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Full Length Article

Associations between anticoagulant treatment pathways and self-reported harms in patients recently diagnosed with venous thromboembolism

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ABSTRACT

Introduction: Understanding potential harms associated with common anticoagulation treatment patterns in patients with venous thromboembolism (VTE) is important for multiple stakeholders. The purpose of this study is to report associations between different anticoagulation patterns and bleeding and emotional harms based on patients' self-reported care experiences.

Methods: Patients at least 18 years of age who had experienced a VTE event in the past two years and completed a national online survey between May and July 2016 were analyzed. The survey assessed the prevalence of self-reported bleeding and emotional harms associated with self-reported anticoagulation treatment patterns and other variables.

Results: Patients mean age was 52.4 (standard deviation 14.4) years and most were female (56.7%) and Caucasian (88.6%). Anticoagulant treatment patterns included warfarin (38.7%), direct oral anticoagulants (26.1%), and those who switched between anticoagulants (17.9%). Self-reported bleeding and emotional harms occurred in 63.6% and 56.3% of patients, respectively. Younger age, experiencing VTE more recently, and a prior history of anxiety, depression, or stroke were associated with increased odds of experiencing bleeding or emotional harm. Compared to warfarin, switching between anticoagulant types was associated with approximately twice the odds of experiencing bleeding harm, while DOAC therapy was associated with lower odds of experiencing emotional harm.

Conclusion: Self-reported bleeding and emotional harms occurred commonly during VTE treatment and were associated with identifiable clinical, demographic, and psychosocial characteristics such as younger age, history of depression and/or anxiety, and more recent VTE diagnosis. Switching between anticoagulants may be a marker for increased harm risk.

1. Introduction

Venous thromboembolism (VTE) is a major national health issue affecting as many as 900,000 people each year in the United States [1]. VTE refers to deep vein thrombosis (DVT), pulmonary embolism (PE), or both, and in the latter cases can be rapidly fatal [1]. Emotional harms, including worry, fear, anxiety, confusion, and depression have been reported in patients with VTE [2–5]. Therefore, VTE is not only a serious medical condition, but can also be stress-inducing and emotionally draining.

Current VTE treatment options consist of various oral and injectable anticoagulants [6]. Warfarin has been the traditional treatment for VTE [7,8], but several new direct oral anticoagulant (DOAC) agents including dabigatran, rivaroxaban, apixaban, and edoxaban have been licensed for VTE treatment [9–12]. Compared with warfarin patients prescribed DOACs require less monitoring, may experience fewer drug-drug interactions, and may not be affected by dietary restrictions [13]. Due to these differences, patients and prescribers have shown an increasing preference for and utilization of DOACs over warfarin [13,14]. In fact, consensus guidelines now recommend DOACs over warfarin for initial treatment of VTE [6].

Identifying the most common anticoagulation VTE treatment patterns is important for several reasons. Utilization trends allow health systems to budget and forecast resource utilization. Furthermore,

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associations between different anticoagulant patterns and various patient outcome variables, such as bleeding, recurrent VTE, medication adherence, satisfaction with care, the extent to which patients feel in control of their health, access to VTE care, and other psychosocial variables, have not been sufficiently identified. Understanding these associations may help explain patients' overall VTE care experiences and inform efforts to improve care.

Qualitative studies exploring the psychosocial impact of VTE have demonstrated the importance of psychological wellbeing during VTE treatment, and have highlighted a potential role for healthcare professionals to identify and support individuals at risk for VTE-related emotional harm [2,3,15]. However, the influence of different VTE treatment patterns on patient's perceptions of emotional wellbeing has not been adequately explored. Therefore, the objective of our study is to report associations between different anticoagulation patterns and bleeding and emotional harms based on patients' self-reported care experiences during VTE treatment.

2. Methods

2.1. Study design

This was a cross-sectional study using self-reported data from a national online VTE survey administered from May to July 2016. The study was approved by the University of Utah's Institutional Review Board (IRB) before initiating data collection. All participants provided informed consent prior to starting the survey.

2.2. Study participants [4]

Patients living in United States who were 18 years of age or older and had at least one self-reported VTE episode (DVT and/or PE) within the past 2 years were eligible and invited to take the survey. Patients diagnosed with cancer within the past 2 years were excluded. Participants were recruited by an independent contract research agency (Hall & Partners, New York, NY) from a nationally representative panel of patients who pre-enrolled to participate in research studies (Research Now®, Research Now Group, Inc., New York, NY). An invitation email was sent to all panel members describing the study and inviting them to enter the survey to answer screening questions related to inclusion and exclusion criteria. Those meeting inclusion criteria gave consent electronically by checking a consent box, and then moved immediately on to the full online survey which was completed in one sitting. The survey remained open until the predetermined sample size of approximately 1000 was achieved. Patients who had clinically implausible data and unrealistic survey completion times were removed from the dataset prior to the final analysis.

2.3. Anticoagulant pattern determination

Individual self-reported anticoagulation regimens were reported for each of three prespecified treatment phases, initial (0–7 days following VTE diagnosis), long-term (8–90 days), and extended (90 + days). Anticoagulant treatment patterns included: 1) injectable anticoagulants only, 2) warfarin, 3) DOACs, 4) switching between warfarin and DOAC therapy, 5) switching between different DOACs, 6) aspirin only, and 7) no anticoagulant medication. Concomitant injectable anticoagulant and aspirin use during treatment was also recorded. An overall anticoagulant pattern determination was recorded based anticoagulant use during the long-term and extended phases. Anticoagulant pattern assignments for each phase and overall were assigned independently by two different reviewers. Disagreements between reviewers were resolved by a third reviewer. For simplicity in the analysis, the seven anticoagulant patterns were consolidated into the following: warfarin, DOACs, switching between anticoagulants (comprised of the two switching patterns), and other (comprised of injectable only, aspirin only and no anticoagulant patterns).

2.4. Outcomes and measures

2.4.1. VTE experiences and anticoagulation therapies

Patients indicated the number of VTE events they had experienced in their lifetimes, the timing of their most recent VTE event (within the past month, between 1 and 3 months ago, 3 to 12 months ago, and > 12 months ago), and whether they had suffered DVT, PE or both. Patients also indicated which anticoagulant medications they had been prescribed for their most recent VTE event. Patients selected single or multiple agents from the following choices: warfarin, DOACs (dabigatran, rivaroxaban, apixaban, edoxaban), injectables (enoxaparin, fondaparinux, and unfractionated heparin), and aspirin. They could also report if no oral anticoagulants were prescribed.

2.4.2. Bleeding harms

Patients self-reported whether they had experienced any of the following since their most recent diagnosis of VTE: a nosebleed that was difficult to control, bleeding from a cut that was difficult to control, excessive bruising, vomiting blood or something that looked like coffee grounds, having blood in urine, or having blood in stool or stools that were black and/or tarry. Patients were also asked to indicate if any of these events caused them to go to the emergency room or hospital. Those who experienced any of these bleeding events were categorized as suffering bleeding harms regardless of whether the event resulted in an emergency room visit or hospitalization.

2.4.3. Emotional harms

Level of current anxiety and depression experienced by patients were assessed by The Hospital Anxiety and Depression Scale (HADS) [16]. This comprises two seven-item subscales for anxiety and depression, each with high previously reported internal consistency. Each item is scored on a 4-point Likert scale such as 0 – 'Not at all', 1 – 'From time to time, occasionally', 2 – 'A lot of the time', and 3 – 'Most of the time.' Patients who scored 11 or greater on anxiety or depression components of HADS were considered as having anxiety, depression, or both. Current VTE emotional distress was quantified with 8 items. Patients were asked the following question: "Thinking about how you feel living now with VTE; please indicate your level of feeling about each of the following." The items were "I feel …" tense, anxious, confused, depressed, afraid, angry, frustrated, or annoyed, each scored on a 5-point Likert scale of 0 – 'Not at all', 1 – 'A little', 2 – 'Moderately', 3 – 'Quite a bit', and 4 – 'Extremely'. Patients who indicated 'Quite a bit' or 'Extremely' with any of the 8 items were considered to suffer emotional distress. These items were summed to give a composite score (range of 0–40) with high internal consistency. To measure the fear of VTE recurrence, patients were asked: "Howoften do you worry about getting another clot in the future?" Responses were scored on a 5-point Likert scale of 0 – 'Not at all', 1 – 'Rarely', 2 – 'Sometimes', 3 – 'Often', and 4 – 'Almost all the time'. Patients who indicated 'Often' or 'Almost all the time' were considered to suffer from fear of recurrent clotting. This is a disease modified version of the breast cancer worries scale, a measure with high internal consistency [16,17].

2.4.4. Demographic and other variables

Patients indicated their age in years, sex, their self-identification of race and ethnicity, their community of residence, insurance type and status, and range of household income. Comorbidities experienced in the prior 2 years including anxiety, DVT, depression, diabetes, heart disease, high blood pressure, high cholesterol, PE, and stroke or TIA were also recorded.

2.5. Statistical analysis

Outcomes were summarized using basic descriptive statistics.

Analysis of variance and Chi-square tests were used to summarize comparisons in baseline characteristics between those who did and did not report experiencing harm and outcomes between treatment patterns. p-Values < 0.05 were considered statistically significant. When significant p-values were obtained in the univariable analysis, pairwise comparisons were tested for significance using a Bonferroni corrected p-value of < 0.0083 ($\alpha = 0.05/6$ pairwise comparisons) for determining statistical significance. Patient characteristics and other factors with p-values < 0.2 in the univariable analysis were entered into multivariable logistic regression models to identify variables associated with harm status.

3. Results

3.1. Patient characteristics

Of 4092 patients contacted by email, a total of 971 patients entered and completed the full survey. The data set was cleaned to remove patients giving nonsensical responses (i.e., not providing variation in answers, completing the survey in an unrealistically short time [i.e., < 6 min], giving manifestly inconsistent responses [e.g., selecting all available anticoagulant therapy options]) resulting in a total of 907 surveys for analysis. Baseline characteristics of the final survey sample are shown in Table 1. Participants had a mean age of 52.4 (standard deviation [SD] 14.4) years with most female (56.7%) and Caucasian (88.6%). Most recent VTE type was DVT for 63.8%, PE for 18.1%, and both for 18.1%. Mean time since most recent VTE episode was 2.2 (SD 1.0) months.

Self-reported comorbidities experienced within the previous two years were common including depression (28.4%), anxiety (26.7%), DVT (84.8%), PE (33.7%), hypertension (45.6%), and hyperlipidemia (38.3%). The most frequently reported anticoagulation treatment patterns were warfarin (38.7%), DOACs (26.1%), and those who switched between warfarin and DOAC or between different DOACs (17.9%).

3.2. Prevalence of harms

The majority of patients (79.5%) experienced at least one type of bleeding or emotional harm following their VTE diagnosis (Table 2). The risk of reporting any harm was higher in younger patients, those with a personal or family history of VTE, those experiencing VTE more recently, and those with prior history of anxiety, depression, or stroke/transient ischemic attack. Anticoagulant therapy treatment pattern was associated with the likelihood of self-reported harms. Compared to any other anticoagulant therapy pattern, patients who received DOAC therapy were less likely to report harm (81.9% vs. 72.6%, respectively, $p = 0.02$), and those who switched between anticoagulation therapy patterns were more likely to report harm (76.8% vs. 92.0%, respectively, $p < 0.0001$). Pairwise comparisons between different anticoagulation therapy patterns revealed that patients who switched between either warfarin and DOACs or between different DOACs were more likely to report harm than those who received warfarin, DOACs, or "Other" types of anticoagulant therapy ($p < 0.0001$ for all). The proportion of patients reporting harm while receiving DOAC therapy was lower than that of patients receiving warfarin (72.6% vs. 79.5%, respectively), but this difference was not statistically significant ($p = 0.052$).

Overall, self-reported bleeding of any severity and emotional harms occurred in 63.6% and 56.3% of VTE patients, respectively (Tables 3 and 4). Those who switched between warfarin and DOACs or between different DOACs experienced significantly higher rates of bleeding (77.8%) than those receiving only warfarin (63.5%, $p = 0.001$), DOACs (58.2%, $p = 0.00005$), or "Other" types of anticoagulant therapy (57.3%, $p = 0.00009$) (Table 3). More patients on warfarin suffered from bleeding harms than those on DOACs (63.5% vs. 58.2%, respectively), but this difference was not statistically significant ($p = 0.2$).

Table 1
Patient demographic and other characteristics.

Characteristic	Total (N = 907)
Age in years, mean (SD)	52.4 (14.4)
Male sex, count (%)	393 (43.3)
Body mass index 30 or more, count (%)	472 (52.0)
Comorbidities in past 2 years, count (%)[a]	
Anxiety	242 (26.7)
Depression	258 (28.4)
DVT	769 (84.8)
PE	306 (33.7)
Diabetes	156 (17.2)
Heart disease	249 (27.5)
High blood pressure	414 (45.6)
High cholesterol	347 (38.3)
Stroke or TIA	77 (8.5)
Most recent clot type, count (%)	
DVT	579 (63.8)
PE	164 (18.1)
Both	164 (18.1)
Number of VTEs in lifetime, median (IQR)	1 (0, 2)
Number of VTEs in last 2 years, median (IQR)	1 (0, 1)
Race, count (%)	
Caucasian	804 (88.6)
African American	55 (6.1)
Asian/Pacific Islander	22 (2.4)
Native American/Alaskan Native	6 (0.7)
Other	20 (2.2)
Family history of VTE, count (%)	328 (36.2)
Months since last VTE, mean (SD)	2.2 (1.0)
Community of residence, count (%)	
Rural	157 (17.3)
Small city or town	283 (31.2)
Suburb	345 (38.0)
Large city	122 (13.5)
Insured, (%)	883 (97.4)
Household income, count (%)	
Poor (< $25 K)	144 (15.9)
Low ($25 K–$49,999)	193 (21.3)
Middle ($50 K–$99,999)	329 (36.3)
High ($100 K or above)	241 (26.6)
Anticoagulant pattern, count (%)	
Warfarin	351 (38.7)
DOAC	237 (26.1)
Switched[b]	162 (17.9)
Other[c]	157 (17.3)

Abbreviations: DOAC (Direct Oral Anticoagulant), DVT (Deep Vein Thrombosis), IQR (interquartile range), PE (Pulmonary Embolism), SD (standard deviation), TIA (Transient Ischemic Attack), VTE (Venous Thromboembolism).

[a] 121 patients switched between warfarin and DOACs, 41 patients switched between DOACs.

[b] 35 patients received injectable anticoagulants only, 79 received aspirin only, 43 reported receiving no anticoagulants.

[c] More than one possible.

Overall patients reported that 34.3% of bleeding episodes required a visit the emergency room or hospitalization (range 7.4% for excessive bruising to 61.5% for vomiting blood or something that looked like coffee grounds).

Patients who switched between warfarin and DOACs or between different DOACs were more likely to report an emotional harm (72.2%) than those receiving only warfarin (54.1%, p = 0.001) or DOACs (46.4%, $p \leq 0.00001$) (Table 4). The difference in reported emotional harm rates between those who switched between warfarin and DOACs or between different DOACs and those who used only "Other" types of anticoagulants was not statistically significant after adjusting the p-value for multiple comparisons ($p = 0.02$). Patients receiving warfarin experienced more emotional harms (54.1%) than patients taking DOAC s (46.4%), but this difference was not statistically significant ($p = 0.07$), nor was the difference in emotional harm reported by those receiving DOACs compared to those receiving "Other" types of

Table 2
Patient demographic and other characteristics summarized by harm status (N = 907).

Characteristics	Any harm (N = 721)	No harm (N = 186)	p-Value
Age in years, mean (SD)	50.8 (14.5)	58.4 (12.4)	0.01
Male count (%)	303 (77.1)	90 (22.9)	0.1
Self-reported comorbidities count (%)[a]			
History of anxiety	214 (29.7)	28 (15.1)	< 0.0001
History of depression	228 (31.6)	30 (16.1)	< 0.0001
History of DVT	616 (85.4)	153 (82.3)	0.3
History of PE	239 (33.1)	67 (36.0)	0.5
History of diabetes	132 (18.3)	24 (12.9)	0.08
History of heart disease	196 (27.2)	53 (28.5)	0.7
History of high blood pressure	323 (44.8)	85 (45.7)	0.9
History of high cholesterol	281 (39.0)	66 (35.5)	0.4
History of stroke	70 (9.7)	7 (3.8)	0.01
Most recent clot type count (%)			
DVT	461 (63.9)	118 (63.4)	0.9
PE	131 (18.2)	33 (17.7)	0.9
Both	129 (17.9)	35 (18.8)	0.8
Number of DVTs in lifetime, median (IQR)	2 (1–3)	1 (1–2)	< 0.0001
Number of PEs in lifetime, median (IQR)	1 (0–2)	0 (0–1)	< 0.0001
Family history of VTE count (%)	285 (39.5)	43 (23.1)	< 0.0001
Months since last VTE, mean (SD)	2.1 (1.0)	2.5 (0.8)	< 0.0001
Anticoagulant pattern count (%)			
Warfarin	279 (38.7)	72 (38.7)	0.9[b]
DOAC	172 (23.9)	65 (34.9)	0.002[b]
Switched	149 (20.7)[c]	13 (7.0)	< 0.0001[b]
Other (LMWH, UFH, fondaparinux, aspirin)	121 (16.8)	36 (19.4)	0.4[b]

SD-standard deviation; DVT-deep vein thrombosis; PE-pulmonary embolism; IQR-interquartile range; VTE-venous thromboembolism; DOAC-direct oral anticoagulant; LMWH-low molecular weight heparin; UFH-unfractionated heparin.

[a] Percent of total experiencing and not experiencing harm.

[b] Compared to any other anticoagulant therapy pattern.

[c] Pairwise comparisons between the switched group and warfarin, DOACs, and "Other" anticoagulant therapy categories were statistically significant, $p < 0.0001$ for all.

anticoagulants after correcting the p-value for multiple comparisons ($p = 0.009$). The odds of reporting emotional harm more than doubled in patients who also experienced bleeding events (odds ratio 2.3, 95% confidence interval 1.7 to 3.0, $p < 0.0001$).

Multivariable logistic regression models indicated that prior history of stroke was associated with increased odds of reporting any harm outcome (odds ratio [OR] 2.90, 95% confidence interval [CI] 1.30–6.60) and bleeding of any severity (OR 2.57, 95% CI 1.42–4.66) (Table 5). Compared to warfarin therapy, switching between anticoagulant types was associated with increased odds of reporting any harm outcome (OR 2.02, 95% CI 1.10–3.90), bleeding of any severity (OR 1.78, 95% CI 1.14–2.79), and bleeding resulting in an ER visit or hospitalization (OR 2.32, 95% CI 1.44–3.76) and DOAC therapy was associated with reduced odds of reporting emotional harm (OR 0.68, 95% CI 0.47–0.98). Increasing age and time since most recent VTE episode were also associated with decreased odds of reporting any harm outcome, bleeding events resulting in an emergency room visit or hospitalization, or emotional harms.

4. Discussion

We found that self-reported anticoagulant therapy patterns were associated with the risk of experiencing bleeding and/or emotional harm during VTE treatment. In particular, patients who switched between warfarin and DOACs or between different types of DOACs reported experiencing significantly higher rates of both bleeding and emotional harms than all the other anticoagulant therapy patterns. Multivariable logistic regression results indicated that compared to warfarin therapy those who switched between anticoagulants were approximately twice as likely to report experiencing a composite harm outcome or bleeding harms. Potential reasons explaining why patients might switch between anticoagulants during VTE treatment include experiencing the types of bleeding and emotional harms assessed in our survey, therapeutic failure, individual patient preferences, or medication costs. Therefore, prospective research with longitudinal follow up and clearly defined reasons for switching is needed to determine whether switching between anticoagulants is a cause or result of treatment-related harms. Patients who switch between anticoagulant therapies may require a heightened level of attention, monitoring, and support including addressing any transportation issues, cost constraints, insurance issues, social support needs, or modifiable bleeding risk factors, such as uncontrolled hypertension, labile INRs, concomitant use of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs), and excessive alcohol use [20]. The multivariable analysis also provided evidence that compared to warfarin therapy patients who were prescribed DOACs had reduced odds of reporting emotional harm. This is an important finding as the proportion of DOAC utilization in VTE patients continues to increase [18,19].

We also found associations between various patient characteristics and increased odds of experiencing harm including younger patients, those with more recent VTE diagnoses, and history of depression, anxiety, diabetes and/or stroke. Awareness of these associations may help clinicians be more vigilant for potential bleeding and emotional harms in patients with these characteristics. Further study is needed to determine if specific interventions such as increased monitoring frequency, enhanced education, or behavioral interventions may reduce the potential for harm [5]. Our results indicate that most patients receiving treatment for VTE will experience bleeding and/or emotional harms and increasing vigilance for potential harm for all patients

Table 3
Proportion of patients with recently diagnosed venous thromboembolism suffering bleeding harms summarized by anticoagulant treatment patterns.

Bleeding types (%)	Total	Warfarin	DOAC	Switched[a]	Other[b]	p-Value
Any	577 (63.6)	223 (63.5)[c]	138 (58.2)[d]	126 (77.8)	90 (57.3)[e]	0.0002
A nosebleed that was difficult to control	145 (16.0)	52 (14.8)	28 (11.8)	47 (29.0)	18 (11.5)	< 0.05
Bleeding from a cut that was difficult to control	300 (33.1)	117 (33.3)	78 (32.9)	62 (38.3)	43 (27.4)	0.2
Excessive bruising	408 (45.0)	176 (50.1)	79 (33.3)	88 (54.3)	65 (41.4)	< 0.05
Vomiting blood or something that looked like coffee grounds	39 (4.3)	7 (2.0)	7 (3.0)	20 (12.3)	5 (3.2)	< 0.05
Having blood in your urine	90 (9.9)	28 (8.0)	16 (6.8)	30 (18.5)	16 (10.2)	< 0.05
Having blood in your stool or stools that were black and/or tarry	96 (10.6)	33 (9.4)	16 (6.8)	30 (18.5)	17 (10.8)	< 0.05

DOAC-direct oral anticoagulant.

[a] 121 patients switched between warfarin and DOACs, 41 patients switched between DOACs.

[b] 35 patients received injectable anticoagulants only, 79 received aspirin only, 43 reported receiving no anticoagulants.

[c] $p = 0.001$ compared to "Switched" group.

[d] $p = 0.00005$ compared to "Switched" group.

[e] $p = 0.00009$ compared to "Switched" group.

Table 4
Proportion of patients with recently diagnosed venous thromboembolism suffering emotional harms summarized by anticoagulant treatment patterns.

Emotional harm type (%)	Total	Warfarin	DOAC	Switched[a]	Other[b]	*p*-Value
Any	511 (56.3)	190 (54.1)[c]	110 (46.4)[d]	117 (72.2)	94 (59.9)	< 0.00001
Anxiety	224 (24.7)	71 (20.2)	43 (18.1)	65 (40.1)	45 (28.7)	< 0.05
Depression	105 (11.6)	40 (11.4)	21 (8.9)	21 (13.0)	23 (14.6)	0.3
Current distress	293 (32.3)	92 (26.2)	60 (25.3)	85 (52.5)	56 (35.7)	< 0.05
Fear of having another clot	368 (40.6)	152 (43.3)	81 (34.2)	73 (45.1)	62 (39.5)	0.09

DOAC-direct oral anticoagulant.
[a] 121 patients switched between warfarin and DOACs, 41 patients switched between DOACs.
[b] 35 patients received injectable anticoagulants only, 79 received aspirin only, 43 reported receiving no anticoagulants.
[c] $p = 0.001$ compared to "Switched" group.
[d] p = 0.00001 compared to "Switched" group.

Table 5
Factors associated with patient-reported harms in the multivariable logistic regression models.

Characteristic	Odds ratio (95% confidence interval)
Composite of harm outcomes	
Age (per year increase)	0.97 (0.96–0.98)
History of stroke	2.90 (1.30–6.60)
Switched between anticoagulant types[a]	2.02 (1.10–3.90)
Months since last VTE episode	0.70 (0.57–0.88)
Any bleeding harm	
History of stroke	2.57 (1.42–4.66)
Switched between anticoagulant types[a]	1.78 (1.14–2.79)
Bleeding harm resulting in ER visit or hospitalization	
Age (per year increase)	0.97 (0.96–0.99)
History of depression	1.78 (1.11–2.86)
History of diabetes	1.64 (1.02–2.62)
Switched between anticoagulant types[a]	2.32 (1.44–3.76)
Months since last VTE episode	0.79 (0.66–0.96)
Any emotional harm	
Age (per year increase)	0.96 (0.95–0.97)
History of anxiety	1.66 (1.09–2.52)
DOAC therapy[a]	0.68 (0.47–0.98)
Months since last VTE episode	0.60 (0.51–0.72)

ER-emergency room; VTE-venous thromboembolism; DOAC-direct oral anticoagulant.
[a] Compared to warfarin therapy.

receiving treatment for VTE may be necessary as harms can substantially affect patient satisfaction, medication adherence, quality of life, and other important factors related to patient outcomes and healthcare costs [4,21]. Carefully questioning patients about bleeding events and how their VTE is affecting them emotionally may be especially important early in therapy, in younger patients, and in those who have switched between anticoagulants. Based on the high harm rates reported by our study participants during VTE treatment, it is reasonable to conclude that anticoagulation therapy management and VTE care experiences require further optimization.

Our study had several strengths as well as limitations. We evaluated a large national sample of recent VTE sufferers which increases the generalizability of our findings. However, because we relied on self-reported VTE events there is a small potential that some patients may not have experienced an actual VTE. We attempted to minimize the potential for this by excluding patients providing implausible responses and completing the survey in an unrealistic timeframe as described in the methods. We acknowledge the possibility, albeit small, that the findings of this study may not be generalizable to patients with objectively diagnosed VTE. We included self-reported perception of harms which focuses on outcomes that are important to patients. We were thus able to quantifiably analyze subjective patient experiences and provide insights into anticoagulation utilization patterns and patient's care experiences in actual clinical practice. On the other hand, patient-reported information relating to comorbidities, VTE history, anticoagulant treatment pathway, and bleeding events is subject to recall bias and potential for under or over-reporting. Patients may have interpreted descriptions of bleeding severity such as "a nosebleed that was difficult to control" or "excessive bruising" differently. It is possible that variability in timing from most recent VTE diagnosis to survey response resulted in differences in frequency of harms reported. We also acknowledge the potential for identification bias associated with the fact that VTE events qualifying patients for survey participation were not objectively verified. In addition, many bleeding events reported by patients in our study would likely not have meet established definitions of bleeding such as the International Society on Thrombosis and Haemostasis criteria for major and clinically relevant non-major bleeding. Study participation was limited to those with online access and patients were limited in racial diversity and age range. The proportion of the panel initially invited to take the survey with actual VTE events is unknown and therefore we are unable to determine the true response rate to our survey.

5. Conclusion

Self-reported bleeding and emotional harms occurred commonly during VTE treatment and were more likely to be reported by patients with identifiable clinical, demographic, and psychosocial characteristics. Switching between warfarin and DOACs or between different DOACs during VTE treatment was associated with the highest rates of both bleeding and emotional harms and may be a marker for patients who require additional support. Compared to warfarin DOAC therapy was associated with reduced odds of experiencing emotional harm. Special care may be required for younger patients, those with more recent VTE diagnosis, and patients with a history of depression, anxiety, stroke, and/or diabetes.

Disclosure statement

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Declaration of competing interest

Dr. Feehan has consulted to Pfizer in the past. All other authors have no conflicts to report.

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