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Variability in Management of Hematologic Malignancy Patients with Venous Thromboembolism and Chemotherapy-Induced Thrombocytopenia

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Venous thromboembolic disease (VTE) is a common complication of hematologic malignancy. The prolonged periods of thrombocytopenia experienced by patients who receive intensive chemotherapy and/or undergo hematopoietic stem cell transplant (HSCT) do not appear to provide protection against VTE; the incidence of symptomatic VTE may be as high as 5% by day 180 post HSCT.¹

The International Society on Thrombosis and Haemostasis (ISTH) has suggested an empiric cut-off of 50,000/uL as the platelet threshold above which therapeutic anticoagulation is “safe”. Accordingly, some guidelines recommend that platelet transfusions be used to maintain a platelet count above this threshold if therapeutic anticoagulation is warranted.² However, these recommendations are not based on high-quality evidence and the risks of multiple platelet transfusions are not trivial.

We surveyed 30 physicians (ten specializing in hematologic malignancies, ten specializing in nonmalignant hematology and ten transfusion medicine specialists) in nineteen different academic centers across the US and Canada. All participants were asked to specify the platelet count above which they would be comfortable having a patient receive either therapeutic- or prophylactic-dose anticoagulation (Figure). In addition to these questions, clinical hematologists were also asked to report their preferred management approach for 3 different case scenarios (Table).

Twenty-four of the 30 physicians (80%) responded to the survey: (seven transfusion medicine specialists, seventeen hematologists). Two out of seven (29%) of the transfusion medicine specialists had >20 years of post-fellowship experience and 29% had 10–20 years. Twenty-four percent of the 17 hematologists had > 20 years of post-fellowship experience and 47% had 10–20 years.

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Authorship and Conflict of Interest

B.T.S. designed research, performed research, analyzed data and wrote the paper. T.G. designed research. E.E. designed research and analyzed data. D.A.G. designed research. The authors have no relevant conflicts of interest to report.

With regard to platelet transfusions for therapeutic anticoagulation, fourteen out of sixteen (88%; 95% CI 62–98%) clinical hematologists favored a threshold of 50,000/ μ L as per the ISTH guidelines. Three out of seven (43%, 95% CI 6.2–80%) transfusion medicine however, were comfortable with a lower threshold of 25,000/ μ L (Figure 1A). Both groups favored a lower platelet transfusion threshold (20,000–30,000/ μ L) for patients receiving prophylactic dose anticoagulation (Figure 1B).

In response to the clinical scenarios, hematologists favored withholding anticoagulation, pending platelet recovery, for catheter-associated thrombosis but indicated that they would transfuse to a platelet threshold of 50,000/ μ L in order to administer therapeutic anticoagulation for acute symptomatic VTE. For the management of symptomatic VTE in a patient who could not achieve a platelet count of 50,000/ μ L, with most respondents indicating a preference to decrease the transfusion threshold to 20,000/ μ L rather than to decrease intensity of anticoagulation or to hold anticoagulation in favor of IVC filter placement (Table).

In conclusion, our survey results revealed a marked degree of variability in the approach to management of anticoagulation in patients with VTE and treatment-related thrombocytopenia. A lower platelet transfusion threshold was favored by more transfusion medicine specialists than hematologists who responded to our survey, but there was no clear consensus in either group. In each case scenario, a variety of different strategies were considered acceptable by clinical hematologists. In light of the current paucity of evidence to guide management in these patients, our findings support the need for prospective trials to better define the risks and benefits of different management strategies for thrombocytopenic patients with hematologic malignancy who have been diagnosed with, or are at risk of acute thrombosis.

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A. Therapeutic dose anticoagulation

B. Prophylactic dose anticoagulation

Figure.

Recommended platelet transfusion thresholds for therapeutic and prophylactic dose anticoagulation

Table

Case Scenario Survey of Malignant and Nonmalignant Hematologists (n = 17)

Case 1: 54 year old woman with AML, incidentally noted to have a catheter-associated thrombosis on chest CT performed for respiratory symptoms on day 3 of induction chemotherapy, platelet count of 15,000. Catheter removal/exchange is not an option. Which of the following would best describe your approach to managing this patient's thrombosis:	
Answer options	Responses
Start full dose anticoagulation, maintain platelet count >50,000/uL with transfusions as needed	29.4%
Start full dose anticoagulation, maintain platelet count >20,000/uL with transfusions as needed	5.9%
Start prophylactic dose anticoagulation, maintain platelet count >20,000/uL with transfusions as needed	23.5%
Keep the line but postpone anticoagulation until platelet count increases	41.1%
Remove the central venous catheter and withhold anticoagulation	0.0%
Case 2a: 62 year old man day +4 after allogeneic hematopoietic cell transplant for myelofibrosis, found to have a segmental PE on CT performed for new onset dyspnea and mild tachycardia without hypoxia. His platelet count is 10,000. Lower extremity compression ultrasonography reveals a proximal DVT of the right leg. Which of the following would best describe your approach to managing this patient's thrombosis:	
Start therapeutic anticoagulation, transfuse to maintain platelet count >50,000/uL	52.9%
Start therapeutic anticoagulation, transfuse to maintain a platelet count >20,000/uL	17.7%
Place an IVC filter and postpone anticoagulation until platelet count spontaneously recovers to >50,000/uL	29.4%
Case 2b: You start the patient on therapeutic anticoagulation with resolution of dyspnea and tachycardia, but after 48 hours and 3 attempts at platelet transfusion, a platelet count above 30,000/uL has not been achieved. There is no evidence of mucocutaneous bleeding. Which of the following most closely describes your approach to management:	
Continue therapeutic anticoagulation, transfuse at least 1 unit of platelets daily until platelet count >50,000/uL (plan to hold all anticoagulation if platelet count is <20,000/uL	17.7%
Continue therapeutic anticoagulation but transfuse platelets for count <20,000/uL	35.3%
Decrease anticoagulation to prophylactic dose, transfuse platelets for count <20,000/uL	23.5%
Hold all anticoagulation until platelet count >50,000/uL	0.0%
Place an IVC filter and hold all anticoagulation until platelet count >50,000/uL	23.5%