention performed under conditions of general anesthesia using myo-relaxants lasts 1 hour or more. At the same time, 80-85% of DVT is clinically symptomatic. In a number of cases, PE develops after discharge from the hospital. All this may give the impression of a relatively low incidence of postoperative thromboembolic complications, but they are justifiably recognized as one of the main causes of postoperative lethality. Feasibility studies take the second place in the structure of mortality in cancer patients, while cancer patients with deep vein thrombosis, PE have a more than three-fold risk of recurrence of thrombosis or thromboembolism with a fatal outcome compared with non-cancer patients [28, 32, 38].

According to published data, postoperative DVT of the lower extremities, which are the main sources of PE, develop in 50-70% of cancer patients, about half of them are already formed on the operating table and most of them are asymptomatic. About 72% of venous thromboses form on the 1st - 3rd day after surgery. In 90-99.3% of cases, the source of PE is located in the basin of the inferior vena cava and is most

often the result of thrombophlebitis of the deep veins of the lower extremities [20, 36, 37]. After obstetric operations, the source of PE may be venous thrombosis of the small pelvis [8]. The trigger mechanism in the development of DVT of the lower extremities is an operation that leads to the activation of the blood coagulation system and a decrease in its fibrinolytic and anticoagulant activity. Hemodynamic disorders in the deep veins of the lower extremities are closely related to hemostatic disorders - muscle relaxants used in endotracheal anesthesia cause paralysis of the muscular-venous pump of the lower leg, as a result of which the linear blood flow velocity in the deep veins of the legs decreases by 50%.

Pathogenesis of pulmonary embolism

After the formation of a blood clot, there are three main ways the process can develop:

1. The thrombus, having arisen, begins to increase in size in the proximal or distal direction and is fixed to the wall of the vein; in the event of a sudden increase in blood flow velocity and pressure in the vein (getting out of bed, coughing, straining, defecating, moving the patient to a gurney), he can break away from the wall of the vessel at the attachment site and become a source of PE. In this case, the thrombus follows the inferior vena cava into the right heart, then into the pulmonary artery, where it becomes stuck:

1) obstruction of the branches of the pulmonary artery increases resistance to blood flow in the small circle and the load on the right ventricle of the heart. A decrease in pulmonary blood flow by more than 50-60% guarantees the development of severe pulmonary hypertension, an increase in tension of the right ventricle of the heart and heart failure;

2) embolism causes intrapulmonary reflexes and the release of vasoactive substances (histamine, serotonin, prostaglandins), leading to vasoconstriction. About 10% of patients develop pulmonary infarction;

3) pulmonary disorders are characterized by a mismatch between ventilation and perfusion - there is a section of the

lung in which there is no blood flow, i.e. dead space increases. Excessive perfusion and a decrease in vascular resistance in other segments of the lungs cause blood shunting from right to left with inadequate blood oxygenation;

4) reflex bronchospasm often occurs;

5) ischemic areas of the lungs quickly lead to atelectasis, which contributes to a violation of the synthesis of surfactant.

II. The reverse development of a blood clot under the influence of proteolytic enzymes and tissue plasminogen activators - this way most of the formed blood clots are spontaneously lysed.

III. The organization of thrombotic masses - a fixed thrombus grows with connective tissue, new capillaries form in it, cavities form and recanalization can occur.

The causative factors of venous thrombotic complications can be divided into blood flow disorders in the veins of the lower extremities, as well as predisposing factors. Violation of the blood flow is caused by varicose veins, compression of blood vessels from the outside (tumors, cysts, inflammatory infiltrates, an enlarged uterus, bone fragments), destruction of the valve apparatus after previous phlebothrombosis. One of the important reasons for the slowdown of blood flow is immobilization, leading to impaired function of the muscular-venous pump, which is detected when:

- marked violation of the contractile function of the myocardium;
- lung diseases (especially with severe respiratory failure, mechanical ventilation);
- sepsis, pneumonia;
- oncological diseases - chemotherapy, hormone therapy, x-ray therapy in cancer patients;
- compression of the veins (tumor, hematoma, etc.);
- diseases of the central or peripheral nervous system;
- patient's age >40 years (with increasing risk, increasing; usual gradations >40, >60 and >75 years);
- bed rest (more than 3 days), a long sitting position (for example, air travel lasting more than 3 hours);

- the use of oral contraceptives containing estrogens, or hormone replacement therapy;
- diseases of the colon;
- nephrotic syndrome;
- obesity
- a history of venous thrombosis and / or pulmonary thrombo-embolism;
- varicose veins;
- a catheter in a central vein;
- pregnancy and the immediate postpartum period (up to 6 weeks).

The first group of reasons includes all factors contributing to the activation of the so-called Virchow triad. All these conditions arise during the early postoperative period in patients with diseases requiring emergency or planned surgery. The development of venous thrombotic complications is possible under the following conditions (percentage of patients with feasibility study of the total number of operated):

- Operations on abdominal organs, including medical or diagnostic laparoscopy (19%).
- Gynecological operations, including treatment and diagnostic curettage of the uterine cavity and cesarean section (11.2%).
- Urological operations, including resection of prostate adenoma (7.1%).
- Neurosurgical operations (24%).
- Operations for malignant tumors of various localization (30%).
- Prosthetics of the joints (knee, hip), as well as combined trauma and fractures requiring surgery or prolonged immobilization (immobilization) of the patient (84%).

Predisposing factors include:

1. Gender - in women, blood clots in the veins are formed more often due to hormonal characteristics.

2. Age - the older the person, the higher the likelihood of thrombosis in the veins.

3. Lifestyle - "sedentary" and slow-moving work contributes to stagnation of blood in the veins.

4. The presence of varicose veins in the lower extremities - the more nodes and the higher the failure of the vein valves, the slower the blood flow through the vessel and the greater the tendency to platelet aggregation.

5. Reception of hormonal contraceptives (combined oral contraceptives), which significantly change the rheological properties of blood.

6. Hereditary disorders of the blood coagulation system - thrombophilia, or a tendency to increased thrombosis.

When examining patients with developing thrombosis, it was established [12, 13] that about half of them had congenital thrombophilia, and in 90% of cases it was due to Leiden mutation, and only 10% fell on all other mutations leading to thrombophilia. Screening of the population for congenital thrombophilia is currently not carried out due to its rather expensive cost. Indications for examination for congenital thrombophilia are the following conditions:

- the presence of thrombosis or thromboembolism in the patient being consulted;
- the presence of thrombosis in relatives of the 1st and 2nd degree of kinship;
- heart attacks, strokes in relatives;
- a history of gestosis and other obstetric pathology.

During the examination, in addition to genetically determined thrombophilia, acquired thrombophilia can also be identified, the main reasons for the development of which at present are: the syndrome of resolved intravascular coagulation (the phase of hypercoagulation), antiphospholipid syndrome (APS) and hyperhomocysteinemia (HHC), which in turn can be either congenital or acquired. Thrombophilia with APS is caused by changes in almost all parts of the coagulation system of blood. Detection of APS in a patient indicates a serious thrombotic risk, and, unfortunately, the patient remains with it for many years, therefore, when clinical risk factors appear, she needs adequate preventive antithrombotic therapy.

Acquired HHC can occur against the background of smoking, abuse of coffee and alcohol, with poor nutrition (lack of folate in food), therefore acquired HHC can be stopped. The situation is much more serious in the presence of congenital HHC, which is caused by mutations in the enzymes methylenetetrahydrofolate reductase or cystathion synthetase. The most significant clinical risk factors [12], which pre-

dispose to the occurrence of venous thrombosis in obstetrics and gynecology, are: varicose disease, hypokinesia, polyhydramnios, and multiple pregnancy.

Risk factors for [12]:

- 1) age - after 40 years, with every decade, the risk of thromboembolic complications doubles;
- 2) The duration of the operation is over 1 hour;
- 3) bed rest;
- 4) pregnancy and the postpartum period;
- 5) oral contraceptives;
- 6) heart disease;
- 7) oncological diseases;
- 8) varicose veins of the lower extremities.

According to the development of thromboembolic complications in patients [3, 21, 33] who undergo surgery, depending on the degree of risk, can conditionally be divided into four groups:

- low risk - up to 40 years, regardless of the duration of the operation and a person older than 40 years with a duration of operation up to 1 hour;
- medium risk - older than 40 years with an operation lasting more than 1 hour, which have a concomitant extra-pathological pathology;
- high risk - all patients, regardless of age, duration of surgery, and the nature of the concomitant pathology, who have signs of chronic venous insufficiency of the lower extremities or have a history of deep vein thrombosis and (or) PE;
- very high risk - over 60 years of age, in which chronic venous insufficiency of the lower extremities is combined with factors such as obesity and prolonged surgery, congestive heart failure).

After surgical interventions in gynecology, the degree of risk development can be estimated from the table [12, 13].

As can be seen from the table, extended surgical interventions: hysterectomy with appendages and without them, operations for uterine prolapse (vaginal-abdominal access), myomectomy with the removal of a large number of nodes penetrating the uterine cavity are at high risk for postoperative rational feasibility study. And large surgical interventions, such as plastic surgeries, conservative myomectomy (removal of 1-3

subserous nodes), removal of the uterine appendages, ovarian resection, supravaginal amputation of the uterus constitute a moderate risk group.

In practice, 3 degrees of risk of postoperative venous thrombo-embolic complications are often distinguished - low, moderate and high. Currently, the most popular scheme for predicting the degree of risk of

postoperative thromboembolic complications, proposed by French anesthetists and approved by the Russian consensus "Prevention of postoperative venous thromboembolic complications" (2000). According to this scheme, with large gynecological operations, the risk level of postoperative venous thromboembolic complications is moderate.

Table. The degree of risk of postoperative venous thrombotic complications in gynecology [12]

Risk	Risk factors associated with surgery	Risk factors associated with the patient's condition
Low (IA)	I. Uncomplicated operations lasting up to 45 minutes: artificial abortion, treatment and diagnostic curettage of the uterine cavity, hysteroscopy, diagnostic laparoscopy (may be with a small operation: diathermocauterization, tubectomy, etc.)	A. None
Moderate (IB, IC, IIA, IIB)	II. Major interventions: plastic surgery, conservative myomectomy (removal of 1-3 sub-rose nodes), removal of the uterine appendages, ovarian resection, supravaginal amputation of the uterus	B. There are risk factors other than a malignant tumor, genetic pathology of hemostasis, antiphospholipid syndrome, hyperhomocysteinemia
High (IIC, IIIA, IIIB, IIIC)	III. Extended interventions: hysterectomy with or without appendages, operations for uterine prolapse (vaginal-abdominal access), conservative myomectomy with removal of a large number of nodes, penetration into the uterine cavity	C. Oncological diseases; deep vein thrombosis and pulmonary thromboembolism (pulmonary embolism) in the anamnesis; genetic pathology of hemostasis; circulation of antibodies to phospholipids

Diagnosis of venous thrombotic complications

The severity of symptoms largely depends on the size of the thrombus and the pool of pulmonary vascular occlusion: pulmonary embolism often occurs under the guise of postoperative pneumonia, pleurisy, acute posterior-infarction myocardial infarction, classical symptoms appear only in 24% of patients: shortness of breath and tachycardia, chest pain, fever, cyanosis, cough, hypotension, heart rhythm disturbances, bronchospasm. The main symptoms include tachycardia, shortness of breath, coughing, after which blood streaks are visible in the sputum, elevated body temperature of the patient. Such complications as deep vein thrombosis of the lower extremities are characterized by severe pain in the lower leg and foot. accompanied by blue or purple skin below the location of

thrombosis. Even slight discomfort in one or both limbs after surgery should not be left without the attention of a doctor, as it may indicate acute leg vein thrombosis. Usually PE is accompanied by bouts of dry cough or hemoptysis with chest pain of various localization. Often the patient has bouts of sudden shortness of breath and a feeling of lack of air. Loss of consciousness may be present.

Massive PE is characterized by severe pain in the chest, shortness of breath, hemoptysis and cyanosis of the skin of the face, neck, earlobes and chest strictly up to the horizontal line between the nipples. Clinical death can instantly occur, without treatment transforming into biological death.

To accurately confirm the diagnosis, the following diagnostic methods are used:

a) echocardiography. The primary diagnostic tool is echocardiography, the so-called distributive examination method, since it cannot accurately confirm the embolism, but it is able to exclude it and direct the diagnosis in time to a specific direction;

b) electrocardiography (especially in dynamics) - signs of overload of the right heart, low voltage and the appearance of SI – QIII syndrome;

c) X-ray of the chest organs reveals a decrease in the intensity of the shadow of the pulmonary vessels, an increase in the transparency of the pulmonary fields corresponding to the embolism region (Westermark symptom). Exudation in the pleural cavity (usually hemorrhagic) or lung tissue infiltration may be detected;

d) a study of the gas composition of arterial blood reveals hypoxemia, hypercapnia and respiratory alkalosis;

e) pulmonary artery angiography is the best way to diagnose pulmonary embolism, the accuracy of the method reaches 100%, but this method is invasive. Angiography of the lungs safely diagnoses pulmonary embolism. Recently, this method was a reference, but now it is inferior to a multi-detector computed tomography (CT). Patients with venous thrombotic complications are not recommended to use angiography, since it increases the risk of mortality in unstable patients and increases the likelihood of bleeding after treatment with thrombolytics;

f) ultrasound examination of the heart - reveals signs of right ventricular overload - dilatation and asinergy of the right ventricle (free wall hypokinesis with normal contractility of the apex), pathological movement of the interventricular septum, tricuspid regurgitation, expansion of the pulmonary artery, absence or decrease fall of the inferior vena cava during inspiration;

g) an ultrasound Doppler study of the veins of the lower extremities allows reliable diagnosis of proximal deep vein thrombosis of the lower extremities in the presence of its symptoms, but has a low sensitivity in the detection of asymptomatic thrombosis;

h) ventilation-perfusion scintigraphy of pulmonary vessels. Used in situations

where CT is contraindicated. In patients belonging to the low-risk group of pulmonary embolism, with a negative result of scintigraphy, embolism is excluded;

i) magnetic resonance imaging (MRI) is often used to examine pregnant women, since they do not carry out radiation exposure;

j) CT at the modern stage of the development of medicine is the most objective way to determine a blood clot in the pulmonary vessels, according to experts of the European Medical Society. For patients with a sufficient degree of risk of thromboembolism, it is enough to use a single-detector CT, while patients with a low probability are used a multi-detector CT, which allows you to determine the diagnosis by 100%. As for MRI, it is commensurate with monodetector CT, but inferior to multidetector CT in its diagnostic value.

A mandatory study for suspected venous thrombotic complications is a D-dimer study, as well as a study of the blood coagulation system (indicators - International Normalised Ratio, fibrin, blood coagulation time, associated partial thrombin time, prothrombin time, prothrombin index). After a comprehensive assessment of the data obtained, treatment begins.

Treatment

Any doctor must remember that mortality with massive PE without treatment is more than 90%, so therapy should be started as soon as possible. The main principle of treatment is to dissolve a blood clot and to correct a violation in blood coagulation. In this regard, in the intensive care unit, the following drugs are intravenously administered to the patient. First of all, it is necessary:

- 1) catheterize the peripheral or central vein;
- 2) establish oxygen therapy, prepare everything for transferring the patient to mechanical ventilation;
- 3) prepare everything for cardiopulmonary resuscitation. The patient should be constantly monitored with blood pressure, heart rate, body temperature, pulse oximetry, electrocardiography. Bed rest is indicated until pain and shortness of breath disappear.

Drug correction is carried out by the following drugs:

- a) heparin 10 000 - 20 000 IU intravenously, but then a continuous intravenous infusion of 1000-1200 IU / h until the associated partial thrombin time is extended by 1.5-2 times (within 7 days). In the future, the introduction of heparin is replaced by indirect anticoagulants. They are prescribed from 3 to 6 months;
- b) disaggregants (0.125 g aspirin, 400-600 mg trental, 250-500 mg ticlide). Of the tablets, warfarin is used in a dose of 10 mg for 5-7 days;
- c) thrombolysis - carried out with the help of iv administration of streptokinase at 250,000 IU for 30 minutes, then a constant infusion of the drug at 100,000-150,000 IU/h during the day is necessary. During the course of thrombolysis, heparin therapy is stopped and begins again no earlier than 4 hours after the termination of streptokinase administration. Thrombolytic therapy is absolutely contraindicated in patients with recently underwent low molecular weight heparins (LMWH), severe hypertension, gastrointestinal bleeding in the last 6 months, during pregnancy, childbirth and in the immediate postpartum period [30];
- d) analgesia with narcotic analgetics;
- e) vasopressor drugs-dopamine-mimetics: dopamine 1% solution - 5 ml, diluted in 200 ml of isotonic glucose solution; β 1-adrenergic agonists: do-butrex 5% solution - 5 ml, dissolved in 200 ml of glucose solution;
- f) restriction of infusion therapy to 10-15 ml / kg / day.

Of the invasive methods of treating pulmonary embolism, the following are known: installing a cava filter in the inferior vena cava, plication, pulmonary thrombectomy, etc. [26]. Indications for surgery are:

1. recurrent PE with adequate anticoagulant therapy;
2. extensive or progressive thrombosis of the inferior vena cava;
3. performed or planned surgery in a patient with transferred PE.

The most important advantage of LMWH compared with unfractionated heparin (UFH) is a more predictable anticoagulant effect, which is associated with greater bioavailability [10, 34]. One of the most im-

portant qualitative differences between LMWH and UFH is the ability not to significantly extend such parameters as associated partial thrombin time, etc., which is mainly associated with exposure to factor Xa and inhibition of the external coagulation pathway. The main difference between the mechanism of action of LMWH on the hemostasis system from UFH is that LMWH possess mainly anti-Xa activity (antithrombin) [16]. To control the effectiveness of the therapy, such markers of intravascular coagulation as thrombin-antithrombin complex, fragments 1 + 2 of prothrombin and especially fibrin / fibrinogen degradation products can be used [7]. Currently, LMWH are widely used in clinical practice for the prevention of venous thrombosis and thromboembolism. Since LMWH are devoid of most of the side effects characteristic of UFH, as well as its anticoagulant effect in response to a fixed dose, they are more predictable, without opinion, LMWH is the drug of choice in the prevention of DVT and PE. Moreover, prophylactic doses of LMWH usually do not exceed 3400 anti-Xa IU and are administered subcutaneously once or twice a day. Thus, LMWH effectively reduce the incidence of postoperative thrombosis (by almost 70%) and do not increase the risk of serious hemorrhagic complications during preoperative administration.

At present, fraxiparin is considered the most promising drug for thromboprophylaxis among LMWH. Fraxiparin also received this recognition from the European Collaborative Study (1991). Fraxiparin, unlike UFH, does not violate the functional state of the hemostasis system, providing a "truly effective" thromboprophylaxis. In addition, in patients receiving fraxiparin, the level of tissue perfusion is significantly higher than in those receiving UFH. The study [16], which included 113 patients operated on for various gynecological pathologies, who in the postoperative period performed prophylaxis of DVT and PE with the help of LMWH, fraxiparin, showed good results. For practical purposes, the following modes of application of fraxiparin can be used: prophylactic doses depending on body weight: less than 50 kg - 0.3 ml; 50-70 kg - 0.4 ml; more than 70 kg - 0.6 ml. Duration

of the use of fraxiparin for prophylactic purposes: during gynecological operations - the first injection 12 hours before the operation, the second injection - 8 hours after the operation, then 1 time per day for 10 days.

Prevention

Despite the steady tendency to increase thromboembolic complications, targeted prophylaxis, if it is carried out in all medical institutions and at all stages of the management of such patients, can significantly reduce the frequency of these formidable complications and reduce postoperative treatment. To reduce the frequency of severe forms of chronic venous insufficiency [4, 23].

All methods of venous thrombotic complications prophylaxis are divided into three main groups - medication, physical, or mechanical, and combined. In widespread practice, only medical prophylaxis is feasible and most effective. However, unfractionated heparin (UFH), traditionally used for this purpose, has a weak antithrombotic activity, despite its pronounced anticoagulation ability. The reason for the low efficacy of UFH lies in its anti-fibrinolytic and pro-aggregative action.

The following drugs are traditionally used for specific drug prophylaxis of venous thrombotic complications:

- anticoagulants (direct and indirect);
- disaggregants - rheologically active colloids.

Low molecular weight heparins (LMWH), the predominance of which over unfractionated heparin have been proved by many studies, are deservedly considered an integral component of the prevention of thromboembolism in operated patients with oncopathology. By blocking factor Xa, LMWH interrupt the coagulation cascade along the external and internal coagulation pathways, while not increasing the frequency of intra- and postoperative bleeding. Indirect anticoagulants are the drugs of choice for the long-term prophylaxis of thrombotic complications [18]. Currently, warfarin is called the gold standard from the drugs of this group because of its lower toxicity, quick action and short (about 2 days) after-action. Antiplatelet agents -

drugs that reduce the functional activity of platelets, used for the prevention and relief of thrombosis in the arterial and microvasculature. Three main groups of antiplatelet agents used in clinical practice can be distinguished: acetylsalicylic acid, dipyridamole, thienopyridines, and platelet IIb/IIIa glycoprotein receptor blockers. When choosing a thromboprophylaxis regimen, it should be remembered that antiplatelet agents are effective in the prevention of arterial thrombosis, but they should not be used to prevent venous thrombosis and thromboembolism. Pharmacoprophylaxis is carried out by early subcutaneous heparin administration (already 2 hours before surgery 5000 U), and then administration at a dose of 5000 U 3-4 times a day for 7-10 days. In addition, patients who do not have contraindications for taking warfarin receive it at a dose of 2.5 mg / day for 1-1.5 months. Unfortunately, one of the first manifestations of asymptomatic thrombosis is life-threatening pulmonary embolism. Therefore, it is important to prevent its occurrence. Over the past 10–20 years, significant progress has been made in the prevention of venous thromboembolic complications. The use of fraxiparin for prophylactic purposes allows to reduce mortality, reduce the incidence of severe forms of chronic venous insufficiency and obtain a tangible economic effect. One of the modern means of preventing venous thrombosis is calcium nadroparin - a long-acting low molecular weight heparin that does not require laboratory monitoring and economically affordable drug. According to [6, 29, 31, 35], in patients who were prescribed bemiparin (zibor), coagulogram indices, in particular Soluble Fibrin Monomeric Complexes, normalized faster. Zibor more effectively reduces intra- and postoperative blood loss compared with enoxaparin in patients with prosthetic joints. The prospect of using perfluorocarbon compounds (perfluororan) in a complex of measures aimed at the prevention of early postoperative thromboembolic complications is justified by a more effective effect on blood rheology and microcirculation compared to the traditional method, and a decrease in the activity of the blood coagu-

lation system and thereby reducing the risk of early thromboembolic complications [14].

Of the synthetic colloids that have an effect on the hemostatic system, dextrans and hydroxyethyl starch preparations (reformed 6%, etc.) deserve attention [5, 17]. According to [2], reformed dextran is the optimal drug for the prevention of thromboembolic complications in cancer patients. The introduction of dextrans leads to a decrease in coagulation factors II, V, VIII. A specific effect reduces platelet adhesion, the activity of von Willebrand factors involved in platelet aggregation disrupts adenosine diphosphate induced platelet aggregation, has an inhibitory effect on factor VII, reduces its activity, blocks the fibrinogen molecule, and increases the sensitivity of the fibrin clot to plasmin.

Thus, the reformed dextran, which has endothelio-protective properties, has a moderately pronounced disaggregant and anticoagulant effect, is effective as part of the comprehensive prevention of thromboembolic complications in cancer patients. Dextrans and antiplatelet agents with a high degree of thromboembolic risk can be used only in combination with heparin preparations, since they themselves do not provide effective thromboprophylaxis. Allergic reactions with the use of medium and large molecular dextrans develop quite often. Mechanical methods of thromboprophylaxis are also ineffective, moreover, inconvenient to use and contraindicated in severe lesions of the vessels of the legs, complicated by the development of trophic ulcers, dermatitis. With regard to thrombosis and thromboembolism, they can be divided into physical and pharmacological. The first group includes early activation of the patient after surgery (on the 2nd-3rd day), wearing compression hosiery before and after surgery, as well as intermittent pneumatic compression [1, 25, 27]. Compression knitwear is made of polyamide microfibers, the material is treated with antibacterial impregnation, silver ions, which do not cause allergies or dermatitis and have a protective function. Intermittent pneumatic compression is the application of a cuff forcing air, alternately on the ankle and thigh with different pressure - 20 mm Hg in the lower leg area and 35 mm Hg in the hip area. This helps

to improve blood flow through the veins of the lower extremities. Wearing compression underwear prevents stagnation of blood in the veins of the lower extremities, which slightly reduces the risk of thrombosis. So, wearing elastic garters to the knee-length reduces the risk of PE to 8.6% in patients with a high degree of risk, while wearing stockings to the groin - up to 3.2%. Wearing compression underwear in patients with a low and moderate risk of venous thrombotic complications does not reduce the risk of thrombosis and thromboembolism.

With a high level of suspicion of thromboembolism, an installation of a cava filter is used as an effective method of prevention. For the period of delivery, surgical intervention or during therapy with thrombolytics, a temporary anti-embolic filter is established. If there is a danger of a thrombus detachment, a permanent cava filter is placed: in this case, a detached thrombus does not enter the heart, but is held by the installed filter.

Prevention is a moving lifestyle and proper nutrition without overeating (obesity is the primary factor leading to the development of venous thromboembolism), it is also a routine examination that allows you to identify serious diseases or malignant neoplasms in time stage. Hormone therapy is prescribed only by a gynecologist, as it is one of the causes of thrombosis. The prevention of venous thrombosis should be given as serious attention as the implementation of the surgical intervention itself. A decrease in the frequency of this postoperative complication will reduce not only the morbidity and mortality associated with it, but also reduce the cost of treating patients with this pathology and its consequences in the acute stage and during relapses.

It should be noted that in patients of moderate and high risk, the cost of diagnostic DVT screening using special instrumental methods (labeled fibrinogen test, compression duplex scanning or phlebography) and the subsequent treatment of complications that have already developed are so high, that currently proposed methods for primary prevention of DVT (prescribing low molecular weight or non-fractionated heparins, intermittent pneumo-

compression, or blood flow acceleration methods) are clinically and economically justified. Ignoring DVT prophylaxis leads not only to an increase in patients suffering from chronic venous insufficiency of the lower extremities of post-thrombotic origin, but also to an increase in the number of fatal outcomes from PE.

Conclusion

The analysis will significantly improve the issues of early diagnosis, the choice of

treatment and prevention of early postoperative thromboembolic complications after gynecological operations.

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