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Mechanisms and Clinical Management of Cancer-Associated Thromboembolism: Challenges and Advances

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Abstract. Cancer-associated thromboembolism (CAT) is a common and highly lethal complication in cancer patients. Tumors and their treatment increase the risk of thrombosis in patients. This article provides a systematic review of the mechanisms of CAT, the mechanism of action of anticoagulant drugs, and their use in the treatment of CAT. Low molecular heparin (LMWH) and new oral anticoagulants (DOACs) are the main therapeutic options recommended by current guidelines. However, in specific patient populations, it is important to individualize the treatment regimen. Recurrent thrombotic and bleeding complications are major challenges in the management of CAT, and future research should focus on optimizing individualized anticoagulation strategies, exploring novel agents, and multimodal combinations to further improve outcomes and reduce the incidence of adverse events, so that the prognosis and quality of life of patients who suffered from cancers can be upgraded a lot.

Keywords: Cancer-associated thromboembolism, anticoagulant, Low molecular heparin, new oral anticoagulants, Clinical Management.

1. Introduction

Cancer-associated thromboembolism, which seriously affecting the survival and prognosis of cancer patients, become one of the most general complications in cancer patients, getting its fatality rate increased. Compared to the general population, cancer patients have a significantly increased risk of thrombosis [1]. This is not only due to the role of cancer itself, but is also closely related to anti-tumor treatments (e.g., chemotherapy, hormone therapy, etc.), which may affect the patient's coagulation system and make cancer patients more susceptible to thrombotic tendencies [2]. Therefore, the prevention and treatment of CAT has become an important part of cancer treatment, and it is necessary for clinicians to deeply understand the mechanism of CAT formation and take effective anticoagulation measures for prevention and treatment. Therefore, how to balance the effect of anticoagulation and safety in the treatment of CAT is a clinical problem that needs to be solved urgently.

Currently, the treatment of CAT mainly relies on anticoagulants, with LMWH and DOACs being the first choice recommended by guidelines. However, the use of LMWH and DOACs in specific patients, such as those with renal insufficiency, those at risk of gastrointestinal bleeding, or those receiving specific chemotherapy regimens, should be used with caution [3]. Individualized treatment regimens, drug side effects, and potential risks all need to be thoroughly evaluated and considered by clinicians. In this article, we will discuss the mechanism of CAT formation, the rationale for anticoagulation, and its clinical application, with the aim of providing clinicians with effective therapeutic strategies.

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2. Mechanisms of cancer-associated thrombosis

The mechanisms of cancer-related thrombosis are complex and include hypercoagulability, vessel wall damage, and hemodynamic changes. First of all, tumor cells secrete a variety of substances that will cause the body to be in a state of hypercoagulability, especially the abnormal production of tissue factor by tumor cells that can activate the exogenous coagulation pathway, and the synthesis of fibrinogen activator inhibitor-1 by tumor cells that can inhibit the fibrinolytic system.[4] Secondly, factors such as radiation therapy, chemotherapy, surgical trauma, and direct invasion of surrounding tissues by the tumor may lead to damage to the vessel wall, exposing subendothelial components, platelet adhesion and coagulation, and activation of the coagulation system, leading to thrombosis. In addition, compression of peripheral blood vessels by the tumor and prolonged postoperative bed rest may result in hemodynamic changes that exacerbate stagnation of blood flow, thereby increasing the risk of thrombosis. The multiple effects of tumor and antitumor therapy make the mechanisms of thrombosis in cancer patients more complex than in the general population.

3. Mechanisms of anticoagulation

The mechanism of action of anticoagulation therapy is to stop the clotting process by blocking key targets in the endogenous and exogenous coagulation pathways. LMWH inhibits factor X activation and prevents fibrin production by enhancing antithrombin I (AT-II) activity [5]. Warfarin reduces vitamin K-related coagulation factor production by inhibiting the conversion of vitamin K in the liver; and the DOACs prevent thrombus formation by directly inhibiting key targets in the coagulation pathway, such as factor Xa or lla [6]. In contrast, DOACs have the advantage of faster onset of action and shorter half-life.

4. Clinical use of anticoagulation in cancer-related thromboembolism

4.1. CAT prevention strategies

CAT has become an important cause of death in oncology patients, and therefore the prevention of CAT is of great importance. All international authoritative guidelines consistently recommend the prevention and treatment of CAT in tumor patients. According to the National Comprehensive Cancer Network (NCCN) guidelines, clinicians can use the Khorana score to assess the risk of patients with suspicious symptoms and select an appropriate anticoagulation regimen [7]. Caprini Risk Assessment Model Combined with D-dimer Assay Provides Higher Accuracy in Patient Risk Assessment [8]. However, thromboembolism does not occur in all patients with tumors, so consistent anticoagulation prophylaxis in all patients may lead to complications such as bleeding. Therefore, risk assessment of patients is important.

4.2. Diagnosis and treatment of CAT

Even when patients are treated with anticoagulation prophylaxis, thrombosis cannot be completely prevented, and the optimal dosage for specific populations has not yet been determined. When a patient presents with suspicious symptoms such as unilateral limb swelling, pain, persistent calf cramps, or swelling of the face or neck, imaging studies, such as ultrasound or enhanced CT, should be performed to make a definitive diagnosis [7]. In addition, anticoagulation carries a certain risk of bleeding, and should be avoided in patients with a recent history of hemorrhage or high-risk bleeding, for which an individualized treatment plan is needed [9].

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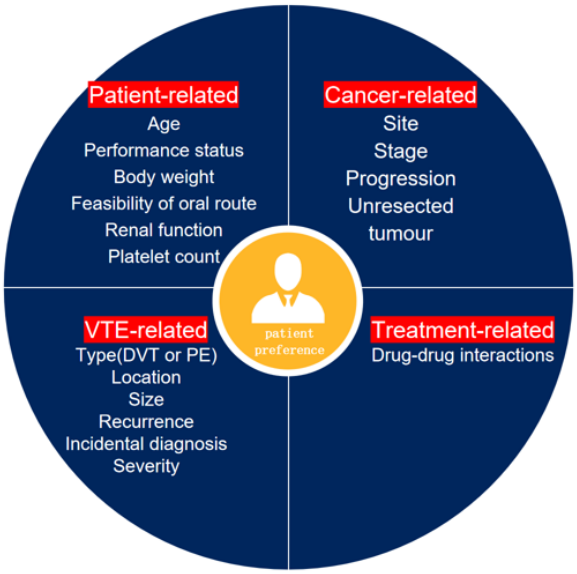

Figure 1. Reference indicators for developing personalized treatment plans for CAT.

4.3. Drug selection

Currently, LMWH and DOACs are the drugs of choice for CAT. LMWH has a good anticoagulant effect and is safe to use in pregnant and breastfeeding women, but may cause osteoporosis and thrombocytopenia and needs to be monitored accordingly [10]. DOACs are fast-acting, have a short half-life, and no direct risk to bone health has been identified, but there may be a higher risk of bleeding in patients with gastrointestinal or genitourinary pathologies and they are contraindicated during pregnancy and lactation [11]. Due to its low cost, warfarin remains an alternative medication for some patients. However, its anticoagulant effect has a long onset and its interactions with other drugs are complex. In patients with contraindications to anticoagulants, inferior vena cava filter implantation (IVCF) can be used as an alternative treatment, but attention should be paid to the possible complications of IVCF [12].

4.4. Application of interventional therapy

In patients who are unable to use anticoagulants, implantation of an inferior vena cava filter (IVCF) is an effective alternative to prevent pulmonary embolism. However, there are some complications associated with the implantation of inferior vena cava filters, such as inferior vena cava occlusion, filter rupture, filter penetration, and so on [13]. could serve as a promising and effective alternative for patients facing only short-term risk of pulmonary embolism and having contraindications to anticoagulation therapy [14].

5. Discussion

Cancer-associated thromboembolism (CAT) is prevalent in cancer patients, and the risk of CAT increases with the intensity of antitumor therapy. Prevention of CAT is essential to improve the quality of life of patients with cancer, but current anticoagulation regimens fall short in terms of efficacy and safety. Although LMWH and the DOACs are the mainstay of treatment for CAT, the risk of recurrent thrombosis and bleeding complications remains a challenge for clinical management. The choice of available drugs needs to take into account individual patient characteristics, such as renal insufficiency, risk of gastrointestinal bleeding, and special circumstances such as pregnancy and lactation.

In addition, there are a number of challenges in the prevention and treatment of CAT, including the development of regimens for specific patient populations, the management of recurrent thrombosis, and

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the control of bleeding risk. Prolonged anticoagulation and regular thrombotic risk assessment can reduce the incidence of recurrent thrombosis, and regular bleeding risk assessment and dose adjustments can reduce the incidence of bleeding complications. However, individual differences limit the effectiveness of current anticoagulation therapy in specific patient populations, and further optimization of anticoagulation regimens is needed to improve the effectiveness and safety of therapy.

Future research should focus on the development of new anticoagulants and explore the possibility of multimodal combinations to improve the management of CAT. At the same time, more accurate risk assessment tools and biomarker testing can be used to customize treatment plans for patients, reduce complications, and further improve treatment outcomes and patient quality of life. Multi-center, long-term follow-up clinical studies are essential to establish a more systematic standardization of anticoagulation therapy. This will not only help to standardize treatment, but also provide safer and more effective treatment options for high-risk patient populations.

6. Conclusion

Cancer-associated thromboembolism (CAT), as a common complication among cancer patients, severely affects the quality of life and prognosis of patients. LMWH and DOACs are the primary means of CAT treatment currently; however, there are still numerous challenges in the management of recurrent thrombosis and bleeding complications. For special patient populations, such as those with renal insufficiency, the risk of gastrointestinal bleeding, and those in pregnancy and lactation, clinicians need to be particularly cautious in selecting appropriate anticoagulation treatment plans. Future studies should focus on optimizing individualized treatment strategies and the development of new anticoagulant drugs and multi-modal combination therapies to enhance the therapeutic effects and quality of life of patients. Through more precise risk assessment and multi-center, long-term follow-up studies, it will be conducive to establishing a more systematic and safe prevention and treatment protocol for CAT, providing cancer patients with superior treatment choices.

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