

# Extended anticoagulation for venous thromboembolism: A survey of the American Venous Forum and the European Venous Forum

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## ABSTRACT

**Objective:** Extended anticoagulation therapy should always be considered after standard treatment of an unprovoked episode of venous thromboembolism (VTE). It can also be considered for selected patients with provoked VTE. However, the evidence-based protocols suggested by some clinical guidelines and risk assessment tools to guide this practice are limited and ambiguous. The goal of the present survey research was to analyze current practices in applying extended anticoagulation therapy for patients with VTE among members of the American Venous Forum (AVF) and European Venous Forum (EVF).

**Methods:** An online survey was created by the AVF Research Committee. The survey consisted of 16 questions to identify the country of practice, specialty, experience of the participating physicians, and their clinical practice patterns in applying extended anticoagulation therapy for VTE patients. The survey was distributed via e-mail to the members of the AVF and EVF.

**Results:** A total of 144 practitioners, 48 AVF members (33%) and 96 EVF members (66%), participated in the survey. Most of the respondents identified themselves as vascular specialists with primary certification in vascular surgery (70%), vascular medicine or angiology (9%), and venous disease or phlebology (3%). Of the 144 respondents, 72% believed that the risk of VTE recurrence will generally outweigh the risk of bleeding for patients with unprovoked VTE. Extended anticoagulation therapy might be used by 97% of providers. Different patterns in real world clinical practice were identified. More than one half of the practitioners estimated the VTE recurrence and bleeding risk subjectively. The antithrombotic drugs most commonly used for secondary prophylaxis were rivaroxaban, apixaban, warfarin, dabigatran, and aspirin, in decreasing order of frequency. Among the reasons selected for not regularly considering extended anticoagulation therapy were the lack of specific clinical practice guidelines (24%), lack of reported evidence (9%), and absence of valid VTE and/or bleeding risk prediction calculators (8%). Twelve participants (8%) stated that extended anticoagulation therapy would not be beneficial for most patients with VTE. Ten participants (7%) indicated that prescribing extended anticoagulation therapy was outside the scope of their specialty.

**Conclusions:** Different practice patterns exist regarding extending anticoagulation therapy beyond the standard treatment for patients with VTE. Major gaps in knowledge remain a serious challenge at least partially explaining the inaccuracy and inconsistency in long-term VTE management. Appropriately designed studies are needed to evaluate risk stratification tools when contemporary best medical therapy is used, accurately predict VTE recurrence and its long-term outcomes, and tailor safe and effective secondary prophylaxis. (*J Vasc Surg Venous Lymphat Disord* 2022;10:1012-20.)

**Keywords:** American Venous Forum; Anticoagulation; Deep vein thrombosis; European Venous Forum; Pulmonary embolism; Survey; Venous thromboembolism; Venous thrombosis

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Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), affects 1 to 2 individuals per 1000 persons annually worldwide.<sup>1,2</sup> Anticoagulation remains the mainstay of treatment for the entire spectrum of venous thromboembolic conditions.<sup>3-7</sup> Clinical practice guidelines have suggested anticoagulation therapy for 3 to 6 months as the standard of care for acute VTE.<sup>3-7</sup> Despite significant progress, many aspects of anticoagulation therapy for VTE have remained unexplored.

VTE is usually considered an acute time-limited condition. However, it will often lead to chronic post-thrombotic changes of the affected segments of the deep venous system. The result of these changes is a tendency for acute VTE to become a chronic recurrent condition with remote regional and systemic effects. At least one third of patients with a first-time unprovoked DVT will experience another symptomatic episode within 10 years after completion of standard anticoagulation therapy.<sup>8</sup> The recurrence risk is highest within the first year after the initial VTE episode but will remain elevated  $\geq 10$  years later.<sup>9,10</sup> The results from a nationwide population-based study from Denmark are consistent with these observations, reporting an increased disease-specific mortality for 30 years after unprovoked VTE.<sup>11</sup>

The VTE recurrence rate can be significantly reduced by extending anticoagulation therapy.<sup>12</sup> However, anticoagulation therapy has been associated with an increased incidence of bleeding.<sup>13</sup> Therefore, extension of anticoagulation therapy requires careful balancing of the VTE recurrence and bleeding risks. The VTE recurrence risk will be reduced only during anticoagulation therapy and increases soon after its discontinuation.<sup>14-16</sup> Therefore, evaluation of the potential benefits of prolonging anticoagulation therapy is a challenge that in many VTE cases will persist indefinitely.

As a reflection of the expanding knowledge in the natural history of VTE<sup>8-11</sup> and the better safety profile of new anticoagulant agents,<sup>17</sup> the tendency to extend anticoagulation therapy beyond the standard treatment duration has been increasing. Clinical guidelines have suggested considering extended anticoagulation therapy for all patients with unprovoked VTE after 3 to 6 months of conventional therapy.<sup>3-7</sup> However, real world clinical practice has not routinely incorporated these recommendations. Several VTE recurrence<sup>18-21</sup> and bleeding<sup>4,22-29</sup> risk stratification tools have been created to facilitate clinical decision making; however, their actual use is unknown. In addition, various agents and therapeutic regimens have been used for extended antithrombotic therapy; however, randomized clinical trials are lacking. The goal of the present survey research was to analyze current practices in applying extended anticoagulation therapy for patients with VTE among

## ARTICLE HIGHLIGHTS

- **Type of Research:** A survey research study
- **Key Findings:** Multiple practice patterns have been in use for extending anticoagulation therapy for patients with venous thromboembolism, which reflects the lack of scientific evidence, lack of convenient and valid risk assessment tools, and lack of strong recommendations within the evidence-based clinical practice guidelines.
- **Take Home Message:** Appropriately designed studies are needed to accurately predict the risk of venous thromboembolism recurrence, guide appropriate long-term follow-up, and tailor safe and effective antithrombotic therapy for secondary prophylaxis.

the members of the American Venous Forum (AVF) and European Venous Forum (EVF).

## METHODS

**Survey design.** The AVF Research Committee developed a survey to evaluate current practices in extending the anticoagulation therapy duration beyond 3 to 6 months for patients with VTE. The survey also aimed to identify any perceived barriers to improving current practices. The survey consisted of 16 questions with preselected answers (Appendix). The questions were created using an iterative and interactive process by the members of the AVF Research Committee. Given the lack of reported data on the topic, no prior validated questionnaires were available to use for our survey. An expert committee was formed from the AVF Research Committee and several outside experts. The questions were developed as a springboard after a comprehensive literature review. This allowed for solidification of the questionnaire format, the development of the necessary items, and the length of the survey. The survey was reviewed and revised multiple times until the final version had been approved by the entire AVF Research Committee and the AVF Executive Committee. The final version of the survey was launched on the AVF website using the MemberClicks platform (MemberClicks LLC, Atlanta, GA). The survey was distributed as a link via e-mail in July 2020 to all AVF and EVF members. Three reminders were also sent by e-mail 1 month apart to nonresponders. The first three questions included the country of practice, specialty, and level of current clinical activity in treating patients with VTE. The remaining questions focused on awareness of the reported evidence and current practices for VTE management. The present study was performed in accordance with the Declaration of Helsinki. Participation in the survey was voluntary and anonymous with no physician-, institution-, or patient-specific identifiers created.

Provision of informed consent for participation was implied by the act of returning the survey to the investigators. A separate signed consent form was not obtained. The study qualified as exempt by the institutional review board.

**Risk prediction models.** The survey inquired about routine use of the following VTE recurrence prediction models: HERDOO2 (hyperpigmentation, edema, redness, D-dimer, obesity, older age, 2 scores) score,<sup>18,19</sup> Vienna prediction model,<sup>20</sup> and DASH (D-dimer, age, sex, hormonal therapy) score.<sup>21</sup> The survey also inquired about the use of the following bleeding risk assessment tools: OBRI (Outpatient Bleeding Risk Index),<sup>22</sup> Kuijjer et al,<sup>23</sup> HEMORR<sub>2</sub>HAGES (hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count or function, rebleeding, hypertension, anemia, genetic factors, excessive fall risk, and stroke),<sup>24</sup> RIETE (Registro Informatizado de Enfermedad Tromboembolica),<sup>25</sup> HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol),<sup>26</sup> ATRIA (anticoagulation and risk factors in atrial fibrillation),<sup>27</sup> ACCP (American College of Chest Physicians),<sup>4</sup> EINSTEIN (once-daily oral direct factor Xa inhibitor rivaroxaban in the long-term prevention of recurrent symptomatic venous thromboembolism in patients with symptomatic deep vein thrombosis or pulmonary embolism),<sup>28</sup> and Hokusai-VTE [comparative investigation of low molecular weight (LMW) heparin/edoxaban tosylate (DUI76b) versus (LMW) heparin/warfarin in the treatment of symptomatic deep vein blood clots and/or lung blood clots].<sup>29</sup>

**Definitions.** Standard anticoagulation was defined as therapeutic anticoagulation therapy within 3 to 6 months after the initial VTE diagnosis. Extended anticoagulation therapy was defined as any form of anticoagulation therapy that had extended beyond the standard period of anticoagulation (>3-6 months). Finally, antithrombotic therapy was used as an umbrella term to encompass treatment with anticoagulation drugs, antiplatelet agents, and sulodexide.

**Statistical analysis.** Statistical analysis was performed using SPSS software, version 26.0 (IBM Corp, Armonk, NY) and Prism 9 software, version 9.1.1 (GraphPad Software, San Diego, CA). Descriptive statistics was used for the data organized in a frequency distribution table in Excel (Microsoft Corp, Redmond, WA). Spearman's rank order correlation coefficient was used to discover possible associations between the country of practice, specialty certification, level of clinical activity, and clinical practice patterns. A *P* value of < .05 was considered statistically significant. Bonferroni's correction was performed to adjust for multiple comparisons.

## RESULTS

**Demographics.** A total of 144 practitioners, 48 AVF members (33%) and 96 EVF members (67%), completed the survey. Most of the respondents were from the United States (31%), followed by Portugal (10%), Argentina (5%), Italy (5%), Switzerland (4%), Poland (4%), Russia (4%), with 2% each from Belgium, Cyprus, Georgia, Germany, Greece, Mexico, Serbia, and Turkey and 1% each from Albania, Chile, Colombia, Denmark, Ecuador, Finland, Iran, Israel, Nepal, and Slovenia. Most respondents had identified themselves as vascular specialists with primary certification in vascular surgery (70%). The remaining had been certified in general surgery (11%), vascular medicine or angiology (9%), venous disease or phlebology (3%), internal medicine (2%), interventional radiology (1%), interventional cardiology (1%), cardiothoracic surgery (1%), plastic surgery (1%), and hematology (1%). Most providers reported seeing more than five patients with VTE per month: 1 to 5 patients/month, 30%; 6 to 10 patients/month, 39%; 10 to 20 patients/month, 17%; and >20 patients/month, 14%.

**VTE and bleeding risk assessments.** Of the participants, 72% believed that, as a general rule, the risk of VTE recurrence outweighed the risk of bleeding for patients with unprovoked VTE. Extended anticoagulation therapy was routinely used by 59% providers, implemented on occasion by 38%, and was never considered by only 3% for patients with first-time unprovoked VTE. The VTE subtypes for which extended anticoagulation therapy could be prescribed are listed in [Table I](#). Of the providers, 85% always estimated both VTE recurrence and bleeding risk when considering the use of extended anticoagulation therapy.

The use of the currently available VTE recurrence risk prediction models is illustrated in [Fig 1](#). Of the participants, 67% reported they did not use risk calculators and estimated the VTE risk subjectively. Various combinations of risk calculators and additional risk factors were used by 6% of the providers. The risk factors that should be considered in the prediction of VTE recurrence according to the survey results are listed in [Table II](#). The other factors included morbid obesity (2%), immobility (1%), smoking (1%), collateralization of venous outflow (1%), factor VIII level in plasma (1%), hormonal therapy (1%), chemotherapy (1%), and indwelling vascular catheters (1%). The use of the bleeding risk assessment tools is presented in [Fig 2](#). One half of participants estimated the risk of bleeding subjectively.

**Implementation of extended therapy.** The drugs most commonly used for extended antithrombotic therapy were rivaroxaban, apixaban, warfarin in the therapeutic dose (international normalized ratio, 2.0-3.0), dabigatran, aspirin, and sulodexide ([Fig 3](#)). Less than 5% of the providers reported using other agents, such as warfarin in a

**Table I.** Usage of an extended anticoagulation regimen for different venous thromboembolism (VTE) subtypes (n = 144)

VTE subtype	Answered "Yes," No. (%) <sup>a</sup>
Recurrent iliofemoral DVT	134 (93.1)
Recurrent femoropopliteal DVT	132 (91.7)
Recurrent PE	130 (90.3)
First-time massive PE	119 (82.6)
First-time unprovoked iliofemoral DVT	115 (79.9)
First-time submassive/nonmassive PE	84 (58.3)
First-time unprovoked femoropopliteal DVT	79 (54.9)
Recurrent isolated distal DVT	72 (50.0)
First-time provoked DVT incited by a nonsurgical factor	33 (22.9)
First-time unprovoked isolated distal DVT	20 (13.9)

DVT, Deep vein thrombosis; PE, pulmonary embolism.  
<sup>a</sup>Total percentage >100% because the question allowed for multiple responses.

subtherapeutic dose (1%), low-molecular weight heparin in a therapeutic dose (1%), edoxaban (1%), and acenocumarol (1%). Most respondents (79%) believed that direct oral anticoagulant agents are associated with a lower bleeding risk compared with warfarin. The remaining participants believed that the risk is the same (12%), higher (3%), or were unsure (6%) about any difference.

More than 95% of the participants followed up their patients at some point during extended treatment. The follow-up intervals selected by the participants were

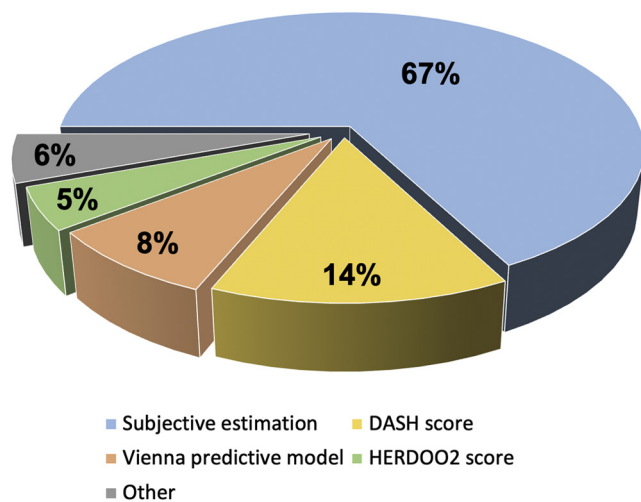
every 3 months (41%), every 6 months (33%), every 12 months (21%), and monthly (1%). One participant (1%) referred patients for follow-up to hematology, and three (2%) reported different follow-up periods determined on a case-by-case basis.

Estimation of the risk/benefit ratio for extended anticoagulation implies a numerical comparison of the risks of specific detrimental effects. The primary end points considered are summarized in Table III. Most respondents reported that the risk of VTE recurrence without anticoagulation therapy should be compared with the risk of major bleeding during anticoagulation therapy. The effects of anticoagulation therapy on mortality and post-thrombotic syndrome were considered less important for decision making.

In answering question 15, regarding the case of a 40-year-old woman taking rivaroxaban 1 year after an unprovoked DVT, 40% would elect to stop anticoagulation therapy, and 13% would continue the therapy, comprising more than one half of the participants. Approximately one of five respondents would refer such a patient to another specialist: the physician who had initially prescribed the anticoagulation therapy (8%) or a hematologist (13%). One quarter of the respondents (26%) did not find any of the preselected answers appropriate. Of these, only three providers (2%) clearly indicated that the risk of bleeding and VTE recurrence should be estimated. Two practitioners (1%) suggested extending anticoagulation therapy with a reduced dose of the same therapeutic agent. Nine physicians (6%) indicated that more information was needed to make the clinical decision. Finally, 21 providers (15%) suggested further evaluation, in various combinations, including history and physical examination, duplex ultrasound, D-dimer measurement, thrombophilia screening, cancer screening, and evaluation for venous obstruction (Supplementary Table, online only).

Among the reasons extended anticoagulation therapy might not be considered on a regular basis for all VTE patients, respondents selected the lack of specific instructions in the clinical practice guidelines (24%), lack of reported evidence (9%), and absence of valid VTE and/or bleeding risk calculators (8%). Twelve participants (12%) believed that extended anticoagulation would not be beneficial for most patients with VTE. Ten respondents (7%) indicated that prescribing extended anticoagulation therapy was outside the scope of their specialty. The cost of treatment (1%), patient refusal (1%), and medical malpractice concerns in the case of a major bleeding episode (1%) were also reported as barriers to extended anticoagulation therapy.

**Correlation analysis.** The correlation analysis did not reveal any meaningful correlations between the



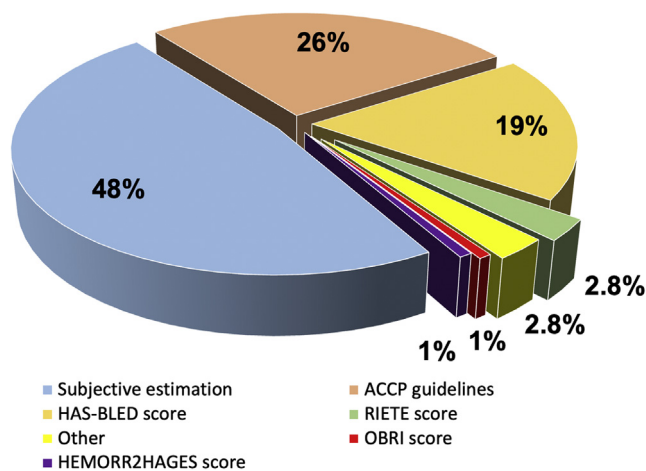
**Fig 1.** Venous thromboembolism (VTE) risk assessment. DASH, D-dimer, age, sex, hormonal therapy; HERDOO2, hyperpigmentation, edema, redness, D-dimer, obesity, older age, 2 scores.

**Table II.** Risk factors for venous thromboembolism (VTE) recurrence (n = 144)

Risk factor	Answered "Yes," No. (%) <sup>a</sup>
Active malignancy	132 (91.7)
Hereditary thrombophilia	130 (90.3)
VTE etiology	108 (75.0)
Acquired thrombophilia	101 (70.1)
Age	98 (68.1)
VTE anatomic extent	85 (59.0)
Elevated D-dimer level	78 (54.2)
Post-thrombotic syndrome	78 (54.2)
Leg paresis/paralysis	69 (47.9)
Residual luminal vein diameter	62 (43.1)
Male gender	50 (34.7)
Other	10 (6.9)

<sup>a</sup>Total percentage >100% because the question allowed for multiple responses.

responses to different survey questions. The practice patterns did not correlate with the country of practice, primary specialty certification, or level of clinical activity. We found a moderate correlation between the responses to survey questions 8 and 10 ( $r = 0.47$ ;  $P < .00001$ ) suggesting that providers using risk stratification scores for VTE recurrence were likely to also use a scoring system for bleeding.



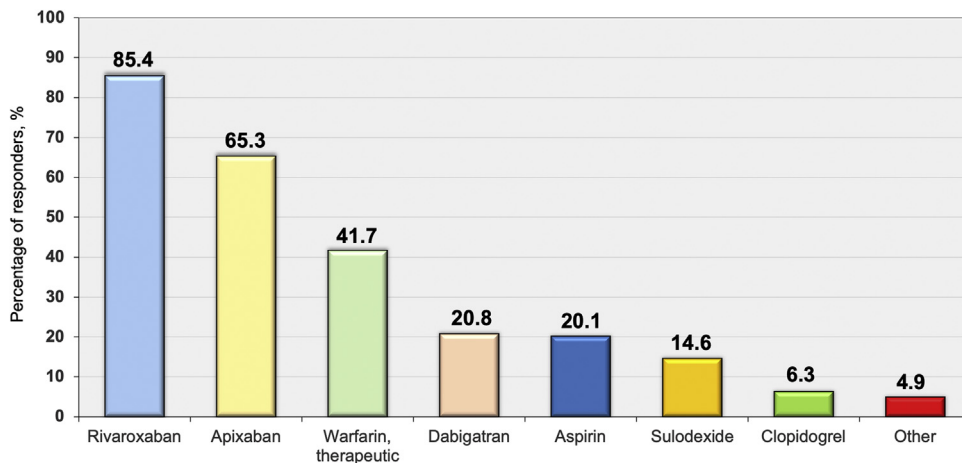
**Fig 2.** Bleeding risk assessment. ACCP, American College of Chest Physicians; HAS-BLED, hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol; HEMORR2HAGES, hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count or function, rebleeding, hypertension, anemia, genetic factors, excessive fall risk, and stroke; OBRI, Outpatient Bleeding Risk Index; RIETE, Registro Informatizado de Enfermedad Tromboembolica.

## DISCUSSION

The present survey research resulted from a collaboration between two large professional societies to better understand the current practices in the use of extended anticoagulation therapy for patients with VTE. The main goal of this manuscript was to provide structured feedback to the survey participants and the rest of the AVF and EVF membership. We hope that our report will increase awareness of the problem, attract more interest, and initiate appropriate discussion and further research activities.

**Which patients might benefit from extended anticoagulation therapy?** More than 90% of providers would consider extended therapy for patients with recurrent VTE (Table I), suggesting that a patient's personal VTE history is a strong and a well-recognized risk factor for recurrence.<sup>3-7</sup> In addition, almost all respondents agreed that unprovoked VTE requires at least the consideration for extended anticoagulation therapy, as delineated by multiple clinical practice guidelines.<sup>3-7</sup> However, it appeared that the anatomic extent of VTE can significantly adjust this decision-making. Patients with more distal DVT and PE with a lower embolic burden were less likely to be treated beyond the standard anticoagulation duration. Further studies are required to address the benefits of extended therapy for this subgroup of patients. The risk of recurrence after VTE provoked by surgery appears to be the same as the incidence of VTE in the general population.<sup>30</sup> Withholding anticoagulation therapy after 3 months of treatment has usually been recommended.<sup>3-7</sup> However, the incidence of another symptomatic episode after VTE provoked by a nonsurgical risk factor has been at least twice higher than that in the general population.<sup>30</sup> According to the survey results, one quarter of the participants might extend anticoagulation therapy in this scenario, which could be an interesting avenue for further research. Patients presenting with PE have a four times greater risk of recurrent symptomatic PE with a threefold greater case-fatality rate compared with patients initially presenting with DVT.<sup>31,32</sup> The latter suggests the need for more aggressive secondary prophylaxis. Most respondents would consider extending anticoagulation therapy for patients with massive PE. However, at present, the clinical guidelines do not support such a practice for patients with provoked massive PE.<sup>3-7</sup> This inconsistency might need further clarification by target studies.

**Challenges in objective VTE recurrence and bleeding risk assessment.** Extended anticoagulation therapy was used by most survey respondents. Thus, most participating providers will somehow estimate the risk of VTE recurrence in their practice. Because risk is a measurable uncertainty, it seems intuitive to estimate VTE recurrence



**Fig 3.** Medications used for extended anticoagulation therapy.

using a numerical scale to mitigate subjectivity and promote reliability in the risk assessment. However, the currently available VTE risk calculators have serious limitations.<sup>18-21</sup> First, they do not recognize the exact anatomic location of VTE as a strong independent risk factor for recurrence.<sup>33,34</sup> They also do not consider residual intraluminal masses as a possible risk factor.<sup>35,36</sup> Second, an optimal threshold for the D-dimer level to predict VTE recurrence has continued to be disputed and inconsistent between the risk scoring tools. Third, at present, no predictive tools assign a magnitude to each major risk factor. Thus, it is unclear which risk factors might play the leading role in the complex synergism of known risk factors. In addition, some patient-related factors, such as undiagnosed nonthrombotic venous outflow obstruction or clinically silent cancer, could be unknown at the time of the decision, rendering accuracy for individual risk calculation even more challenging. The

American Society of Hematology has recommended against the routine use of prognostic scores to guide the duration of anticoagulation therapy.<sup>6</sup> However, these guidelines have also suggested that clinicians and patients could use prognostic scores when the balance between risks and benefits is uncertain. Balancing the risks and benefits will always have some level of uncertainty and disagreement between providers unless measured using the same objective tool.

Major bleeding during anticoagulation therapy is likely to be encountered more frequently in clinical practice than that reported in clinical trials.<sup>37</sup> Hence, extrapolation of the bleeding risk from randomized trials, as some providers might do, introduces inaccuracy into the bleeding risk assessment. However, the current objective estimation of the bleeding risk is also imprecise. First, only one half of bleeding risk scores were designed specifically for patients with acute VTE.<sup>23,25,28,29</sup> Second, the safety profiles for the different anticoagulant agents are not equivalent.<sup>38-42</sup> Third, subtherapeutic anticoagulation therapy mitigates the risk of bleeding and deserves to be considered and further investigated.<sup>43,44</sup> To add more complexity, many patients will receive antiplatelet therapy, nonsteroidal anti-inflammatory drugs, and/or antisecretory medications, which could change the overall bleeding risk. It is also well-known that the bleeding risk is the highest at the beginning of anticoagulation therapy and decreases over time.<sup>13</sup> These factors and the dynamic nature of the bleeding risk are not recognized by the risk prediction tools.

**The current state of extended therapy.** Two thirds of the practitioners considered VTE recurrence as a more clinically relevant event than bleeding, potentially biasing them toward more aggressive anticoagulation therapy. Most respondents elected to discontinue anticoagulation therapy for a young female patient with an

**Table III.** Clinical outcomes suggested for calculation of risk/benefit ratio for extended anticoagulation therapy (n = 144)

Risk factor	Answered "Yes," No. (%) <sup>a</sup>
Major bleeding	126 (87.5)
VTE recurrence	117 (81.3)
Case-fatality rate of bleeding	79 (54.9)
Severe post-thrombotic syndrome	72 (50.0)
Case-fatality rate of VTE recurrence	71 (49.3)
Moderate post-thrombotic syndrome	37 (25.7)
Minor bleeding	24 (16.7)
Mild post-thrombotic syndrome	18 (12.5)
Other	2 (1.4)

VTE, Venous thromboembolism.

<sup>a</sup>Total percentage >100% because the question allowed for multiple responses.

unprovoked DVT (question 15). The information in the question was intentionally incomplete for important clinical variables, because iliofemoral DVT, a high residual thrombus burden, or a high D-dimer level might justify continuation of anticoagulation therapy if the bleeding risk is low. This inconsistency is an excellent example of real-world practice. The variety of answers illustrates the lack of standardization, limited usage of the risk calculators, and different opinions regarding which risk factors are clinically relevant.

The main finding from our survey was that at least one half of physicians estimated the risk of VTE recurrence and the risk of bleeding subjectively. Subjective estimation does not contribute to unbiasedness, transparency, repeatability, or reproducibility in the assessment of the risk and benefits of extended anticoagulation therapy. The subjective approach is also a serious obstacle to the development of a structured algorithm in VTE management. Because a physician's ability to predict for major bleeding might not be better than that expected by chance,<sup>22</sup> more consistent usage of the risk prediction calculators could prove helpful. A wider use of the risk calculators would also be an opportunity to standardize the current care protocols. These speculations, however, should be considered carefully. The poor usage of VTE and bleeding risk prediction tools could be partially explained by the inherent limitations in these tools. Different scoring systems have demonstrated poor performance for bleeding risk prediction in external validation studies, including the ACCP guidelines.<sup>45-47</sup> In some patient subgroups, such as cancer patients or the elderly, the bleeding risk scores also might not be accurate.<sup>48,49</sup> It is unclear whether using the available risk calculators will lead to better outcomes for VTE patients. Hence, from an evidence-based medicine viewpoint, any strategy to extend anticoagulation therapy will be an educated guess that remains hampered by the limited data.

The lack of evidence, valid risk assessment models, and clear clinical practice guidelines were reported by almost one half of the respondents as barriers for extended anticoagulation therapy for VTE. The clinical practice guidelines for VTE management are constantly improving and represent a reasonable pragmatic approach.<sup>6,7</sup> However, the guidelines cannot solve the problem of the lack of evidence. The high variability in the personal interpretation of the guidelines could be a sign of the weak evidence and limited applicability of these guidelines in real-world clinical practice. Until more accurate, reliable, and validated instruments emerge, secondary VTE prophylaxis strategies run the risk of remaining highly inconsistent between physicians.

**Future research directions.** Surveys are valuable tools that, along with registries, help to better understand real-world practices. The next step might be to involve more physicians and other professional societies devoted

to VTE to provide more robust data. Use of the Delphi protocol could be useful to develop an algorithm for extended anticoagulation therapy. An ideal method to improve extended anticoagulation therapy seems to be the development of a single comprehensive VTE recurrence and bleeding risk prediction tool using a large prospective cohort of patients with VTE, followed by external validation and standardization. A randomized trial comparing such a tool with guidelines-based physician decisions would be imperative to prove its superiority. The suggested VTE risk factors (Table II) and clinical end points (Table III) could be considered for future risk prediction models.

**Study limitations.** To the best of our knowledge, the present study is the first survey study of a difficult and controversial topic. Owing to the response rate obtained, biases could have been introduced and the statistical power could have been insufficient. The present findings must be corroborated and clarified by the ongoing investigation. The present survey did not include several subpopulations of VTE patients requiring a separate discussion, such as cancer-associated VTE. Some questions might have seemed overly simple, such as question 4; however, these were intended to understand the global picture rather than clarifying practice details. Some standardized answers, such as "hereditary thrombophilia," might seem incomplete; however, a more accurate set of answers would have made the question too complex for a short screening survey. Finally, the survey criticizes current practices without providing a clear solution to the issue. However, identification of this knowledge gap might be an important first step toward achieving better outcomes.

## CONCLUSIONS

We found different practice patterns for extending anticoagulation therapy beyond the standard treatment for patients with VTE. Improving awareness and continuous education on the current evidence and clinical practice guidelines are important tasks for practicing physicians with the active participation of professional societies. However, the major gaps in knowledge remain a serious challenge and can at least partially explain the inaccuracy and inconsistency in long-term VTE management. Appropriately designed studies are required to evaluate risk stratification tools when contemporary best medical therapy is used, accurately predict VTE recurrence and its long-term outcomes, and tailor safe and effective secondary prophylaxis.

The American Venous Forum (AVF) research committee included Maxim Shaydakov (committee chair), Windsor Ting (chair-elect), Mikel Sadek (past chair), Faisal Aziz (research council chair), Jose Diaz, Peter Henke, Nicos Labropoulos, Rafael Malgor, Andrea Obi, Sarah Onida, André van Rij, and Ruben Velletaz. The authors express

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## AUTHOR CONTRIBUTIONS

Conception and design: MES

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*Additional material for this article may be found online at [www.jvsvenous.org](http://www.jvsvenous.org).*

**APPENDIX (online only).**

**Survey questions.**

Question 1. What is your country of practice?  
\_\_\_\_\_

Question 2. What is your specialty certification?

- a. Vascular surgery
- b. Cardiothoracic surgery
- c. General surgery
- d. Interventional radiology
- e. Interventional cardiology
- f. Primary care
- g. Hematology
- h. Other (*please specify*): \_\_\_\_\_

Question 3. How many patients with venous thromboembolism (VTE) do you see per month?

- a. Less than 5
- b. 5-10
- c. 10-20
- d. More than 20

Question 4. In considering extended anticoagulation, which of these risks is more important in patients with unprovoked VTE in the long term?

- a. Bleeding during anticoagulation therapy
- b. Recurrence of VTE

Question 5. How often do you prescribe extended anticoagulation in patients with a first-time unprovoked VTE after completion of 3 months of active treatment?

- a. In all cases
- b. In most cases
- c. In some cases
- d. Never

Question 6. In which cases would you prescribe extended anticoagulation?  
(*indicate all that apply*)

- a. First-time unprovoked isolated distal deep vein thrombosis (DVT)
- b. First-time unprovoked femoropopliteal DVT
- c. First-time unprovoked iliofemoral DVT
- d. First-time provoked DVT incited by a nonsurgical factor
- e. First-time massive pulmonary embolism (PE)
- f. First-time submassive/nonmassive PE
- g. Recurrent isolated distal DVT
- h. Recurrent femoropopliteal DVT
- i. Recurrent iliofemoral DVT
- j. Recurrent PE
- k. Other (*please specify*): \_\_\_\_\_

Question 7. In order to prescribe extended anticoagulation, do you always estimate:

- a. Risk of bleeding
- b. Risk of VTE recurrence
- c. Risk of both bleeding and VTE recurrence
- d. Other (*please specify*): \_\_\_\_\_

Question 8. What do you use to estimate an individual's risk of VTE recurrence?

- a. HERDOO2 (hyperpigmentation, edema, redness, D-dimer, obesity, older age, 2 scores) score<sup>18,19</sup>
- b. Vienna predictive model<sup>20</sup>
- c. DASH (D-dimer, age, sex, hormonal therapy) score<sup>21</sup>
- d. None of the above — I do not use predictive models but estimate subjectively
- e. Other (*please specify*): \_\_\_\_\_

Question 9. Which of these risk factors should be considered to predict VTE recurrence? (*indicate all that apply*)

- a. Age
- b. Male gender
- c. D-dimer
- d. Residual luminal vein diameter
- e. VTE anatomic extent
- f. VTE cause
- g. Active malignancy
- h. Hereditary thrombophilia
- i. Acquired thrombophilia
- j. Post-thrombotic syndrome
- k. Leg paresis/paralysis
- l. Other (*please specify*): \_\_\_\_\_

Question 10. How do you estimate an individual's risk of bleeding in VTE patients?

- a. OBRI (Outpatient Bleeding Risk Index) score<sup>22</sup>
- b. Kuijer score<sup>23</sup>
- c. HEMORR2HAGES (hepatic or renal disease, ethanol abuse, malignancy, older age, reduced platelet count or function, rebleeding, hypertension, anemia, genetic factors, excessive fall risk, and stroke) score<sup>24</sup>
- d. RIETE (Registro Informatizado de Enfermedad Tromboembolica) score<sup>25</sup>
- e. HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol) score<sup>26</sup>
- f. ATRIA (anticoagulation and risk factors in atrial fibrillation) score<sup>27</sup>
- g. ACCP (American College of Chest Physicians) guidelines<sup>4</sup>
- h. EINSTEIN (once-daily oral direct factor Xa inhibitor rivaroxaban in the long-term prevention of recurrent symptomatic venous thromboembolism in patients with symptomatic deep vein thrombosis or pulmonary embolism) score<sup>28</sup>
- i. Hokusai-VTE [comparative investigation of low molecular weight (LMW) heparin/edoxaban tosylate (DU176b) versus (LMW) heparin/warfarin in the treatment of symptomatic deep-vein blood clots and/or lung blood clots] score<sup>29</sup>
- j. None of the above — I do not use predictive models but estimate subjectively
- k. Other (*please specify*): \_\_\_\_\_

Question 11. What medications do you use for extended secondary prevention of VTE? (*indicate all that apply*)

- a. Warfarin, therapeutic (international normalized ratio [INR], 2.0-3.0)

- b. Warfarin, subtherapeutic (INR, 1.0-2.0)
- c. Rivaroxaban
- d. Dabigatran
- e. Apixaban
- f. Aspirin
- g. Clopidogrel
- h. Sulodexide
- i. Other (*please specify*): \_\_\_\_\_

Question 12. The long-term bleeding risk of DOACs (direct oral anticoagulation agents) used for extended prophylaxis compared with warfarin is

- a. The same
- b. Higher
- c. Lower
- d. Unsure

Question 13. How often do you reevaluate patients on extended anticoagulation to determine continuing therapy?

- a. Every 3 months
- b. Every 6 month
- c. Every year
- d. Never — duration is established initially
- e. Other (*please specify*): \_\_\_\_\_

Question 14. Which of these criteria should be utilized to estimate the risk/benefit ratio of extended anticoagulation? (*indicate all that apply*)

- a. The incidence of minor bleeding on anticoagulation
- b. The incidence of major bleeding on anticoagulation
- c. Case-fatality rate of bleeding on anticoagulation
- d. The incidence of VTE recurrence
- e. Case-fatality rate of VTE recurrence

- f. The incidence of mild post-thrombotic syndrome after VTE recurrence
- g. The incidence of moderate post-thrombotic syndrome after VTE recurrence
- h. The incidence of severe post-thrombotic syndrome after VTE recurrence
- i. Other (*please specify*): \_\_\_\_\_

Question 15. A 40-year-old woman who is taking rivaroxaban for an unprovoked DVT that happened 1 year ago comes to your office asking whether she should keep taking the drug. She has never had any bleeding complications. What would you recommend?

- a. Stop anticoagulation
- b. Continue anticoagulation
- c. Send the patient back to physician who first initiated anticoagulation
- d. Send the patient to her primary care physician
- e. Refer the patient to a hematologist
- f. Other (*please specify*): \_\_\_\_\_

Question 16. If you do not regularly prescribe extended anticoagulation in your practice, please explain why:

- a. It is not beneficial for most patients
- b. Lack of specific guidelines to indicate when and how this should be done
- c. Lack of reported evidence to support such practice
- d. Absence of valid VTE/bleeding risk scales to guide decision-making
- e. It is not my specialty
- f. Other (*please specify*): \_\_\_\_\_

**Supplementary Table (online only).** Different practice patterns revealed by the answers to question 15 (n = 144)

Evaluation	Answered "yes," no. (%) <sup>a</sup>
History <sup>b</sup>	13 (9.0)
Physical examination	12 (8.3)
Duplex ultrasound	12 (8.3)
D-dimer level	9 (6.3)
DVT location	9 (6.3)
Thrombophilia screening	7 (4.9)
Cancer screening	3 (2.1)
Mobility status evaluation	1 (0.7)
Venous obstruction evaluation	1 (0.7)

DVT, Deep vein thrombosis.  
<sup>a</sup>Total percentage >100% because question 15 allowed for multiple responses.  
<sup>b</sup>Present illness, medical history, family history, subjective data.