Received: 31 December 2019 | Revised: 9 April 2020 | Accepted: 16 April 2020

DOI: 10.1002/rth2.12361

BRIEF REPORT

Underuse of medical thromboprophylaxis in mobile elderly inpatients: The SWITCO65+ cohort

Marc Blondon MD, MS[1] | Andreas Limacher PhD[2] | Marc Righini MD[1] | Drahomir Aujesky MD, MS[3] | Marie Méan MD[4]

[1]Division of Angiology and Hemostasis, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

[2]CTU Bern, University of Bern, Bern, Switzerland

[3]Division of General Internal Medicine, Bern University Hospital, Bern, Switzerland

[4]Division of General Internal Medicine, University of Lausanne, Lausanne, Switzerland

Correspondence
Marc Blondon, Division of Angiology and Hemostasis, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland
Email: marc.blondon@hcuge.ch

Funding information
This study was supported by the Swiss National Science Foundation (grant 33CSCO-122659/139470). The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Handling Editor: Susan Kahn

Abstract

Background: Hospital-associated venous thromboembolism (HA-VTE) can be prevented by pharmacologic thromboprophylaxis. Thrombotic risk assessment models (RAMs) are essential tools to improve inadequately prescribed thromboprophylaxis. Among cases of HA-VTE, our study objectives are to explore the classifications of available thrombosis RAMs, the adequacy of thromboprophylaxis and risk factors for inadequate thromboprophylaxis.

Methods: We identified cases of HA-VTE occurring during medical hospitalizations within a multicenter Swiss venous thromboembolism (VTE) cohort (2009-2013). We calculated the proportion of VTE cases deemed at high risk with 4 VTE RAMs (Geneva, Simplified Geneva, Padua, and Improve) and the adequacy of administered pharmacologic thromboprophylaxis, and explored risk factors for underprescription of thromboprophylaxis in high-risk inpatients.

Results: Among 66 medical inpatients with HA-VTE, 60.6% had pulmonary embolism. The sensitivities of the Geneva, Simplified Geneva, Padua, and Improve RAMs were 86.4%, 80.3%, 72.7%, and 57.6%, respectively. The proportion of inadequate thromboprophylaxis was high, as 62.5%-71.1% of high-risk inpatients had not received it. Among the high-risk group according to the Simplified Geneva RAM, absence of immobilization was the only variable significantly associated with an inadequate use of thromboprophylaxis (odds ratio, 3.59; 95% confidence interval, 1.08-11.88).

Conclusions: We found a dramatically high proportion of inadequate medical thromboprophylaxis among inpatients who suffered from HA-VTE. This reinforces the need for global and local quality-improvement efforts to promote adequate use of thromboprophylaxis in elderly inpatients. Mobility may favor the underuse of thromboprophylaxis, and clinicians should stay alert to other thrombotic risk factors in mobile inpatients.

KEYWORDS

anticoagulants, hospitalization, inpatients, quality improvement, risk assessment, thrombosis, venous thromboembolism

Essentials

- The prescription of medicine to prevent abnormal blood clots in hospital should be matched to the risk .
- We evaluated use of this medicine in 66 older medical inpatients with hospital-associated VTE.
- The use of this medicine was inadequate in most inpatients.
- Mobile inpatients were at greater risk of an inadequate use of clot prevention.

1 | INTRODUCTION

Venous thromboembolism (VTE) is a recognized complication of hospitalizations. About half of deep vein thrombosis (DVT) and pulmonary embolism (PE) occurs during the hospital stay or in the 3 months thereafter.[1] This is highly relevant among older adults, who are more likely to be hospitalized and at a greater multifactorial risk of VTE.[2]

The use of pharmacologic thromboprophylaxis reduces the risk of VTE by half but remains complex, as it needs to be tailored to individual thrombotic and bleeding risks, using risk assessment models (RAMs). Hospital-based practice reports suggest that hospitalists overprescribe thromboprophylaxis among low-risk inpatients and underprescribe thromboprophylaxis among high-risk inpatients.[3,4]

Study aims were, in a contemporary cohort of older adults who had a hospital-associated venous thromboembolism (HA-VTE), to describe classifications of 4 thrombotic RAMs, the adequacy of prescription of thromboprophylaxis, and the risk factors for underprescription of thromboprophylaxis in high-risk medical inpatients.

2 | METHODS

The Swiss Cohort of Elderly Patients With Venous Thromboembolism (SWITCO65+) is a prospective multicenter cohort study of older (≥65 years) patients with acute VTE, with approval of Ethics Committees from all participating centers.[5] Briefly, between 2009 and 2012, consecutive inpatients with objectively diagnosed symptomatic pulmonary embolism (PE) or non–catheter-related lower-limb DVT were included in 9 Swiss university and nonuniversity large hospitals.

For this study, we included medical inpatients with symptomatic HA-VTE, defined as an acute objectively confirmed VTE event occurring during a hospital stay (after the day of admission). The decision to use thromboprophylaxis during the index hospital stay was at the discretion of the physician in charge, without broad use of a RAM at the time.

2.1 | Definition of variables

We evaluated the Geneva RAM,[6] the Simplified Geneva RAM (sGR),[7,8] the Padua RAM,[9] and the Improve RAM[10] (Table 1), which classify inpatients as low risk or high risk for HA-VTE. Information on previous VTE, known thrombophilia, active cancer, and body mass index was collected. To inform the reason for admission, we used the occurrence of respiratory/cardiac failure and infection during the past 3 months. For immobilization, we used a variable combining bed rest >72 hours and/or fracture/cast of the leg. Variables of hemiparesis, hemiplegia, and paraplegia, and prior varicose vein surgery were used for lower-limb paralysis and chronic vein insufficiency, respectively. Unavailable data (nephrotic syndrome and stay in intensive care unit/cardiac care unit) were assumed to be absent, given their low reported prevalence in such patients (1.6%[6] and 6.4%,[10] respectively).

In-hospital pharmacologic thromboprophylaxis was defined as prophylactic doses of unfractionated heparin, low-molecular-weight heparin (enoxaparin, nadroparin) or fondaparinux prior to the HA-VTE. Thromboprophylaxis was deemed inadequate when not used in a high-risk inpatient.

2.2 | Population

Among the 170 inpatients with HA-VTE in SWITCO65+, we excluded 21 because of therapeutic anticoagulation prior to the VTE diagnosis, and 83 surgical inpatients.

2.3 | Statistical analysis

We estimated the proportion of inpatients classified as high risk for HA-VTE by the 4 different RAMs (Table 1), reported distribution of the scores of the RAMs, and compared the proportion of use of thromboprophylaxis between low-risk and high-risk participants, according to the 4 RAMs (chi-squared test), individually or when combined. All proportions are accompanied by a 95% Wilson confidence interval (CI).

In secondary analysis, we compared the distribution of prespecified individual variables from the RAMs, bleeding- and geriatric-specific variables between cases of high-risk HA-VTE with and without adequate thromboprophylaxis (based on the sGR), using logistic regression adjusted for age and sex.

3 | RESULTS

The 66 medical inpatients with HA-VTE had a mean age of 75 years, with a low prevalence of obesity (Table 2). HA-VTE

TABLE 1 Hospital-associated VTE RAMs (items and points)

Geneva RAM Low risk 0-2 High risk ≥ 3		Simplified Geneva RAM Low risk 0-2 High risk ≥ 3		Padua RAM Low risk 0-3 High risk ≥ 4		Improve RAM Low risk 0-2 High-risk ≥ 3	
Malignancy	2	Previous VTE	3	Active cancer	3	Previous VTE	3
Myeloproliferative syndrome	2	Hypercoagulable state	2	Previous VTE	3	Thrombophilia	2
Previous VTE	2	Cancer or myeloproliferative syndrome	2	Reduce mobility (3 days)	3	Cancer	2
Hypercoagulable state	2	Cardiac or respiratory failure	2	Thrombophilia	3	Lower-limb paralysis	2
Cardiac failure	2	Acute infection or rheumatic disease	2	Recent trauma or surgery (1 mo)	2	Immobilization (7 d)	1
Respiratory failure	2	Immobilization	2	Age > 70 y	1	Age > 60 y	1
Recent stroke (<3 mo)	2	Age > 60 y	1	Cardiac or respiratory failure	1	ICU or CCU stay	1
Recent myocardial infarction (<1 mo)	2	BMI > 30 kg/m^2	1	Acute myocardial infarction or ischemic stroke	1		
Acute infection	2	Recent stroke or myocardial infarction	1	Acute infection or rheumatic disease	1		
Acute rheumatic disease	2			BMI > 30 kg/m^2	1		
Nephrotic syndrome	2			Hormonal treatment	1		
Immobilization (<30 min/d)	2						
Age > 60 y	1						
BMI > 30 kg/m^2	1						
Hormonal treatment	1						
Recent travel (>6 h)	1						
Chronic venous insufficiency	1						
Pregnancy	1						
Dehydration	1						

Abbreviations: BMI, body mass index; CCU, coronary care unit; ICU, intensive care unit; RAM, risk assessment model; VTE, venous thromboembolism.

events were PE (60.6%) and proximal (28.8%) and distal DVT (10.6%). The median duration between hospital admission and HA-VTE was 6 days, and the median length of hospitalization, including the treatment for VTE, was 23.5 days. The overall use of pharmacologic thromboprophylaxis was 34.8%. Mechanical thromboprophylaxis was seldom used (3%) and only in combination with pharmacologic thromboprophylaxis.

We found differences in the proportion of inpatients classified as high risk by the different RAMs (Table 3), varying from 57.6% for the Improve RAM to 86.4% for the sGR ($P < .001$). For the 4 RAMs, the use of pharmacologic thromboprophylaxis did not significantly differ between low-risk and high-risk inpatients. Further, when considering all 4 RAMs together, the use of thrombophylaxis was similar between inpatients with 0 high-risk scores (2/6; 33%), ≥1 high-risk scores (21/60; 35%), ≥2 high-risk scores (21/56; 38%), ≥3 high-risk scores (14/45; 31%), and all 4 high-risk scores (11/35; 31%).

According to the sGR, thromboprophylaxis was underprescribed in 36 of 57 high-risk inpatients (63.2%; 95% CI, 50.2-74.5). When we explored risk factors for this underprescription of thromboprophylaxis (Table 4), the median sGR was similar (5.0 in each group). Thromboprophylaxis was more frequently inadequately lacking in men, inpatients without recent respiratory or cardiac failure, and inpatients without recent immobilization. There was no difference according to a personal history of VTE, thrombopenia, or age-specific variables (high risk of fall). When adjusting for age and sex, absence of immobilization was significantly associated with an inadequate use of thromboprophylaxis (odds ratio [OR], 3.59; 95% CI, 1.08-11.88).

4 | DISCUSSION

In this cohort of older inpatients with HA-VTE, the use of pharmacologic thromboprophylaxis was dramatically inadequate: Most inpatients with HA-VTE, who were considered at high risk at the time of admission, did not benefit from thromboprophylaxis. When exploring potential risk factors for this finding, we found that care providers had underprescribed thromboprophylaxis to inpatients who were mobile.

In accordance with the literature, this study confirms that among inpatients who suffered from HA-VTE, the original Geneva RAM or sGR classifies more patients at high risk of VTE than the Improve RAM.[7] By consequence, the use of those 2 RAMs potentially generates a greater use of thromboprophylaxis with a greater sensitivity.[7]

Our finding of inadequate thromboprophylaxis prescription in over half of HA-VTE cases is in accordance with previous estimates. Thus, in large Swiss hospitals, up to 55% of medical inpatients had inadequate thromboprophylaxis prescription as deemed by the Geneva RAM.[6,11] Similar findings were also reported in other countries[12] and in studies focusing on medically ill hospitalized elderly patients.[13]

TABLE 2 Baseline characteristics of the 66 medical inpatients with hospital-acquired VTE

All participants (n = 66)	
Characteristic	**Median (IQR) or n (%)**
Age, y	75 (70-83)
Women	30 (46)
Obesity	10 (15)
Previous VTE	20 (30)
Known thrombophilia	2 (3)
Active cancer	20 (30)
Recent severe infection or sepsis	27 (41)
Recent acute respiratory and/or cardiac failure	13 (20)
Recent bed rest >72 h or fracture/cast of lower extremity	26 (39)
Recent stroke or myocardial infarction	7 (11)
Recent major surgery	6 (9)
Recent major bleeding	15 (23)
Platelets <150 g/L	9 (14)
Low physical activity	37 (56)
High risk of fall	42 (64)
Concomitant antiplatelet therapy	21 (32)

[a]n (%) or median (IQR).
[b]Adjusted for age and sex.
[c]Per increasing decade.

Whether immobilization is a trigger for thromboprophylaxis administration remains debated,[4,12,14] and this is further complicated by the heterogeneity of the definition of immobilization.[15] In a retrospective study of older patients hospitalized in internal medicine, low mobility was not significantly associated with adequacy of thromboprophylaxis prescription, whereas in a multicenter chart audit of 29 Canadian hospitals including consecutive patients admitted for an acute medical illness (mean age, 70 years), immobilization was independently associated with greater use of thromboprophylaxis (OR, 1.60; 95% CI, 1.45-1.77).[12] Our findings of a 3-times-greater risk of inadequate thromboprophylaxis prescription in mobile inpatients also suggests that immobilization plays an important role in the clinical decision to administer thromboprophylaxis in elderly inpatients and leads to overlooking other important HA-VTE risk factors in mobile patients.

It could be argued that all patients with VTE in our study should have received thromboprophylaxis. However, given the side effects and resources used by our current thromboprophylactic regimens, the strategy of tailoring thromboprophylaxis to a high-risk group with a high, but not perfect, sensitivity is most rational. Some improvement in RAM discrimination may come in the future from machine learning, but one should not expect perfect prediction even from very complex RAM.[16]

Strengths of this study are the prospective and multicentric design and the use of stringent, objective criteria to define VTE. We also focused on HA-VTE occurring during the hospital stay, when the prevention of thromboprophylaxis may be most efficient. Our study has 3 main limitations. First, our small study sample size limits the power to observe predictors of inadequate thromboprophylaxis. Second, the lack of a control group (participants without VTE) limited the comparative evaluation of the performance of the RAMs, that is, no estimates of specificity, discrimination, or calibration. Third, our study was not designed to analyze VTE cases occurring within 90 days after a previous hospitalization; therefore, our findings can be truly generalized only to inpatients who develop HA-VTE.

In conclusion, our findings reinforce the need for global and local quality-improvement efforts to promote an adequate use of thromboprophylaxis and limit the burden of HA-VTE in elderly medical inpatients. Mobility may favor the underuse of thromboprophylaxis, and clinicians should stay alert to other thrombotic risk factors in mobile inpatients.

TABLE 3 Characteristics of the RAMs and use of thromboprophylaxis among the 66 medical inpatients with hospital-acquired VTE

			Use of pharmacologic thromboprophylaxis, % (95% CI)		
	Median (IQR)	**Cases categorized as high risk, % (95% CI)**	**Low-risk inpatients**	**High-risk inpatients**	***P* value**
Simplified Geneva RAM	5.0 (3.0-7.0)	86 (76-92)	22 (6-55)	37 (26-50)	.39
Geneva risk RAM	4.0 (3.0-6.0)	80 (69-88)	46 (23-71)	32 (21-46)	.34
Padua risk RAM	5.0 (3.0-7.0)	73 (61-82)	28 (13-51)	38 (25-52)	.46
Improve risk RAM	3.0 (2.0-4.0)	58 (46-69)	43 (27-61)	29 (17-45)	.24

TABLE 4 Baseline characteristics of the 57 medical inpatients at high thrombotic risk according to the Simplified Geneva RAM, with the inadequate use of thromboprophylaxis

High-risk participants (n = 57)			
Characteristic	**Inadequate lack of thromboprophylaxis[a] (n = 36)**	**Use of thromboprophylaxis[a] (n = 21)**	**Odds ratio for inadequate lack of thromboprophylaxis[b] (95% CI)**
Age, y	74 (67-83)	75 (70-84)	0.62 (0.28-1.37)[c]
Women	12 (33)	13 (62)	0.39 (0.12-1.28)
Obesity	6 (17)	2 (10)	3.33 (0.51-20.0)
Previous VTE	14 (39)	6 (29)	2.94 (0.75-11.1)
Known thrombophilia	2 (6)	0 (0)	Not estimable
Active cancer	14 (39)	6 (29)	1.18 (0.33-4.17)
Recent severe infection or sepsis	16 (44)	11 (52)	0.61 (0.18-2.04)
Recent acute respiratory and/or cardiac failure	6 (17)	7 (33)	0.34 (0.09-1.32)
Recent bed rest >72 h or fracture/cast of lower extremity	12 (33)	14 (67)	0.28 (0.08-0.93)
Recent stroke or myocardial infarction	4 (11)	1 (5)	1.96 (0.19-20.0)
Recent major surgery	2 (6)	4 (19)	0.26 (0.04-1.72)
Recent major bleeding	9 (25)	4 (19)	1.61 (0.40-6.67)
Platelets <150 g/L	12 (14)	9 (14)	1.03 (0.16-6.66)
Low physical activity	21 (58)	12 (57)	1.61 (0.47-5.56)
High risk of fall	23 (64)	15 (71)	1.11 (0.30-4.17)
Concomitant antiplatelet therapy	15 (42)	5 (24)	2.78 (0.78-10.0)

[a]n (%) or median (IQR).

[b]Adjusted for age and sex.

[c]Per increasing decade.

ACKNOWLEDGMENTS

The authors thank all SWITCO65+ investigators and key personnel for their contribution: K. Jaeger, B. Frauchiger, J. Osterwalder, N. Kucher, J. Cornuz, S. Trelle, O. Bulla, C.M. Matter, M. Husmann, M. Banyai, M. Aschwanden, M. Egloff, L. Mazzolai, O. Hugli, and H. Bounameaux. Trial Registration: http://clinicaltrials.gov. Identifier: NCT00973596.

RELATIONSHIP DISCLOSURE

MB, MR, DA, and MM declare nothing to report. AL reports grants from Swiss National Science Foundation during the conduct of the study, and he is affiliated with CTU Bern, University of Bern, which has a staff policy of not accepting honoraria or consultancy fees. However, CTU Bern is involved in design, conduct, or analysis of clinical studies funded by not-for-profit and for-profit organizations. In particular, pharmaceutical and medical device companies provide direct funding to some of these studies. For an up-to-date list of CTU Bern's conflicts of interest, see http://www.ctu.unibe.ch/research/declaration_of_interest/index_eng.html.

AUTHOR CONTRIBUTIONS

MB, AL, MR, DA, and MM contributed to the concept and design of this analysis, interpreted the data, critically wrote and revised the intellectual content, and approved the final version of the manuscript. AL analyzed the data.

TWITTER

Marc Blondon @MarcBlondon

REFERENCES

1. Spencer FA, Lessard D, Emery C, Reed G, Goldberg RJ. Venous thromboembolism in the outpatient setting. Arch Intern Med. 2007;167:1471–5.
2. Engbers MJ, van Hylckama VA, Rosendaal FR. Venous thrombosis in the elderly: incidence, risk factors and risk groups. J Thromb Haemost. 2010;8:2105–12.
3. Cohen AT, Tapson VF, Bergmann J-F, Goldhaber SZ, Kakkar AK, Deslandes B, et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. Lancet. 2008;371:387–94.
4. Spirk D, Nendaz M, Aujesky D, Hayoz D, Beer JH, Husmann M, et al. Predictors of thromboprophylaxis in hospitalised medical patients. Explicit ASsessment of Thromboembolic RIsk and Prophylaxis for Medical PATients in SwitzErland (ESTIMATE). Thromb Haemost. 2015;113:1127–34.
5. Mean M, Righini M, Jaeger K, Beer HJ, Frauchiger B, Osterwalder J, et al. The Swiss Cohort of Elderly Patients With Venous Thromboembolism (SWITCO65+): rationale and methodology. J Thromb Thrombolysis. 2013;36:475–83.
6. Nendaz M, Spirk D, Kucher N, Aujesky D, Hayoz D, Beer JH, et al. Multicentre validation of the Geneva Risk Score for hospitalised medical patients at risk of venous thromboembolism. Explicit ASsessment of Thromboembolic RIsk and Prophylaxis for

Medical PATients in SwitzErland (ESTIMATE). Thromb Haemost. 2014;111:531–8.
7. Blondon M, Spirk D, Kucher N, Aujesky D, Hayoz D, Beer JH, et al. Comparative performance of clinical risk assessment models for hospital-acquired venous thromboembolism in medical patients. Thromb Haemost. 2018;118:82–9.
8. Blondon M, Righini M, Nendaz M, Glauser F, Robert-Ebadi H, Prandoni P, et al. External validation of the simplified Geneva risk assessment model for hospital-associated venous thromboembolism in the Padua cohort. J Thromb Haemost. 2019;18:676–80.
9. Barbar S, Noventa F, Rossetto V, Ferrari A, Brandolin B, Perlati M, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. J Thromb Haemost. 2010;8:2450–7.
10. Spyropoulos AC, Anderson FA, Fitzgerald G, Decousus H, Pini M, Chong BH, et al. Predictive and associative models to identify hospitalized medical patients at risk for VTE. Chest. 2011;140:706–14.
11. Nendaz MR, Chopard P, Lovis C, Kucher N, Asmis LM, Dorffler J, et al. Adequacy of venous thromboprophylaxis in acutely ill medical patients (IMPART): multisite comparison of different clinical decision support systems. J Thromb Haemost. 2010;8:1230–4.
12. Kahn SR, Panju A, Geerts W, Pineo GF, Desjardins L, Turpie AGG, et al. Multicenter evaluation of the use of venous thromboembolism prophylaxis in acutely ill medical patients in Canada. Thromb Res. 2007;119:145–55.
13. Pavon JM, Sloane RJ, Pieper CF, Colon-Emeric CS, Cohen HJ, Gallagher D, et al. Poor adherence to risk stratification guidelines results in overuse of venous thromboembolism prophylaxis in hospitalized older adults. J Hosp Med. 2018;13:403–4.
14. Goldin M, Cohen J, Makhnevich A, Mulvany C, Akerman M, Sinvani L. Patterns and outcomes of prescribing venous thromboembolism prophylaxis in hospitalized older adults: a retrospective cohort study. J Thromb Thrombolysis. 2018;45:369–76.
15. Ye F, Bell LN, Mazza J, Lee A, Yale SH. Variation in definitions of immobility in pharmacological thromboprophylaxis clinical trials in medical inpatients: a systematic review. Clin Appl Thromb Hemost. 2018;24:13–21.
16. Nafee T, Gibson CM, Travis R, Yee MK, Kerneis M, Chi G, et al. Machine learning to predict venous thrombosis in acutely ill medical patients. Res Pract Thromb Haemost. 2020;4:230–7.

How to cite this article: Blondon M, Limacher A, Righini M, Aujesky D, Méan M. Underuse of medical thromboprophylaxis in mobile elderly inpatients: The SWITCO65+ cohort. *Res Pract Thromb Haemost*. 2021;5:142–147. https://doi.org/10.1002/rth2.12361