Venous thromboembolism management practices and knowledge of guidelines: a survey of Australian haematologists and respiratory physicians

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TITLE: Venous thromboembolism management practices and knowledge of guidelines: a survey of Australian haematologists and respiratory physicians

Abstract

Background

~~Venous thromboembolism (VTE) is a leading cause of preventable mortality in Australia.~~

Current international clinical practice guidelines do not adequately address all clinical scenarios in the management of ~~VTE~~ venous thromboembolism (VTE) and no comprehensive Australian guidelines ~~are yet to be developed~~exist. ~~Our~~ We~~research~~ aimed to identify areas of uncertainty in VTE management and whether self-reported practice ~~by respiratory physicians and haematologists~~ is consistent with ~~current international clinical~~ guidelines.

Methods

We conducted an ~~national~~ Australian cross-sectional online survey consisting of 53 questions to investigate doctors' VTE management practices. The survey was distributed ~~nationally~~ to consultant and trainee/registrar haematologists and respiratory physicians ~~via email~~ with the aid of participating medical societies.

Results

Seventy-one haematologists and 110 respiratory physicians responded to the survey. ~~Sixty-six percent of those who completed the survey~~The majority of survey respondents were 31-50 years old and ~~the majority~~ worked in teaching hospitals and in the acute care setting. ~~The median number of years spent working in their speciality was 9 [IQR (4, 19)].~~ Under-treatment was reported for high-risk pulmonary embolism (PE) and duration of anticoagulation for first episode unprovoked PE (32% and 83% respectively). Over-treatment was reported in areas of thrombolysis for intermediate-risk PE (16%) and duration of anticoagulation for first episode provoked PE (41%). Uncertainty and variations in doctors' management approaches were also found.

Conclusion

This survey demonstrated significant over-treatment, under-treatment and variability in the practice of VTE management. The findings highlight the need for the development and implementation of national guidelines for the management of VTE in Australia.

MeSH Terms:

Venous Thromboembolism, Physicians, Uncertainty, Surveys and Questionnaires, Australia

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Introduction

Venous thromboembolism (VTE) is a leading cause of preventable mortality in Australia. In 2008 there were 14,716 reported cases nationally, costing the medical system an estimated $1.72 billion, as well as creating a significant economic burden through loss to the workforce.[1]

Despite the availability of multiple management guidelines there are still significant areas of uncertainty in management.[2] This is largely due to the variable prognoses of individuals with VTE and gaps in the evidence base for several important clinical scenarios. In particular, significant doubt remains regarding the optimal treatment of ~~sub-massive or~~ intermediate-risk pulmonary embolism (PE).

The major institutions to publish guidelines on the management of VTE are the National Institute for Health and Care Excellence (NICE), the European Society of Cardiology (ESC) and the American College of Chest Physicians (ACCP) who have most recently published guidelines in 2012, 2014 and 2016 respectively.[3-5] These guidelines are extensive, however, there is variation in their coverage and recommendations in part due to recent changes in the evidence base. The lack of a comprehensive Australian guideline creates significant uncertainty for treating clinicians leading to discrepancies in national standards of practice. Variation in practice has been observed in prior studies, although, none of the studies addresses all areas of management and there is limited information regarding Australian practice.[6-11]

This study aimed to identify the extent to which self-reported VTE management practices of Australian haematologists and respiratory physicians are consistent with currently available international guidelines. The outcomes of this study will ~~inform~~ aid the development of national clinical guidelines for the investigation and management of VTE. In addition, by identifying gaps in knowledge, the study highlights important areas for training and education.

Methods

Study design and ethics

We conducted a cross-sectional survey of haematologists and respiratory physicians currently working within Australia. Both consultants and registrars/trainees were eligible to participate. The study was approved by the Melbourne Health Human Research Ethics Committee (Project number QA2015182).

Survey development

A draft survey was developed after an extensive literature review and review of current clinical practice guidelines. The draft survey was reviewed by 10 physicians (respiratory physicians, general physicians and haematologists) at the Royal Melbourne Hospital and Peter McCullum Cancer Centre who provided expert advice on question content and survey design. An online version of the survey was developed using Survey Monkey® (www.surveymonkey.com) and accessible via web-link. It consisted of 53 questions and took ten minutes to complete.

Survey procedure

An email containing a the link to the survey was sent to members of The Australasian Society of Thrombosis and Haemostasis, The Haematology Society of Australia and New Zealand (HSANZ) and The Thoracic Society of Australia and New Zealand (TSANZ). After an initial poor response rate reminder emails were sent on at least one further occasion.

Surveys were also distributed at TSANZ and HSANZ scientific meetings.

Statistical analysis

Statistical analysis was conducted using STATA IC 14.1 (StataCorp, College station, TX, USA). Denominators for percentage calculations were adjusted to account for missing data. Chi square analysis was used to identify differences in survey responses between haematologists and respiratory physicians. Multivariate logistic regression was used to determine which demographic or physician specific factors were related to physician responses. All relevant clinical and demographic factors for which data was collected were included in the analysis including specialty, sex, years of clinical experience, metropolitan or regional practice, private hospital workplace and reported use of guidelines. P< .05 was considered statistically significant.

Results

Participation and demographics

Of an estimated 505 haematologists and 630 respiratory physicians registered in Australia in December 2015,[12] 71 and 110 respectively responded to the survey. ~~Six haematologists and 11 respiratory physicians were excluded as they~~Respondents who did not complete beyond the demographic section were excluded. Providing a response rate of 13% for haematologists and 16% for respiratory physicians. This is a conservative estimate based on the number of doctors registered with the Australian Health Practitioners Regulation Agency in 2016 rather than the number who are members of the societies who distributed the survey.

Sixty-six percent of respondents were 31-50 years old, the median number of years spent working in their speciality was 9 [IQR (4, 19)] and over 84% worked in teaching hospitals and in the acute care setting (Table 1). The responses to survey questions are summarised in the following text and ~~in Table 2. This t~~Table 2 includes a breakdown by specialist type for all responses which differed significantly between respiratory physicians and haematologists.

Multivariate logistic regression was used to identify physician specific factors associated with specific management practices ~~(Table 3). .~~ All statistically significant results are presented in Table 3.

Knowledge and use of guidelines

Doctors were more familiar with the Australian Therapeutic Guidelines (ATG)[13] and ACCP's 2012 and 2016[5] guidelines (47%, 44% and 54% respectively) than the ESC[4] and NICE[3] guidelines (21% and 27%). Five percent of doctors were not familiar with any of these guidelines.

Seventy-seven percent of doctors agreed they usually base clinical decisions on one or more of these guidelines.

Initial assessment of pulmonary embolism

The vast majority of doctors (96%) were familiar with the Wells score for assessing the probability of having a VTE, however, 38% said they would rarely or never calculate and record it. Sixty-one percent of doctors were familiar with the Pulmonary Embolism Severity Index (PESI). Only 25% regularly use the PESI/simplified PESI (sPESI) whereas ~~M~~most doctors ~~would also~~ regularly use cardiac biomarkers (60%) and/or imaging[1] (74%). ~~whereas only 25% regularly use the PESI/simplified PESI (sPESI).~~

Managing low-risk pulmonary embolism

Fifty-six percent of respondents usually admit a patient with low-risk PE for one to two days (where social circumstances and co-morbidities permit early discharge). Only 4% usually admit for three to five days and 40% would treat at home or discharge within 24 hours.

Sixty-six percent of doctors surveyed would recommend anticoagulation for a patient without cancer or a deep venous thrombosis (DVT) who has an incidental asymptomatic single sub-segmental PE (SSPE) found on computed tomography pulmonary angiogram (CTPA) or ventilation perfusion (VQ) scan.

Managing high-risk pulmonary embolism

The majority of doctors surveyed would recommend thrombolysis for ~~a~~ patients with high-risk PE without contraindications to thrombolysis (68%). However, 18% indicated they would rarely or never recommend thrombolysis and 14% indicated they would only recommend thrombolysis sometimes. Using thrombolysis never or rarely was almost four times more likely amongst haematologists, six times more likely amongst doctors in private hospitals and showed a slight association with increasing years of clinical experience (Table 3).

[1] Computed tomography pulmonary angiogram or echocardiography.

Managing intermediate-risk pulmonary embolism

~~Reported r~~Recommendations for thrombolysis

The majority of doctors (84%) do not recommend the use of thrombolysis for patients with intermediate-risk PE in those without contraindication to thrombolysis. More doctors would frequently or always recommend thrombolysis for patients with elevated troponin and right ventricular dysfunction (RVD) on echocardiography (16%) than for patients with elevated troponin and RVD dysfunction on CTPA (7%). Six percent of doctors said they would sometimes recommend thrombolysis for patients with elevated troponin and no evidence of RVD on CTPA or echocardiography (Figure 1).

Ninety percent of respondents reported discussing the risks and benefits of thrombolysis with their patients. However, 22% of them stated that patient preferences do not influence their decision to use thrombolysis much or at all for intermediate-risk PE.

Only 8% of doctors surveyed said they had used half-dose thrombolysis ~~for a patient with intermediate-risk PE~~ in this patient group.

Recommendations for cardiac monitoring

~~The vast majority of doctors (91%)~~Ninety-one percent of doctors would recommend cardiac monitoring for patients with both elevated serum troponin and features of RVD on CTPA or echocardiography. Sixty-two percent recommend ~~cardiac~~ monitoring for patients with features of RVD on CTPA or echocardiogram but without ~~elevation of serum~~elevated troponin. While 49% recommend ~~cardiac~~ monitoring for patients with an elevated ~~serum~~ troponin but without features of RVD ~~on CTPA or echocardiogram~~.

Screening for thrombophilia and malignancy

For patients with a first episode unprovoked PE, 88% of doctors would frequently or always recommend patients are up-to-date with ~~current~~ national screening tests.[2] Fifty-four percent would recommend a thrombophilia screen, however, only 17% recommend a computed tomography (CT) chest/abdomen/pelvis or CT abdomen/pelvis to screen for occult malignancy in patients over 40 years of age.

Follow-up of pulmonary embolism

Thirty-five percent of respondents routinely order a VQ scan before cessation of anticoagulation for unprovoked PE, whereas 5% would routinely order a CT. Seventeen percent ~~said they would~~ routinely order either.

Sixteen percent of doctors routinely use echocardiogram during follow-up of individuals with unprovoked PE. Fifty-one percent use echocardiography during the follow-up of patients who had features of RVD and/or pulmonary hypertension detected at the time of initial diagnosis and 45% in those with persisting symptoms (multiple answers were possible for this question).

[2] Mammography for breast cancer, faecal occult blood testing for bowel cancer and Papanicolaou testing for cervical cancer.

Choice of anticoagulant

Assuming there are no contraindications, 76% of doctors prefer to prescribe new oral anticoagulants ~~(NOACs)~~ over vitamin K antagonists ~~(VKAs)~~ for patients with PE ~~who do not have~~without cancer.

Long term management of VTE in patients without transient risk factors

Only 40% of doctors stated they would recommend aspirin for patients ceasing anticoagulation after an episode of unprovoked PE. Only 18% of doctors said they frequently or always use follow-up d-dimer tests to guide duration of anticoagulation in unprovoked PE.

Duration of anticoagulation

Forty-one percent of doctors said they would anticoagulate first episode provoked PE for a six or 12 month period (Table 4). Most doctors (83%) would also recommend anticoagulation for fixed periods of six or 12 months for patients with unprovoked first episode PE. For first episode PE with active cancer, unprovoked second episode PE and first episode PE with significant irreversible risk factors other than cancer, the majority of doctors would recommend indefinite[3] anticoagulation (81%, 65% and 63% respectively).

Discussion

The survey ~~demonstrated~~ revealed considerable variability in VTE management practices across multiple areas ~~of VTE management~~. Some of this variation may be due to discrepancies and~~/or~~ gaps in recommendations from the ATG, NICE, ESC and ACCP as 77% of respondents said they base management decisions on one or more of these guidelines. Table 5 describes some of the areas where recommendations are absent or vary between these publications.[4]

For the purpose of this discussion we have classified areas of variability in practice into three broad categories: areas of uncertainty, over-treatment and under-treatment. A practice was only considered over or under-treatment if results deviated from a recommendation which is consistent across the three guidelines in Table 5. We acknowledge more recent recommendations may be supported by better evidence.

Areas of uncertainty

Weighing patients' preferences

Patient's preferences for thrombolysis in intermediate-risk PE are important due to the nature of the risks, including debilitating stroke and intracranial haemorrhage,[14] and benefits of treatment. Surprisingly, 10% of doctors reported they do not discuss the risks and benefits of thrombolysis with their intermediate-risk patients and 22% of those who do said patient preferences do not influence their decision to thrombolyse 'much or at all'.

Thrombophilia and cancer screening in first episode unprovoked pulmonary embolism

The results indicate that thrombophilia screening for patients with first episode unprovoked PE is ordered with varying frequency. This is consistent with findings from an American retrospective study which

[3] Until the clinical risk of recurrent VTE no longer outweighs the risk of bleeding e.g. once there is no longer evidence of active cancer or there is a change in the underlying bleeding risk.
[4] The ATG were excluded as they are not comprehensive.

showed thrombophilia testing is performed in an ~~largely~~ unstructured manner.[15] Guidance in this area is limited (Table 5) and epidemiological data from the German MAISTHRO registry[24] and multination REITE registry[16, 17] did not clearly identify patient groups who will ~~are likely to~~ benefit from testing. It is also unclear if test results are altering management decisions.

With regards to cancer screening, 12% of doctors do not regularly recommend being up-to-date with national screening programmes, while 17% regularly order a screening CT abdomen/pelvis in over 40 year olds. The NICE guidelines recommend consideration of a screening CT abdomen/pelvis in patients over 40 if initial investigations for cancer are negative,[8] however, several more recent publications do not.[21-24] Australian guidelines ~~would help to~~could unify the approach and may reduce ~~costs associated with~~ unnecessary screening.

Aspirin use

The ACCP's 2016 guidelines recommend aspirin for patients ceasing anticoagulation for an unprovoked PE (Table 5).[5] This recommendation is supported by two RCTs published in 2012.[18, 19] Despite this, only 40% of respondents ~~would~~ recommend aspirin in this instance.

Management of low-risk pulmonary embolism

The survey showed that 66% of doctors would anticoagulate patients with asymptomatic SSPE without concomitant DVT. These findings are consistent with those of a 2013 European survey.[8] ~~Based on retrospective data, t~~The ACCP's 2016 guideline recommends that these patients should not receive anticoagulation (Table 5).[5] There are no published ~~randomised controlled trials~~RCTs on the subject[20] and the other guidelines do not make a recommendation.

Follow-up scans

Sixteen percent of doctors routinely request echocardiogram during the follow-up of individuals with unprovoked PE. Routine use is unlikely to be beneficial for identifying CTEPH,[21] although, two moderate sized cohort studies indicate that follow-up echocardiography may be useful to diagnose CTEPH in a subset of patients.[22, 23] The ESC's guideline has recommendations for follow-up screening of patients at risk of CTEPH, although, none of the guidelines consider follow-up imaging for other indications (Table 5). Thirty-five percent of ~~survey~~ respondents order a VQ scan for routine follow-up on cessation of anticoagulation after unprovoked PE. Evidence regarding the usefulness of follow-up imaging to tailor anticoagulation duration is limited. A small study from 2015 found the risk of recurrent VTE was not associated with residual thromboembolic obstruction on CT.[24] However, VQ single photon emission computed tomography may be useful for tailoring the duration of anticoagulation based on resolution of perfusion defects.[25-27]

Further research is required to establish the utility of ordering tests in this situation. ~~Research should focus on whether routine testing changes important clinical outcomes such as VTE recurrence and is cost-effective.~~

Areas of uncertainty in duration of anticoagulation

Anticoagulation practices were variable for unprovoked second episode PE and first episode PE with significant irreversible risk factors other than cancer. Discrepancies in guideline recommendations broadly reflect this (Table 5). These results are consistent with findings from the European REITI registry which found heterogeneous anticoagulation practices.[6]

Areas of under-treatment

The major guidelines recommend using thrombolysis for high-risk PE unless the patient has a clear contraindication (Table 5).[3-5, 13, 28] However, the results of this survey suggest there is a level of under-treatment of high-risk PE by some physicians which is consistent with results from overseas studies. Analysis of the American EMPEROR registry showed that in the period 2006-2008 only seven of 58 patients admitted with high-risk PE received thrombolysis.[9] This study also found a trend of reduced mortality in the thrombolysis group compared with those who did not receive thrombolysis, although, the study was underpowered to detect a true difference.[9] ~~Similar results were noted in one European study~~A European study found similar results.[10]

There was also a tendency to under-treat ~~in the management of~~ first episode unprovoked PE. The majority of physicians surveyed (73%) said they would recommend anticoagulation for periods of six or 12 months (Table 4) despite guidelines recommending ~~an~~ indefinite anticoagulation[5] (Table 5).[3-5]

Areas of over-treatment

A ~~concerning finding of this survey was that a~~ significant proportion of doctors surveyed (41%) indicated they would anticoagulate first episode provoked PE for a period of six or 12 months despite consistent guideline recommendations for three months of anticoagulation (Table 5). Results from the REITE registry study suggest that such variable anticoagulation practices may increase the risk for fatal bleeding.[6]

Our survey also ~~found evidence of~~suggested over-treatment in the management of intermediate-risk PE, although to a lesser degree. In particular, 16% of doctors surveyed indicated they would frequently or always recommend thrombolysis for normotensive patients with elevated cardiac biomarkers and evidence of RVD on echocardiogram (Figure 1) with haematologists four times more likely than respiratory physicians to make this recommendation (Table 2). However, guidelines recommend thrombolysis be considered for this group of patients only if there is haemodynamic or clinical deterioration (Table 5).

The Australian context

Our findings are consistent with the Care Track Australia study which showed that the level of compliance with guidelines for VTE prevention and management requires improvement.[11] Efforts have been undertaken by the National Health and Medical Research Council to ~~produce and~~ implement VTE prophylaxis strategies across Australia,[29] however, these strategies have not included the management of acute VTE. A 2014 study of post-surgical VTE in New South Wales suggested urgent policy action on all VTE management is required as the mortality rate of VTE had not changed over the period of 2002-2009.[30]

Limitations

The major limitation of this study was the low response rate. However, the survey respondents' demographic distribution is consistent with national data[31, 32] and we believe the sample represents an adequate cross-section of haematologists and respiratory physicians.

Considerable effort was made to increase the response rate including multiple reminders and attendance at scientific meetings. Although a high response rate is preferable, non-response rate is not a good

[5] Minimum three months anticoagulation followed extended anticoagulation until the clinical risk of recurrent VTE no longer outweighs the risk of bleeding.

indicator of the size of non-response bias alone[33, 34] and our rate is similar to other surveys of Australian doctors.[35-37]

Implications for practice and future research

This survey highlighted key areas of over-treatment, under-treatment and uncertainty in VTE management. The development and implementation of a national evidence based clinical practice guideline may reduce this variability and improve ~~management of VTE~~VTE management in Australia. There are many areas where clinical uncertainty exists due to gaps in the evidence base ~~and these~~which may be addressed by future research, however in the interim, consensus statements may discourage an excessive reliance on tests of unclear utility and help to facilitate the development of unified treatment pathways. This study provides data on which areas guidelines need to focus. In addition it is likely that specific interventions will be needed to promote the uptake of guidelines and encourage behavioural change.

Venous thromboembolism is a common condition managed by general practitioners, emergency physicians, general physicians, specialist physicians and surgeons. It is important to engage all relevant clinicians and stakeholders for guideline development and future surveys of VTE management should include practitioners not covered by ~~the current~~this survey.

Future prospective cohort studies that link management practices to patient outcomes will provide data about variations in practice and outcomes. One study has been established, but larger studies including multiple centres are needed.[38, 39] Guideline development could also facilitate the development of nationally standardised audit tools to evaluate ~~the management of VTE~~VTE management ~~in both the inpatient and outpatient setting~~.

Conclusion

This survey of respiratory physicians and haematologists has demonstrated significant variability in ~~practice in the management of VTE~~VTE management. Some of which relates to areas of clinical uncertainty which are either not covered by current guidelines or for which guideline recommendations are inconsistent. There were also deviations from consistent guideline recommendations, in particular there is evidence of over-treatment of patients with provoked PE and patients with intermediate-risk PE and under-treatment of patients with high-risk PE. The findings highlight the urgent need for the development and implementation of national guidelines for the management of VTE in Australia.

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Tables

Table 1. Demographic data by specialty area of practice

	Respiratory physicians (%, N=99)	Haematologists (%, N=65)
Sex		
Male	63.6	55.4
Female	36.4	43.1
Declined to answer	0	1.5
Age		
20-40	52.5	52.3
41-50	27.3	23.1
51-60	14.1	18.5
61+	6.1	6.2
Position		
Consultant	73.7	69.2
Registrar/trainee	26.3	30.8
Setting		
Acute hospital inpatient care	93.9	84.6
Acute hospital consultative/liaison	42.4	58.5
Community care	4.0	4.6
Outpatient	59.6	66.2
Private	35.4	32.3
Laboratory	0	6.2
Region		
Metropolitan	93.9	84.6
Regional	6.1	12.3
Metro and regional	0	3.1
Hospital type		
Teaching hospital	90.9	89.1
District general hospital	2.0	0
Private hospital	7.1	6.3
Community care	0	1.6
Laboratory	0	3.1
Years worked in specialty area		
Median years (q_1, q_3)	9 (4, 16)	10 (4, 20)

N = sample size; q_1 = first quartile; q_3 = third quartile, † laboratory

Table 2. Variation of venous thromboembolism management practice between groups

	Total (%)	Haematologists (%)	Respiratory physicians (%)	P value
Doctors who are familiar with the ACCP's 2012 guidelines (N = 164)	54.3	73.9	41.9	<.001
Doctors who agreed they base clinical decisions on a discussed guideline (N = 163)	76.7	85.9	70.7	0.025
Doctors who admitted familiarity with the PESI score (N = 146)	61.0	48.0	67.7	0.021
Doctors who frequently or always calculate and record the Wells score in patients suspected of having a PE (N = 162)	28.4	37.5	22.5	0.038
Doctors who frequently or always order cardiac biomarkers for patients with intermediate-risk PE (N = 141)	68.8	55.3	75.5	0.015
Doctors who frequently of always thrombolyse intermediate-risk PE with RVD on echocardiography and elevated troponin (N = 141)	16.3	27.7	10.6	0.01
Doctors who never or rarely thrombolyse high-risk PE in patients without contraindications (N = 142)	17.6	29.2	11.7	0.01
Doctors who generally discuss the risks and benefits or thrombolysis with their patients (N = 140)	90.0	82.6	93.6	0.041
Doctors who would recommend aspirin for patients with unprovoked PE who are ceasing anticoagulation (N = 137)	40.1	54.4	33.0	0.016
Doctors who frequently or always use D-dimer tests to guide the duration/continuation of anticoagulation in unprovoked PE (N = 143)	18.2	30.4	10.3	0.002

N= Sample size; ACCP = American College of Chest Physicians; PESI = Pulmonary Embolism Severity Index; PE = Pulmonary embolism; RVD = Right ventricular dysfunction

Table 3. Multivariate logistic regression results showing variables associated with survey responses

Doctors response	Variable	OR	P value	95% CI
Doctors who are familiar with the ACCP's 2012 guidelines	Respiratory physicians	0.23	<.001	.11 - .48
Doctors who are familiar with the ACCP's 2016 guidelines	Agreed they base clinical decisions on a discussed guideline[‡]	5.4	<.001	2.1 – 13.7
Doctors who are familiar with the ESC guidelines	Agreed they base clinical decisions on a discussed guideline[‡]	3.2	.048	1.0 – 10.1
Doctors who never or rarely thrombolyse high-risk PE in patients without contraindications	Haematologists	3.7	.013	1.3 – 10.5
	More clinical experience	1.1	.048	1.0 – 1.1
	Primarily work in a private hospital	6.0	.030	1.2 – 29.9
Doctors who frequently of always thrombolyse intermediate-risk PE with RVD on echocardiography and elevated troponin	Haematologists	3.9	.008	1.4 – 10.4
Doctors who would anticoagulate first episode provoked PE for three months	More clinical experience	0.96	.031	0.92 – 0.99
Doctors who are familiar with Wells score	More clinical experience	0.86	.015	0.76 – 0.97
	Private hospital	0.091	.039	0.009 – 0.89
Doctors who frequently or always calculate and record the Wells score in patients suspected of having a PE	Respiratory physicians	0.44	.031	0.21 – 0.93
Doctors who admitted familiarity with the PESI score	Respiratory physicians	2.6	.016	1.2 – 5.7
	Agreed they base clinical decisions on a discussed guideline[‡]	2.6	.029	1.1 – 6.1
Doctors who frequently or always use the PESI for initial assessment of PE severity	Agreed they base clinical decisions on a discussed guideline[‡]	6.9	.012	1.5 – 31
Doctors who frequently or always use cardiac biomarkers for initial assessment of PE severity	Respiratory physicians	2.6	.015	1.2 – 5.7
	More clinical experience	0.95	.016	0.91 – 0.99
Doctors who frequently or always use imaging[†] for the initial assessment of PE severity	Agreed they base clinical decisions on a discussed guideline[‡]	3.0	.017	1.2 – 7.4

Doctors who frequently or always order cardiac biomarkers for patients with intermediate-risk PE	Respiratory physicians	3.4	.035	1.1 – 10.8
	Agreed they base clinical decisions on a discussed guideline‡	3.1	.019	1.2 – 8.0
	More clinical experience	0.95	.034	0.91 – 1.0
Doctors who generally discuss the risks and benefits or thrombolysis with their patients	Respiratory physicians	3.6	.034	1.1 – 11.5
Doctors who recommend cardiac monitoring in patients with elevated troponin and RVD on CT or echocardiography	More clinical experience	0.91	.008	0.85 – 0.97
Doctors who recommend cardiac monitoring for patients with RVD on CT or echocardiography but without elevated troponin	Male	0.44	.048	0.19 – 0.99
Doctors who frequently or always use D-dimer tests to guide the duration/continuation of anticoagulation in unprovoked PE	Respiratory physicians	0.2	.002	0.072 – 0.54
Doctors who agreed they prefer NOACs over VKAs for patients with PE without cancer or contraindications	Agreed they base clinical decisions on a discussed guideline‡	3.1	.013	1.3 – 7.4

OR = odds ratio; CI = confidence interval; ACCP = American College of Chest Physicians; ESC = European Society of Cardiology; PE = pulmonary embolism; RVD = right ventricular dysfunction; CT = computed tomography; NOACs = new oral anticoagulants; VKAs = vitamin K antagonists; PESI = Pulmonary Embolism Severity Index ; † CT chest or echocardiography; ‡ Discussed guidelines were the American College of Chest Physicians: 9th edition, American College of Chest Physicians: 10th edition, The European Society of Cardiology, the National Institute for Health and Clinical Excellence or the Australian Therapeutic Guidelines.

Table 4. Self-reported recommended duration of anticoagulation by haematologists and respiratory physicians in five clinical scenarios

	Generally less than three months (%)	Generally three months (%)	Generally six months (%)	Generally 12 months (%)	Generally indefinitely† (%)	Lifelong (%)
Provoked‡ first episode PE (N=145)	0.7	57.2	39.3	1.4	0.7	0.7
Unprovoked§ first episode PE (N=145)	0	4.8	66.9	15.9	11.0	1.4
Unprovoked second episode PE (N=145)	0	0	1.4	0.7	64.8	33.1
First episode PE with significant irreversible risk factors (other than cancer) (N=144)	0	3.5	16.7	4.9	63.2	11.8
First episode PE with active cancer (N=144)	0	0	4.9	3.5	80.6	11.1

† Until it appears that the clinical risk of recurrent VTE no longer outweighs the risk of bleeding e.g. once there is no longer evidence of active cancer or there is a change in the underlying bleeding risk; ‡ PE which occurs in the presence of transient or mutable risk factors; § PE with no identifiable risk factors; N = sample size; PE = pulmonary embolism

Table 5. Comparison of current guideline recommendations published by NICE, ESC and ACCP

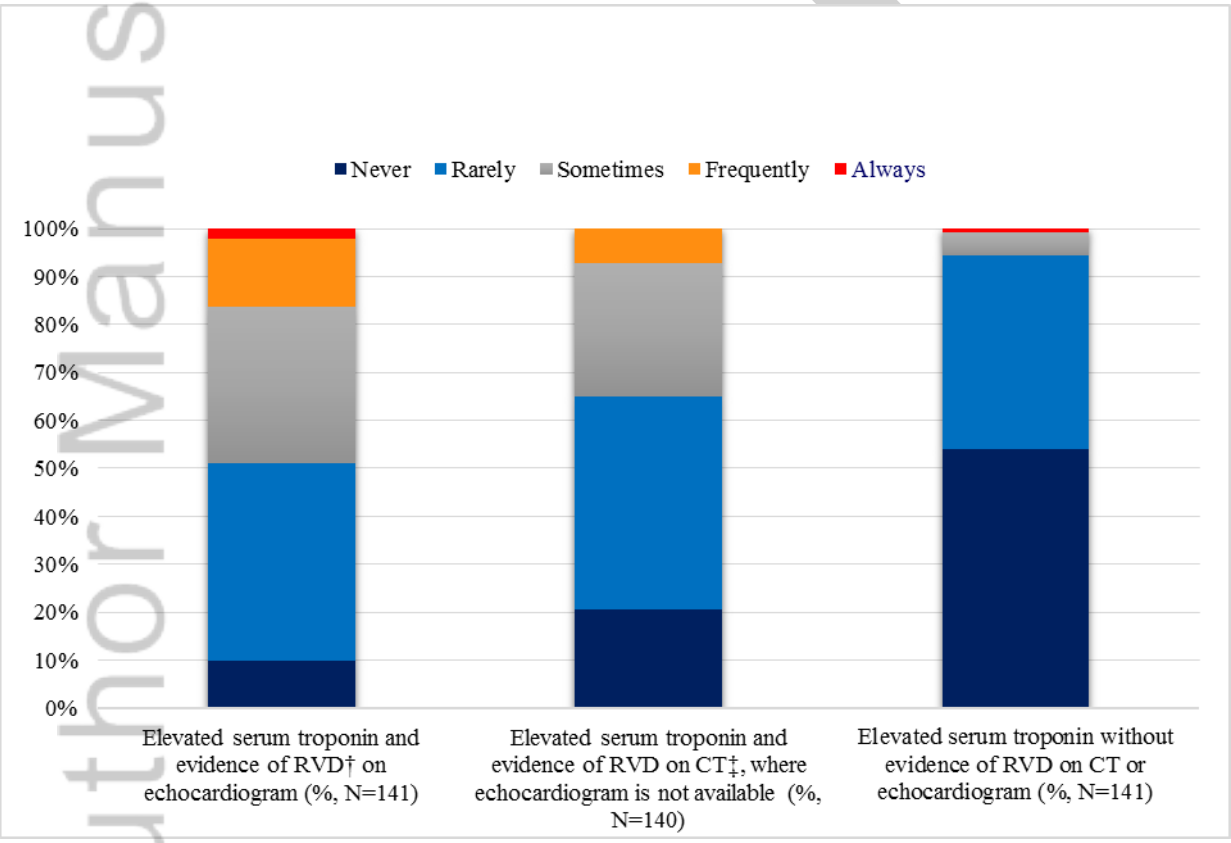
	NICE[3]	ESC[4]	ACCP 2016[5]
Duration of anticoagulation			
Provoked first episode PE	Three months.	Three months.	Three months.
Unprovoked first episode PE	Minimum three months with extended anticoagulation after assessment of recurrent VTE and bleeding risk.	Minimum three months with extended anticoagulation to be considered if low bleeding risk.	Minimum three months with indefinite anticoagulation[†] provided low/moderate bleeding risk.
Unprovoked second episode PE	No specific recommendation. See recommendation for first episode unprovoked PE.	Indefinite anticoagulation.[†]	Indefinite[†] for low/moderate bleeding risk; three months for high bleeding risk.
First episode PE with irreversible risk factors other than cancer	No specific recommendation.	No specific recommendation. However, the discussion says patients with thrombophilia[‡] can be considered for indefinite anticoagulation[†] after a first episode unprovoked PE.	No specific recommendation. However, the discussion says no single risk factor increases the relative risk of recurrent VTE enough to alter management over those otherwise specified.
First episode in the presence of active cancer	Six months, then re-assess and consider extending.	Three to six months, consider indefinite anticoagulation.[†]	Indefinite anticoagulation.[†]
Thrombophilia screen after unprovoked PE	Consider antiphospholipid antibodies if ceasing anticoagulation. Screen for hereditary thrombophilias[‡] if family history of VTE[§] and ceasing anticoagulation.	Not discussed.	Not discussed.
Cancer screen after unprovoked PE	Hx, Ex, CXR, FBE, Ca^{2+}, LFT, Urinalysis. Consider CT abdomen/pelvis in patients >40.	Screening may be restricted to Hx, Ex, basic laboratory tests and CXR.	Not discussed.
Follow-up scans	Not discussed.	Routine VQ scan not recommended. If persistent dyspnoea, evaluation for CTEPH with VQ scan should be considered. No other recommendations.	Not discussed.
NOACs for management of VTE	VKAs are recommended over NOACs. Rivaroxiban may be considered.	NOACs should be considered as alternatives to VKA.	NOACs recommended over VKA.
Thrombolysis for intermediate-risk PE	Do not offer thrombolysis to patients with intermediate-risk PE.	Thrombolysis for intermediate-risk PE is not recommended unless there are signs of haemodynamic decompensation.[¶]	Thrombolysis for intermediate-risk PE is not recommended unless there are signs of deterioration.[††]

Thrombolysis for high-risk PE	Thrombolysis should be considered.	Thrombolysis is recommended.	Thrombolysis is recommended in patients without high bleeding risk.
Anticoagulation of asymptomatic SSPE	Not discussed.	No specific recommendation.	Not recommended unless there is concomitant DVT or a high-risk of VTE recurrence.
Early discharge of low-risk PE	Not discussed.	Consider early discharge and home treatment over inpatient stays of five days or more.	Home treatment or an inpatient stay of fewer than five days is recommended over an inpatient stay of five days or more.
Aspirin after cessation of anticoagulation for unprovoked PE	Not discussed.	Aspirin should be considered.	Aspirin is recommended.
Cardiac monitoring	Not discussed.	No specific recommendation. States that intermediate-risk PE requires 'close monitoring'.	No specific recommendation. States that patients with severe symptoms or marked cardiopulmonary impairment should be monitored closely for deterioration.

† Until it appears the clinical risk of recurrent VTE no longer outweighs the risk of bleeding e.g. once there is no longer evidence of active cancer or there is a change in the underlying bleeding risk; ‡ lupus anticoagulant, protein C or S deficiency, homozygous factor V Leiden or homozygous PTG20210A; § VTE in a first degree relative; ¶ The ESC recommend close monitoring for cardiac decompensation in patients with RVD and elevated cardiac biomarkers[4]; †† Deterioration may include: increase in heart rate, drop in systolic BP, an increase in jugular venous pressure, worsening gas exchange, signs of shock, progressive right heart dysfunction on echocardiography or an increase in cardiac biomarkers.[5]
PE = pulmonary embolism; VTE = venous thromboembolism; NOACs = new oral anticoagulants; Hx = history; Ex = examination; CXR = chest x-ray; FBE = full blood examination; LFT = liver function tests; VQ = ventilation perfusion scan; VKA = vitamin K antagonists; SSPE = sub-segmental pulmonary embolism; DVT = deep venous thrombosis.

Figures

Figure 1. Self-reported frequency of recommending thrombolysis for intermediate-risk PE without contraindications in three clinical scenarios.



† RVD = right ventricular dysfunction; ‡ CT = computer tomography pulmonary angiogram; N = sample size

Appendix A: Questionnaire

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