

THE ASSOCIATION BETWEEN D-DIMER AND DEEP VEIN THROMBOSIS LOCATION AND ITS ABILITY TO PREDICT PULMONARY EMBOLISM, a retrospective pilot study

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Abstract

Background In lower limb deep vein thrombosis; it is important to identify proximal from distal deep vein thrombosis as it carries the highest risk of pulmonary embolism. It is known that D-dimer has a great role in deep vein thrombosis diagnosis. Yet, the use of D-dimer to predict the location of deep vein thrombosis and the risk of pulmonary embolism in deep vein thrombosis patients has not been investigated before.

Objective To address the correlation between D-dimer and the location of deep vein thrombosis and to study the efficacy of D-dimer to predict risk of PE in patients with proximal or extensive deep vein thrombosis.

Method We included 110 consecutive patients who were hospitalized with the diagnosis of deep vein thrombosis, with or without a concomitant diagnosis of PE, and with D-dimer measured at initial presentation. We categorized the location of deep vein thrombosis as: distal, proximal, and extensive. In the analysis, patients were grouped into high-risk (patients with Proximal or Extensive deep vein thrombosis and pulmonary embolism) and low risk group (patients without pulmonary embolism).

Results There was no significant association between D-dimer level and the location of deep vein thrombosis ($p=0.519$). However, D-dimer level was greater among patients with pulmonary embolism (9.6mg/L) than among patients without pulmonary embolism (7.4mg/L), ($p=0.027$). D-dimer was a significant predictor of pulmonary embolism as patients with proximal or extensive deep vein thrombosis had 8-folds increased risk of pulmonary embolism than patients with D-dimer less than 4.75mg/L (OR=7.9, $p=0.013$).

Conclusion Though D-dimer was not significantly associated with the location of deep vein thrombosis, it was a significant predictor of pulmonary embolism in patients hospitalized with proximal or extensive deep vein thrombosis.

Background

The annual overall incidence of venous thromboembolism (VTE) is estimated to be approximately 100 per 100,000 persons (half of them with deep vein thrombosis) [1]. In Saudi Arabia, it is estimated that 25,000 people develop VTE annually [2]. Lower limb deep vein thrombosis (DVT) is the main source of pulmonary embolism (PE). Patients with proximal (i.e. above the knee) carry the highest risk of PE (approximately 66%) compared to patients with distal DVT (i.e. below the knee) (33%) [3]. D-dimer results from fibrin degradation and it is the laboratory indicator of thrombus formation and lysis anywhere in the body [4]. It is an inexpensive and feasible test that has a major role in the diagnosis of Venous Thromboembolism. A negative D-dimer is sufficient to rule out a diagnosis of DVT in patients with low or intermediate pretest probability on Well's score [5]. D-dimer test has always been interpreted as positive (usually $>0.5\text{mg/L}$) which is highly suggestive of DVT or negative ($<0.5\text{mg/L}$) which makes DVT a less likely diagnosis. Little concern was made regarding how positive the test is (i.e. the level of D-dimer). Several Studies have investigated D-dimer beyond its diagnostic value in patients with PE; in attempt to use D-dimer as a biomarker or predictor of the severity of PE [6,7,8]. These studies have shown an association between higher level of D-dimer and the severity of PE, with a higher level of D-dimer indicating a more extensive PE [6, 9]. Furthermore, studies proved the prognostic value of D-dimer in predicting mortality in patients with pulmonary embolism [7,8] when high level of D-dimer was associated

with increased mortality. One study showed that the higher the D-dimer level the higher the overall mortality in patients with pulmonary embolism. According to that study for every 1000ng/ml increase in D-dimer the overall mortality increased by 10% among patients with PE [7].

The utility of D-dimer in patients with DVT is still confined to its diagnostic value (i.e to rule out DVT diagnosis) giving its high sensitivity and negative predictive value [10]. Until now the use of D-dimer to predict the location of DVT or the risk of developing PE in DVT patients has not been investigated. To our knowledge; there is no study that examined the use of D-dimer as a predictor of the most serious complication associated with lower limb DVT; i.e. pulmonary embolism. We conducted this study to shine a light on the correlation between D-dimer level and the location of DVT and the ability of D-dimer of to predict pulmonary embolism among patients who are diagnosed with proximal or extensive DVT.

Objectives:

To assess whether D-dimer level is associated with the location of lower limb DVT (distal, Proximal, Extensive) and the incidence of symptomatic PE in these patients. In addition, to determine the efficacy of D-dimer to risk stratify patients with lower limb DVT to high risk group (patients who developed PE on top of proximal or extensive DVT) and low risk group (those who are diagnosed proximal or extensive DVT but did not develop PE), and to find a D-dimer level above which patients can be considered high risk of developing PE.

Materials & Methods

This is a retrospective study which included 110 consecutive patients, between January 2015 and December 2017, who were admitted to the hospital with a diagnosis of DVT confirmed by ultrasonography, with or without a concomitant diagnosis of PE at initial presentation, and D-dimer level measured at initial presentation. Inpatients who developed DVT during hospitalization were excluded.

Data which consisted of (patient's age and gender, symptoms of DVT(as unilateral leg swelling, pain, hotness), duration of symptoms, length of hospital stay, location of DVT (distal, proximal, or extensive), location of proximal DVT (popliteal, femoral, or iliac), presence of malignancy, pregnancy or recent surgery which are considered as confounder that may interfere with D-dimer level, D-dimer level and finally the occurrence of pulmonary embolism either at initial presentation or later during hospitalization) was collected from patients' electronic medical records and medical files into a designed data sheet. The extracted data was de-identified (without names, National ID number, contact number, or geographical data) to assure patients confidentiality.

D-dimer was measured using the rapid quantitative turbidimetric D-dimer assay which has a negative predictive value of 97.7% [11] and was reported in mg/L. The diagnosis of DVT was confirmed by whole leg compression ultrasonography. "Distal DVT" was defined [as anterior tibial, posterior tibial or peroneal vein thrombosis]; "Proximal DVT" was defined [as popliteal, femoral, or external iliac vein thrombosis], while "Extensive DVT" was defined [as thrombosis involving the whole leg (extending from below to

above the popliteal vein)]. The diagnosis of pulmonary embolism was confirmed by Spiral CT angiography. During the analysis we grouped the patients into a high-risk group (patients who developed PE on top of proximal or extensive DVT) and low risk group (those who are diagnosed proximal or extensive DVT but did not develop PE).

Statistical Analysis:

The power analysis was performed using G*power software (version 3.1.9.2] to determine the minimum sample size needed for this study. For a medium effect size ($f^2 = 0.15$) and an alpha level = 0.05, the minimum sample size needed to achieve a .80 power was 55.

Descriptive data was expressed by mean, standard deviation, median, minimum and maximum for continuous variables and frequencies for categorical variables.

For bivariate analysis; the non-parametric Spearman correlation was used to assess the association between D-dimer and length of hospital stay and duration of symptoms. The Kruskal-Wallis test was used to establish the association between D-dimer and location of DVT and site of proximal DVT. Finally, the Mann-Whitney test was used to assess the differences in D-dimer values between the patients with PE and without PE.

A multinomial logistic regression was conducted to model the relationship between the independent variable D-dimer and membership to the three groups of DVT location (distal, proximal, extensive) and it was adjusted for age and gender. Malignancy, pregnancy and surgery could not be included as covariates since there were not cases of malignancy, pregnancy or surgery for the distal category of DVT. We ran two models where we used D-dimer as continuous and then as two groups: below and above the value its median (=4.39)

We used ROC curves to study the feasibility of using Dimer level to identify patients at high risk. In particular, the area under the curve (AUC) is used to estimate the accuracy of Dimer levels to separate high risk from moderate/low risk patients. An area of 1 represents a perfect diagnostic test and an area of .5 represents a worthless test, in the sense that flipping a coin would provide the same level of accuracy. The following point system is commonly used to interpret the value of the area under the curve: .90-1 = excellent (A), .80-.90 = good (B), .70-.80 = fair (C), .60-.70 = poor (D), .50-.60 = fail (F). These curves were used to establish a cutoff that will provide optimal values of sensitivity and specificity. [12]

Finally, the correlation between D-dimer and occurrence of PE was addressed with a logistic regression to model the likelihood of developing a Pulmonary Embolism based on D-dimer. The model was adjusted for age, gender, surgery and DVT (proximal vs extensive). D-dimer was categorized into two groups according to the suggested cutoff level from the ROC curve: below and above the value of 4.75.

Results

Main Patient Characteristics:

Sixty-four of patients were female and the average age was 44.8 with 65.5% of the patients had proximal DVT, a 28.2% had extensive DVT and only 6.4% were diagnosed as having distal DVT. Most of the patients with proximal DVT had thrombosis at the femoral vein 52.8%, 26.4% at the popliteal and 20.8% at the iliac vein. The incidence of PE in the sample was 11%, (12 out of 110) either upon presentation or during hospital stay (average length of stay was 6 days). All patients with PE were from the proximal or the extensive group (50% each). All of them were hemodynamically stable. Only two of our patients had malignancy, 24 % developed DVT post-operatively and 8% during pregnancy. The duration of DVT symptoms ranged from 1 day to 20 days (Table 1).

Table 1.

Descriptive Characteristics of Study Sample (N=110)

The association between D-dimer level and DVT Location:

Though D-dimer level was lower in the distal Group (Mean=6.13, SD=6.1) than the proximal (Mean=7.2, SD=7.9) and the extensive (Mean=8.8, SD=8.8) groups, there was no significant association between level of D-dimer and the location of DVT, according to the Kruskal-Wallis test (H=1.31, P=0.519). D-dimer also was not found to be significantly related to the site of proximal DVT (H=2.01, P=0.366). (See *Appendix A for further details*).

The association between D-dimer level and Length of hospital stay, duration of DVT symptoms:

A positive weak correlation was found between D-dimer level and length of hospital stay ($r=.24$, $p=.015$). However, there was no correlation between duration of DVT symptoms and level of D-dimer.

The association between D-dimer level and pulmonary embolism:

Interestingly, patients with PE had a greater D-dimer level (mean=9.6 6.5 mg/L) than patients without PE (mean=7.4 8.2 mg/L) as shown by an-Whitney test (P=0.027). (see *Appendix A for further details*)

D-dimer level to predict DVT Location:

Even on multinomial logistic regression analysis which was adjusted for age, gender, and surgery using D-dimer as continuous variable (Model 1), we found that there was not a significant improvement in the model with predictors compared to the model with only the intercept (H=4.43, $p=.619$). As seen in (Table 2), the unique contribution of D-dimer was not statistically significant, in other words, D-dimer does not significantly predict the location of DVT (H=.688, $p=.709$).

Table 2

Unique contributions of predictors in multinomial logistic regression predicting DVT location

As reported in (Table 3) under Model 1, D-dimer level does not significantly predict membership to the proximal group rather than the distal group (OR=1.03, 95%CI= [.91-1.2], p=.657), neither it predicts membership to the extensive group rather than the distal group (OR=1.05 , 95%CI =[.92-1.2], p=.502). As seen under Model 2 in (Table 3), we obtained similar results when D-dimer was categorized into 2 categories: above and below the median value (4.39 mg/L). When using D-dimer quartiles to create 4 groups (<=2.72, 272 to 4.39, 4.39 to 9.48 and >9.48) results did not provide any significant findings either. (See Appendix B for further details).

Table 3

Parameter estimates of multinomial logistic regression predicting DVT location

The correlation between D-dimer and High-Risk Group (defined as patients who developed PE on top of proximal or extensive DVT):

We risk-stratified the patients based on the risk of pulmonary embolism; into high risk group (those are the patients with proximal or extensive DVT who had symptomatic PE upon presentation or later during hospital stay) and low risk group (patients with DVT who did not develop PE) to try to find its association with D-dimer level. We found that higher level of D-dimer was associated with the high-risk group, according to a ROC curve analysis (Figure 1). The Area Under the Curve (AUC) suggested that D-dimer is a fair test to classify patients as high risk (according to our definition) (AUC=.700, 95%CI= [.583, .817]). The cutoff for D-dimer suggested to classify the patient as high risk is **4.75 mg/L** with a sensitivity of 66% and specificity of 63%. (See Appendix C to see more detail about the curve coordinates).

Figure legend (1): *The value of AUC is .700, which indicates that D-dimer is a fair test to classify patients as high-risk of PE*

The predictive value of D-dimer of PE:

A binary logistic regression model (adjusted for age, gender, surgery and DVT) to find the ability of the suggested cutoff level of D-dimer (4.75 mg/L) to predict PE in patients with proximal or extensive DVT showed that D-dimer is a significant predictor of PE. Results are reported in (Table 4). In particular, patients with proximal or extensive DVT who have a D-dimer level above 4.75 mg/L are at 8-folds increased risk of PE than patients with D-dimer less than 4.75mg/L [OR=7.9 (95% CI, 1.55 – 40.39); p=0.013].

Table 4.

Logistic regression for D-dimer's cut-off predicting PE, controlling for age, gender and DVT location.

Discussion

Most of our patients had proximal DVT and only (6%) were with distal DVT, that can be attributed to the fact that most of the asymptomatic DVT are distal DVT [13]. Patients with extensive DVT had higher D-dimer level than proximal group and distal group, but we could not establish a significant relationship between D-dimer level and location of DVT, or with the site of proximal DVT (popliteal, femoral, and iliac) with P value = 0.519 and 0.336, respectively.

In the contrary to our results, a pilot study [14], included 249 patients with suspected DVT, 50 of which had confirmed DVT, found that high D-dimer was significantly correlated with proximal DVT. They concluded that patients with D-dimer more than 1000 ng/ml are at increased risk of proximal DVT. Though we had a larger sample size (110 patients), the percentage of distal DVT (6%) was lower than their study (34%).

In our study, higher D-dimer level was associated with an increase in length of hospital stay ($p=0.015$), but there was no correlation between level of D-dimer and duration of symptoms (ranging from 1 day to 20 days).

Interestingly, we found that D-dimer level is higher in patients with PE compared to patients who did not develop PE ($P=0.027$). We further proved that when we classified the patients into high risk group (patients who developed PE on top of proximal or extensive DVT) and low risk group and we found that D-dimer is a fair test to risk stratify patients with proximal or extensive DVT into high risk of PE (according to ROC curve figure 1). We suggest 4.75 mg/l as a cut-off level above which patients with proximal or extensive DVT can be considered as high-risk for developing PE. This cut-off has a sensitivity of 66% and a specificity of 63%; implying that the probability to correctly identify patients with proximal or extensive DVT as high risk of PE when they have D-dimer above 4.75 mg/L is 66%.

In patients with PE; several studies have found a significant association between D-dimer level and the extend of PE. A prospective study concluded that higher levels of D-dimer was associated with a greater perfusion defect on patients with PE who are hemodynamically stable. They found that D-dimer more than 4000micr/l (4mg/L) was associated with perfusion defect > 50% [2]. another study found that high D-dimer was also significantly associated with the proximity of PE as main pulmonary arteries PE was associated with high D-dimer (9.2 mg/l) while lobar and segmental PE patients had D-dimer of 3.8 and 1.4 mg/l respectively [6].

We examined the predictive value of D-dimer for occurrence PE in patients with proximal or extensive DVT using the cut-off of 4.75mg/l. The logistic regression model shows that D-dimer is a significant predictor of PE, ($OR=7.9$, $p=0.013$). In particular, patients with proximal or extensive DVT is at 8-folds increased risk of PE than patients with D-dimer less than 4.75mg/l. To our knowledge, there is no other study examined the ability of D-dimer to predict PE in patients with DVT.

The prognostic value of D-dimer in patients with PE was also examined in two studies derived from the RIETER Registry of VTE. They have linked higher level of D-dimer with increased mortality in patients with acute symptomatic PE [7,8].

Grau E et al showed that PE patients with D-dimer more than 5000ng/ml are at 2.9-fold increased risk of overall mortality compared to patients with D-dimer less than 5000ng/ml [7].

The Second study assessed the association between D-dimer and 15-day mortality in patients with acute PE. Patients with higher D-dimer (4200 ng/ml) had a higher overall mortality rate 7% compared to 2.7% in patients with lesser D-dimer (<1050ng/ml) [8]. Both studies concluded that level of D-dimer is a strong, independent predictor of overall and PE-related mortality (at 15 days and 3-months) among patients with acute symptomatic PE. On the other hand; one retrospective study which involved 292 patients failed to show a similar significant association between high D-dimer and increased rate of in-hospital overall or PE-related mortality among patients with stable acute pulmonary embolism [15]. Though rate of mortality was 2.9% in patient with D-dimer > 5000 ng/ml compared to 0% with D-dimer <5000 ng/ml; it was not statistically significant (P value 0.06). This has been shown in one more study [16]. Though in one prospective study, that included 699 patients with VTE found that high D-dimer level (>8 mg/l) is associated with decreased overall survival; this finding was limited to the patients with malignancy (P <0.001) while this association was statistically nonsignificant (P<0.282) in patients without malignancy [17].

Limitation of the study:

Our study lacks the balance between the three groups of DVT, with distal DVT representing only 6.4% of the sample, that might have affected the variation in the sample and therefore the results. Moreover, the small percentage of PE patients (only 11%) may have influenced the statistical analysis. Large, prospective studies are needed to evaluate the use of D-dimer beyond its diagnostic value as a predictor for DVT location and incidence of PE in DVT patients.

Conclusion:

Though level of D-dimer is not significantly associated with the location of DVT, it is a significant predictor of PE in patients hospitalized with proximal or extensive DVT. Based on our results, this can be applied to the daily practice by being more careful with the patients with proximal or extensive DVT and D-dimer level above 4.75mg/l by admitting those patients into a monitored area and early administration of anticoagulation as they are at increased risk of developing pulmonary embolism. While those patients with D-dimer level less than 4.75 mg/l are at lower risk of developing PE during hospitalization and they are more suitable for early discharge to complete the treatment as outpatients.

Declarations

Ethics approval and consent to participate: The ethical approval of King Abdulaziz Specialist Hospital - Taif was obtained. Written informed consent was waived by the ethical committee.

Consent for publication: not applicable

Availability of data and materials: the datasets used and analyzed during this study are available from the corresponding author on reasonable request.

Competing interests: the authors declare that they have no conflict of interests

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Authors' contributions:

SA formulated the study concept and design and was a major contributor in data interpretation and writing the manuscript.

AA, TG, MA, AA, JM performed data collection from patients' medical records, double data entry, contributed to data analysis

MA contributed to the study design and revised the manuscript.

All authors read and approved the final manuscript

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References

- 1- Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. *Arch Intern Med.* 1998;158(6):585-93.
- 2- Al-Hameed FM, Al-Dorzi HM, Al-Momen AM, Algahtani FH, Al-Zahrani HA, Al-Saleh KA, et al. The Saudi Clinical Practice Guideline for the treatment of venous thromboembolism. Outpatient versus inpatient management. *Saudi Med J.* 2015;36(8):1004-10.
- 3- Horii Y, Yoshimura N, Hori Y, Takaki S, Takano T, Inagawa S, et al. Correlation between the site of pulmonary embolism and the extent of deep vein thrombosis: evaluation by computed tomography pulmonary angiography and computed tomography venography. *Jpn J Radiol.* 2011;29(3):171-6.
- 4- Adam SS, Key NS, Greenberg CS. D-dimer antigen: current concepts and future prospects. *Blood.* 2009;113(13):2878-87.
- 5- Bates SM, Jaeschke R, Stevens SM, Goodacre S, Wells PS, Stevenson MD, et al. Diagnosis of DVT: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012;141(2 Suppl):e351S-e418S.

- 6- Ghanima W, Abdelnoor M, Holmen LO, Nielssen BE, Ross S, Sandset PM. D-dimer level is associated with the extent of pulmonary embolism. *Thromb Res.* 2007;120(2):281-8.
- 7- Grau E, Tenías JM, Soto MJ, Gutierrez MR, Lecumberri R, Pérez JL, et al. D-dimer levels correlate with mortality in patients with acute pulmonary embolism: Findings from the RIETE registry. *Crit Care Med.* 2007;35(8):1937-41.
- 8- Lobo JL, Zorrilla V, Aizpuru F, Grau E, Jiménez D, Palareti G, et al. D-dimer levels and 15-day outcome in acute pulmonary embolism. Findings from the RIETE Registry. *J Thromb Haemost.* 2009;7(11):1795-801.
- 9- Galle C, Papazyan JP, Miron MJ, Slosman D, Bounameaux H, Perrier A. Prediction of pulmonary embolism extent by clinical findings, D-dimer level and deep vein thrombosis shown by ultrasound. *Thromb Haemost.* 2001;86(5):1156-60.
- 10- Righini M, Perrier A, De Moerloose P, Bounameaux H. D-Dimer for venous thromboembolism diagnosis: 20 years later. *J Thromb Haemost.* 2008;6(7):1059-71.
- 11- Michiels JJ, Gadisseur A, van der Planken M, Schroyens W, Berneman Z, De Maeseneer M, et al. Diagnosis of deep vein thrombosis: how many tests do we need? *Acta Chir Belg.* 2005;105(1):16-25.
- 12- Kumar R, Indrayan A. Receiver operating characteristic (ROC) curve for medical researchers. *Indian Pediatr.* 2011;48(4):277-87.
- 13- Yamashita Y, Shiomi H, Morimoto T, Yoneda T, Yamada C, Makiyama T, et al. Asymptomatic Lower Extremity Deep Vein Thrombosis - Clinical Characteristics, Management Strategies, and Long-Term Outcomes. *Circ J.* 2017;81(12):1936-44.
- 14- G Z. Correlation between Deep Vein Thrombosis Location and D-Dimer Values: A Pilot Study. *Journal of Vascular Medicine & Surgery.* 2014;2(2).
- 15- Stein PD, Janjua M, Matta F, Alrifai A, Jaweesh F, Chughtai HL. Prognostic value of D-dimer in stable patients with pulmonary embolism. *Clin Appl Thromb Hemost.* 2011;17(6):E183-5.
- 16- Bova C, Pesavento R, Marchiori A, Palla A, Enea I, Pengo V, et al. Risk stratification and outcomes in hemodynamically stable patients with acute pulmonary embolism: a prospective, multicentre, cohort study with three months of follow-up. *J Thromb Haemost.* 2009;7(6):938-44.
- 17- Paneesha S, Cheyne E, French K, Bacchu S, Borg A, Rose P. High D-dimer levels at presentation in patients with venous thromboembolism is a marker of adverse clinical outcomes. *Br J Haematol.* 2006;135(1):85-90.

Tables

Table 1.

Descriptive Characteristics of Study Sample (N=110)

Patient Characteristics	Mean \pm SD	n	%
Age	44.8 \pm 21.4		
Gender			
male		40	36.4
female		70	63.6
Malignancy			
No		106	98.1
Yes		2	1.9
Pregnancy			
No		101	91.8
Yes		9	8.2
Post-Operative			
No		82	75.9
Yes		26	24.1
Length of hospital stay (days)	6.65 \pm 4.11		
Duration of DVT symptoms (days)	4.44 \pm 4.25		
DVT location			
distal		7	6.4
proximal		72	65.5
extensive		31	28.2
Site of proximal DVT			
popliteal		19	26.4
femoral		38	52.8
iliac		15	20.8
Presence of pulmonary embolism			
No		97	89.0
Yes		12	11.0
D-dimer level	7.62 \pm 8.04 mg/L		

Table 2

Unique contributions of predictors in multinomial logistic regression predicting DVT location

Predictor	<i>Model 1</i>			<i>Model 2</i>		
	χ^2	df	p	χ^2	df	p
Age	1.60	2	.449	1.74	2	.419
Gender (male)	1.69	2	.430	2.22	2	.330
D-dimer level	.688	2	.709			
D-dimer's cut-off				1.87	2	.393

Model 1: multinomial logistic regression to predict DVT extension where D-dimer is included as continuous variable (named D-dimer level)

Model 2: same multinomial logistic regression model where D-dimer has been categorized into less or equal to 4.39 mg/dl or over 4.39 mg/dl (named D-dimer's cut-off)

χ^2 indicates the difference in -2 log-likelihoods between final model and the model when the predictor is removed; D-dimer's was dichotomized according to values below or above its median (=4.39).

Table 3

Parameter estimates of multinomial logistic regression predicting DVT location

Predictor	<i>Model 1</i>		<i>Model 2</i>	
	<i>OR</i>	<i>p</i>	<i>OR</i>	<i>p</i>
Proximal DVT location				
Age	.977	.210	.977	.201
Gender (female)	1.11	.903	.943	.944
D-dimer level	1.03	.657		
D-dimer (<= 4.39 mg/L)			.348	.245
Extensive DVT location				
Age	.981	.327	.982	.352
Gender (male)	2.01	.433	1.89	.478
D-dimer level	1.05	.502		
D-dimer (<= 4.39 mg/L)			.497	.460

Distal DVT is the reference group.

OR: odds ratio

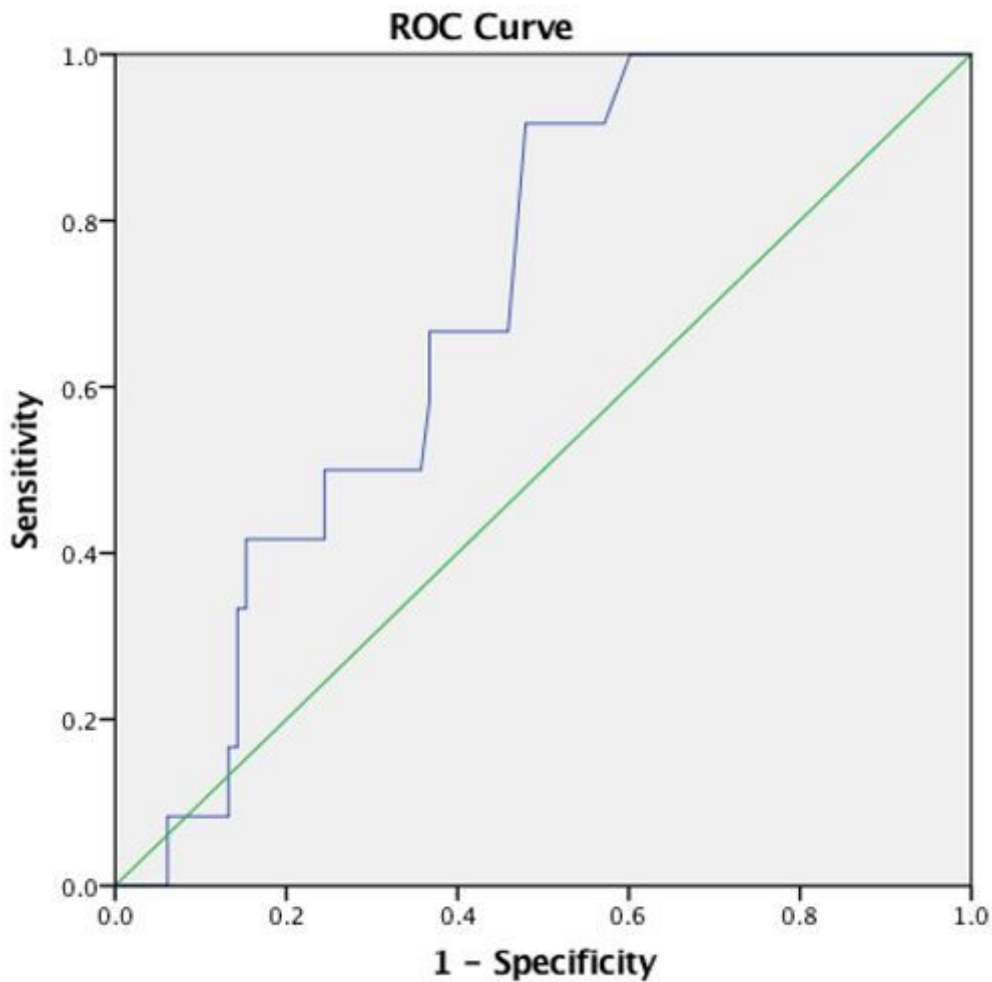
Table 4.

Logistic regression for D-dimer's cut-off predicting PE, controlling for age, gender and DVT location.

Predictor	OR	95% CI	Wald	p
Age	1.03	[.998 , 1.06]	3.25	.071
Gender (female)	.149	[.029 , .774]	5.13	.024
DVT location (proximal)	.237	[.058 , .961]	4.06	.044
D-dimer (> 4.75)	7.91	[1.55 , 40.39]	6.17	.013

Reference categories for gender is male, for DVT location is extensive and for D-dimer is below or equal to 4.75 mg/dl; analysis restricted to patients with proximal or extensive DVT.

Figures



Diagonal segments are produced by ties.

Figure 1

The value of AUC is .700, which indicates that D-dimer is a fair test to classify patients as high-risk of PE

Supplementary Files

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