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Original Research Article

Reducing ultrasound in diagnosing deep vein thrombosis by using clinical scores and D-dimer testing

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ABSTRACT

Background: To reduce unnecessary venous ultrasound examination in cases suspected to have deep venous thrombosis (DVT) in emergency department by using D dimer and wells score. venous duplex is widely used to diagnose DVT increasing burden on ultrasound in overcrowded emergency department. Authors can decrease this burden by using clinical probability scores and D dimer.
Methods: This is prospective study done on 50 consecutive patients suspected to have DVT represented to emergency department of Menoufia University Hospital during the period from June 2018 to June 2019. Full history, physical examination, assessment of clinical probability score, d dimer level and results of venous duplex collection.
Results: According to wells score, the majority of cases diagnosed as DVT were of high probability group 13(68.4%), 5 patients with moderate probability and only one patient with low probability was diagnosed as DVT. The mean of D dimer level in cases diagnosed as DVT is (4173.6±2173.1) and in cases without DVT is (927.4±1064.6). Using wells score and D dimer together, sensitivity is 100%, Specificity is 94%. PPV is 90%, and NPV is 100% in predicting DVT. All cases with negative d dimer and low risk probability do not have DVT.
Conclusions: Based on this result, using wells score and d dimer level in early work up of patients suspected to have DVT will decrease overusing and cost of venous duplex.

Keywords: Clinical probability, D-dimer, Deep venous thrombosis, Venous duplex, Wells score

INTRODUCTION

Because of complications of deep venous thrombosis (DVT) as pulmonary embolism and post-phlebitic syndrome, DVT is associated with increased morbidity and mortality.[1] Therefore, diagnosis of DVT accurately will decrease its complications and its mis-diagnosis will make patients at risk of bleeding because of anticoagulant used in treatment of DVT.[2]

Diagnosing patients suspected to have DVT is a difficult challenge as it has non- specific symptoms and signs.[3] Previously, the gold standard for diagnosis of DVT was venography but now it not preferred as it is expensive and invasive.

On the contrary, venous ultrasound is reliable, safe and non- invasive for detecting VTE so it became the corner stone tool in diagnosis of VTE.[4] Only 15%~28% of suspected cases with DVT have actually thrombosis with venous duplex examination.[5]

In addition, it costs money and needs a specialist to perform so anew strategy is needed for diagnosis of DVT. A newer approach for diagnosis includes a combination of D-dimer level and clinical probability score (wells score) can decrease unnecessary ultrasound examination for cases suspected to have DVT.[6]

The aim of this current study is to reduce unnecessary venous ultrasound examination as a diagnostic tool in

cases suspected to have DVT in emergency department by using D-dimer and wells clinical probability score.

METHODS

This is prospective comparative study. Fifty consecutive patients suspected to have DVT represented to emergency department of Menoufia University Hospital during the period from June 2018 to June 2019 and referred to radiologist to confirm presence or absence of DVT.

Data from cases were collected in pre-organized data sheet by the researcher. Data collected from cases included demographic data as age, sex and body mass index (BMI). Data regarding past medical history, risk factors for DVT, and clinical examination of all cases were collected.

Classification of cases according to clinical probability score (wells score) into low, moderate, and high risk for DVT. Blood sample for d-dimer level for all suspected cases. Diagnosis by venous duplex whether cases have DVT (proximal or isolated distal DVT) or absence of DVT.

Data were collected, tabulated, statistically analyzed using a personal computer with Statistical Package of Social Science (SPSS) version 20, where the following statistics were applied. Two types of statistics were done: Descriptive statistics as number, percentage, mean and standard deviation (SD).

Analytic statistics included Chi-squared test ($\chi 2$), Fischer exact test, Student t-test, Mann-whiteny test, Kruskal Waills test. ROC curve (is graph called a Receiver Operating Characteristics curve it is a plot of the true positive rate against the false positive rate for different possible cut-off of diagnostic test or marker), sensitivity (also called the true positive rate) and specificity (also called the true negative rate). P value >0.05 to be statistically insignificant, p value ≤0.05 to be statistically significant, and p value ≤0.001 to be highly statistically significant.

RESULTS

The study was conducted on 50 patients, males represented 26 (52%), females represented 24 (48%), the mean age was (45±7.4), and the mean BMI was (28.6±3.8) as shown in table 1. Most of patients have no past history medical history representing about 20 (40%) of cases, 9 (18%) of cases had DM, 9 (18%) had HTN, 5 (10%) had CHF, 2 (4%) had COPD, 1 (2%) had Behcet disease, and 4(8%) had active cancer. Only 19 (38%) of cases have DVT while the remaining 31 (62%) have no DVT.

Regarding risk factors as shown in table 2 active cancer, immobilization, and recently bedridden for ≥3 days, or major surgery within the previous 12 weeks requiring general or regional anesthesia were statistically significant in relation to DVT. Oral contraception pills, hormonal replacement therapy, family history of disease, and previously documented deep vein thrombosis were statistically non-significant in relation to DVT.

Table 1: Demographic data, medical history among studied patients, and presence or absence of DVT by duplex in studied patients (n=50).

	Variables	No (%)
Sex	Male	26 (52)
	Female	24 (48)
Age in years	Mean ±SD	45±7.4
	Range	26-75
	Median	44
BMI	Mean ±SD	28.6±3.8
	Range	22-38
	Median	28.5
History medical disease	No	20 (40)
	DM	9 (18)
	HTN	9 (18)
	Caner	4 (8)
	CHF	5(10)
	Bechet	1 (2)
	CPOD	2 (4)
Final diagnosis by duplex ultrasound	DVT	19 (38)
	No DVT	31 (62)

Clinical probability Wells score in DVT group was low risk in one case, moderate risk in 5 cases, and high risk in 13 cases. There is highly significant relation between increased wells score and DVT.

The mean level of D-dimer was (4173.6±2173.1) in DVT group and was (927.4±1064.6) in non DVT group. There was significant relation between DVT and increased d dimer level. Regarding clinical picture as shown in table 3 redness, hotness, and leg pain showed significant relation with non DVT group.

Localized tenderness along the distribution of the deep venous system and entire leg swelling showed significant relation with DVT.

Calf swelling at least 3 cm larger than that on the asymptomatic side and pitting edema confined to the symptomatic leg showed non-significant relation with DVT.

Regarding sensitivity, specificity and accuracy of D-dimer for predictor of DVT as shown in table 4, this study shows that at cutoff point (≥575) sensitivity is 94.9%, Specificity is 58.2%. PPV is 58%, NPV is 95% in predicting DVT. Area under ROC for D-dimer is 0.92.

Table 2: Comparison between patients with DVT and patients without DVT regarding risk factors, wells score and D-dimer level (n=50).

Variables		DVT (n=19)		Not DVT (n=31		Test of sig.	P value
		No	%	No	%		
Active cancer	Yes	4	21.1	0	0	FXT=8.3	0.01 S
	No	21.1	78.9	31	100		
Immobilization	Yes	6	31.6	2	6.5	FXT=5.5	0.04 S
	No	13	68.4	29	93.5		
Recently bedridden for ≥ 3 days, or major surgery within the previous 12 weeks requiring general or regional anesthesia	Yes	7	36.8	4	12.9	FXT=3.9	0.05 S
	No	12	63.2	27	87.1		
Oral contraception pills	Yes	3	15.7	2	6.4	FXT=1.11	0.32 NS
	No	16	84.3	29	93.6		
Hormonal replacement therapy	Yes	0	0	1	3.2	FXT=0.62	0.62 NS
	No	19	100	30	96.8		
Family history of disease	Yes	1	5.3	1	3.2	FXT=0.12	0.72 NS
	No	18	94.7	30	96.8		
Previously documented deep vein thrombosis	Yes	12	63.2	14	45.2	χ^2=1.52	0.25 Ns
	No	7	36.8	17	54.8		
Wells score	Low	1	5.3	22	71	FXT=26.2	0.00** (<0.001) HS
	Moderate	5	26.3	7	22.6		
	High	13	68.4	2	6.5		
D-dimer	Mean±SD	4173.6±2173.1		927.4±1064.6		U=4.9	0.00** (<0.001) HS

FXT=Fisher's Exact test, χ^2=chi-saqure, U= Mann- whiteny test, NS=Non-significant, HS=High significant.

Table 3: Comparison between patients with DVT and patients without DVT regarding clinical presentation (n=50).

Variables		DVT No=19		Not DVT No=31		Test of sig.	P value
		No	%	No	%		
Redness and hotness	Yes	0	0	9	29	FXT=6.7	0.008 S
	No	19	100	22	71		
Leg pain	Yes	1	5.3	19	61.3	χ^2=15.4	0.00** (<0.001) HS
	No	18	94.7	12	38.7		
Localized tenderness along the distribution of the deep venous system	Yes	12	36.2	0	0	FXT=25.7	0.00** (<0.001) HS
	No	7	36.8	31	100		
Entire leg swelling	Yes	13	68.4	6	19.4	χ^2=12.07	0.001 S
	No	6	31.6	25	80.6		
Calf swelling at least 3 cm larger than that on the asymptomatic side	Yes	4	21.1	13	41.9	χ^2=2.2	0.13 NS
	No	15	78.9	18	58.1		
Pitting edema confined to the symptomatic leg	Yes	12	63.2	14	45.2	χ^2=1.52	0.25 Ns
	No	7	36.8	17	54.8		

Table 4: Sensitivity, specificity and accuracy of D-dimer for prediction of DVT.

	AUC	P	Cut off	Sensitivity	Specificity	PPV	NPP	95% CI
D-dimer	0.92	<0.001	≥575	94.9%	58.2%	58%	95%	0.84-0.99

Table 5: Sensitivity, specificity and accuracy of total wells score for prediction of DVT.

	AUC	P	Cut off	Sensitivity	Specificity	PPV	NPP	95% CI
Wells score	0.93	<0.001	≥1.5	94.7%	77.4%	72%	96%	0.86-0.99

Regarding sensitivity, specificity and accuracy of total wells score as predictor of DVT as shown in table 5, this study shows that at cutoff point (≥1.5) sensitivity is 94.7%, Specificity is 77.4%. PPV is 72%, NPV is 96% in predicting DVT. Area under ROC for wells score is 0.93.

Using wells score and d dimer together as shown in table 6, sensitivity is 100%, Specificity is 94%. PPV is 90%, and NPV is 100% in predicting DVT.

Table 6: Validity of combined D-dimer and wells score for diagnosis of DVT.

	D-dimer and wells score
Sensitivity	100%
Specificity	94%
NPV	100%
PPV	90%

DISCUSSION

This study included 50 consecutive patients suspected to have DVT represented to emergency department of Menoufia University Hospital. 19 of them were diagnosed to have DVT and the remaining 31 cases did not have DVT. Regarding socio-demographic data and past medical history of all studied cases as shown in Table 1 males represented 26 (52%), females represented 24 (48%), the mean age was (45±7.4), and the mean BMI was (28.6±3.8). Regarding risk factors for DVT as shown in Table 2, this study shows that active cancer was observed in 4 (8%) cases, immobilization was observed in 5 (10%), recently bedridden for ≥ 3 days, or major surgery within the previous 12 weeks requiring general or regional anesthesia was observed in 11 (22%), previously documented deep vein thrombosis was observed in 2(4%) of cases, oral contraception pills in 5(10%), hormonal replacement therapy in 1 (2%), and family history of DVT 2 (4%).

This study shows (as shown in Table 2) that, immobilization, active cancer, and recently bedridden for ≥3 days, or major surgery within the previous 12 weeks requiring general or regional anesthesia, showed significant relation with DVT. This can be explained by increased venous stasis and probability of DVT.

This goes in accordance with results of Diana et al in retrospective sub study as it also showed significant relation between immobilization, and recently bedridden cases with DVT.[7] Rolf et al disagrees with these results regarding relation between being bed ridden and DVT as the relation was nonsignificant.[8] In this study, other risk factors (as shown in Table 2) as OCP, HRT, previous history of DVT, and family history of DVT showed nonsignificant relation with DVT. The study reported by Rolf et al agrees with these results regarding risk factors as OCP, HRT, and previous DVT as it showed nonsignificant relation between them and DVT.[8]

Patients were subdivided into 3 groups using wells score Low, moderate and high probability (as shown in table 2). Low probability represented 23 (46%), moderate probability represented 12 (24%), and high probability represented 15 (30%) of patients.

The majority of cases diagnosed as DVT were of high probability group (as shown in table 5) 13(68.4%), 5 patients with moderate probability and only one patient with low probability was diagnosed as DVT. Michelangelo S et al agrees with these results.[9]

Regarding d dimer, this study shows that the mean of d dimer level in cases diagnosed as DVT is (4173.6±2173.1) and in cases without DVT is (927.4±1064.6) (as shown in Table 2). There is highly significant relation between presence of DVT and high levels of d dimer that is agreed by results of Michelangelo et al.[9] Regarding clinical picture (as shown in Table 3), localized tenderness along the distribution of the deep venous system was observed in 12 (24%) of cases, entire leg swelling was observed in 19 (38%), calf swelling at least 3 cm larger than that on the asymptomatic side was observed in 17 (34%), pitting edema confined to the symptomatic leg in 26 (52%) of cases, redness and hotness and tenderness in 9 (18%) of cases, and leg pain in 20(40%) of cases.

These results show that there is significant relation between localized tenderness along the distribution of the deep venous system, entire leg swelling and DVT. Also showed non-significant relation between calf swelling, pitting edema confined to the symptomatic leg and DVT.

These results show also significant relation between hotness, redness, and leg pain with non DVT group. This goes in accordance with results of Diana G et al in retrospective Sub study regarding localized tenderness along the distribution of the deep venous system, entire leg swelling as both showed significant relation with DVT and also significant relation between hotness, redness, and leg pain with non DVT group.[7] Diana G et al disagrees with these results regarding calf swelling and pitting edema as both were significantly related to DVT.[7] A study by Rolf P et al disagrees with these results regarding relation between entire leg swelling, calf swelling and DVT as non-significant relation between entire leg swelling and DVT was found and significant relation between calf swelling and DVT was found.[8]

However, Rolf P et al agrees with these results regarding localized tenderness along the distribution of the deep venous system which was significantly related to DVT and pitting edema which was non-significantly related to DVT.[8] Reducing the unnecessary venous ultrasound use in cases with suspected DVT is the corner stone of this study using wells clinical probability score and d dimer in emergency department.

Regarding sensitivity, specificity and accuracy of D-dimer for predictor of DVT as shown in table 4, this study shows that at cutoff point (≥575) sensitivity is 94.9%, Specificity is 58.2%. PPV is 58%, NPV is 95% in predicting DVT. Area under ROC for D-Dimer is 0.92. A study by Blair A et al used cutoff point (≥500) and results were near to this study as sensitivity is 98.0%, Specificity is 55.4%, and NPV was 99.8%.[10] However, PPV was 11.4%. Another study by Der et al used cutoff point (≥500) and results were near to this study as sensitivity is 95.8%, Specificity is 57.4%, and NPV was 99.4%.[11] Another study by Mahmut et al used cutoff point (≥500) and results were near to this study as sensitivity is 95.2%, Specificity is 55.3%, NPV was 96.2%, and PPV was 48.7.[12] Regarding sensitivity, specificity and accuracy of total wells score as predictor of DVT as shown in table 5, this study shows that at cutoff point (≥1.5) sensitivity is 94.7%, specificity is 77.4%.

PPV is 72%, NPV is 96% in predicting DVT. Area under ROC for wells score is 0.93. The study reported by Shrey M et al used 2 different cutoff points one cutoff point at 1 and other cutoff point at 2.[13] At cutoff point (1) sensitivity is 100%, Specificity is 36%. PPV is 9%, NPV is 100% in predicting DVT. At cutoff point (2), sensitivity was 67%, Specificity was 90%. PPV was 31%, NPV was 98% in predicting DVT. Another study by D Gatot and A Mardia used different cutoff point for wells score (≥3) at which both sensitivity and Specificity was 80.6% in predicting DVT.[14] This difference can be explained by small sized sample and different characters in each sample.

Using wells score and d dimer together as shown in table 6, sensitivity is 100%, Specificity is 94%. PPV is 90%, and NPV is 100% in predicting DVT. Great improvement of sensitivity, specificity, PPV and NPP in predicting and excluding DVT with combination of both d dimer and wells score.

CONCLUSION

Based on this result, using wells score and d dimer level in early work up of patients suspected to have DVT will decrease cost and overusing of venous duplex. Using wells score and d dimer together resulted in sensitivity of 100%, Specificity of 94%. PPV of 90%, and NPV of 100% in predicting DVT. Great improvement of sensitivity, specificity, PPV and NPP in predicting and excluding DVT. In this study, all cases with low risk using wells score and negative d dimer don does not have DVT. Using this in emergency medicine will reduce unnecessary ultrasound examination decreasing the burden on emergency department.

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