Received: 4 August 2023 | Revised: 16 November 2023 | Accepted: 20 November 2023

https://doi.org/10.1016/j.rpth.2023.102286

RESEARCH LETTER

Implementation of a cancer-associated thrombosis prevention program at a rural cancer center

1 | INTRODUCTION

Cancer-associated thrombosis (CAT) is the second leading cause of death in patients with cancer and is preventable [1,2]. Venous thromboembolism (VTE) risk assessment and prophylaxis in high-risk patients who are at low risk of bleeding are recommended for outpatients with cancer initiating therapy [3–6]. Given that nearly 1 in 5 patients with cancer live in rural areas in the United States, the study of effective models of VTE prevention in these settings is imperative [7]. To effectively reduce VTE events in patients with cancer at rural clinics, an increased understanding of the barriers to CAT prevention is needed.

CAT prevention in community cancer centers with a predominately rural population has not been well studied [8,9]. A successful model for guideline implementation (the Vermont model) was based in an academic setting [9]. The program used a multidisciplinary approach, which included hematology and thrombosis specialists, pharmacists, and nursing staff, who were involved in various aspects of VTE education and risk assessment. Our objectives were to study the impact of implementation of this effective model for CAT prevention in a rural cancer center and to assess barriers to implementation.

2 | METHODS

2.1 | CAT prevention program implementation

We deployed a prospective intervention program (the Vermont model) to prevent CAT at a rural cancer center, Central Vermont Medical Center [9]. Central Vermont Medical Center serves a rural catchment (>98% rural), offering services of medical hematology and oncology, surgery, and radiation oncology through the National Life Cancer Treatment Center.

Forty-seven providers across 9 rural cancer clinics in Maine, Vermont, and New Hampshire were surveyed via email in advance of program deployment to determine potential and perceived barriers. The survey response rate was 9%. Barriers were also assessed qualitatively following the completion of the study. Resources developed for the Vermont model were modified in advance and included transformation of the electronic health record (EHR) screening tool to a paper tool and printed education materials for patients and providers. An integrated workflow with existing cancer clinic processes was developed. Adaptations made for implementation in the rural setting included use of paper-based VTE risk scoring, VTE assessment and education provided by advanced practice providers and physicians (not primary nursing as in the original model), and final decision making regarding prophylactic anticoagulation made by the oncologist or oncology advanced practice provider without pharmacy or hematology input.

The cancer patient population characteristics and outcomes were assessed via retrospective chart review. VTE risk assessment, education, and prophylaxis were compared for 6.5 months before and after program implementation. Patients were excluded if they received hormonal therapy only or had a confirmed diagnosis of VTE at the time of initiation of cancer therapy.

2.2 | Data collection

Data collection was conducted by chart review, including Khorana risk score elements [10]. Because a risk assessment was not performed on all patients, identification of high-risk patients is reported for those patients identified via chart review and Khorana risk score calculation. High risk of VTE was defined as ≥3 points on either the Khorana or PROTECHT score.

2.3 | Statistical analysis

Means and SDs were used to summarize data for continuous variables, and percentages were used to describe categorical variables. Comparisons between continuous variables were performed using a 2-sample independent *t*-test. Associations between categorical variables were examined using chi-squared tests or Fisher's exact tests. When there were no patients in a category (value of 0), 0.5 was inserted for 0, and the association was tested using Fisher's exact test. Statistix 8 (Analytical Software) was used to perform the statistical analyses.

2.4 | Institutional review board

This study was exempt from review by the University of Vermont Institutional Review Board, and patient informed consent was waived.

TABLE 1 Characteristics of patients initiating cancer-directed therapy at a rural cancer center.

Characteristic	Before implementation (n = 82)	After implementation (n = 69)	P value
Age (y), mean (SD)	65.4 (12.5)	67.8 (11.3)	.22[a]
Sex, male, n (%)	50 (61.0)	36 (52.2)	.28[b]
BMI (kg/m^2), mean (SD)	27.8 (6.9)	27.8 (7.4)	.99[a]
Medical history, n (%)			
Prior VTE diagnosis	7 (8.5)	5 (7.2)	.77[b]
Bleeding history	1 (1.2)	0	1.00[c,d]
Reason for therapy, n (%)			.50[b]
New cancer	60 (73.2)	45 (65.2)	
Recurrent/ progressive disease	17 (20.7)	17 (24.6)	
Unknown	5 (6.1)	7 (10.1)	
Cancer stage, n (%)			
Stage 1	8 (9.8)	9 (13.0)	.35[b]
Stage 2	7 (8.5)	12 (17.4)	
Stage 3	24 (29.3)	19 (27.5)	
Stage 4	37 (45.1)	27 (39.1)	
Unclassified	6 (7.3)	2 (2.9)	
VTE risk factors, n (%)			
Very high–risk cancer type	3 (3.7)	1 (1.4)	.63[c]
High-risk cancer type	30 (36.6)	29 (42.0)	.50[b]
Low hemoglobin concentration (<10 g/dL)	9 (11.0)	9 (13.0)	.70[b]
High BMI (≥35)	10 (12.2)	7 (10.1)	.69[b]
High platelet count (≥350 × 10^9/L)	10 (12.2)	9 (13.0)	.88[b]
High leukocyte count (>11 × 10^9/L)	7 (8.5)	11 (16.0)	.16[b]
Gemcitabine	8 (9.8)	3 (4.4)	.23[c]
Platinum-based therapy	43 (52.4)	27 (39.1)	.10[b]
Khorana risk score (VTE risk), n (%)			.60[b]
Low risk (0)	16 (19.5)	16 (23.2)	
Intermediate risk (1-2)	52 (63.4)	45 (65.2)	
High risk (≥3)	14 (17.1)	8 (11.6)	

Percentages were calculated for count data based on preimplementation and postimplementation participants/patients.

BMI, body mass index; VTE, venous thromboembolism.

[a]Two-sample independent t-test.

[b]Chi-square test for independence.

[c]Fisher's exact test (P values for the 2-tailed test are reported).

[d]0.5 was inserted for the 0 value.

3 | RESULTS

3.1 | Patient characteristics

Characteristics of the patient population are presented in Table 1. The preimplementation (n = 82) and postimplementation (n = 69) cohorts were not significantly different in age (65.4 vs 67.8 years, P = .22), sex (61% male vs 52% male, P = .28), body mass index (27.8 vs 27.8, P = .99), and disease stage (stage I, 9.8% vs 13%; stage II, 8.5% vs 17.4%; stage III, 29.3% vs 27.5%; stage IV, 45.1% vs 39.1%; unclassified, 7.3% vs 2.9%; P = .35). Prior history of VTE diagnosis and bleeding history were low in both cohorts (8.5% in the preimplementation cohort and 7.2% in the postimplementation cohort).

VTE risk factors were similar in the cohorts before and after program implementation (Table 1). Close to half of the patients had a cancer type with a high or very high risk of VTE in the preimplementation (40.3%) and postimplementation (43.4%) cohorts. Patients' VTE score profiles were similar (P = .60) before and after implementation, with most patients, 63.4% (preimplementation cohort) and 65.2% (postimplementation cohort), having an intermediate risk of VTE. Less than a fifth, 17.1% (preimplementation cohort) and 11.6% (postimplementation cohort), were identified as being at high risk of VTE.

3.2 | Impact of CAT prevention program

VTE risk assessment increased from 1.2% to 39.1% in patients following the implementation of the CAT prevention program (P < .000001) (Table 2). No patients were documented as high risk of VTE by the clinical team prior to implementation despite chart review identifying 17.1% as high risk for VTE (data not shown). After implementation, 75% (6 of 8) of the patients with a high risk of VTE were documented as high risk by the clinical team (Table 2).

TABLE 2 Venous thromboembolism risk assessment, education, and prophylaxis after cancer-associated thrombosis prevention program implementation.

Outcomes	All patients			Patients with HR VTE		
	Before implementation (*n* = 82)	After implementation (*n* = 69)	*P* value	Before implementation (*n* = 14)	After implementation (*n* = 8)	*P* value
Documented VTE risk assessment, *n* (%)	1 (1.2)	27 (39.1)	<.000001	0	6 (75.0)	.0004[a]
VTE education, *n* (%)	5 (6.1)	26 (37.7)	<.000001	1 (7.1)	5 (62.5)	.011
VTE prophylaxis, *n* (%)	0	3 (4.3)	.097[a]	0	1 (12.5)	.38[a]

All *P* values were calculated using Fisher's exact test (*P* values for the 2-tailed test are reported). Risk score missing data were not considered.
HR VTE, high risk of venous thromboembolism; VTE, venous thromboembolism.
[a]0.5 was inserted for the 0 value.

Patient education on thrombosis risks and prevention predominantly occurred during the prechemotherapy education session. The documentation of VTE-specific patient education increased from 6.1% to 37.7% ($P < .000001$), showing a significant impact of the program in the total patient population (Table 2). For those at the highest risk of VTE, the CAT prevention program increased the percentage of all patients at high risk of VTE receiving VTE education from 7.1% to 62.5%, $P = .011$ (Table 2).

Primary prophylaxis for VTE was not prescribed for any patient initiating cancer-directed therapy prior to program implementation. After program implementation, 12.5% of all high-risk patients received VTE prophylaxis ($P = .38$). For high-risk patients identified by the clinical team as high risk of VTE (not via chart review), 16.7% (1 of 6) of those patients were prescribed VTE prophylaxis (data not shown).

3.3 | Qualitative assessment of the Vermont model program implementation

In the rural cancer setting, the leading factor identified to improve VTE education and risk assessment rates was incorporation of the risk assessment tool into the EHR. In contrast to VTE education and assessment rates, program implementation had a modest impact on patients prescribed anticoagulation prophylaxis. This compares to 93.8% of high-risk patients who received VTE prophylaxis in the initial Vermont model implemented at an academic cancer center [9]. Patient nonacceptance of anticoagulation therapy was not identified by the treatment team as a reason for low VTE prophylaxis rates. Barriers to prescription of anticoagulation therapy included concerns regarding potential copays and concerns regarding bleed risk. The limited pharmacy constraints and lack of hematology/anticoagulation-specific expertise in the rural clinic remain a barrier to implementation of VTE prophylaxis guidelines.

4 | CONCLUSIONS

Rural cancer centers can effectively increase rates of VTE prevention guideline adherence using a low-resource implementation model. Major barriers to implementation included limited resources for EHR integration and provider time constraints. VTE prophylaxis in the high–VTE-risk population was lower than seen in prior studies, in part due to perceived increased bleed risk and copay concerns. Additional strategies are needed to increase the prescription of anticoagulation for at-risk patients.

ACKNOWLEDGMENTS

The authors would like to acknowledge the clinical care team members and administrative leadership at the Central Vermont Medical Center Cancer Center who supported this study.

FUNDING

The research reported here was supported by grant U54 GM115516 from the National Institutes of Health for the Northern New England Clinical and Translational Research Network.

ETHICS STATEMENT

This study was exempt from review by the University of Vermont Institutional Review Board, and patient informed consent was waived.

AUTHOR CONTRIBUTIONS

Study design and implementation: C.E.H. and E.T. Data collection: H.M.F. Data analysis and statistical evaluation: H.M.F. and S.K. Data interpretation: H.M.F., S.K., and C.E.H. Writing/approving manuscript: all authors.

RELATIONSHIP DISCLOSURE

There are no competing interests to disclose.

Heather M. Feldman[1]
Eswar Tipirneni[2]
Shamima Khan[3]
Steven Ades[4]
Allison Holm[5]
Chris E. Holmes[6]

[1]University of Vermont Cancer Center, University of Vermont, Burlington, Vermont, USA
[2]Texas Oncology, San Antonio, Texas, USA
[3]Division of Public Health, Larner College of Medicine, University of Vermont, Burlington, Vermont, USA
[4]Division of Hematology and Oncology, University of Vermont Cancer Center, University of Vermont, Burlington, Vermont, USA
[5]Data Management Office, University of Vermont Health Network, Burlington, Vermont, USA
[6]Division of Hematology and Oncology, Larner College of Medicine, University of Vermont, Burlington, Vermont, USA

Handling Editor: Prof Cihan Ay

Correspondence
Chris E. Holmes, Division of Hematology and Oncology, University of Vermont, 111 Colchester Avenue, Given Building, Burlington VT 05401, USA.
Email: ceholmes@uvm.edu

TWITTER

Chris E. Holmes @ChrisHolmesMD

REFERENCES

[1] Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. *J Thromb Haemost*. 2007;5:632–4.
[2] Streiff MB. Thrombosis in the setting of cancer. *Hematology Am Soc Hematol Educ Program*. 2016;2016:196–205.
[3] Elshoury A, Schaefer JK, Lim MY, Skalla DP, Streiff MB. Update on guidelines for the prevention of cancer-associated thrombosis. *J Natl Compr Canc Netw*. 2022;20:1–8.
[4] Farge D, Frere C, Connors JM, Ay C, Khorana AA, Munoz A, et al. 2019 International clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer. *Lancet Oncol*. 2019;20:e566–81.
[5] Key NS, Khorana AA, Kuderer NM, Bohlke K, Lee AYY, Arcelus JI, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO clinical practice guideline update. *J Clin Oncol*. 2020;38:496–520.
[6] Siragusa S, Armani U, Carpenedo M, Falanga A, Fulfaro F, Imberti D, et al. Prevention of venous thromboembolism in patients with cancer: guidelines of the Italian Society for Haemostasis and Thrombosis (SISET)(1). *Thromb Res*. 2012;129:e171–6.
[7] Kirkwood MK, Hanley A, Bruinooge SS, Garrett-Mayer E, Levit LA, Schenkel C, et al. The state of oncology practice in America, 2018: results of the ASCO practice census survey. *J Oncol Pract*. 2018;14:e412–20.
[8] Ades S, Holmes CE. Implementing guidelines to prevent cancer associated thrombosis: how can we do better? *Res Pract Thromb Haemost*. 2023;7:100038. https://doi.org/10.1016/j.rpth.2023.100038
[9] Holmes CE, Ades S, Gilchrist S, Douce D, Libby K, Rogala B, et al. Successful model for guideline implementation to prevent cancer-associated thrombosis: venous thromboembolism prevention in the ambulatory cancer clinic. *JCO Oncol Pract*. 2020;16:e868–74.
[10] Verso M, Agnelli G, Barni S, Gasparini G, LaBianca R. A modified Khorana risk assessment score for venous thromboembolism in cancer patients receiving chemotherapy: the Protecht score. *Intern Emerg Med*. 2012;7:291–2.