NIH-PA Author Manuscript

Clinical features from the history and physical examination that predict the presence or absence of pulmonary embolism in symptomatic emergency department patients: results of a prospective, multi-center study

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Abstract

Study Objective—Prediction rules for pulmonary embolism (PE) employ variables explicitly shown to estimate the probability of PE. However, clinicians often use variables that have not been similarly validated, yet are implicitly believed to modify probability of PE. The objective of this study was to measure the predictive value of 13 implicit variables.

Methods—Patients were enrolled in a prospective cohort study from 12 centers in the United States; all had an objective test for PE (D-dimer, CT angiography, or V/Q scan). Clinical features including 12 predefined previously validated (explicit) variables and 13 variables not part of existing prediction rules (implicit) were prospectively recorded at presentation. The primary outcome was VTE (venous thromboembolism: PE or deep venous thrombosis), diagnosed by imaging up to 45 days after enrollment. Variables with adjusted odds ratios from logistic regression with 95% confidence intervals not crossing unity were considered significant.

Results—7,940 patients (7.2% VTE+) were enrolled. Mean age was 49±17 years and 67% were female. Eight of 13 implicit variables were significantly associated with VTE; those with an adjusted OR >1.5 included non-cancer related thrombophilia (1.99), pleuritic chest pain (1.53), and family history of VTE (1.51). Implicit variables that predicted no VTE outcome included: substernal chest pain, female gender, and smoking. Nine of 12 explicit variables predicted a positive outcome of VTE, including unilateral leg swelling, recent surgery, estrogen, hypoxemia and active malignancy.

Conclusions—In symptomatic outpatients being considered for possible PE, non-cancer related thrombophilia, pleuritic chest pain, and family history of VTE increase probability of PE or DVT. Other variables that are part of existing pretest probability systems were validated as important predictors in this diverse sample of US Emergency department patients.

Keywords

Prediction; decision rules; logistic regression; D-dimer; pulmonary embolism

Background

Chest pain and shortness of breath are the two most common symptoms associated with pulmonary embolism (PE). Together these symptoms are responsible for 10 million visits annually to United States emergency departments (EDs).[1] The concern for morbidity and mortality directly caused by failing to diagnose PE has lead to an increase in the use of D-dimer testing, and CT angiography, particularly in ambulatory patients. [2−3] Pretest probability prediction rules have been designed with the goal of increasing the net efficiency of the diagnostic workup for PE. These systems employ predictor variables that have been qualitatively defined in words, quantitatively defined by statistical testing, incorporated into algorithms or scoring systems [4−6] and subsequently validated in clinical practice. [7−8] Accordingly, we submit that variables vetted through this process allows their designation as explicit predictors.

Importance

A survey of community and academic emergency clinicians indicated frequent use of unstructured reasoning when they formulate a pretest probability of PE.[9] We have inferred from these data that clinicians employ many clinical variables they implicitly assume to be associated with PE that have not previously been used in published decision rules. We speculate that the rationale for implicit predictors may have originated in textbook chapters, review articles, lectures by experts, and from structured and unstructured didactics in academic medical centers, as well as an extrapolation from the perceived pathophysiology.

Goals of This Investigation

This study examines the individual predictive value of a battery of predictor variables that were prospectively recoded by a large sample of ED clinicians who ordered diagnostic testing for PE in 7,940 patients. The aim was to compute and compare the adjusted odds ratios for 13 predefined implicit variables (assumed to be predictive but not part of existing pretest probability or scoring systems) that are commonly taught and used as rationale to initiate, delay,

or obviate testing for PE versus 12 explicit predictor variables (with origin in published prediction rules for PE).

Methods

Theoretical construct of the model

Figure 1 depicts what the authors believe to be the current state of thinking among both researchers and clinicians regarding risk factors for PE in the ED. The clinical predictors on the left generally push decision-making towards testing for PE, whereas the variables on the right generally decrease desire to order CT testing for PE, and items over the fulcrum are the grey-zone, implicit predictors. At present, the no published data teach how much these implicit predictors weigh or where they should be placed in the scale diagrammed in Figure 1. To address this unknown, this study presents a preplanned analysis of a large database of ED patients evaluated for PE, with bedside predictor variables and outcomes collected and recorded under a unified, rigorous protocol. This allows a simultaneous examination of multiple explicit (traditional) and implicit (assumed) predictor variables for PE in a single logistic regression equation. This methodology allows a head-to-head comparison of the predictive value of these predictors.

Study Design and Setting

This was a prospective observational study conducted in 12 emergency departments in the US, from July 1, 2003 until November 30, 2006 using methodology previously described in a report validating a low risk PE prediction rule (the PERC rule).10 However, data from one of the sites (Christchurch, New Zealand) that was collected and complete for validation of the PERC rule was not complete with respect to analysis of all data elements required for this manuscript and therefore not included in this analysis.10 This study was approved by the Institutional Review Boards for the conduct of human subject research at all institutions. Ten of 12 sites were required to obtain verbal or written consent, 2 sites were issued a waiver of requirement of informed consent. The 12 sites included nine teaching hospitals, four of which were located in a suburban setting, four in an urban setting, and one in a rural setting. All three community practice hospitals were located in a suburban setting. The study had an experienced central coordinator (in Charlotte, NC) who visited each site for initiation, worked full-time on this project during the entire period of enrollment and whose sole responsibility was to oversee compliance of each site with the study protocol.

Selection of Participants

Patients were enrolled in the ED and included if they had signs or symptoms that the treating physician interpreted as sufficient to warrant testing for PE and they indicated willingness to participate by process of informed consent. We excluded patients who were already being treated for venous thromboembolic disease (VTE: PE or deep venous thrombosis-DVT) with therapeutic levels of anticoagulation, and patients with computed tomography (CT), ventilation perfusion scintillation (VQ) or duplex Doppler testing, performed within the preceding 30 days that was diagnostic of PE or DVT, respectively. We excluded patients with overt circulatory shock, respiratory failure, or co-morbid conditions that included likely death in the next few days. We also excluded patients with social circumstances that have been highly predictive of loss to follow-up including homelessness or imprisonment. All subjects enrolled had to have testing with at least one of the following: D-dimer blood test, CT angiography of the pulmonary arteries, or VQ scan. Patients evaluated for possible DVT only, without physician suspicion for PE, were not enrolled.

Data Collection and Processing

Trained research personnel sequentially monitored ED physician orders for PE testing during either randomly assigned shifts or during periods when research personnel were available to perform consecutive enrollment. This was a non-interventional observational study and clinicians could evaluate for PE by the method of their choice, but the study protocol recommended an algorithm that used pretest probability assessment followed by selective use of a quantitative D-dimer, CT angiography or VQ scan. Patients with low pretest probability and a negative D-dimer or a CT angiography read as negative for PE or a normal VQ scan were considered to not have PE at enrollment. All patients without a diagnosis of VTE at enrollment were followed to determine possible new diagnosis of VTE within the next 45 days.

Explicit predictor variables were obtained from four published standard pretest probability models; Wells[4], revised Geneva[8], Charlotte Criteria[6], and a decision rule designed to exclude PE (the PERC rule).[11] With the exception of the "alternative diagnosis more likely" component of Wells' score, we considered all variables contained in one or more of these published models to be "explicit". Variables that are absent from the above models, but commonly used in routine care as an indication to test for PE were defined *a priori* in our analysis as "implicit" predictor variables. (Table 1) The rationale for including each implicit variable, and its written definition came from the collective experience of the authors during the design of the web-based data collection instrument.

All subjects had a structured interview with data recorded at the point of care using a web-based collection instrument with preformed fields and drop down menus to prevent miss-keyed or missing data.[12] Sites used either the clinician to enter the data or the information was conveyed directly to a research assistant by the clinician and supported by the medical record. Users could not upload the form until all data fields were populated. All clinical data including signs, symptoms, and variables were entered prior to results of final PE testing while patients were in the ED. All decisions about admission, further evaluation, and anticoagulation were made by treating physicians independent of the study protocol.

Outcome Measure—The primary outcome for this study was PE or DVT diagnosed during the index ED visit or hospitalization or during the subsequent 45 days. Follow-up was performed 45 days after the index visit for all enrolled subjects via telephone interview, medical record review or search of the Social-Security Death Index as previously described.[13] Patients and medical records were queried for subsequent acute care visits, hospitalization, cardiopulmonary imaging, tests for VTE, new or changed anticoagulation, or death. The criterion standard for the diagnosis of VTE required diagnosis and intent to treat either PE or DVT within 45 days. Diagnosis of PE required CT documented by an attending radiologist as positive for acute filling defect of a pulmonary artery or VQ scan documented as high probability for PE, or autopsy positive for PE. Diagnosis of DVT required a venous duplex ultrasound-Doppler examination of the arm or leg interpreted as positive for DVT. Treatment was deemed present with medical record evidence of the intent to institute systemic anticoagulation, or actual systemic anticoagulation for at least 90 days, or inferior vena cava filter placement.

Analytical plan

Baseline patient characteristics are reported as means with standard deviations and proportions with 95% confidence intervals. (95% CI) The primary data analysis was done by entering 25 independent (predictor) variables into a logistic regression equation to determine beta coefficients and converting them to adjusted odds ratios (OR). Some continuous variables were dichotomized based on previous convention in the literature associated with PE (age, hypoxemia, tachycardia), or clinical convention (fever, BMI). Prior to analysis, the cohort was

known to contain 568 patients with the dependent variable of VTE present. Based on a conservative conventional ratio of subjects with the outcome of interest to number of candidate variables of 20:1, this would allow the ability to test at least 25 candidate variables. Significance was defined as adjusted odds ratios with 95% CI that do not cross 1.00. Statistical calculations were made using Stata statistical software version 10 (StataCorp LP, College Station, Texas). We screened all data elements for any miss-keyed or nonsense data extensively by graphical analysis, histograms, and tabular examination of extreme values at the end of the range (for continuous data), and by one way tables reporting all categories including missing for categorical data. This was reconciled with focused re-examination of the medical record when available.

Results

Characteristics of Study Subjects

Not all patients who were eligible provided informed consent or were capable of adequate followup. The rate of refusal of informed consent in otherwise eligible subjects was 5.0%. The rate of subjects excluded due to foreseeable inability to achieve follow-up was 3.9% (e.g. homelessness, imprisonment). The final sample comprised 7,940 ED patients who underwent formal testing for PE ordered by 477 unique clinicians. The mean patient age was 49.0 years (SD±17.3). Median age was 47 years (25th–75th IQR 36 to 61). Females comprised 67% of the sample. Race and ethnicity are described in Table 2. At the end of 45-day follow up, 568/7940 (7.2%; 95% CI 6.6 to 7.7%) met the criterion standard definition of PE or DVT. Most VTE (552) were diagnosed at the index visit (Figure 2).

Patients reported chest pain (72%) and dyspnea (70%) as the most common presenting symptoms. Half of all patients were discharged from the ED, 36% were admitted to a floor bed, 12% to a 24-hour ED observation/short stay unit, and 2% were admitted to an ICU.

Main Results

Table 3 shows the results of the primary data analysis. In 284 records we were unable to fully impute or correct miss-keyed, missing or non-sense data and these were not included in the final logistic regression model. We compared 25 predictor variables including 13 that we believe to be implicit predictors and 12 that are explicit predictors. Eight of 13 implicit predictor variables tested were significant in the multivariate model. Three were positively associated with VTE (non-cancer related thrombophilia [OR=1.99], pleuritic chest pain [OR=1.53], and family history of VTE [OR=1.51]) and three that were negatively associated with VTE (female gender [OR=0.60], current smoking [OR=0.60], and substernal chest pain [OR=0.60]). Both the presence of tachypnea (respiratory rate >24 breaths/minute) and patient perception of dyspnea were associated with increased likelihood of VTE [OR 1.26 for both] but with lower limits of the 95% confidence interval of 1.02 and 1.00 respectively. Several predictor variables often cited as providing rationale for test ordering were not statistically significant including: pregnancy or post-partum state, sudden onset of symptoms, obesity (body mass index >=30), and past history of treated but currently inactive malignancy. Nine of the 12 explicit predictor variables were associated with VTE. The strongest associations included: patient history of VTE (OR=2.90), unilateral leg swelling (OR=2.60), recent surgery within 4 weeks (OR=2.27), estrogen use (OR=2.31), pulse oximetry saturation <95% (OR=2.10), active cancer (OR=1.92), and immobilization exclusive of travel (OR=1.72). However, some explicit variables that are currently part of pretest probability prediction rules and taught as being associated with PE were not significant in our analysis. Hemoptysis, trauma within 4 weeks, and shock index>1.0 were not statistically associated with the outcome of VTE.

Limitations

Physicians were not mandated to follow universal imaging algorithms and therefore it is possible that some patients may have had non-recognized VTE. The study used a thorough, validated follow up methodology, and results include a post-index VTE rate similar to protocolized management trials[7,17] suggesting that this effect is unlikely to have been to a degree that threatens validity of findings. It is also likely that the observational nature of this work explains why the prevalence of disease was lower than has been observed in other studies[18] or recent controlled trials of imaging studies. [17, 19–20] In contrast to the strict qualifying process required for a management study or a clinical trial, the present work was designed to collect a large, relatively unbiased sample of patients with heterogeneous clinical characteristics known to clinicians at the time they ordered a test for PE in the emergency department; we believe our findings represent real-world, current acute care practice in the United States.

We are unaware of a method to estimate the probability of type II-like error with a multivariate logistic regression equation (i.e., failure to recognize a truly significant predictor). Nonetheless, we believe it is likely that this analysis failed to find significance for variables that truly are important predictors of PE in the ED. Specifically, the variable of trauma had an odds ratio of 0.78 with confidence interval of 0.37–1.65. The explicit definition of trauma that appeared to the user in a pop-up box on the data form was as follows: "traumatic injury requiring hospitalization within the previous 4 weeks." The word "hospitalization" was not further defined, although the user had to choose which body systems were injured. It is possible that trauma would have been significant if the definition were more specific or more restrictive (e.g., trauma requiring >3 consecutive days hospitalization in the previous 4 weeks). This possibility of a type II-like error could also apply to our findings about pregnancy. Our sample had a low number of pregnant patients and the confidence interval around this variable is wide.

We did not perform interobserver agreement analysis on this sample as most explicit variables are part of the Wells score or other pretest probability systems that have been extensively applied and validated in a variety of practice settings. The implicit variables are either objective data elements (BMI, tachypnea, fever) or are relatively clear binary elements from the history (recent pregnancy, inactive malignancy). In earlier work in which 21 variables were analyzed to create a prediction rule, we performed inter-observer agreement and found that of the 15 significant predictors, only 2 (immobility and sudden onset) were not included in the model due to low values of Cohen's Kappa (0.30 and 0.48)[11] However, we acknowledge that some elements such as dyspnea may be abstracted differently by different observers and this must be considered in interpreting these findings.

Most importantly, we wish to highlight the distinction between the present research, designed to predict the short-term outcome of PE, versus epidemiological research designed to assess for clinical factors that cause PE. Studies such as the Longitudinal Investigation of Thromboembolism Etiology (LITE) study[21] report the outcomes of patients followed over time to determine biological and clinical factors that cause VTE in the general population. Factors that increase risk of PE in the general public (e.g., obesity) may not be important predictors of PE among symptomatic patients in the ED setting.

Discussion

This is a large, heterogeneous cohort of acute care patients studied to prospectively quantify the association of patient characteristics known at the time of test ordering with the outcome of VTE. We found that 7.2% of all subjects had PE or DVT at the index visit or during the subsequent 45 days. The variables with the strongest associations with VTE were for patient history of VTE, unilateral lower extremity swelling, recent surgery, estrogen use, oxygen

saturation less than 95%, active cancer and patient history of thrombophilia. These findings are consistent with previous studies of pretest probability prediction rules [4–6] and help to further identify the most important variables that should maximally heighten PE suspicion for the clinician at the time of test ordering.

We believe that many other variables used to guide clinical decisions in EDs and clinics are based on dogma, rather than evidence. Our investigation of these variables is unique. To our knowledge, no previously published evidence has directly compared and quantified the predictive value of pleuritic chest pain, substernal chest pain, dyspnea, estrogen use, family history of VTE, and patient history of a thrombophilic condition for the outcome of VTE. Though some past reports [5] have investigated some of these variables, this is the first report of a large number of them in aggregate, investigated with a priori determined definitions and standardized follow up in the current multi-detector CT era. Furthermore, none of these variables are part of either the currently used Wells score or the revised Geneva score.

Despite the fact that this work focuses on acutely symptomatic patients at the point of test ordering and therefore is not applicable to the question of development of VTE over time, many of our findings are consistent with previous studies of VTE epidemiology. Significant predictors in both epidemiology studies and our work include active cancer, previous VTE, increased age, and recent surgery. [14–16]

The findings related to smoking, female gender, and race need special comment. Both female gender and current smoking were significantly predictive of not having VTE in this cohort with ORs of 0.6. One possible explanation of this finding is that it is a function of over-testing for PE among females and smokers. A disproportionate percentage of females were enrolled in this study (2:1 ratio) and the rate of PE among females was higher on a univariate basis (54.4% vs. 45.6%), but after adjustment for age and estrogen, the independent effect of female gender appeared to predict reduced likelihood of VTE. Disproportionate enrollment of females in studies of PE diagnosis has been seen in other reports and suggests women may be more likely to be tested for PE than men. We strongly urge that this observation not be interpreted as evidence that women are at lower risk for PE. They are not. With respect to smoking and VTE it must be remembered that the manner in which these data elements were obtained does not lend itself to interpretation of causality over time and it may well be that sustained tobacco is causally related to development of VTE in the general population. However we found it to be significantly associated with not having VTE ultimately diagnosed during or after ED testing. We believe that two obvious points can be combined to provide a rational explanation for this observation. First, smoking is a common problem (about one-third of adult ED patients smoke), and second, smoking-related damage to the airways often manifests symptoms that suggest possible PE (but after diagnostic testing and an observation period, no PE ever turns up). It is also important to note that race as a predictor variable was not modeled. In summary, these variables need further analysis and this report does not suggest that female gender, smoking or race should be used as independent factors in the decision to test or not test for PE.

We observed that several clinical characteristics that we believe are assumed by clinicians to predict the presence of VTE were actually not significant independent predictors in the multivariate logistic regression analysis applied to our cohort and had confidence intervals that crossed 1.0. These include sudden onset of symptoms, obesity, and past history of now inactive cancer. One potential interpretation of these data is that acutely symptomatic patients who are otherwise low risk for PE, who have none of the above significant predictor variables but only one or several of the non-significant characteristics such as sudden onset, non-pleuritic substernal chest pain, inactive malignancy, or obesity perhaps should not be considered to be at increased likelihood of PE based on these characteristics alone.

Teachers, practitioners and researchers may find use for these data. Teachers of emergency medicine might use the odds ratio data in Table 3 to prepare lectures and "chalk talks" to students of emergency medicine on the initial approach to patients with possible PE. Practitioners may wish to document these significant predictors when considering whether or not to test for PE, and may wish to add them as standard elements to chief complaint-based, templated charting systems. Researchers may consider testing the predictors we found to be significant in a new decision rule or management algorithm, (our group has no current plans to do so).

Conclusion

In this large sample of symptomatic ED patients tested for PE, several clinical characteristics that are not part of existing prediction rules were identified as significantly associated with the outcome of PE or DVT within 45 days. These included patient history of thrombophilic condition, pleuritic chest pain, and family history of VTE. Predictors from existing pretest probability scoring systems that were validated here as strongly associated with the outcome of VTE included: history of past PE or DVT, unilateral leg swelling, surgery within the past 4 weeks requiring general anesthesia, estrogen use, oxygen saturation of less than 95%, and active or metastatic malignancy. Future decision rules for PE should include these variables and clinicians who use an unstructured approach should use these variables accordingly to help them estimate the pretest probability of PE.

Acknowledgments

ABBREVIATION LIST

CI	95% Confidence Intervals
CT	Computed Tomography
DVT	Deep Venous Thrombosis
ED	Emergency Department
ICU	Intensive Care Unit
OR	Adjusted Odds Ratio
PE	Pulmonary Embolism
VQ	Ventilation Perfusion Scintillation
VTE	Venous Thromboembolism– Pulmonary Embolism or Deep Venous Thrombosis

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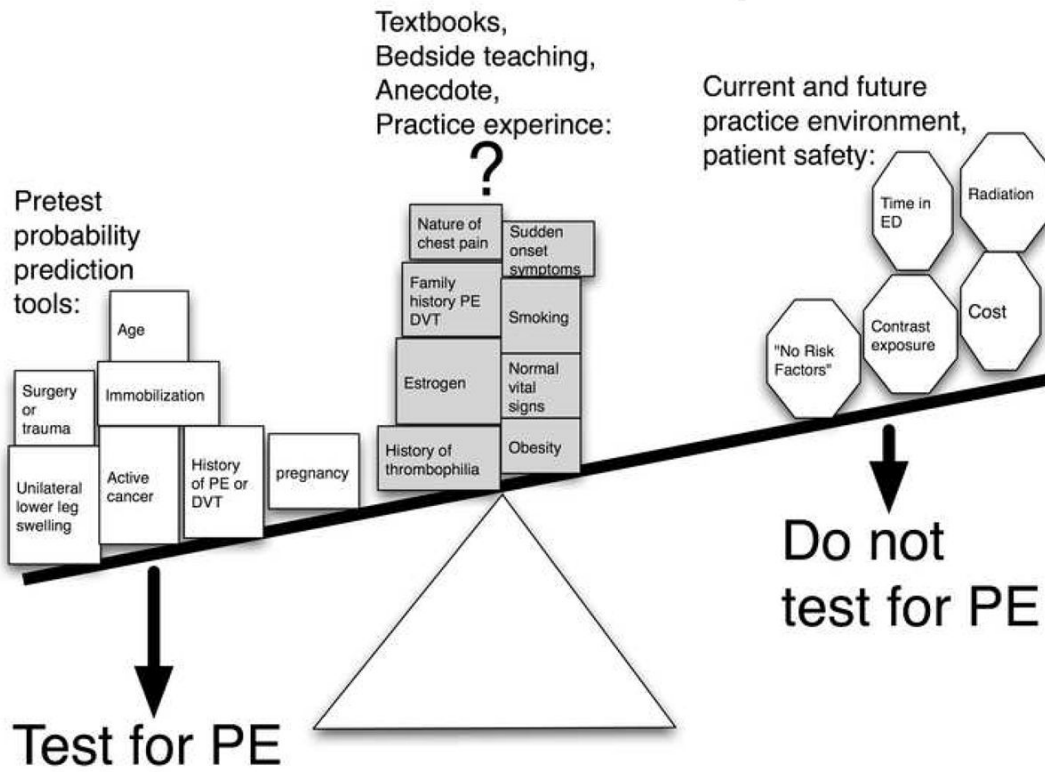
Figure 1.
Theoretical construct of the test vs. no test decision
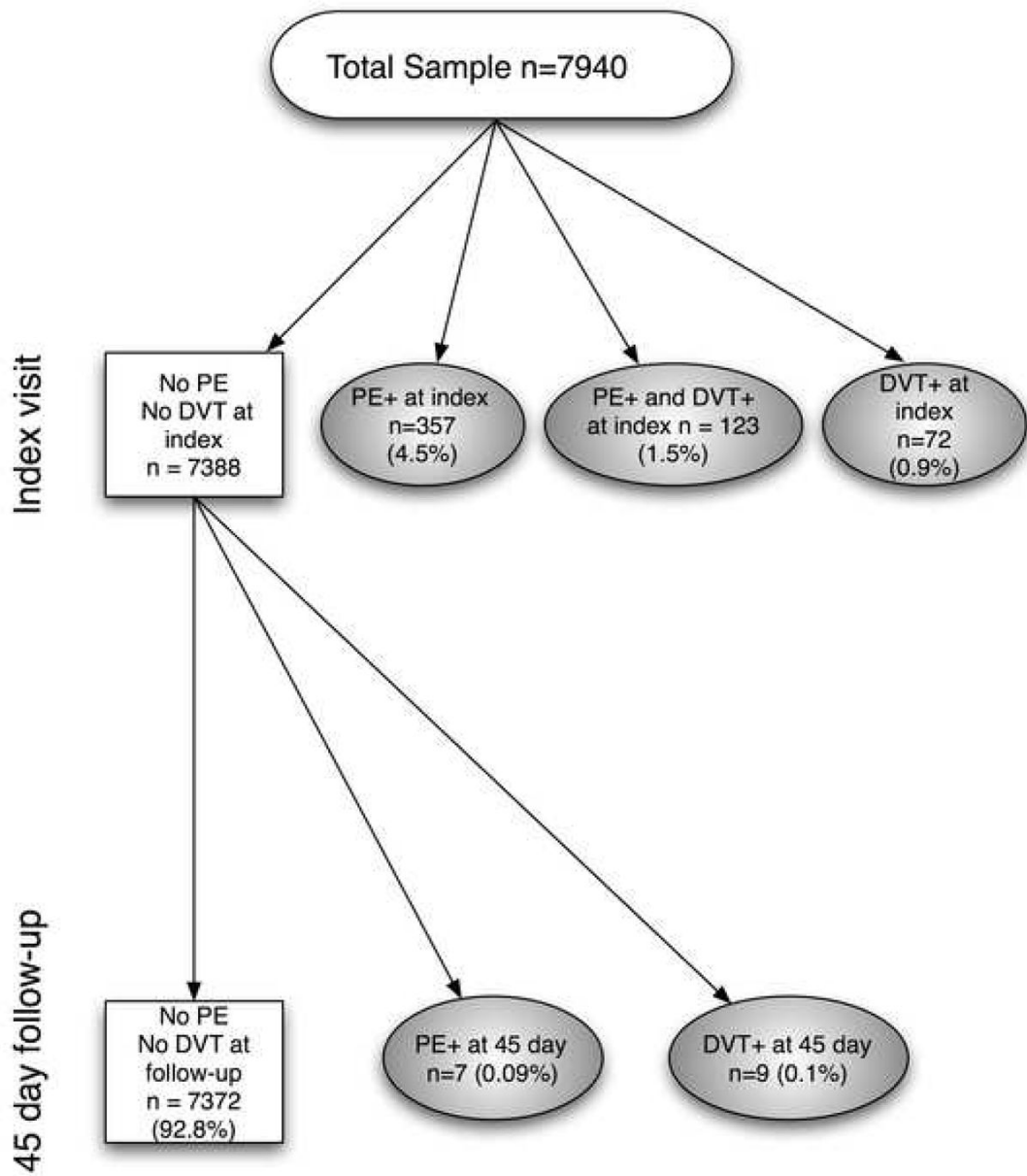
Figure 2.
Flow diagram showing diagnostic outcome of all patients. The study design did not allow for patients to have an endpoint of lost to follow-up

Table 1

Categorization and definition of predictor variables

Explicit predictor variables:	
	Probability system:
Unilateral leg swelling	**W,G,C, P**
Surgery within the previous 4 weeks (requiring general anesthesia)	**W,G,C, P**
Trauma within the previous 4 weeks (requiring hospitalization)	**W, P**
Immobilization (any of the following: generalized body immobility for 48 hours in the prior 2days, bedridden status, paralysis/paresis, or limb in cast/external fixator)	**W**
Hemoptysis	**W,G,C, P**
Patient history of VTE	**W,G, P**
Pulse >94 [*]	**G**
Active malignancy: (current chemotherapy, radiation therapy, or palliative care)	**W,G**
Shock index > 1.0 (SI = pulse divided by systolic blood pressure)	**C**
Age > 50 years	**C,P**
Hypoxemia (oxygen saturation <95% on pulse oximetry)	**C, P**
Estrogen: (current use)	**P**
Implicit predictor variables:	
Female gender	
Pregnancy or post partum state	
Thrombophilic condition (non-cancer related): any of the following known in the ED: Factor V Leiden mutation, protein C or S deficiency, prothrombin mutation, anti-phospholipid antibody syndrome, or sickle cell disease (SS or SC)	
Smoking tobacco currently	
Sudden onset of symptoms	
Sub-sternal chest pain (located behind the sternum)	
Pleuritic chest pain (between clavicles & costal margin, that changes with respiration)	
Dyspnea: (patient perception of shortness of breath or difficulty breathing)	
Inactive malignancy (not being treated with chemotherapy, radiation, or palliative care)	
Obesity (body mass index-BMI >=30)	
Fever (temperature >= 38.0° C)	
Tachypnea (respiratory rate > 24 breaths/minute)	
Family history of VTE	

[*] tachycardia was also part of the PERC rule (>99 beats per minute) and the Wells score (>100 beats per minute)

W = Wells score, G = Geneva score, C = Charlotte rule, P= PERC rule

Table 2

Patient characteristics

Total n= 7940	n	% or mean	95% CI or SD
DEMOGRAPHICS:			
Age		49.0	+/− 17.3
Female	5328	67.1%	66.1 to 68.1%
White	4541	57.2%	56.1 to 58.3%
Black	2704	34.0%	33.0 to 35.1%
Hispanic	482	6.1%	5.6 to 6.6%
Asian	74	0.9%	0.7 to 1.2%
Other race	139	1.8%	1.5 to 2.1%
CLINICAL CHARACTERISTICS:			
Chest pain	5697	71.8%	70.7 to 72.7%
Dyspnea	5587	70.4%	69.3 to 71.4%
Wells score <=4	6694	84.3%	83.5 to 85.1%
Wells score >4	1246	15.7%	14.9 to 16.5%
OUTCOME:			
Admitted (inpatient)	3029	38.4%	37.4 to 39.5%
Admitted (emergency observation unit)	982	12.5%	11.7 to 13.2%
Discharged	3868	49.1%	48.0 to 50.2%
PE/DVT at index visit	552	7.0%	6.4 to 7.5%
PE or DVT at follow-up only	16	0.2%	0.1 to 0.3%

CI = confidence interval

SD = standard deviation

PE = pulmonary embolism

DVT = deep venous thrombosis

Table 3

Logistic regression model output for all predictor variables (12 explicit and 13 implicit)

	n (%)	Adjusted OR	95% CI	P value
Explicit predictor variables:				
Patient history of VTE	858 (10.8%)	2.90	2.32 to 3.64	<0.001
Unilateral leg swelling	710 (8.9%)	2.60	2.05 to 3.30	<0.001
Surgery within the previous 4 weeks	520 (6.6%)	2.27	1.70 to 3.02	<0.001
Estrogen use currently	663 (8.4%)	2.31	1.63 to 3.27	<0.001
Hypoxemia (saturation <95%)	1,544 (19.4%)	2.10	1.70 to 2.60	<0.001
Active or metastatic cancer	489 (6.2%)	1.92	1.43 to 2.57	<0.001
Immobilization	763 (9.6%)	1.72	1.34 to 2.21	<0.001
Age > 50 years[*]	3,467 (43.7%)	1.35	1.10 to 1.67	0.005
Pulse >94 beats/minute[†]	3,234 (40.7%)	1.52	1.24 to 1.87	<0.001
Shock index > 1.0	834 (10.5%)	1.26	0.96 to 1.65	0.093
Hemoptysis	227 (2.9%)	0.78	0.46 to 1.32	0.353
Trauma within the previous 4 weeks	90 (1.1%)	0.78	0.37 to 1.65	0.520
Implicit predictor variables:				
Personal history of non-cancer related thrombophilia	149 (1.9%)	1.99	1.21 to 3.3	0.007
Pleuritic chest pain	3,660 (46.1%)	1.53	1.26 to 1.86	<0.001
Family history of VTE	820 (10.3%)	1.51	1.14 to 2.00	0.004
Female gender	5,328 (67.1%)	0.57	0.47 to 0.69	<0.001
Smoking tobacco currently	1,839 (23.2%)	0.59	0.46 to 0.76	0.001
Sub-sternal chest pain	2,909 (36.6%)	0.58	0.46 to 0.72	<0.001
Pregnancy or post partum state[‡]	285 (3.6%)	0.60	0.29 to 1.26	0.180
Sudden onset of symptoms	4,407 (55.5%)	0.88	0.73 to 1.06	0.175
Obesity (body mass index >=30)	2,885 (36.3%)	1.13	0.93 to 1.38	0.214
Tachypnea (RR > 24)	1,667 (21.0%)	1.26	1.02 to 1.56	0.035
Dyspnea	5,587 (70.4%)	1.26	1.00 to 1.58	0.048
Pat history of malignancy, now inactive	512 (6.4%)	0.82	0.56 to 1.18	0.284
Fever (temperature >= 38.0° C)	292 (3.7%)	1.13	0.76 to 1.69	0.536

[*] Age > 65 years from the revised Geneva score was alternatively used in the multivariate model but resulted in no qualitative difference in the adjusted odds ratio. (data not shown)

[†] pulse > 100 from the Wells score and pulse 75–94 from revised Geneva score were each used in the multivariate model sequentially and resulted in no qualitative difference in the adjusted OR. Pulse >94 beats per minute is reported here in the final model as it resulted in the largest pseudo R^2 (data not shown)

[‡] Post partum included pregnancy within past 4 weeks

Univariate association of predictor variable stratified by VTE positive and negative groups: (for web appendix)

Predictor variable	VTE positive	%	VTE negative	%
Patient history of VTE	155/568	27.3%	703/7372	9.5%
Unilateral leg swelling	135/568	23.8%	575/7372	7.8%
Surgery within the previous 4 weeks	86/568	15.1%	434/7372	5.9%
Estrogen use currently	51/568	9.0%	612/7372	8.3%
Hypoxemia (saturation <95%)	240/567	42.3%	1304/7349	17.7%
Active or metastatic cancer	85/568	15.0%	404/7372	5.5%
Immobilization	125/568	22.0%	638/7372	8.7%
Age > 50 years*	340/567	60.0%	3127/7367	42.4%
Pulse >94 beats/minute†	317/568	55.8%	2917/7372	39.6%
Shock index > 1.0	110/565	19.5%	724/7341	9.9%
Hemoptysis	20/568	3.5%	207/7372	2.8%
Trauma within the previous 4 weeks	9/568	1.6%	81/7372	1.1%
Personal history of non-cancer related thrombophilia	26/568	4.6%	123/7372	1.7%
Pleuritic chest pain	274/568	48.2%	3386/7372	45.9%
Family history of VTE	76/568	13.4%	744/7372	10.1%
Female gender	309/568	54.4%	5019/7371	68.1%
Smoking tobacco currently	85/568	15.0%	1754/7372	23.8%
Sub-sternal chest pain	121/568	21.3%	2788/7372	37.8%
Pregnancy or post partum state‡	8/568	1.4%	277/7372	3.8%
Sudden onset of symptoms	285/568	50.2%	4122/7372	55.9%
Obesity (body mass index >=30)	216/560	38.6%	2669/7249	36.8%
Tachypnea (RR > 24)	193/562	34.3%	1474/7316	20.1%
Dyspnea	449/568	79.0%	5138/7372	69.7%
Pat history of malignancy, now inactive	40/568	7.0%	472/7372	6.4%
Fever (temperature >= 38.0° C)	36/559	6.4%	256/7207	3.6%