CHEST®

State of Practice: Management Practice for Thromboprophylaxis in Acutely Ill Medical Patients

VOLUME 2, ISSUE 5

CHEST Clinical Perspectives™

Introduction

Venous thromboembolisms (VTEs) encompass both deep vein thrombosis and pulmonary embolisms and are a major public health concern.[1] Each year, as many as 900,000 individuals in the United States are affected by VTEs, and up to 11% of these individuals will die as a result of the condition. Thrombus formation can be due to hypercoagulability, venous stasis, or injury to blood vessel walls.[2] Common risk factors for VTEs include genetic susceptibility, chronic illnesses (such as heart and lung disease), and advanced age. Individuals hospitalized for acute medical illnesses are particularly susceptible to developing VTEs due to vascular injury resulting from surgery and/or a lack of movement during hospitalization. This risk of thrombus formation continues after discharge, and the majority will occur during the first 3 months after hospitalization.[3,4] However, in many cases, thromboprophylaxis is not administered during hospitalization.[5]

VTEs are often preventable, and mechanical and/or pharmacologic interventions may be used for antithrombotic therapy.[2] Mechanical prophylaxis includes compression stockings and pneumatic compression devices that apply pressure to the leg and promote circulation and thereby reduce thrombi formation. Pharmacologic therapies inhibit thrombus formation by targeting different parts of the biological pathways that lead to clot formation. More specifically, pharmacologic interventions used for thromboprophylaxis include fibrinolytic factors, antiplatelet agents (such as aspirin), and anticoagulants.[6] Regardless of their mechanism of action, all classes of drug therapies used for thromboprophylaxis are accompanied by an increased risk of bleeding events.

Anticoagulants are the most utilized types of drugs for VTE prophylaxis, and common classes include heparins, vitamin K antagonists (VKAs), and non-vitamin K antagonist oral anticoagulants (NOACs).[6] Heparins, which may be fractionated or unfractionated, are naturally occurring sugars (glycosaminoglycans) that inhibit clot formation by enhancing antithrombin, a key coagulation inhibitor. Inhibition of thrombin indirectly leads to the inhibition of factor Xa and thrombin. Inhibition of factor Xa inhibits both arms of the coagulation pathway, while thrombin inhibition prevents the conversion of fibrinogen to fibrin. Examples of low-molecular-weight heparin (LMWH) include dalteparin and enoxaparin. Vitamin K is critical to multiple steps of the coagulation cascade, and VKAs, such as warfarin, are also effective at preventing coagulation. One drawback to VKA therapy, however, is that patients must be carefully monitored while receiving VKA therapy because variations in drug metabolism, chances of drug-drug interactions, and dietary vitamin K intake may affect drug efficacy. Finally, NOACs (also known as direct-acting oral anticoagulants) directly inhibit factor Xa or thrombin. FDA-approved thrombin inhibitors include dabigatran, and approved factor Xa inhibitors include rivaroxaban, apixaban, and edoxaban. NOACs have fewer drug-drug interactions than VKAs and do not require routine monitoring while offering significantly lower bleeding risk than VKAs.[6-9]

In October 2019, the FDA approved rivaroxaban for thromboprophylaxis therapy for patients with acute medical illness during and after hospitalization. In the MAGELLAN trial, once daily orally administered rivaroxaban was compared with once daily subcutaneously administered enoxaparin in a group of about 8,000 patients 40 years of age or older.[10] Rivaroxaban was shown to be noninferior to enoxaparin in an initial 10-day standard therapy period. In a subsequent 35-day extended therapy period, rivaroxaban was

shown to be superior to a placebo-control in reducing the risk of VTEs after hospital discharge. However, this reduction in risk was accompanied by an increase in major bleeding events. Therefore, current use indications for posthospitalization rivaroxaban are for patients who are not at a high risk for bleeding.

Practice guidelines for thromboprophylaxis are evolving as new therapeutic options become available. The American College of Chest Physicians (CHEST) recommends thromboprophylaxis for all acutely ill patients with an increased risk of VTE formation.[11]

For patients who develop VTE, the most updated CHEST guidelines for antithrombotic therapy recommends the use of NOACs (dabigatran, rivaroxaban, apixaban, or edoxaban) over VKAs in patients without cancer for initial and extended therapy.[12] However, the guidelines show no preference for one NOAC over another. The rationale for the updated recommendations is that NOACs have similar efficacy to VKAs in reducing clotting with a reduced risk of bleeding without the need for routine monitoring. In cases where NOACs are not used, CHEST recommends the use of VKAs over LMWH. LMWH is only recommended for cancer patients and when VTEs recur while receiving other anticoagulant therapies. These recommendations by CHEST are in contrast to the most recent guidelines released by the American Society of Hematology for VTE in the setting of malignancy, which still recommends the use of LMWH over NOACs and recommends inpatient LMWH alone over the use of inpatient LMWH therapy with outpatient therapy.[13] CHEST also recommends that the initial antithrombotic therapy for VTE be used for 3 months and only continued indefinitely for patients who are at a low to moderate risk for bleeding and who are being treated for their first unprovoked event. Once anticoagulants are stopped, aspirin can be used daily by patients with no contraindications.

Pulmonologists and intensivists play a key role in the management of thromboprophylaxis in acutely ill patients. Therefore, their knowledge and attitude surrounding the use of various therapies can significantly affect patient wellbeing and reduce VTE-related morbidity and mortality. In the present study, we will focus on pulmonologists' and intensivists' VTE management practices and their attitudes toward traditional and novel thromboprophylaxis therapies.

BACKGROUND AND PURPOSE

In this issue of *CHEST Clinical Perspectives*, CHEST is undertaking primary research with pulmonologists and intensivists to understand their approach to ordering thromboprophylaxis in acutely ill medical patients for the purpose of reducing risk of VTE. Specifically, this issue focuses on the extent to which management practice has evolved given the introduction of novel anticoagulants. The objectives of this research are to:

- Understand current practice related to ordering thromboprophylaxis, as well as the therapies used with acutely ill medical patients.
- Understand the attitudes toward thromboprophylaxis from a risk and benefit standpoint that underlie decision-making related to deployment of therapy.
- Assess therapeutic, clinical, and administrative factors that impact management choices and the adoption of novel anticoagulants.
- Assess familiarity with and influence of the MAGELLAN study.
- Identify differences in management based on practice tenure and setting (academic vs community-based).

METHODOLOGY

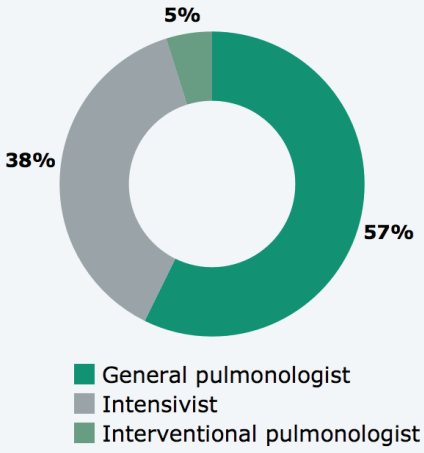
CHEST conducted an online survey with a sample of 103 pulmonologists and intensivists randomly selected from the CHEST member database. Respondents were screened to ensure that they are in active clinical practice. Respondents were sent a link to the survey from CHEST, and data were collected during February 12 to 20, 2020.

Descriptive statistics were used to assess distributions of the data across important demographic variables. Inferential statistics were used to assess differences in descriptive and behavioral measures, which were cross-tabulated by practice setting data. Depending on data type, a two-tailed independent samples t-test and a chi-square test were used to test for statistical significance ($P < .1$ considered statistically significant).

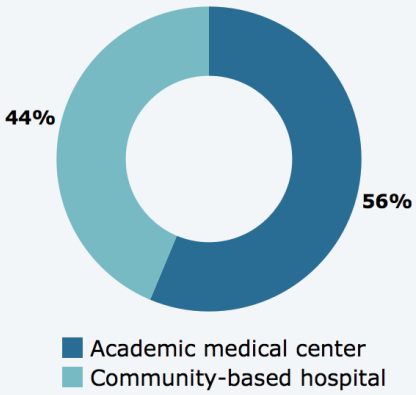
RESPONDENT PROFILE

The majority of the respondent base is composed of general pulmonologists (57%) and intensivists (38%). The respondent base was an even mix of clinicians by practice setting and tenure (with a slight skew toward younger physicians practicing in academic environments). The vast majority reported seeing patients across a variety of hospital and office settings.

Specialty

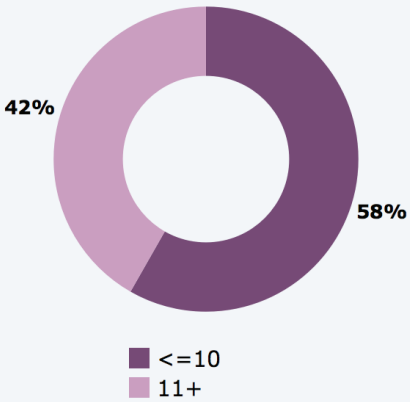


Practice Setting



Q: Are you a ...
Which of the following best describes your primary hospital affiliation?

Years in Practice



Patient Care Setting

ICU	87%
Office or pulmonary clinic	83%
General inpatient or pulmonary unit (not an ICU)	77%
Other	2%

Q: How many years has it been since you completed your pulmonary fellowship? In what settings do you see patients?
PLEASE CHECK ALL THAT APPLY.

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Self-reported role in managing risk of VTE

The majority of respondents say they are either the clinician who is primarily responsible for setting therapeutic strategy for management of VTE risk in acutely ill medical patients (73%) or are making recommendations to that effect (19%). However, respondents who report setting the therapeutic strategy for their patients are more likely to be in academic centers and are less likely to be familiar with the MAGELLAN study.

Managing the Risk of Venous Thromboembolism VTE-Related Events

	Total	<=10 Years in Practice	11+ Years in Practice	Familiar With MAGELLAN	Not Familiar With MAGELLAN
I set therapeutic strategy and order medications.	73%	82%	60%	54%	82%
I make recommendations regarding medications to reduce VTE risk.	19%	13%	28%	40%	9%
Another clinician, eg, hospitalist, is primarily responsible for this aspect of patient management.	8%	5%	12%	6%	9%

Q: Thinking specifically about your acutely ill medical (nonsurgical) patient population, which of the following statements best describes your role in managing the risk of venous thromboembolism (VTE)-related events?

Frequency of order

Frequency of ordering thromboprophylaxis is relatively high, with respondents reporting, on average, that they ordered thromboprophylaxis for 18.2 out of their last 20 acutely ill medical patients. Respondents with longer practice tenure (11 years or longer) were more likely than their counterparts to order thromboprophylaxis. On average, thromboprophylaxis was ordered for 18 out of the last 20 of these patients seen. No variation is observed by practice setting.

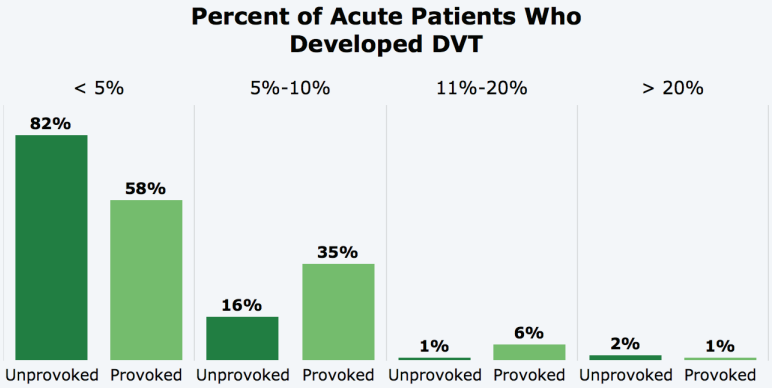
Patients Received Thromboprophylaxis During Their Inpatient Stay

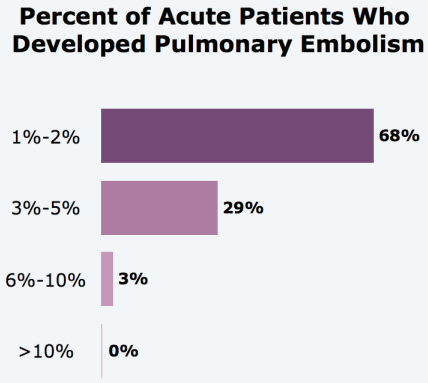
	Total	<=10 Years in Practice	>10 Years in Practice
Percent ordering thromboprophylaxis on all 20 patients	36%	25%	51%
Mean number of patients (out of last 20)	18.20	17.90	18.70

Q: Thinking of the last 20 acutely ill medical patients under your care, how many of those patients received thromboprophylaxis during their inpatient stay? INSERT WHOLE NUMBER BETWEEN 0 AND 20.

Experience with VTE-related events

Most respondents report comparatively lower frequency of VTE-related events: 58% say that fewer than 5% of their patients experience provoked DVT; 82% say that fewer than 5% experience unprovoked DVT; and 68% say that 1% to 2% of their patients experience pulmonary embolism.





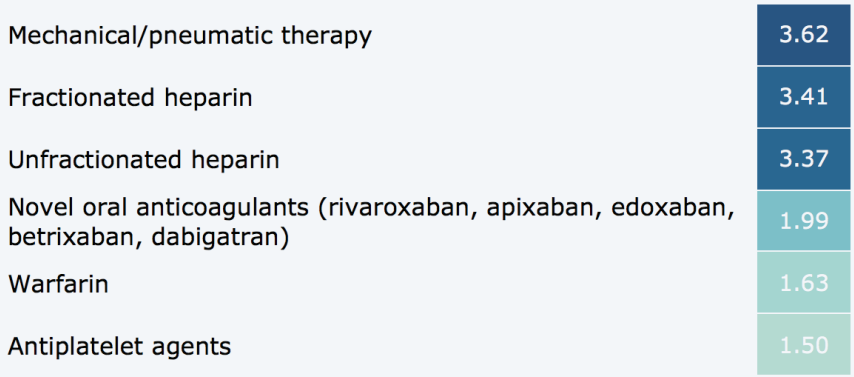
Q: Thinking about your acutely ill medical patients not admitted with a VTE diagnosis or need for anticoagulation for any reason, what percentage developed DVT (provoked and unprovoked)?
What percent of your acutely ill medical patients developed a pulmonary embolism?

CHOICE OF THERAPIES AND TREATMENT PLANNING

Current reported deployment of therapies

Respondents say they are most likely to use mechanical/pneumatic therapy (but not necessarily used as sole method), followed by fractionated and unfractionated heparin. Reported use of novel anticoagulants, warfarin, and antiplatelet agents is much less frequent. Community-based pulmonologists report greater deployment of novel anticoagulants compared with their academic-based counterparts.

Mean Frequency of Thromboprophylaxis Therapies Used With Acute Patients



Q: How frequently do you use the following thromboprophylaxis therapies with your acutely ill medical patients?

Respondents who are familiar with the MAGELLAN study report more frequent use of novel anticoagulants.

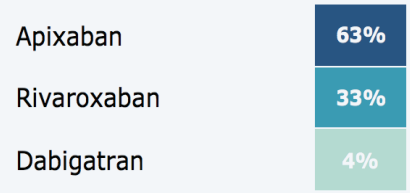
Frequency of Novel Oral Anticoagulants Used With Acute Patients

	Total	Familiar With MAGELLAN	Not Familiar With MAGELLAN
Rarely	42%	26%	50%
Never	32%	31%	32%
On some patients	22%	31%	18%
On most patients	3%	9%	0%
On all patients	1%	3%	0%

Q: How frequently do you use the following thromboprophylaxis therapies with your acutely ill medical patients?

Respondents who report using novel oral anticoagulants say they are most likely to use apixaban (63%), followed by rivaroxaban (33%). Interpret with caution- small base size.

Preferred Novel Oral Anticoagulant



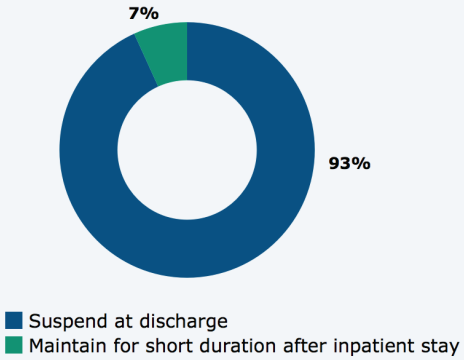
Interpret with caution: small base size.

Q: When using a novel oral anticoagulant for thromboprophylaxis in your acutely ill medical patients, which one do your prefer?

Post-discharge management practice

Nearly all respondents (93%) indicate that they suspend thromboprophylaxis at discharge.

Post-discharge Management Practice



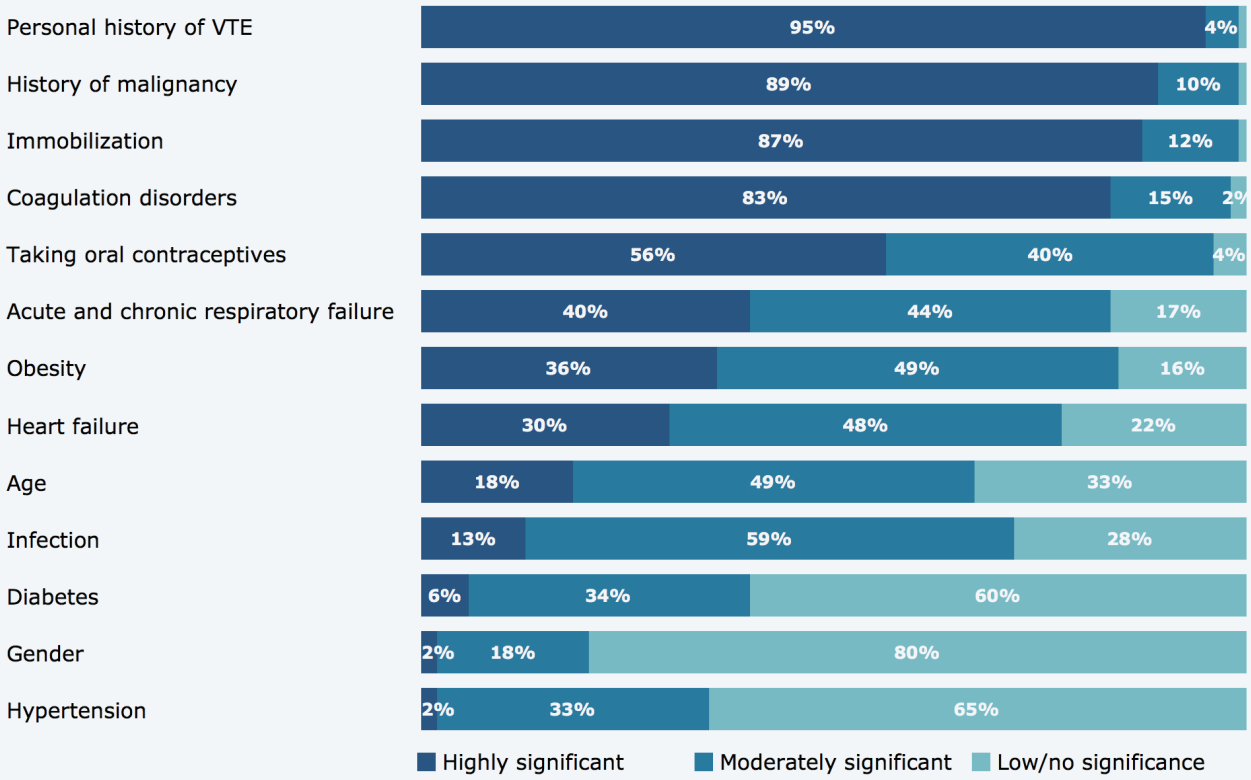
Q: Do you typically continue thromboprophylaxis after discharge or discontinue upon discharge?

IMPACT OF CLINICAL INDICATIONS AND RISK FACTORS ON DECISION MAKING

Significance of risk factors in pursuing thromboprophylaxis

Select factors are highly significant in driving the decision to order thromboprophylaxis in acutely ill medical patients, namely history of VTE, history of malignancy, immobilization, and coagulation disorders. There is a variety of factors, however, that respondents are more divided on when it comes to triggering thromboprophylaxis, including taking oral contraceptives, acute and chronic respiratory failure, obesity, and heart failure. Community-based providers and those with longer tenures in practice are more likely to order thromboprophylaxis in patients with heart failure and acute respiratory failure.

Significance of Risk Factors in Pursuing Thromboprophylaxis

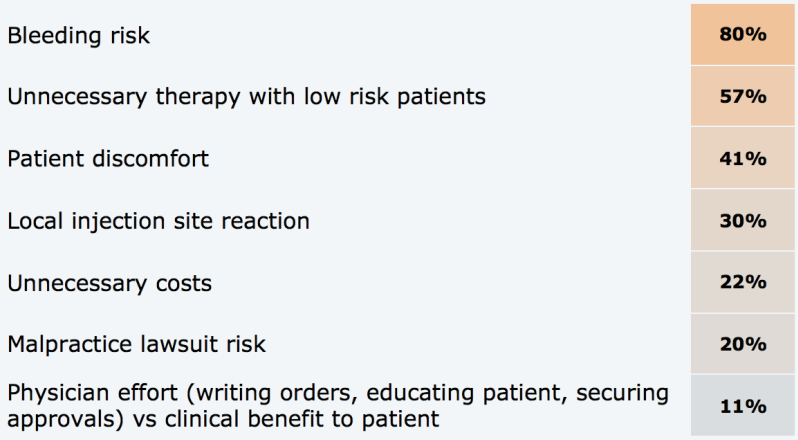


Q: How significant are the following risk factors in driving your decision to pursue thromboprophylaxis?

Risks and concerns when considering thromboprophylaxis

While the primary risk that respondents consider when ordering thromboprophylaxis is bleeding (80%), a significant portion also mention other concerns, including ordering an unnecessary therapy for a low risk patient (57%), potential patient discomfort (41%), and local injection site reaction (30%).

Risks or Concerns Considered When Considering Thromboprophylaxis

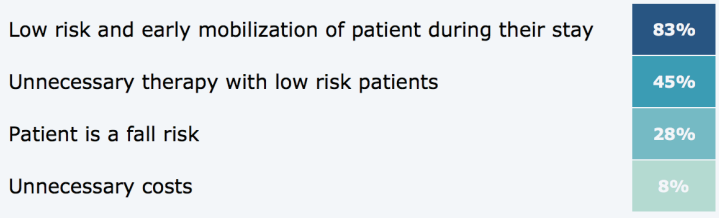


Q: What risks or concerns do you associate with the initiation and continuation of thromboprophylaxis for your acutely ill medical patients? PLEASE CHECK ALL THAT APPLY.

Rationale for not pursuing thromboprophylaxis in acutely ill medical patients.

The most frequently cited rationale for not pursuing thromboprophylaxis in acutely ill medical patients is the assessment that they are low risk combined with early mobilization during their stay (83%). Other reiterate the potential for an unnecessary therapy with low risk patients (45%). Fall risk is mentioned by a smaller share of respondents (28%).

Rationale for Not Pursuing Thromboprophylaxis in Acute Patients



Q: What would be your rationale for NOT prescribing VTE prophylaxis in your hospitalized acutely ill medical patients? PLEASE CHECK ALL THAT APPLY.

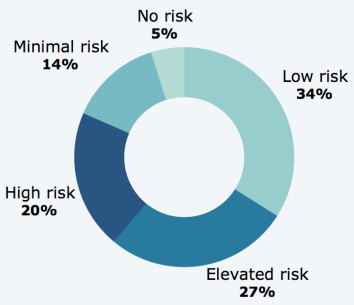
REVIEW OF PATIENT CASE THERAPEUTIC RECOMMENDATIONS

To provide a window to clinical decision-making, respondents were presented with three patient cases (Patients A, B, and C) for review. Each patient faced unique circumstances; however, all could be classified as acutely ill medical patients. After reviewing a brief overview of their history and clinical indicators, respondents were asked the following questions:

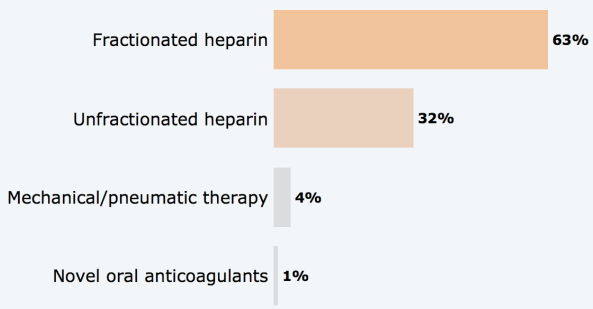
- The degree of risk associated with pursuing thromboprophylaxis with the patient.
- Which therapy would they order for the patient and the rationale for not ordering thromboprophylaxis.
- Assessment as to whether or not the patient is a candidate for extended post-discharge prophylaxis.

Respondents are divided with regard to their assessment of the risk level associated with pursuing thromboprophylaxis with this patient. Half (47%) consider the risk high or elevated and half (48%) consider it low or minimal. All respondents indicate they would pursue thromboprophylaxis with the patient and virtually all indicate they would order heparin (63% fractionated and 32% unfractionated).

Risk Level Associated With Pursuing Thromboprophylaxis



Choice of Therapy



Percent Considering Patient A Candidate for Extended Post-discharge Prophylaxis

	Total	<=10 Years in Practice	11+ Years in Practice	Familiar With MAGELLAN	Not Familiar With MAGELLAN
No	81%	88%	70%	63%	90%
Yes	19%	12%	30%	37%	10%

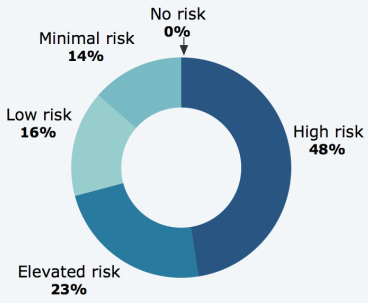
Patient A

Q: Patient A is a 32-year-old previously healthy woman who is hospitalized in the ICU with influenza. Her course was complicated by acute respiratory failure requiring mechanical ventilation. She is now mildly sedated, and her oxygen requirements are decreasing. You are hopeful to extubate her in the next 1 to 2 days. Her platelets are 115K, and she has not had any bleeding complications during her hospital stay. She has maintained adequate urine output, and renal function is preserved. What degree of risk do you associate with pursuing thromboprophylaxis with this patient?

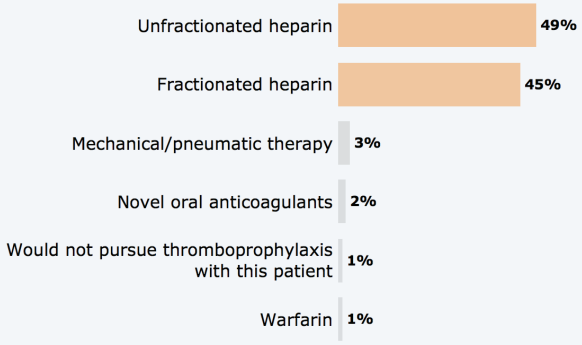
The vast majority of respondents (81%) do not consider Patient A to be a candidate for extended post-discharge prophylaxis. There is some differentiation of response by practice tenure, with respondents who have more than 11 years in practice post-fellowship being more likely to indicate that Patient A is a candidate for extended post-discharge prophylaxis (30% vs 12% among respondents with shorter tenure). Further, respondents who are familiar with the MAGELLAN study are more likely to view Patient A as a candidate for extended therapy.

Respondents are much more likely to consider Patient B as high risk for thromboprophylaxis. As with Patient A, the therapy of choice is heparin (49% unfractionated, 45% fractionated).

Risk Level Associated With Pursuing Thromboprophylaxis



Choice of Therapy



Percent Considering Patient B Candidate for Extended Post-discharge Prophylaxis

	Total	Academic Setting	Community Setting	<=10 Years in Practice	11+ Years in Practice	Familiar With MAGELLAN	Not Familiar With MAGELLAN
No	60%	70.69%	46.67%	70%	47%	43%	69%
Yes	40%	29.31%	53.33%	30%	53%	57%	31%

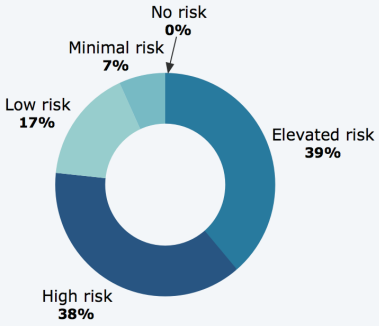
Patient B

Q: Patient B is 76-year-old man with a history of hypertension, chronic renal insufficiency with baseline creatinine of 1.5, and colon cancer that has been surgically resected 3 months ago. He presents to the ED with a right-lower-lobe pneumonia. He has noted significant shortness of breath and has not been very active for the last several days. His family notes he has been confused intermittently and has had difficulty with an unsteady gait over the last month. He was seen and assessed by pulmonary in the ED, and he is admitted to the medical step down unit for close monitoring. He is requiring high flow oxygen and intermittent bi-level noninvasive ventilation. What degree of risk do you associate with pursuing thromboprophylaxis with this patient?

While respondents are more likely to consider Patient B a candidate for extended post-discharge prophylaxis (40%), there is differentiation in this assessment when comparing academic (only 30% see Patient B as a candidate) and community-based respondents (53% consider Patient B a candidate). Also, those who are familiar with MAGELLAN are also more likely to view Patient B as a candidate.

The vast majority of respondents (77%) consider Patient C to be at high or elevated risk in pursuing thromboprophylaxis. While heparin is once again identified as the antithrombolytic agent most likely to be ordered, there is variation between academic and community-based providers. Academic providers are near unanimous in saying they would order heparin, while community-based providers are more likely to vary across therapies, including heparin, warfarin, and mechanical therapy.

Risk Level Associated With Pursuing Thromboprophylaxis



Choice of Therapy

	Total	Academic Setting	Community Setting
Fractionated heparin	48%	57%	36%
Unfractionated heparin	37%	41%	31%
Mechanical/pneumatic therapy	8%	2%	16%
Warfarin	5%	0%	11%
Novel oral anticoagulants	3%	0%	7%

Percent Considering Patient C Candidate for Extended Post-discharge Prophylaxis

	Total	Academic Setting	Community Setting	<=10 Years in Practice	11+ Years in Practice
Yes	51%	34%	73%	42%	65%
No	49%	66%	27%	58%	35%

Patient C

Q: Patient C is a 55-year-old woman with pulmonary arterial hypertension (PAH) receiving dual oral therapy who presented to the clinic with increased shortness of breath, swelling, and new onset ascites. She was directly admitted to the pulmonary service for diuresis and management. She was seen and assessed. An echocardiogram and CT pulmonary angiogram were ordered to further assess the cause of her worsening condition. Echocardiogram shows progressive pulmonary hypertension and worsening of right-sided heart dilation and dysfunction. Her CTPA did not reveal any evidence of pulmonary embolism. Lab results were notable for a creatinine value of 1.3, hemoglobin value of 9.8, and platelets of 82 K. She was then transferred to a higher level of care to pursue right-sided heart catheterization and possible IV pulmonary hypertension medication. She is alert. She is able to get up to a bedside commode with assistance but is not able to ambulate due to shortness of breath and lightheadedness. What degree of risk do you associate with pursuing thromboprophylaxis with this patient?

More so than Patients A and B, respondents consider Patient C to be a candidate for extended post-discharge prophylaxis. Again, community-based providers and those with longer post- fellowship practice tenures are more likely to consider Patient C a candidate for post-discharge therapy.

FACTORS INFLUENCING SHIFTS IN ANTI-VTE STRATEGY

Reported changes in approach to thromboprophylaxis

As indicated in the table below, frequency of use of thromboprophylaxis therapies is largely unchanged compared to 5 to 10 years ago. Heparin remains the most frequently used agent (a decline is noted in the use of unfractionated heparin). Mechanical therapy remains commonplace, but reported frequency of use is lower. There does not appear to be a significant uptake in the use of novel anticoagulants.

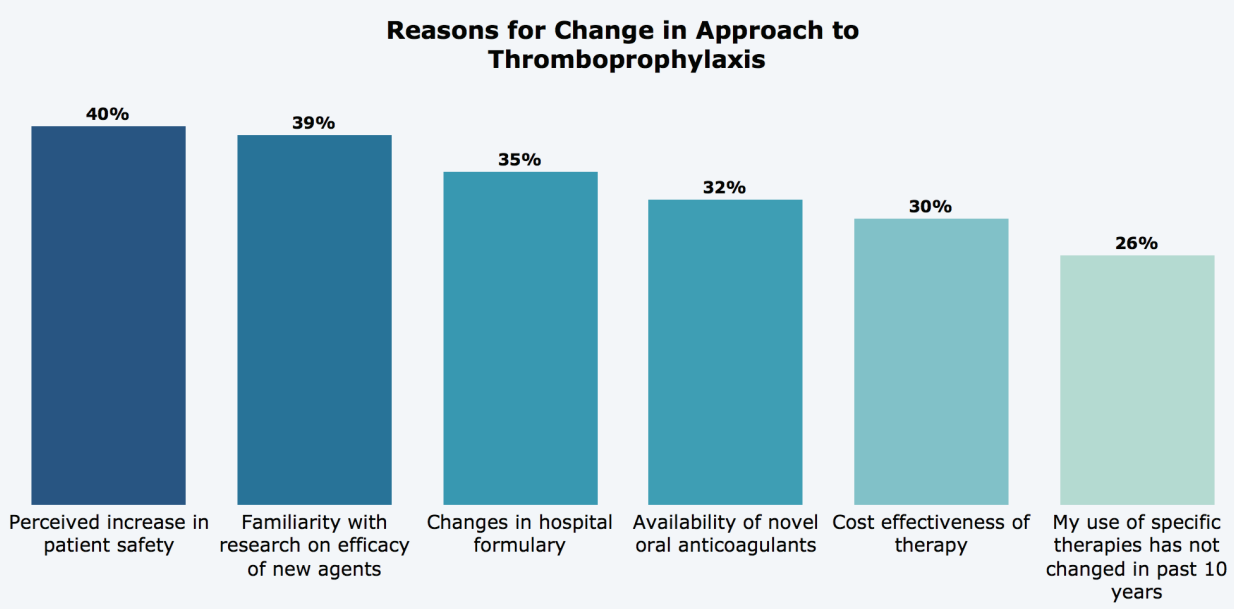
Reported Frequency of Use of Thromboprophylaxis Therapies
(Percent of Most/All Patients)

	5-10 years ago	Currently
Mechanical therapy	62%	50%
Unfractionated heparin	55%	46%
Fractionated heparin	51%	51%
Novel anticoagulants	3%	4%
Warfarin	6%	1%
Antiplatelet therapy	3%	2%

Q: Thinking back to 5 to 10 years ago, how frequently did you use the following thromboprophylaxis therapies with you acutely ill medical patients?

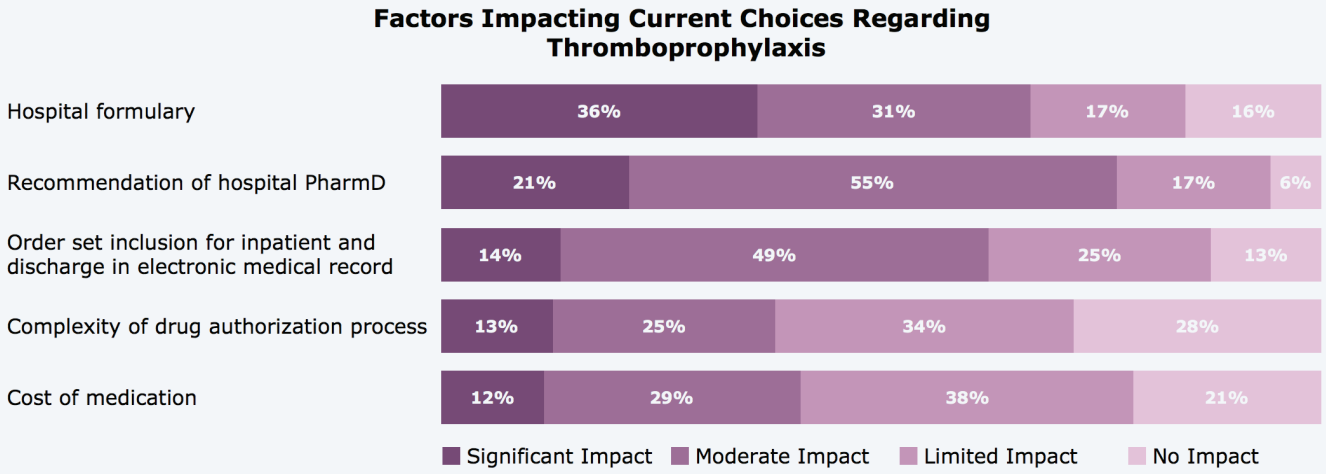
Reasons for change in approach to thromboprophylaxis

While 26% of respondents say that their approach to thromboprophylaxis has not changed in the past 5 to 10 years, others report that a variety of factors related to changes in therapeutic agents and efficacy, hospital formularies, and cost effectiveness have played a role in the frequency with which they use different antithrombolytic agents. Perceived increase in patient safety is cited most frequently (40%), followed by research demonstrating the effectiveness of new agents (39%), changes in hospital formulary (35%), availability of new agents (32%), and perceived cost effectiveness (30%). Respondents who are familiar with the MAGELLAN study are much more likely to cite the presence of new agents as their leading reason for changes in their approach to thromboprophylaxis.



Q: Why, if at all, has your frequency of use of specific thromboprophylactic therapies changed compared with 5 to 10 years ago? PLEASE CHECK ALL THAT APPLY.

In terms of the factors that have the biggest impact on their current choice of antithrombolytic agents, respondents say that hospital formulary and hospital pharmacy recommendations have the biggest impact on their choice of agent. Cost and complexity of drug authorizations are less likely to be cited as issues impacting current choices.



Q: To what extent do the following factors impact your current choices regarding thromboprophylaxis for your acutely ill medical patients?

Institutional VTE risk reduction actions

Respondents report that hospitals have taken a number of steps to raise awareness regarding thromboprophylaxis. The vast majority of respondents (81%) say their institution has implemented standard guidelines for thromboprophylaxis. A variety of supporting activities are identified: check-listing (routine assessment of need for thromboprophylaxis) is mentioned by 73% of respondents, followed by electronic medical record alerts (63%), and diagnosis-specific order sets for thromboprophylaxis (48%). While educational interventions are mentioned less frequently, 47% say their institution has utilized computer-based educational programs; thromboprophylaxis is reported as a subject of CME/grand rounds by 20% of respondents.

Institutional practices do not vary substantially in academic vs community-based facilities; however, academic centers are much more likely to have implemented check-listing protocols.

Institutional Actions to Reduce Risk of VTE

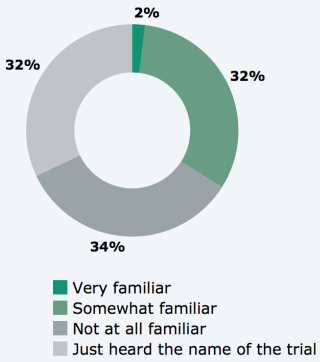
	Total	Academic Setting	Community Setting
Have implemented standard guidelines for thromboprophylaxis	81%	83%	78%
Check-listing (routine assessment of need for thromboprophylaxis in acutely ill medical patients)	73%	81%	62%
Electronic alerts generated within the patient's electronic medical record	63%	64%	62%
Utilize computer-based educational interventions on thromboprophylaxis	48%	52%	42%
Have implemented diagnosis-specific order sets for thromboprophylaxis	47%	43%	51%
Topic of CME/grand rounds	20%	26%	13%

Q: Which of the following things does your practice or institution do to reduce risk of VTE-related events among your acutely ill medical patients? PLEASE CHECK ALL THAT APPLY.

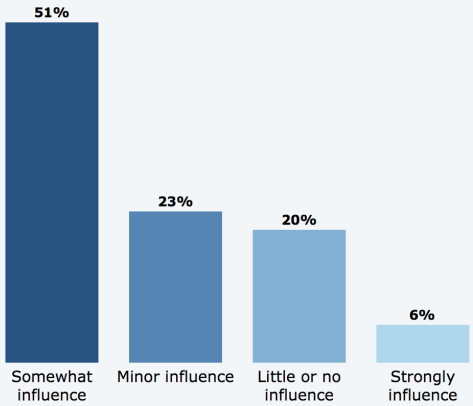
FAMILIARITY AND IMPACT OF THE MAGELLAN STUDY

Only a third of respondents (34%) report any degree of familiarity with the MAGELLAN study assessing the efficacy and safety of rivaroxaban administered during and after discharge. Familiarity levels do not vary by site of care. While the base size is small, among those who are familiar with MAGELLAN, half (57%) say it has had a degree of influence on their approach to reducing the risk of VTE-related events in their acutely ill medical patients.

Familiarity With MAGELLAN



Impact of MAGELLAN Study on Approach to Reducing Risk of VTE-Related Events



Q: The MAGELLAN Study is a clinical trial assessing the efficacy and safety of rivaroxaban administered for 35 days, as compared with enoxaparin administered for 10 days and followed by placebo, in a heterogeneous population of patients 40 years of age or older with reduced mobility and an acute medical illness requiring hospitalization. How familiar are you with MAGELLAN?

To what extent do the findings of the MAGELLAN study influence your approach to reducing the risk of VTE-related events in your acutely ill medical patients?

KEY TAKEAWAYS

- Pulmonologists and intensivists play an important role in managing the risk of VTE-related events.
- The majority of pulmonologists and intensivists routinely ordered prophylaxis but were reluctant to recommend extended therapy in patient cases reviewed.
- Most surveyed pulmonologists and intensivists were not familiar with the MAGELLAN study, and this translated to an underutilization of novel oral anticoagulants.
- Pulmonologists and intensivists do not universally agree on the risk factors that warrant an order for thromboprophylaxis therapy.
- Academic and community-based institutions have implemented standard guidelines for thromboprophylaxis, but community-based practices have a lower frequency of utilization of routine assessment of the need for thromboprophylaxis.
- Advancing knowledge regarding novel oral anticoagulants, the benefits of extended thromboprophylaxis, and the need for routine risk assessment are important for reducing the risk of VTE-related events in acutely ill medical patients.

DISCUSSION

Pulmonologists and intensivists play an important role in managing the risk of VTE-related events. In this study, most of the respondents routinely ordered thromboprophylaxis or strongly influenced decisions for managing VTE-related events. In keeping with CHEST recommendations for acutely ill hospitalized patients, the vast majority of surveyed practitioners ordered thromboprophylaxis for recent patients. While prophylaxis was not used in 100% of the cases, this finding is encouraging. The ENDORSE trial published in 2008 indicated that only approximately 40% of medically ill patients received VTE prophylaxis according to CHEST recommendations set at that time.[14] If the current results can be extrapolated to the larger population, adherence to CHEST recommendations may be increasing. While the likelihood of utilizing prophylaxis was similar across practice settings, respondents with longer practice tenure were more likely to administer prophylaxis.

Overall, the survey reflects a low utilization of novel anticoagulants. Survey respondents prefer to utilize traditional therapies, such as mechanical therapy and fractionated or unfractionated heparins. Although the first NOAC was approved for VTE prophylaxis in 2012, respondents report that the frequency of use for NOACs is largely unchanged compared with 5 to 10 years ago. Here, practitioners are continuing to use therapies that they are most familiar with. Elsewhere, other published studies have reported increased use of NOACs

throughout North America when treating VTE.[15,16] Survey respondents cited bleeding risk as a contributing factor when considering thromboprophylaxis. A low utilization of NOACs may be influenced by the fact that FDA-approved reversal agents for NOACs have only become available within the last 5 years. A reversal agent for dabigatran became available in 2015, and reversal agents for rivaroxaban and apixaban (the two most utilized NOACs in this study) became available in 2018.[17] It is also possible that a lack of knowledge on new clinical studies contributes to this clinical inertia, as only 34% of respondents were familiar with the MAGELLAN trial. Practitioners who were familiar with the trial were more likely to use NOACs. However, they were not the ones most likely to play deciding roles in thromboprophylaxis use. In this study, it is clear that knowledge translated to action. Therefore, an increase in post-hospital NOAC use could result from further educating health-care practitioners, and, especially, younger providers, regarding late-stage clinical trials highlighting the benefits of NOACs for the population at risk for post-discharge VTE.

The majority of patient cases presented in this study indicated a benefit for extended anticoagulant therapy. Yet, the majority of the respondents would suspend therapy at discharge. Concerns about bleeding risk and lack of knowledge regarding the benefits of extended prophylaxis likely contribute to the reluctance to continue therapy after discharge.[10] The majority of at-risk patients are likely to develop VTEs within 3 months after discharge, and hospital stays are generally short.[3,4] Therefore, education around the benefits of extended therapy is critical for lowering the incidence of VTE-related events.

One barrier to the implementation of thromboprophylaxis guidelines is deciding whom to treat. Across the board, surveyed pulmonologists and intensivists agreed that certain factors, such as a history of VTEs or malignancy, immobilization, and coagulation disorders, warranted the use of thromboprophylaxis in acutely ill patients. However, respondents were divided on factors such as obesity and heart failure, use of oral contraceptives, and respiratory failure. In such cases, using a risk assessment model may be beneficial. Risk assessment models were not addressed in the current CHEST antithrombotic therapy guidelines, but the previous edition utilized scoring systems to help to identify at-risk patients who would benefit from thromboprophylaxis.[11,12] For example, the Padua risk assessment model stratifies patients according to nine baseline features, including age, obesity, and history of VTE.[11] Patients receiving a higher score are considered to have a greater risk of developing VTEs and are recommended to receive thromboprophylaxis. More recently, the validated IMPROVE VTE risk score calculator has been combined with measurements of the biomarker, D-dimer, a fibrin degradation product that is indicative of thrombus formation and

degradation.[18] A combination of the risk score with D-dimer levels further improves the risk stratification of patients. With better methods for routinely assessing VTE risk, practitioners may be more confident in deciding when to administer post-hospital thromboprophylaxis.

Since VTE was identified as a major public health concern in 2008, many institutions have been implementing VTE prevention protocols to standardize patient care. Effective VTE protocols are simple and incorporate education on best practice guidelines, assess barriers to implementing guidelines, and integrate actionable steps into clinical practice guidelines to ensure that at-risk patients receive prophylaxis.[19] In this study, VTE prevention practices were similar in academic and community-based settings. Standard guidelines and diagnosis-specific order sets were implemented, and alerts were generated in the patient's medical records. However, community-based settings reported less structured routine assessment of VTE risk in acutely ill patients. Routine VTE risk and bleeding risk assessments are the cornerstones of an effective VTE prevention protocol and the first step to ensuring that risk-appropriate prophylaxis is administered that also takes into consideration patient comorbidities.[19] While respondents from both community-based and academic settings report having some education on VTE prophylaxis via CME/grand rounds, there is a clear need for education surrounding the importance and benefits of routine risk assessment. With appropriate risk assessment, VTE incidence and VTE-related financial burdens can also be reduced as each hospital-associated VTE event can result in an increased cost of over $10,000.[19]

Pulmonologists and intensivists are key players in the management of VTE risk in acutely ill patients. Therefore, their knowledge around best practice guidelines and VTE risk factors will greatly affect the results of any VTE prevention programs. To shift VTE-management practices, there needs to be an increase in knowledge around novel oral anticoagulants, post-hospitalization anticoagulation, and institutional guidelines for implementing.

EDUCATIONAL OPPORTUNITIES

- Education around the MAGELLAN study and other late-stage clinical trials highlighting the benefit of NOACs.
- Education around the best practices for thromboprophylaxis including the benefits of extended thromboprophylaxis.
- Education around the importance of routine assessment of the need for thromboprophylaxis.

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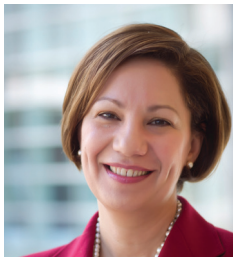

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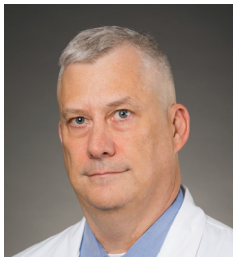

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