Thrombosis Research 173 (2019) 124–130

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Association between insurance status, anticoagulation quality, and clinical outcomes in patients with acute venous thromboembolism

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ARTICLE INFO

Keywords:
Aged
Insurance status
Pulmonary embolism
Venous thromboembolism
Venous thrombosis

ABSTRACT

Introduction: A higher level of health insurance coverage may be related to better quality of care and outcomes. Whether insurance status is associated with anticoagulation quality and clinical outcomes in patients with venous thromboembolism (VTE) is unknown.

Methods: We studied 819 elderly patients treated with vitamin K antagonists for VTE in a Swiss prospective multicenter cohort (09/2009–12/2013). The study outcomes were the anticoagulation quality, defined as the time spent in the therapeutic INR range, and clinical events, i.e. the time to a first VTE recurrence, major bleeding, and mortality. We assessed the association between insurance status (private vs. general), anticoagulation quality, and clinical outcomes using regression models, adjusting for potential confounders.

Results: Although the unadjusted mean percentage of time spent in the therapeutic INR range (2.0–3.0) was slightly higher in patients with private vs. general insurance (65% vs. 61%; p = 0.030), the adjusted difference was not statistically significant (1.53%, 95% CI −1.97 to 5.04). Patients with private insurance had a lower 36-month cumulative incidence of major bleeding (9.7% vs. 15.7%; $p = 0.018$). After adjustment, privately insured patients had a lower risk of major bleeding compared to patients with general insurance (sub-hazard ratio 0.57, 95% CI 0.32 to 0.98). Insurance status was not associated with recurrent VTE or mortality.

Conclusion: Privately insured patients spent somewhat more time in therapeutic INR range and had a lower rate of major bleeding than generally insured patients. Basic (general) health insurance may be a marker of lower anticoagulation quality and higher risk of major bleeding.

1. Introduction

The lack of health insurance has been associated with suboptimal processes of care and poor disease-related outcomes primarily due to impaired access to healthcare [1–3]. However, even among patients with insurance coverage, the level (intensity) of coverage may also be related to processes of care and patient outcomes. Evidence suggests that a higher level of health insurance coverage may be associated with better access to healthcare, quality of care, and outcomes in patients with cardiorespiratory disorders, such as heart failure [4], acute coronary syndrome [5,6], chronic asthma [7], and COPD [8,9].

Switzerland is a country with mandatory health care coverage, which offers a universal access to health care [10]. All Swiss are obliged to purchase a basic insurance policy that covers a large portion of the costs of medical outpatient and inpatient treatment. The compulsory basic insurance can be supplemented by voluntary private insurance plans that allow for coverage of additional treatment options (e.g., guaranteed access to almost all private and public providers in Switzerland, financial contributions to prevention and health promotion measures, and coverage for regular medical check-ups and uninsured drugs) not covered by the basic insurance. Among others, private insurance policy holders are also entitled to receive care from the most senior and experienced physicians in the hospital. Approximately 35% of the Swiss population have a supplemental private insurance [11].

Acute venous thromboembolism (VTE), defined as deep vein thrombosis (DVT) and/or pulmonary embolism (PE), is a life-threatening medical condition that often requires initial hospitalization and long-term clinical and laboratory monitoring [12]. A single center

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https://doi.org/10.1016/j.thromres.2018.11.011
Received 8 May 2018; Received in revised form 1 November 2018; Accepted 11 November 2018
Available online 12 November 2018
0049-3848/

retrospective U.S. study demonstrated that uninsured patients admitted with acute VTE were hospitalized for nearly two additional days and were more than two times as likely to return to the emergency department within 30 days as insured patients [13]. The differences were explained by a limited access to outpatient health care. However, whether patients with acute VTE who have a higher level of health insurance coverage experience a better quality of care and long-term clinical outcomes than those with a basic health insurance is unknown. We therefore prospectively examined whether private insurance coverage is associated with a better quality of anticoagulation and clinical outcomes in a multicenter Swiss cohort study of elderly patients with acute VTE.

2. Methods

2.1. Cohort sample

The study was conducted between September 2009 and December 2013 as part of the SWIss venous Thromboembolism COhort (SWITCO65+), a prospective multicenter cohort study that assessed long-term medical outcomes and quality of life in elderly patients with symptomatic VTE from all five university and four high-volume hospitals in Switzerland. Consecutive patients aged ≥65 years with acute, objectively confirmed, symptomatic DVT and/or PE were identified in the in- and outpatient services of all participating study sites. Exclusion criteria were catheter-related thrombosis, thrombosis at a different site than lower limb, insufficient German or French-speaking ability, impossibility to follow up (i.e., terminal illness), an inability to provide informed consent (i.e., severe dementia), or previous enrollment in the cohort. A detailed description of the study methods was published previously [14]. All participants provided written informed consent. The study was approved by the institutional review board at each participating site. For the present study, we considered all patients of the original cohort who were treated with vitamin K antagonists (VKA) within 30 days of VTE diagnosis.

2.2. Baseline data collection

For all enrolled patients, trained study nurses prospectively collected baseline demographic (age, gender, living status, educational level,) type (provoked, unprovoked, cancer-related) and localization of the index VTE (PE ± DVT, isolated distal DVT), vital signs at presentation (blood pressure), comorbid conditions (body mass index, smoking status, prior VTE, history of major bleeding, alcohol consumption, level of physical activity, the risk of falls, arterial hypertension, diabetes mellitus, cerebrovascular disease, cardiovascular disease, chronic lung disease, chronic liver and renal disease, inflammatory bowel disease, active cancer, recent major surgery), laboratory findings (hemoglobin, platelets, cardiac troponin, D-Dimer, C-reactive protein), baseline medications (preexisting anticoagulation therapy, concomitant antiplatelet therapy, polypharmacy), and VTE-related treatments (type of VKA used [phenprocoumon, acenocoumarol], thrombolysis, the insertion of a vena cava filter, or thromboembolectomy). Information about the patient's insurance status (general vs. private) was abstracted from the patient's medical record. All information was recorded on standardized data collection forms.

2.3. Study outcomes

Our study outcomes were the quality of anticoagulation, expressed as the percentage of time spent in a given International Normalized Ratio (INR) range (< 2.0, 2.0–3.0, and > 3.0) according to the Rosendaal method [15], and adverse clinical events, i.e. the time to a first recurrent VTE, major bleeding, or death from all causes. Recurrent VTE was defined as a new or recurrent, fatal or non-fatal, symptomatic, and objectively confirmed PE or DVT, as previously described [14]. Major bleeding was defined as a fatal bleeding, bleeding in a critical location (intracranial, intraspinal, intraocular, retroperitoneal, intraarticular, pericardial, or intramuscular with compartment syndrome), a bleeding with reduction of hemoglobin ≥20 g/l, or a bleeding leading to the transfusion of ≥2 units of packed red blood cells [16].

Follow-up included one telephone interview and two face-to-face evaluations during the first year of study participation and then semi-annual contacts, alternating between face to-face-evaluations and telephone calls as well as periodic hospital chart reviews. As part of the follow-up interview/visits, study nurses obtained information about the date and type of VTE recurrence, bleeding events, and death. Study nurses recorded INR values and the duration of initial anticoagulation throughout follow-up. A committee of three blinded clinical experts adjudicated all outcomes. The committee classified the cause of all deaths as definitely due to PE (i.e., confirmed by autopsy or death followed a clinically severe PE), possibly due to PE (i.e., death in a patient who died suddenly or unexpectedly), due to bleeding, or due to another cause. Death was judged to be bleeding-related if it followed an intracranial hemorrhage or a bleeding episode leading to hemodynamic deterioration [17].

2.4. Statistical analysis

We compared baseline characteristics by insurance coverage using the chi-squared test and the non-parametric Wilcoxon rank-sum test as appropriate. We also compared the percentage of time spent in a given INR range (< 2.0, 2.0–3.0, > 3.0) between generally and privately insured patients, excluding the first seven treatment days [15].

We used linear regression to examine the association between insurance status and the time spent in a given INR range. We adjusted for known risk factors of anticoagulation quality, including age, female gender, living status, education, body mass index, smoking status, alcohol consumption, physical activity, diabetes mellitus, chronic heart failure, chronic liver disease, active cancer, polypharmacy, and type of VKA used [18–25]. We also examined the percentage of time spent in the therapeutic INR range (2.0–3.0) by adverse clinical outcomes.

We estimated the cumulative incidence of VTE recurrence, major bleeding, and overall mortality by insurance using the Kaplan-Meier technique and compared groups using the log-rank test. We examined the association between insurance and the time to a first VTE recurrence using competing risk regression, accounting for death as a competing event [26]. The strength of the association in the Fine-Gray model is reflected by the sub-hazard ratio (SHR). We adjusted for known risk factors of VTE recurrence (age, gender, type (provoked, unprovoked, cancer-related) and localization of the index VTE (PE ± DVT, isolated distal DVT), body mass index, prior VTE, inflammatory bowel disease) [27–32]. We used the same model to assess the association between insurance and major bleeding, adjusting for known risk factors of bleeding (age, gender, overt pulmonary embolism, history of major bleeding, alcohol consumption, physical activity, risk of falls, arterial hypertension, diabetes mellitus, cerebrovascular disease, chronic heart failure, chronic liver disease, chronic renal disease, active cancer, recent major surgery, anemia, low platelet count, concomitant antiplatelet therapy, polypharmacy) [33–41]. Finally, we also examined the association between insurance and the time to death using Cox regression, adjusting for age, systolic blood pressure, physical activity, diabetes mellitus, active cancer, anemia, ultra-sensitive troponin, D-dimer, high-sensitivity C-reactive protein, polypharmacy [42]. All three models were adjusted for periods of anticoagulation as a time-varying covariate. In all regression models, we performed multiple imputations for missing values [43]. All analyses were done using Stata 14.2 (Stata Corporation, College Station, Texas).

3. Results

3.1. Study sample

Of the 1003 patients initially enrolled in SWITCO65+, we excluded 184 patients who did not receive VKAs (n = 132), had < 2 INR values measured (n = 40), refused the use of their data (n = 8), or withdrew their consent (n = 4). Thus, the final study sample comprised 819 patients with acute VTE. Median age (75.0 years [interquartile range (IQR) 69.0–81] vs. 75.0 years [IQR 70.0–81.0], p = 0.851) and female gender (47% vs. 48%, p = 0.803) did not differ between analyzed and excluded patients.

Overall, 616 patients (75%) had general and 203 (25%) private insurance coverage. Patients with general insurance were more likely to be women (49% vs. 39%, p = 0.012), to live at home alone (37% vs. 28%, p = 0.032), and to have less than high school education (60% vs. 45%, p < 0.001) than privately insured patients (Table 1). Patients with general insurance had a higher body mass index (27.3 [IQR 24.5–30.5] vs. 26.3 [IQR 23.9–29.4], p = 0.013), reported fewer standardized alcoholic drinks per week (1.0 vs. 4.0, p < 0.001), were more likely to have arterial hypertension (66% vs. 58%, p = 0.035) and a high risk of fall (48% vs. 33%, p < 0.001), and were more likely to receive acenocoumarol as an anticoagulant (38% vs. 26%, p = 0.002) than privately insured patients. The median follow-up duration was 30 months (IQR 24–41).

3.2. Insurance status and anticoagulation

The median initial anticoagulation duration was 11.5 months (IQR 5.9–28.7) and was similar in generally and privately insured patients (11.7 months [IQR 5.9–28.5] vs. 11.1 months [IQR 5.8–29.4] p = 0.953). The unadjusted mean percentage of time spent in the therapeutic INR range (2.0–3.0) was statistically significantly lower in generally than in privately insured patients (61% vs. 65%; p = 0.030),

Table 1
Baseline characteristics by insurance status.

Characteristic	All (N = 819)	General (N = 616)	Private (N = 203)	p-Value	Missing
	n (%) or median (interquartile range)				
Patient age	75.0 (69.0;81.0)	75.0 (69.0;81.0)	74 (70.0;80.0)	0.508	0 (0)
Female gender	382 (47)	303 (49)	79 (39)	0.012	0 (0)
Living status				0.032	0 (0)
- At home with someone else	515 (63)	372 (60)	143 (70)		
- At home alone	284 (35)	227 (37)	57 (28)		
- In a nursing home	20 (2)	17 (3)	3 (1)		
Educational level				< 0.001	2 (0)
- Less than high school	460 (56)	369 (60)	91 (45)		
- High school graduate	206 (25)	148 (24)	58 (29)		
- Post-secondary[a]	151 (18)	97 (16)	54 (27)		
Type of VTE				0.949	0 (0)
- Unprovoked[b]	556 (68)	418 (68)	138 (68)		
- Provoked[c]	186 (23)	139 (23)	47 (23)		
- Cancer-related[d]	77 (9)	59 (10)	18 (9)		
Localization of VTE				0.013	0 (0)
- DVT only	234 (29)	180 (29)	54 (27)		
- DVT + PE	118 (14)	76 (12)	42 (21)		
- PE only	467 (57)	360 (58)	107 (53)		
Systolic BP < 100 mm Hg	25 (3)	17 (3)	8 (4)	0.479	16 (2)
Body mass index	27.1 (24.4;30.1)	27.3 (24.5;30.5)	26.3 (23.9;29.4)	0.016	3 (0)
Current or past smoker	380 (46)	285 (46)	95 (47)	0.935	2 (0)
Prior VTE	244 (30)	185 (30)	59 (29)	0.086	0 (0)
History of major bleeding[e]	75 (9)	63 (10)	12 (6)	0.069	1 (0)
Standardized alcoholic drinks/week[f]	2.0 (0.0;7.0)	1.0 (0.0;7.0)	4.0 (0.0;10.0)	< 0.001	4 (0)
Low physical activity[g]	277 (34)	217 (35)	60 (30)	0.170	2 (0)
High risk of falls[h]	364 (44)	297 (48)	67 (33)	< 0.001	1 (0)
Arterial hypertension[i]	527 (64)	409 (66)	118 (58)	0.035	0 (0)
Diabetes mellitus	128 (16)	105 (17)	23 (11)	0.058	0 (0)
Cerebrovascular disease[j]	73 (9)	61 (10)	12 (6)	0.089	0 (0)
Cardiovascular disease[l]	12 (1)	9 (1)	3 (1)	1.000	0 (0)
Chronic heart failure	59 (7)	46 (7)	13 (6)	0.754	0 (0)
Chronic lung disease[m]	111 (14)	89 (14)	22 (11)	0.237	0 (0)
Chronic liver disease[n]	10 (1)	10 (2)	0 (0)	0.131	0 (0)
Chronic renal disease[o]	154 (19)	124 (20)	30 (15)	0.098	0 (0)
Inflammatory bowel disease[p]	26 (3)	16 (3)	10 (5)	0.109	0 (0)
Active cancer[q]	77 (9)	59 (10)	18 (9)	0.890	0 (0)
Recent major surgery[r]	117 (14)	89 (14)	28 (14)	0.908	0 (0)
Anemia[s]	275 (34)	218 (35)	57 (28)	0.079	56 (7)
Platelet count < 150 G/l	111 (14)	85 (14)	26 (13)	0.905	56 (7)
Ultrasensitive cTnT > 14 pg/ml	346 (42)	270 (44)	76 (37)	0.069	109 (13)
D-dimer > 3000 ng/ml	287 (35)	214 (35)	73 (36)	0.930	124 (15)
Highly sensitive CRP > 40 mg/l	238 (29)	187 (30)	51 (25)	0.120	107 (13)
AC prior to index VTE	37 (5)	26 (4)	11 (5)	0.443	0 (0)
Antiplatelet therapy[t]	269 (33)	194 (31)	75 (37)	0.168	0 (0)
Polypharmacy[u]	402 (49)	314 (51)	88 (43)	0.063	0 (0)
Type of VKA used				0.002	0 (0)
- Acenocoumarol	288 (35)	235 (38)	53 (26)		
- Phenprocoumon	531 (65)	381 (62)	150 (74)		
Thrombolysis[v]	26 (3)	20 (3)	6 (3)	1.000	0 (0)

(continued on next page)

Table 1 (*continued*)

Characteristic	All (N = 819)	General (N = 616)	Private (N = 203)	p-Value	Missing
	n (%) or median (interquartile range)				
Inferior vena cava filter	6 (1)	5 (1)	1 (0)	1.000	0 (0)
Thromboembolectomy[k]	2 (0)	1 (0)	1 (0)	0.435	0 (0)
Managed as outpatients	149 (18)	111 (18)	38 (19)	0.834	0 (0)

Abbreviations: VTE, venous thromboembolism; DVT, deep vein thrombosis; PE, pulmonary embolism; BP, blood pressure; cTnT, cardiac troponin T; CRP, C-reactive protein; AC, anticoagulation; VKA, vitamin K antagonist.

[a] Diploma from a university or an equivalent institution.

[b] Absence of major surgery, estrogen therapy, immobilization, or active cancer during the last three months before the index VTE.

[c] Major surgery, estrogen therapy, or immobilization (bed rest > 72 h, fracture or cast of the lower extremity, voyage in sitting position > 6 h) during the last 3 months before the index VTE.

[d] Leukemia, lymphoma, or metastatic or non-metastatic solid cancer requiring surgery, chemotherapy, radiotherapy, or palliative care during the last three months before the index VTE, excluding local skin tumors such as basal cell carcinoma and spinal cell carcinoma.

[e] Bleeding that led to a hospital stay or transfusions.

[f] Self-reported average weekly amount of alcoholic beverages during the last 12 months measured as standardized alcoholic beverages.

[g] Mostly lying/sitting activity or avoidance to climb stairs/carry light weight.

[h] Self-reported fall during the last year or problems with gait, balance, or mobility.

[i] Treated or untreated.

[j] Defined as a known history of ischemic or hemorrhagic stroke or a transient ischemic attack.

[k] Defined as any acute heart failure episode NYHA class III or IV, or myocardial infarction during the last 3 months.

[l] Any known chronic lung disease such as chronic obstructive pulmonary disease, active asthma, lung fibrosis, cystic fibrosis, or bronchiectasis.

[m] Liver cirrhosis, chronic hepatitis (B, C, autoimmune, etc.), chronic liver failure or hemochromatosis. Fatty liver is not considered a chronic liver disease.

[n] Chronic renal disease (i.e. chronic renal failure with or without hemodialysis) such as diabetic or hypertensive nephropathy, chronic glomerulonephritis, chronic interstitial nephritis, myeloma-related nephropathy, or cystic kidney disease.

[o] History of Crohn's disease or ulcerative colitis.

[p] Leukemia, lymphoma, or non-metastatic solid cancer requiring chemotherapy, radiotherapy, surgery, or palliative care during the last three months, excluding local skin tumors such as basal cell carcinoma and spinal cell carcinoma.

[q] Surgery requiring general or spinal anesthesia during the last 3 month.

[r] Hemoglobin < 13 g/dl in men or < 12 g/dl in women.

[s] Concomitant use of any antiplatelet therapy, such as aspirin, clopidogrel, prasugrel, aspirin/dipyridamole, or use of non-steroidal anti-inflammatory drugs.

[t] Defined as the current prescription of > 4 different drugs, including St. John's wort.

[u] Defined as the administration (systemic or catheter-based) of any thrombolytic (urokinase, streptokinase, alteplase, reteplase, or tenecteplase).

[v] Defined as an embolus/thrombus fragmentation using a catheter or a removal of thrombus/embolus by a surgical intervention.

Table 2
Anticoagulation quality by insurance status.

Outcome	All (N = 819)	General (N = 616)	Private (N = 203)	p-Value
INR range	Mean percentage of time spent in a given INR range (SD)			
< 2.0	22.7 (21.3)	23.3 (22.0)	20.8 (19.2)	0.162
2.0–3.0	62.4 (22.6)	61.4 (22.8)	65.3 (21.6)	0.030
> 3.0	15.0 (17.0)	15.4 (17.5)	13.8 (15.3)	0.262

Abbreviations: INR, international normalized ratio; SD, standard deviation.

whereas the percentage of time spent above (> 3.0) and below (< 2.0) the therapeutic INR range did not differ by insurance status (Table 2). After adjustment for risk factors of poor anticoagulation control, patients with private insurance spent somewhat more time in the therapeutic and less time in the supra- and sub-therapeutic INR range than patients with general insurance, but the difference did not achieve statistical significance (Table 3).

3.3. Anticoagulation quality and clinical outcomes

As shown in Table 4, the unadjusted mean percentage of time spent in therapeutic INR range (2.0–3.0) of patients with VTE recurrence did not differ statistically significantly from patients without VTE recurrence (60% vs. 63%, p = 0.167), whereas patients with a major bleeding spent statistically significantly less time in therapeutic INR range than those without major bleeding (54% vs. 64%, p < 0.001). Patients, who ultimately died, spent less time in therapeutic INR range than those who survived (49% vs. 65%, p < 0.001).

3.4. Insurance status and clinical outcomes

Overall, 106 patients (12.9%) had a first recurrent VTE, 103 (12.6%) had a first major bleeding, and 111 patients (13.6%) died during follow-up. While the 36-month cumulative incidence of recurrent VTE and overall mortality did not differ by insurance status, the 36-month cumulative incidence of major bleeding was statistically significantly lower in privately than in generally insured patients (9.7% vs. 15.7%, p = 0.018) (Fig. 1, Panel B).

After adjustment for potential confounders and periods of anticoagulation as a time-varying covariate, insurance status was not associated with recurrent VTE or overall mortality. However, patients with private insurance had a lower risk of major bleeding compared to generally insured patients (SHR 0.57, 95% confidence interval (CI) 0.32–0.98) (Table 5).

4. Discussion

Our results demonstrate that patients receiving VKAs for VTE who had private health insurance spent somewhat more time in the therapeutic INR range and had a statistically significantly lower risk of major bleeding than patients with general insurance. The insurance status was not associated with the risk of recurrent VTE or overall mortality. To our knowledge, our study is the first work that examined the association between the level of health insurance and anticoagulation quality and clinical outcomes.

Table 3
Adjusted mean differences of the percentage of time spent in a given INR range in generally and privately insured patients.

Outcome	Adjusted mean difference in %[a] (95%-CI)	p-Value
INR < 2.0		
General insurance	Reference	–
Private insurance	−0.76 (−4.15 to 2.64)	0.662
INR 2.0–3.0		
General insurance	Reference	–
Private insurance	1.53 (−1.97 to 5.04)	0.392
INR > 3.0		
General insurance	Reference	–
Private insurance	−0.78 (−3.56 to 2.01)	0.585

Abbreviations: INR; international normalized ratio; CI; confidence interval.
[a] Adjusted for age, female gender, living status, education, body mass index, smoking status, alcohol consumption, physical activity, diabetes mellitus, chronic heart failure, chronic liver disease, active cancer, polypharmacy, type of vitamin K antagonist, and periods of anticoagulation as a time-varying covariate.

Table 4
Anticoagulation quality by adverse clinical outcomes.

Outcome	Mean percentage of time spent within an INR range of 2.0–3.0 (SD)	p-Value
VTE recurrence		0.167
- Yes (n = 106)	59.5 (25.9)	
- No (n = 713)	62.8 (22.0)	
Major bleeding		< 0.001
- Yes (n = 103)	54.4 (22.3)	
- No (n = 716)	63.5 (22.4)	
Overall mortality		< 0.001
- Yes (n = 111)	48.7 (22.5)	
- No (n = 708)	64.5 (21.8)	

Abbreviations: INR, international normalized ratio; SD, standard deviation; VTE, venous thromboembolism.

Interestingly, although privately insured patients spent more time in the therapeutic INR range than generally insured patients, the quality of anticoagulation did not significantly differ after adjusting for other known factors of poor anticoagulation control, such as physical activity [21], smoking status [21,44], polypharmacy [18,45], and type of VKA [24,25]. This finding indicates that a lower level of insurance does not represent an independent risk factor (for which there would be no plausible biological explanation) but merely a marker of poorer anticoagulation control and that the higher anticoagulation quality in privately insured patients in the unadjusted analysis must rather be explained by differences in sociodemographic factors, comorbid conditions, or treatments that are known to be associated with a lower quality of anticoagulation. For instance, privately insured patients were significantly less likely to be women [18,44], to have a lower educational level [46], to receive acenocoumarol [24,25], and somewhat less likely to have diabetes mellitus [19,47,48] and polypharmacy [18,45] than generally insured patients. Indeed, supplementary private insurance plans are often purchased by higher income, more health conscious populations [49,50]. Because the access to health care is guaranteed irrespective of the level of insurance coverage in Switzerland, disparities in care access are unlikely to be responsible for differences in anticoagulation control between generally and privately insured patients.

Despite adjustment for multiple bleeding risk factors, privately insured patients were statistically significantly less likely to develop major bleeding in our study. There are several potential explanations for the association between the level of insurance coverage and the risk of major bleeding. First, the lower rate of major bleeding among

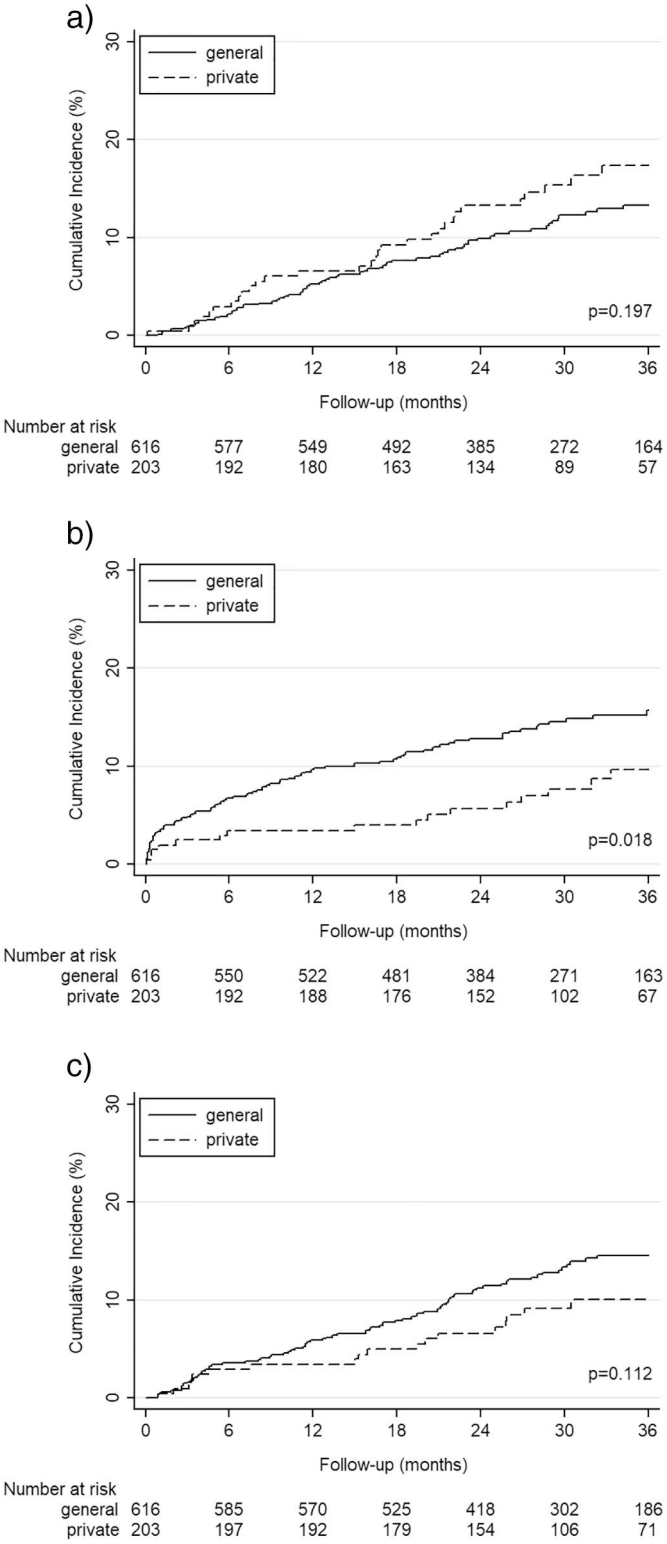

Fig. 1. Panel A. Kaplan-Meier estimates of a first recurrent venous thromboembolic event by insurance status. The 36-month cumulative incidence of a first recurrent venous thromboembolic event was 13.3% for patients with general and 17.4% for patients with private insurance (p = 0.197 by the log-rank test).
Panel B. Kaplan-Meier estimates of a first major bleeding event by insurance status. The 36-month cumulative incidence of a first major bleeding event was 15.7% for patients with general and 9.7% for patients with private insurance (p = 0.018 by the log-rank test).
Panel C. Kaplan-Meier estimates of overall mortality by insurance status. The 36-month cumulative incidence of death was 14.6% for patients with general and 10.1% for patients with private insurance (p = 0.112 by the log-rank test).

Table 5
Association between insurance status and clinical outcomes.

Outcome	Unadjusted SHR (95%-CI)	p-Value	Adjusted SHR[c] (95%-CI)	p-Value
VTE recurrence	106/819		106/819	
General insurance	Reference	–	Reference	–
Private insurance	1.27 (0.83 to 1.93)	0.266	1.33 (0.86 to 2.05)	0.207

Outcome	Unadjusted SHR (95%-CI)	p-Value	Adjusted SHR[a] (95%-CI)	p-Value
Major bleeding	103/819		103/819	
General insurance	Reference	–	Reference	–
Private insurance	0.52 (0.31 to 0.89)	0.016	0.57 (0.32 to 0.98)	0.044

Outcome	Unadjusted HR (95%-CI)	p-Value	Adjusted HR[b] (95%-CI)	p-Value
Overall mortality	111/819		111/819	
General insurance	Reference		Reference	–
Private insurance	0.63 (0.39 to 1.02)	0.062	0.67 (0.41 to 1.11)	0.120

Abbreviations: VTE, venous thromboembolism; SHR, sub-hazard ratio; CI, confidence interval; HR, hazard ratio.

[a] Adjusted for age, gender, type (provoked, unprovoked, cancer-related) and localization of the index VTE (PE ± DVT, isolated distal DVT), body mass index, prior VTE, inflammatory bowel disease, and periods of anticoagulation as a time-varying covariate.

[b] Adjusted for age, gender, overt pulmonary embolism, history of major bleeding, alcohol consumption, physical activity, risk of falls, arterial hypertension, diabetes mellitus, cerebrovascular disease, chronic heart failure, chronic liver disease, chronic renal disease, active cancer, recent major surgery, anemia, low platelet count, concomitant antiplatelet therapy, polypharmacy, and periods of anticoagulation as a time-varying covariate.

[c] Adjusted for age, systolic blood pressure, physical activity, diabetes mellitus, active cancer, anemia, ultra-sensitive troponin, D-dimer, high-sensitivity C-reactive protein, polypharmacy, and periods of anticoagulation as a time-varying covariate.

privately insured patients could be a direct consequence of the somewhat higher percentage of time spent in the therapeutic INR range. Privately insured patients also spent somewhat less time in the supra-therapeutic INR range (> 3.0) than generally insured patients (13.8% vs. 15.4%), although the difference was not statistically significant. Strong evidence suggests that the quality of anticoagulation is directly related to the risk of developing major bleeding [51]. Indeed, patients who experienced major bleeding spent less time in a therapeutic INR range than those without this complication in our analysis. Second, privately insured patients are likely to be wealthier, better educated, and healthier and therefore, may have a lower bleeding risk than generally insured patients. In our study, privately insured patients had a higher educational level, were less likely to live alone, and had a lower risk of falls and a lower prevalence of arterial hypertension than generally insured patients. Although we made multiple adjustments for socioeconomic and patient baseline characteristics, the lower risk of major bleeding in privately insured patients may still be explained by unmeasured, residual confounding. Our findings are consistent with the results from a Canadian population-based cohort study including 166,742 elderly patients receiving warfarin therapy for atrial fibrillation, in which a lower socioeconomic status was found to be a risk factor for hemorrhage and hemorrhage-related mortality [52]. Although the intensity of anticoagulant monitoring did not differ by socioeconomic status, patients with lower socioeconomic status displayed a greater number of comorbid conditions and exposure to drugs that might heighten the risk of hemorrhage [52]. Overall, our results indicate that patients with a lower level of health insurance are more prone to have a lower anticoagulation quality and major bleeding. Whether more intensive surveillance of such patients could reduce the risk of major bleeding is uncertain.

Patients, who ultimately died, spent less time in the therapeutic INR range than those who survived (49% vs. 65%, $p < 0.001$). As our study was not designed to examine the association between anticoagulation quality and adverse clinical outcomes, we cannot say whether a lower anticoagulation quality is simply a marker of illness severity or whether the anticoagulation quality had a direct impact on survival in our analysis. It is also conceivable that patients who died early may have had less time to achieve a therapeutic INR range (reverse causation).

Our study has several potential limitations. First, our study enrolled exclusively patients aged 65 years or older with acute VTE. We thus cannot generalize our results to younger patients or those with other indications for anticoagulation. Second, patients with severe dementia and with insufficient language skills, which are known risk factors for poor anticoagulation control [18,45,53], were not enrolled in the study. As patients with limited language skills are less likely to have private health insurance, the exclusion of such patients may have decreased the association between insurance status and anticoagulation quality and major bleeding. Finally, because direct oral anticoagulants were not yet authorized for treatment of acute VTE in Switzerland at the time of patient enrollment, none of the patients was treated with direct oral anticoagulants. The more expensive direct oral anticoagulants, which do not need regular monitoring and provide a more stable anticoagulation intensity than VKAs [54,55], may have the potential to reduce disparities in anticoagulation quality and major bleeding between patients with basic and supplemental insurance plans.

In conclusion, our results demonstrate that in patients receiving VKAs for acute VTE, those with private insurance coverage had a somewhat better quality of anticoagulation and a lower rate of major bleeding than patients with general insurance coverage. Our findings indicate that in a country with universal health coverage, basic (general) health insurance may be a marker of lower anticoagulation quality and a higher risk of major bleeding compared to supplementary, higher-level (private) insurance plans. Whether a more intensive surveillance of generally insured patients with VTE or the use of direct oral anticoagulants instead of VKAs has the potential to improve anticoagulation quality and to reduce the major bleeding risk, is unknown.

Funding

The study was supported by a grant from the Swiss National Science Foundation (no. 33CSCO-122659/139470). The sponsor had no role in study design, data collection, site monitoring, data analysis, data interpretation, or writing of the manuscript.

CRediT authorship contribution statement

Brigitta Zumbrunn: Writing - original draft. **Odile Stalder:** Formal analysis. **Marie Méan:** Writing - review & editing. **Andreas Limacher:** Formal analysis. **Tobias Tritschler:** Writing - review & editing. **Nicolas Rodondi:** Funding acquisition, Writing - review & editing. **Drahomir Aujesky:** Conceptualization, Funding acquisition, Methodology, Writing - original draft.

Acknowledgements

This study was supported by the Swiss National Science Foundation (33CSCO-122659/139470). We thank all collaborators of the SWITCO65+ study.

Conflict of interest

The authors declare that they have no conflict of interest.

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