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Prevention of Thrombosis in Oncohematological Patients

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Abstract: Cancer patients are at high risk of thrombotic complications, which worsen the outcomes of anticancer treatment and occupy one of the leading places among the causes of death. Thrombosis in a cancer patient increases the risk of death by 30 times, which is associated with the development of fatal thromboembolism and a more aggressive course of the tumor process.

Keywords: thromboprophylaxis, thromboembolic complications, thrombosis, leukemia, lymphomas, multiple myeloma.

The leading role in the pathogenesis of thrombotic complications is played by disturbances in the hemostasis system caused both directly by the tumor and by methods of treatment. Low molecular weight heparins are considered the basis for the specific prevention of thromboembolic complications in cancer patients. The use of low molecular weight heparins after surgery and during chemotherapy effectively reduces the incidence of venous thrombosis. Direct oral anticoagulants are promising drugs for oral administration and are indicated as one of the treatment options for patients with tumor-associated thrombosis with a low risk of bleeding and no drug interactions with ongoing systemic chemotherapy.

All oncosurgical patients who are operated on an emergency basis are at high risk for venous thromboembolic complications. Depending on the circumstances, prevention of venous thromboembolic complications can be started both before and after surgery. In cases where mechanical methods of preventing venous thromboembolic complications are indicated, their use should be started before surgery.

In the presence of urgent indications for surgery and the possible duration of preoperative preparation for at least 6 hours, thromboprophylaxis should be carried out in full (non-drug and drug) similar to that for planned interventions.

In the presence of emergency indications for surgery (usually for peritonitis or bleeding), pre-and intraoperative thromboprophylaxis is reduced to non-drug measures (elastic compression of the lower extremities). The introduction of anticoagulants should begin as early as possible in the postoperative period. In the case of an emergency intervention for ongoing bleeding, drug thromboprophylaxis is possible only with verified achievement of final hemostasis.

Mechanical measures to prevent venous thromboembolic complications should be continued until full recovery of motor activity.

Drug prevention of venous thromboembolic complications at moderate risk should continue until discharge, but not less than 7-10 days after surgery. In patients with a high risk of venous thromboembolic complications, it is advisable to prolong drug prophylaxis up to 28-35 days, regardless of the timing of discharge from the hospital, if there are no contraindications.

The feasibility of extending prophylaxis up to 28 days has been demonstrated after major operations for malignant neoplasms in the abdominal cavity or in the pelvic cavity in patients with persistent risk factors for venous thromboembolic complications (incompletely resected neoplasm, obesity, history of venous thromboembolic complications). After major onco-orthopedic operations, prolongation of prophylaxis up to 35 days is justified.

For long-term prevention of venous thromboembolic complications in these situations, low molecular weight heparins should be used.

Cancer patients are characterized by a high risk of developing thrombotic complications, which worsen the outcomes of anticancer treatment and occupy one of the leading places among the causes of death [1, 2]. Modern studies have shown that cancer increases the risk of deep vein thrombosis and pulmonary embolism by 4–7 times. At autopsy, signs of thromboembolic complications are found in 50% of cancer patients, while pulmonary embolism causes death in 15% of patients, in the rest it is a “favorable” background for other fatal complications [5, 4]. Thromboembolic complications most often develop in patients with biologically aggressive tumors, such as a tumor of the pancreas, stomach, ovaries, kidneys, liver, especially in the presence of metastases. However, the results of studies conducted in recent years indicate that there are more cases of thromboembolic complications in patients with oncohematological diseases, such as acute leukemia, lymphomas, multiple myeloma, than in patients with solid tumors [3, 6].

On the other hand, when studying all cases of thrombosis, according to various authors, in 5–10% of patients, thrombosis becomes the first manifestation of a malignant process, while most neoplasms are detected within the first 6–12 months after a thrombotic episode. A meta-analysis that included 10 studies and 2316 patients with a clinically unprovoked episode of venous thromboembolic complications (VTEC) showed that the incidence of malignant tumor detection over a 12-month follow-up period was 5.2 (4.1–6.5) % [6, 8].

Along with an increased risk of VTEC, oncosurgery is associated with a serious risk of HO, which may be higher than the threat of VTEC. Such a balance of risks is due to the often-occurring extensive phenomena of tumor decay, an expanded volume of oncological operations (especially when large vessels are involved in the tumor conglomerate), as well as the formation of large wound surfaces with a mass of crossed and coagulated or bandaged vessels. This is especially true for patients with tumor processes of the head and neck. Therefore, in extensive oncological operations, the problem of reducing the incidence of VTEC should be considered in close connection with the parallel risk of developing bleeding from the tumor, high intra- and postoperative blood loss against the background of large wound surfaces, and post-hemorrhagic coagulopathy.

Risk factors for postoperative hemorrhagic complications:

- ✓ age over 75 years;
- ✓ a history of gastrointestinal bleeding;
- ✓ a history of peptic ulcer disease;
- ✓ hemorrhagic stroke in history;

- ✓ chronic diseases of the liver or kidneys with severe functional insufficiency;
- ✓ simultaneous therapy with antiplatelet agents;
- ✓ coagulopathy with a state of hypocoagulation (including DIC);
- ✓ medical hypocoagulation (international normalized ratio > 3 and/or activated partial thromboplastic time > 120 s).

Thus, cancer patients are considered to be at high risk of developing thrombotic complications. Thromboembolic complications are often the cause of hospitalization of cancer patients, reduced effectiveness and even termination of treatment. In addition, a decrease in the survival of patients with thrombosis is associated with the development of fatal pulmonary embolism, a more aggressive course of the tumor process, and a deterioration in the quality of life of patients [2, 30].

The main mechanisms of activation of the hemostasis system during antitumor drug treatment are damage to vascular endothelial cells, direct activation of platelets, an increase in the level of von Willebrand factor, a decrease in fibrinolytic activity and the level of natural anticoagulants due to hepatotoxicity, and, finally, the release of procoagulants and cytokines by tumor cells, damaged during cytostatic therapy. In addition, the use of immunomodulators (thalidomide and lenalidomide) stimulates the release of secondary cytokines (interleukins 6 and 1), which exacerbates hypercoagulability [4, 26].

Embolic thrombi include floating thrombi, which have a single fixation point in the distal region. The proximal part of such a thrombus is freely located in the bloodstream and can change its position with a change in venous pressure. Non-embolic thrombi are considered occlusive and parietal.

Proved the need for adequate anticoagulant therapy as the basis for the treatment of patients with venous thromboembolic complications (including asymptomatic). Parenteral administration of anticoagulants in case of reasonable suspicion of deep vein thrombosis of the lower/upper extremities and/or pulmonary embolism should be started before the instrumental verification of the diagnosis (in conditions where further tactics of managing the patient have not yet been determined, it is reasonable to use unfractionated heparin – 5000 IU intravenously as a bolus with switching to intravenous infusion).

All patients with deep vein thrombosis of the lower/upper limbs of the lower limbs are shown elastic compression. Prior to the instrumental examination, patients with deep vein thrombosis of the lower/upper extremities should be prescribed strict bed rest to reduce the risk of pulmonary embolism. After examination, patients with occlusive and parietal forms of venous thrombosis can immediately be activated.

If venous thromboembolic complications occur during anticancer drug therapy, it should be interrupted. The resumption of anticancer treatment is possible after the disappearance of clinically significant manifestations of venous thromboembolic complications (local inflammation, pulmonary heart failure), taking into account the prognosis of the tumor process against the background of adequate anticoagulant therapy.

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