

**BRIEF REPORT**

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

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## 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

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## 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.<sup>1</sup> This is highly relevant among older adults, who are more likely to be hospitalized and at a greater multifactorial risk of VTE.<sup>2</sup>

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.<sup>3,4</sup>

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 ( $\geq 65$  years) patients with acute VTE, with approval of Ethics Committees from all participating centers.<sup>5</sup> 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,<sup>6</sup> the Simplified Geneva RAM (sGR),<sup>7,8</sup> the Padua RAM,<sup>9</sup> and the Improve RAM<sup>10</sup> (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%<sup>6</sup> and 6.4%,<sup>10</sup> 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<br>Low risk 0-2<br>High risk $\geq 3$ |   | Simplified Geneva RAM<br>Low risk 0-2<br>High risk $\geq 3$ |   | Padua RAM<br>Low risk 0-3<br>High risk $\geq 4$ |   | Improve RAM<br>Low risk 0-2<br>High-risk $\geq 3$ |   |
|--|---|---|---|---|---|---|---|
| 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 <sup>2</sup>                                  | 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 <sup>2</sup>                      | 1 |   |   |
| Nephrotic syndrome                               | 2 |   |   | Hormonal treatment                              | 1 |   |   |
| Immobilization (<30 min/d)                       | 2 |   |   |   |   |   |   |
| Age > 60 y                                       | 1 |   |   |   |   |   |   |
| BMI > 30 kg/m <sup>2</sup>                       | 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 thromboprophylaxis was similar between inpatients with 0 high-risk scores (2/6; 33%),  $\geq 1$  high-risk scores (21/60; 35%),  $\geq 2$  high-risk scores (21/56; 38%),  $\geq 3$  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.<sup>7</sup> By consequence, the use of those 2 RAMs potentially generates a greater use of thromboprophylaxis with a greater sensitivity.<sup>7</sup>

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.<sup>6,11</sup> Similar findings were also reported in other countries<sup>12</sup> and in studies focusing on medically ill hospitalized elderly patients.<sup>13</sup>

**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)               |

<sup>a</sup>n (%) or median (IQR).

<sup>b</sup>Adjusted for age and sex.

<sup>c</sup>Per increasing decade.

Whether immobilization is a trigger for thromboprophylaxis administration remains debated,<sup>4,12,14</sup> and this is further complicated by the heterogeneity of the definition of immobilization.<sup>15</sup> 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).<sup>12</sup> 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.<sup>16</sup>

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

|                       | Median (IQR)  | Cases categorized as high risk, % (95% CI) | Use of pharmacologic thromboprophylaxis, % (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 <sup>a</sup> (n = 36) | Use of thromboprophylaxis <sup>a</sup> (n = 21) | Odds ratio for inadequate lack of thromboprophylaxis <sup>b</sup> (95% CI) |
| Age, y  | 74 (67-83)  | 75 (70-84)                                      | 0.62 (0.28-1.37) <sup>c</sup>  |
| 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)   |

<sup>a</sup>n (%) or median (IQR).

<sup>b</sup>Adjusted for age and sex.

<sup>c</sup>Per increasing decade.

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## RELATIONSHIP DISCLOSURE

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## 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.

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