

# Patterns of Venous Thromboembolism Prophylaxis During Treatment of Acute Leukemia: Results of a North American Web-Based Survey

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## Abstract

**Venous thromboembolism commonly occurs in patients with acute leukemia. We surveyed North American providers, and of the 151 responses, approximately half reported using pharmacologic anticoagulation during induction and consolidation treatment, while 15% did not use prophylaxis and 36% used mechanical methods and ambulation. These data highlight the need for further investigation and development of evidence-based guidelines for prophylaxis in this at-risk population.**

**Background:** Venous thromboembolism (VTE) occurs in 2% to 12% of patients with acute leukemia (AL) despite disease- and therapy-associated thrombocytopenia, and it can be associated with significant morbidity and mortality. Because of the few high-quality studies, there are no evidence-based guidelines for VTE prophylaxis in this patient population. We sought to determine the spectrum of practice regarding prevention of VTE in patients with AL during induction and consolidation therapies. **Methods:** We conducted a 19-question Web-based survey directed at North American providers caring for these patients. One hundred fifty-one of 215 responses received were eligible for analysis, with a response rate of 20.9% among physicians who treated leukemias. **Results:** Overall, 47% and 45% of providers reported using pharmacologic VTE prophylaxis during induction and consolidation phases, respectively. Approximately 15% of providers did not provide any VTE prophylaxis, while 36% used mechanical methods and ambulation. Among providers who did not recommend pharmacologic prophylaxis, the most commonly cited reasons were the perceived high risk of bleeding (51%), absence of data supporting use (38%), and perceived low risk of VTE (11%). **Conclusion:** Large, prospective studies are needed to define the safest and most effective approach to VTE prevention in patients with AL.

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## Introduction

Hematologic malignancies are associated with a significant risk of venous thromboembolism (VTE), comparable to that of higher-risk solid tumors including brain, pancreatic, and ovarian cancer.<sup>1</sup> Studies of acute leukemia (AL) patients have demonstrated an incidence of VTE ranging from 2.2% to 12%, with thrombotic events occurring before diagnosis, at the time of diagnosis, or during treatment.<sup>2-7</sup> The pathogenesis of VTE in AL patients is multifactorial. Leukemic cells produce procoagulant, proteolytic, and fibrinolytic factors including tissue factor and cancer procoagulant.<sup>8-10</sup> Blast cells secrete proinflammatory cytokines such as tumor necrosis factor alpha and interleukin 1 $\beta$ , whose downstream effects lead to a thrombotic

tendency.<sup>8-10</sup> Chemotherapy also contributes to a prothrombotic state via direct endothelial damage and destruction of leukemic cells as well as through liver injury causing reduced synthesis of natural anticoagulants (protein C, protein S, antithrombin).<sup>8-10</sup> In particular, L-asparaginase decreases production of antithrombin.<sup>10</sup> Indwelling central venous catheters (CVC), immobility, infections, and use of high-dose steroids are other thrombotic risk factors.<sup>11</sup>

Given prolonged thrombocytopenia during induction and consolidation therapies, pharmacologic prophylaxis and treatment of VTE can be challenging. This underscores the importance of developing safe and effective methods of VTE prevention in this at-risk population. To date, there have been no large, prospective studies addressing VTE prophylaxis in AL patients, nor are there evidence-based guidelines to assist clinicians. On the basis of our experience and the lack of consensus guidelines, we hypothesized that there would be a wide range in provider practice regarding methods of VTE prevention in patients with AL. To determine the current individual practices in North America, we devised a Web-based survey of VTE prophylaxis practice among clinicians caring for patients with AL.

## Methods

To determine current practices of VTE prophylaxis among health care providers, we devised an anonymous 19-question Web-based survey (Supplemental Figure 1 in the online version) utilizing SurveyMonkey software (<http://SurveyMonkey.com/>). The survey was approved by the Johns Hopkins institutional review board and distributed by e-mail to members of Eastern Cooperative Oncology Group—American College of Radiology Imaging Network (ECOG-ACRIN) centers on October 22, 2014, by the ECOG-ACRIN Clinical Education and Awareness Team. Four reminders were sent at 2-week intervals, with the survey closing on December 8, 2014. The collected data were de-identified and stored on a password-protected computer and analyzed using descriptive statistics.

## Results

The survey was distributed to an e-mail list that had 6446 recipients, of whom 3628 were physicians. Of those physicians, 723 have treated leukemia patients. We received a total of 215 responses and included responses only from clinicians who reported directly managing care of leukemia patients. Of the total 215 respondents, 64 were excluded for the following reasons: 52 respondents did not directly manage medical care of AL patients, 3 referred AL patients to other centers, 5 left blank responses to all questions regarding VTE prophylaxis, 1 was a duplicate entry, and 3 described their position as support or office staff.

On the basis of the 151 analyzed responses, the response rate for all physicians was 4.2% and the response rate for physicians who treat leukemia was 20.9%. The final sample included 151 responses from clinicians based in the United States ( $n = 147$ ) and Canada ( $n = 4$ ), representing 88 different institutions and 37 states or provinces. Sixty-four percent of respondents were men, and 84% were between the ages of 31 to 60 years. Ninety-four percent were board certified in hematology and/or oncology. The complete characteristics of the survey population are listed in Table 1.

Provider patterns of VTE prophylaxis for AL during induction and consolidation therapies excluding acute promyelocytic leukemia

**Table 1** Characteristics of Survey Respondents

Characteristic	n (%)
<b>Country of Practice</b>	
United States	147 (97)
Canada	4 (3)
<b>Gender</b>	
Male	96 (64)
Female	55 (36)
<b>Age</b>	
20-30 years	1 (1)
31-40 years	41 (27)
41-50 years	46 (30)
51-60 years	40 (27)
61-70 years	18 (12)
71-80 years	5 (3)
<b>Job Description</b>	
Clinical researcher	77 (51)
Clinician	53 (35)
Clinical educator	7 (5)
Clinician + researcher	10 (7)
Translational researcher	2 (1)
Basic science researcher	2 (1)
<b>Time After Fellowship Training</b>	
0-5 years	38 (25)
6-10 years	29 (19)
11-20 years	34 (23)
21 years or more	45 (30)
Other	5 (3)
<b>Type of institution of practice</b>	
University affiliated/public	103 (68)
Private	40 (27)
Veterans' administration	2 (1)
Other	6 (4)
<b>No. of AL Patients Treated Yearly (Institution)</b>	
<25	35 (23)
25-50	29 (19)
51-100	33 (22)
101-150	34 (23)
≥151	16 (11)
Unsure	4 (3)
<b>No. of AL Patients Treated Yearly (Provider)</b>	
<25	74 (49)
25-50	55 (36)
51-100	15 (10)
101-150	4 (3)
≥151	3 (2)
<b>Presence of VTE Prophylaxis Order Set for AL Patients</b>	
Yes	36 (24)
No	105 (70)
Unsure	10 (7)

Abbreviations: AL = acute leukemia; VTE = venous thromboembolism.

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