Cancer Therapy & Oncology
International Journal
ISSN: 2473-554X

Juniper Publishers
key to the Researchers

Editorial
Volume 29 Issue 1 - May 2025
DOI: 10.19080/CTOIJ.2025.29.556251

Cancer Ther Oncol Int J

Treatment of Cancer-Associated Venous Thromboembolism in Thrombocytopenic Cancer Patients

Nahla A. M. Hamed*

Professor of Clinical Haematology, Faculty of Medicine, Alexandria University, Egypt

Submission: May 03, 2025; **Published:** May 15, 2025

Corresponding author: Nahla A. M. Hamed, Professor of Clinical Haematology, Faculty of Medicine, Alexandria University, Egypt

Abstract

The optimum treatment of venous thromboembolism in thrombocytopenic cancer patients is a challenging issue due to the high risk of bleeding complications and thrombosis recurrence in these patients. Anticoagulant therapy in patients with platelets more than 50×10^9/L has been associated with a low risk of bleeding. This provides a rationale for use anticoagulant drugs in full-dose within the first month since the index event, the period with the highest risk for venous thromboembolism (VTE) recurrence. Oral administration of direct oral anticoagulants (DOACs) and their lack of routine monitoring make them increasingly used in these patients. However, factors such as drug-drug interactions, chemotherapy used, tumor location, and renal function may influence their safety and efficacy.

Keywords: Venous Thromboembolism; Active Cancer; Thrombocytopenia; Vena Cava Filter; Abelacimab

Abbreviations: CAT: Cancer-Associated Thrombosis; VTE: Venous Thromboembolism; CRT: Catheter Related Thrombosis; LMWH: Low-Molecular-Weight Heparin; DOACs: Direct Oral Anticoagulants; VKAs: Vitamin K Antagonists

Introduction

Cancer-associated thrombosis (CAT), is a term used to define diagnosis of venous thromboembolism (VTE) in patients with active cancer [1]. The commonest site of VTE in cancer patients is deep veins of the lower limbs. Other sites of VTE presentation are pulmonary veins and cerebral veins. Unusual sites of VTE are portal veins, splanchnic, and mesenteric veins while the internal jugular vein is a rare site of deep vein thrombosis in cancer patients. Cancer patients are predisposed to upper-extremity deep vein thrombosis (UE-DVT) as a result of central venous catheters use [2]. CAT is the second leading cause of death after cancer progression among cancer patients. VTE in non-cancer patients have better outcome than those in cancer patients. They have increased risk of recurrent VTE and anticoagulation-related bleeding due to several factors, such as disease- and treatment-related thrombocytopenia [1]. Appropriate management of VTE in cancer patients is challenging due to the need to balance risk of bleeding with the increased risk of VTE recurrence [2].

Risk Features for Cancer-Associated VTE Progression/ Recurrence

Acute VTE [i.e. within 1 month since the index event], higher VTE burden (e.g., segmental or more proximal pulmonary embolism, proximal lower extremity DVT), and recurrent VTE are a higher risk for progression/recurrence of venous thrombosis [3]. Lower risk for VTE progression/recurrence, include subacute (30-90 days since the index event) or chronic VTE (more than 90 days since the event) or a less severe clinical presentation, e.g. isolated subsegmental pulmonary embolism, distal DVT (VTE in veins distal to the popliteal vein i.e, in the peroneal, anterior tibial, and posterior tibial veins), catheter-related thrombosis (CRT), incidental VTE events or [1] autologous haematopoietic stem cell transplantation) [3]. Age less than 65 years, pulmonary embolism as initial VTE and an interval less than 3-month between initial VTE and cancer diagnosis are considered by the Computerized Registry of Patients with Venous Thromboembolism (RIETE) as risk factors

for recurrence of VTE [2]. VTE recurrence after cancer treatment should prompt assessment for a new primary malignancy or cancer recurrence [2]. Different models of risk assessment are used in cancer patients to predict VTE risk. The Ottawa model can be utilized to predict risk of VTE recurrence in cancer patients [2]. Most patients with CAT were not identified as high risk by current risk assessment models. It should be considered that the majority of patients included in the development of these risk scores had solid tumors rather than haematological cancers [4].

Management Plan of CAT

The anticoagulation strategy was influenced by the degree of thrombocytopenia and the time interval from diagnosis of CAT. The first month of treatment of VTE with anticoagulant therapy is considered a high-risk period for occurrence of recurrent bleeding and thrombosis, with a higher rate of VTEs recurrence in patients with acute VTE. Anticoagulant therapy in patients with mild thrombocytopenia (platelets more than 50×10^9/L) has been associated with a low bleeding risk. Modification in anticoagulant therapy are generally recommended when platelets are 25-50 $\times$ 10^9/L (severe thrombocytopenia), since the risk of bleeding increases below this threshold. Additional factors associated with higher bleeding risk, include a history of prior major bleeding, the type of haematological disease, treatment influenced management as well as increasing prothrombin time, creatinine and bilirubin. When the platelet counts are below 25 $\times$ 10^9/L (very severe thrombocytopenia), discontinue anticoagulant treatment. The full dose of antithrombotic therapy must be restarted, if the indication persists even between cycles of treatment once the platelet count is consistently above the threshold for full antithrombotic medication [3].

Treatment of CAT in Patients with Mild Thrombocytopenia

Full-dose anticoagulant treatment is recommended by current guidelines in patients with mild thrombocytopenia (platelet count more than 50×10^9/L) and acute VTE with high-risk features for VTE progression. Platelet transfusions are added if the platelet count are less than 50 $\times$ 10^9/L [5]. Therapeutic-dose anticoagulation is generally considered safe in these patients. The type and dose of anticoagulant is recommended in accordance with patients without thrombocytopenia [1].

Treatment of CAT in Patients with Severe Thrombocytopenia

Two main approaches are suggested by the International Society on Thrombosis and Haemostasis guidelines for managing cancer patients with severe degree of thrombocytopenia and high risk for CAT: a) complete anticoagulation with transfusion support if necessary, or b) dose-modified anticoagulation (50% of the prophylactic dose of low-molecular-weight heparin, LMWH). No significant difference in bleeding or recurrent thrombosis between full dose and modified dose anticoagulation groups was found by Cancer-Associated Venous Thrombosis and Thrombocytopenia and the United Kingdom study. However, The North American Thrombocytopenia Related Outcomes with Venous thromboembolism study demonstrated a significantly lower risk of bleeding events in those receiving modified dose anticoagulation when compared to those receiving full dose anticoagulation, without an increased risk of VTE recurrence [4]. Reduction of LMWH dose by 50% or prophylactic LMWH doses are recommended in acute VTE patients with a lower risk for thrombus progression and in patients with non-acute VTE [3]. Direct oral anticoagulants (DOACs) should currently be avoided in patients with platelets less than 50×10^9/L. There is lack of data on their use in this setting. In addition, the increased bleeding risk with prophylactic LMWH doses makes DOACs a less safe option in such cases [3].

Inferior Vena Cava (IVC) Filters

IVC filters are associated with a high rate of side effects and complications, such as local bleeding, DVT and dislocation. IVC filters has to be used on a case by-case basis in the following situations: a) patients with acute VTE and are at high risk for clot progression or PE recurrence or b) in the presence of absolute contraindications for anticoagulation, including those having severe persistent thrombocytopenia or having active bleeding. Filters should be considered in selected high-risk patients only for a limited period until therapeutic anticoagulation is feasible [6].

Venous Thrombosis at Atypical Sites

i. Patients having cancer-associated thrombosis of splanchnic vein and concurrent severe thrombocytopenia should be treated on a case-by-case basis, in line with recommendations for treatment of VTE at typical sites with low or intermediate risk for VTE progression. These patients are preferably treated with an intermediate or prophylactic dose of anticoagulation until platelet count recovery and rise of platelets above 50 x 10^9/L [6].

ii. According to available guidelines, treatment of catheter-related thrombosis (CRT) is suggested to be based on treatment of VTE at low or intermediate risk for VTE progression and/or recurrence. Reduced-dose anticoagulation is suggested for patients with CRT and platelet counts less than 50 x10^9/L and temporary discontinuation of anticoagulants when the platelets are less than 25 x10^9/L [1]. The current guideline recommends catheter removal in the presence of infection, completion of therapy or malfunction of the catheter only [6]. A previous consensus-based decision suggested that patients must be on anticoagulation for at least 3 to 5 days before central venous catheter removal following an acute ischaemia of CRT for UE-DVT, not evidence-based [6].

iii. It is suggested to use modified dose of anticoagulation primarily in patients with VTE and thrombocytopenia after HSCT. Resuming adequate anticoagulation (reduced dose, at platelets 25- 50x10^9/L; therapeutic dose, at platelets more than 50 x

How to cite this article: Nahla A. M. Hamed. Treatment of Cancer-Associated Venous Thromboembolism in Thrombocytopenic Cancer Patients. Canc Therapy & Oncol Int J. 2025; 29(1): 556251. DOI: 10.19080/CTOIJ.2025.29.556251

10^9/L) is suggested after platelet reconstitution. Reduced risk of VTE recurrence was observed in patients resuming anticoagulant therapy after engraftment [1].

How Anticoagulants Should be Chosen for CAT Patients?

Current practice shifted towards use of LMWH and DOACs because vitamin K antagonists (VKAs) need regular laboratory monitoring, as well as they have narrow therapeutic range, need dietary restrictions, and their drug-drug interactions with commonly used chemotherapeutic agents such as 5-fluorouracil and their less predictable pharmacology [2]. VKAs is used only when neither DOAC nor LMWH are considered appropriate [7]. American Society of Haematology guidelines suggested that VKAs might be superior to DOACs and LMWH in patients with severe renal insufficiency (creatinine clearance less than 30 mL/min) [6].

Many existing guidelines including the CHEST, Canadian Expert Consensus, and National Comprehensive Cancer Network (NCCN) recommend DOACs primarily for CAT patients then LMWH as an alternative. It is advisable to use LMWH as an alternative to DOAC in specific circumstances, including potential drug malabsorption (e.g., after gastrointestinal resection), impairment of hepatic or renal function, a high risk of haemorrhage (thrombocytopenia), a history of bleeding, tumors located in the genitourinary tract, gastrointestinal tract, or intracranial region, active mucosal lesions, and unresected mucosal tumors, or when administered together with antiplatelet therapy or concurrent medications that may lead to significant drug-drug interactions [7]. particularly inducers and inhibitors of P-glycoprotein and cytochrome P450 3A4. Drugs known to interact with DOACs are immune-modulating agents (dexamethasone, cyclosporine, tacrolimus), topoisomerase inhibitors (etoposide), tyrosine kinase inhibitors (nilotinib), antimitotic agents (vinblastine, paclitaxel), hormonal agents (bicalutamide), and anthracyclines (idarubicin) [6]. Patients with Child–Pugh class B or C hepatic function should not take drugs such as rivaroxaban, apixaban and edoxaban that are highly dependent on hepatic metabolism [6].

Appropriate Duration of Anticoagulation

The recurrence rate of VTE within the first 6 months after the index event (4.5%) exceeded that between 6 to 12 months (1.1%) as shown in the TiCAT trial. The 2024 NCCN guidelines recommended that the duration of anticoagulant therapy should not be less than 3 months or continue as long as the cancer is active or undergoing treatment [7]. For symptomatic catheter-associated DVT, anticoagulant treatment is considered for at least 3 months or as long as the catheter is in place [8]. American Society of Haematology Guidelines recommended anticoagulant therapy for more than six months [7]. For non-catheter-associated DVT or PTE, long-term anticoagulation was advised when the cancer is active, being treated, or if risk factors for recurrence persist [7]. Active cancer is defined as one of the following: cancer diagnosed within the previous 6 months; cancer for which treatment had been administered within 6 months; cancer that is not in complete remission, recurrent or regionally advanced or metastatic cancer [6] The previously mentioned guidelines included general recommendations relevant to all populations, as well as indication-specific for certain subgroups [6]. Generally, decisions regarding long-term therapy should be regularly evaluated, balancing benefits against risks, including bleeding, recurrence risk, cost, patient preference, and expected survival [7].

Future Direction

Factor XI inhibitors are being evaluated for prevention and treatment of VTE in various settings. Abelacimab is a fully human monoclonal antibody that acts by inhibiting factor XI activation and activity. It is currently under study in randomized clinical trials for treating acute VTE in patients with active cancer [2].

Conclusion

The following factors must be considered when treating cancer-associated thrombosis in thrombocytopenic cancer patients: patient's risk for recurrent thromboembolism, patient's risk for bleeding as well as the degree and duration of thrombocytopenia. The risk of thrombosis must be balanced versus the risk of bleeding when treating CAT in patients having thrombocytopenia.

References

1. Moik F, Ay C (2024) Treatment of VTE in the thrombocytopenic cancer patient. Hematology Am Soc Hematol Educ Program 1: 259-269.
2. Dave HM, Khorana AA (2024) Management of venous thromboembolism in patients with active cancer. Cleve Clin J Med 91(2): 109-117.
3. Leader A, Hofstetter L, Spectre G (2021) Challenges and advances in managing thrombocytopenic cancer patients. J Clin Med 10(6): 1169.
4. Tan Y, Carrier M, Curry N, Desborough M, Musgrave K, et al. (2024) Cancer complicated by thrombosis and thrombocytopenia: still a therapeutic dilemma. Bleeding, Thrombosis Vas Bio 3(s1): 115.
5. Abbas U, MacKenzie R, Khan U, Fatima R, Wang TF, et al. (2025) Anticoagulant management of cancer-associated thrombosis and thrombocytopenia: a retrospective chart review. Res Pract Thromb Haemost 9: e102684.
6. Falanga A, Leader A, Ambaglio C, Bagoly Z, Castaman G, et al. (2022) EHA guidelines on management of antithrombotic treatments in thrombocytopenic patients with cancer. HemaSphere 6: e750.
7. Wan T, Song J, Zhu D(2025) Cancer-associated venous thromboembolism: a comprehensive review. Thrombosis J 23:35.
8. National Comprehensive Cancer Network (2025) Cancer-associated venous thromboembolic disease.

How to cite this article: Nahla A. M. Hamed. Treatment of Cancer-Associated Venous Thromboembolism in Thrombocytopenic Cancer Patients. Canc Therapy & Oncol Int J. 2025; 29(1): 556251. DOI: 10.19080/CTOIJ.2025.29.556251

DOI: 10.19080/CTOIJ.2025.29.556251

How to cite this article: Nahla A. M. Hamed. Treatment of Cancer-Associated Venous Thromboembolism in Thrombocytopenic Cancer Patients. Canc Therapy & Oncol Int J. 2025; 29(1): 556251. DOI: 10.19080/CTOIJ.2025.29.556251