

Role of D-Dimer Assay in Early Detection of Suspected Deep Vein Thrombosis in Obese Individuals

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Abstract

Background: Role of D-dimer assay in suspected high risk obese patients has not been explored much. Therefore, purpose of this study is to ascertain the place of D-dimer assay in diagnosis of Deep vein thrombosis (DVT) in obese patients. **Methods:** Patients attending outdoor or admitted in surgery ward of hospital, presenting with history and examination suggestive of DVT, at high risk of developing DVT and having Body Mass Index >25 kg/m² were included. D-dimer assay and ultrasonography (USG) was done at the time of admission, ultrasound was repeated at one week (if the first examination was negative for DVT) and at one month. Out of total 70 suspected cases, D-dimer levels were compared in relation to cases which were finally diagnosed as DVT by USG and those in whom DVT was excluded. Sensitivity, specificity, positive predictive value, and negative predictive value for the D-dimer test were calculated. **Results:** 70 suspected cases of DVT (32 males & 38 females) were included with mean age of 55.59±13.59 y and with mean BMI of 27.7±1.7. No statistical difference between vital parameters of diagnosed and excluded cases of DVT was found. The sensitivity and specificity of D dimer were found to be 100.0% & 35.5% respectively. Positive predictive value was 46.29% and Negative predictive value was 100.0%. **Conclusions** The sensitivity and negative predictive value of semiquantitative latex D-dimer assay for deep venous thrombosis are high. Deep vein thrombosis in obese individuals can be ruled out on the basis of D-dimer assay.

Keywords: D-Dimer; Deep Vein Thrombosis; Obesity; Ultrasonography; D-dimer in obesity.

Introduction

Deep venous thrombosis (DVT) is a potential cause of in hospital mortality. If DVT is not managed soon it can lead to pulmonary embolism (PE), a deadly sequel of DVT. Studies showed that higher BMI and obesity tend to increase the chances of DVT and its complications [1].

A meta analysis study has shown that chances of first spontaneous venous thromboembolism among obese people is more than twice that of individual with normal BMI [2]. Clinicians have to diagnose and treat obese patient of PE. Moreover, imaging limitations are being faced by clinicians in the diagnosis of DVT [3].

Early diagnosis and anticoagulant therapy can be a life saver in Patients of DVT. Accurate diagnosis of deep vein thrombosis reduces, to a great extent the risk of thromboembolic complications. Venography has been looked up to as the core diagnostic tool for deep venous thrombosis but it has lot of disadvantages as being expensive and time-consuming procedure with limited availability. Venography has been replaced by compression ultrasonography (CUS) in many hospitals which has a sensitivity and negative predictive value of 95% and 98% respectively for proximal DVT [4]. This also has some disadvantage as it needs to be repeated within one week in order to detect any progression from a distal DVT to the proximal system, increasing the cost of diagnostic evaluation and decreasing the efficiency of this procedure. Only about 25% of suspected cases of DVT actually have thrombosis [5,6]. Therefore there is utter need for other procedures

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to diagnose a case of DVT. In this scenario the role of D- dimer in evaluation of DVT patients with obesity can be looked upon with much hope.

D – dimer is a fibrin degradation product. D-dimer concentration can indirectly indicate whether a thrombus is formed or not. In this aspect there is use of monoclonal antibodies specific for D-dimer fragment.

Monoclonal antibodies can help to differentiate fibrin-specific clot from non-cross-linked fibrin and from fibrinogen. Some studies suggest that a normal D-dimer concentration can be used to exclude thromboembolic processes [7]. On the other hand in case of abnormal D-dimer concentrations other methods of diagnostic significance should be done.

Keeping in mind the increasing burden of obesity in general population, commensurate attention is required to form effective strategies to prevent and diagnose VTE in this group of patients. Therefore the purpose of this study is to ascertain the role of D-dimer assay in the diagnosis of Deep vein thrombosis in obese patients.

Material and Methods

Selection of Patients

One hundred twenty six patients of either sex in the age group of 25 to 75 years, attending outdoor or admitted in surgery ward of associated hospital presenting with history and examination suggestive of deep vein thrombosis and at high risk of developing DVT were initially considered for the study. Out of the above, 70 patients were finally selected according to the stated inclusion criteria, rest were excluded. A Written, informed consent was taken from all patients. This study was approved by the research ethics committee of the institute.

Inclusion Criteria

- Patients presenting with history and examination suggestive of deep vein thrombosis, such as calf pain, swelling in leg, redness in leg, dilation of surface vein, calf tenderness, pain on dorsiflexion of foot, pain on squeezing of calf
- Chronic tobacco user
- Prolonged immobilization
- Prolong surgery
- Obese individuals as indicated by BMI > 25 (kg/m²)

Exclusion Criteria

Patients with the following condition

- Critically ill
- Trauma
- Hemorrhage
- Sepsis
- Receiving anti-coagulant therapy
- BMI < 25 (kg/m²)

Methods

In all patients demographic details & history were noted followed by clinical examination including BMI estimation by an expert and investigations which included colour Doppler ultrasonography of the symptomatic leg and D-dimer assay (Table 1). Colour Doppler ultrasonography was done using real-time B-mode with compression, with a 7.5-MHz or a 5.0-MHz transducer. Two areas of the leg were examined: the common femoral vein at the inguinal ligament and the popliteal vein at the knee-joint line traced down to the point of the trifurcation of the calf veins. Veins were scanned in the transverse plane only. Lack of compressibility was the sole criterion for an abnormal result; A vein was considered fully compressible if no residual lumen was seen. D-dimer assay was done by Latex agglutination slide test which is a semiquantitative assay. D dimer value $\geq 0.5 \mu\text{g/ml}$ was considered positive.

Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences, version 16.0. Descriptive statistical analysis [mean \pm standard deviation (SD)] was performed for continuous variables. For D-dimer assay, out of the total 70 suspected cases of DVT, D-dimer levels were compared in relation to cases which were finally diagnosed as DVT by USG and those in whom DVT were excluded. Sensitivity, specificity, positive predictive value, and negative predictive value for the D-dimer test were calculated

Result

Study group comprised of a total of 70 suspected cases of DVT (32 males & 38 females). Mean age was 55.59 ± 13.59 y and mean BMI was 27.7 ± 1.7 . Baseline vital parameters were compared in DVT positive patients and DVT excluded cases (Table 2). Number

of cases positive for D-dimer and Colour Doppler USG at the time of admission and at one month follow up is presented (Figure 1) and final number of diagnosed

cases out of all suspected cases is shown (Table 3). Final table shows utility of D- dimer assay in diagnosing cases of DVT (Table 4).

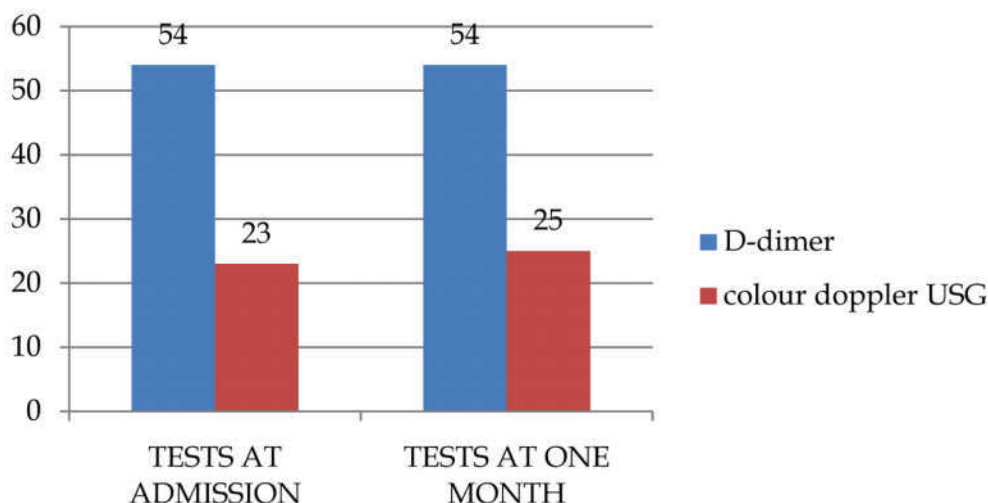


Fig. 1: Comparison of D- dimer at the time of admission and USG at the time of admission and at one month follow up (N=70)

Table 1: Study protocol

Selection of Patient	Based on Inclusion Criteria
At the time of admission	D dimer assay Colour Doppler Ultrasonography
At one week	Colour Doppler Ultrasonography if the first examination was negative for DVT. If the ultrasonography was positive for DVT, then patient was treated with anticoagulants.
At one month	Colour Doppler Ultrasonography

Table 2: Vital parameters in diagnosed and excluded cases of DVT (N=70)

Parameters	DVT Diagnosed (total cases 25) Mean \pm SD	DVT Excluded (total cases 45) Mean \pm SD	P value
Pulse (beats/min)	80.1 \pm 10.7	78.4 \pm 12.6	P = 0.5708
Systolic blood pressure (mm Hg)	134.2 \pm 18.6	132.8 \pm 16.4	P = 0.7488
Diastolic blood pressure (mm Hg)	78.2 \pm 12.2	76.4 \pm 10.6	P = 0.5381
Respiratory rate/min	17.2 \pm 3.2	16.6 \pm 2.8	P = 0.4173

Table 3: Total no. of patients diagnosed as DVT by USG (N=70)

D dimer + ve	54
Diagnosed as DVT(by USG)	25
Excluded or not having DVT	45

Table 4: Performance of D-dimer in suspected cases of DVT

	Percentage	95% CI
Sensitivity	100.0	83.41-100.0
Specificity	35.5	22.28-51.57
Positive predictive value	46.29	32.84-60.27
Negative predictive value	100.0	75.92-100

Discussion

This study was done to ascertain the role of D-dimer assay in diagnosing the cases of Deep vein thrombosis in obese individuals.

It appears that D-dimer has an important place in deciding which cases of suspected deep-vein thrombosis according to history and clinical examination should be subjected to colour Doppler ultrasound rather than subjecting all patients to ultrasound.

D-dimer assessment tends to decrease the disadvantages imposed by ultrasound as this can be done conveniently and is rapid. A negative D-dimer test can rule out the diagnosis of deep-vein thrombosis, obviating any further investigations.

Previous work in this area shows that the brighter aspect of D-dimer assay is the high negative predictive value in patients suspected of deep-vein thrombosis, which is the same as we have observed. Also, D- dimer should be used as an initial tool for excluding DVT [8,9]. P S Wells et al in 2003 in their study "Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis" have shown that D-dimer assay has high negative predictive value [10].

Others have reported high sensitivity of D dimer for the diagnosis of DVT and a high specificity at a pre-specified cutoff of 0.5 µg/ml [11,12]. SM Bates et al have reported an overall sensitivity of 96%, a negative predictive value of 98%, a specificity of 45% and positive predictive value of 29% [13]. Wee-Shian Chan et al in 2008 have also found high sensitivity and high negative predictive value [14]. Whereas some are of opinion that ultrasonography and clinical assessment are only of true value [15-18].

When we compared the vital parameters of diagnosed and excluded cases of DVT there comes out to be no difference among the two. It has also been shown in another study stating that majority of patients remain asymptomatic [19].

There is a review article on how difficult it is to diagnose pulmonary embolism in the obese patient [20]. In our study, we have focused on this high risk category that is obesity in adults and elderly. Some previous work has been done in children and other high risk patients such as pregnant females [14,21].

Thus so far, the good thing about D-dimer comes out to be its ability to exclude the cases not having deep vein thrombosis and this tends to lower the necessity of performing ultrasound in all patients.

Conclusion

The sensitivity and negative predictive value of semiquantative latex D-dimer assay for deep venous thrombosis are high. Deep vein thrombosis in obese individuals can be ruled out on the basis of D-dimer assay.

References

1. Klovaite J, Benn M, Nordestgaard BG. Obesity as a causal risk factor for deep venous thrombosis: a Mendelian randomization study. *J Intern Med.* 2015 May;277(5):573-84.
2. Genyan Yang, Christine De Staercke, and W. Craig Hooper. The effects of obesity on venous thromboembolism: A review. *Open J Prev Med.* 2012 November; 2(4):499-509. doi:10.4236/ojpm.2012.24069.
3. Uppot RN, Sahani DV, Hahn PF, Kalra MK, Saini SS, Mueller PR. Effect of obesity on image quality: fifteen-year longitudinal study for evaluation of dictated radiology reports. *Radiology* 2006;240:435-439.
4. Kraaijenhagen RA, Lensing AW, Wallis JW, van Beek EJ, ten Cate JW, Büller HR. Diagnostic management of venous thromboembolism. *Baillieres Clin Haematol.* 1998;11:541-86.
5. Cogo A, Lensing AW, Koopman MM, Piovella F, Siragusa S, Wells PS et al. Compression ultrasonography for diagnostic management of patients with clinically suspected deep vein thrombosis: prospective cohort study. *BMJ.* 1998;316:17-20.
6. Birdwell BG, Raskob GE, Whitsett TL, Durica SS, Comp PC, George JN et al. The clinical validity of normal compression ultrasonography in outpatients suspected of having deep venous thrombosis. *Ann Intern Med.* 1998;128:1-7.
7. Tapson VF. Acute pulmonary embolism. *N Engl J Med.* Mar 6 2008;358(10):1037-52.
8. Perrier A, Desmarais S, Miron MJ, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet* 1999;353:190-5.
9. Kraaijenhagen RA, Piovella F, Bernardi E, et al. Simplification of the diagnostic management of suspected deep vein thrombosis. *Arch Intern Med* 2002;162:907-11.
10. Wells PS, Anderson DR, Rodger M, et al. "Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis". *N. Engl. J. Med.* 2003;349(13): 1227-35.
11. S. Goodacre, F.C. Sampson, A.J. Sutton, S. Mason, F. Morris, "Variation in the diagnostic performance of D-dimer for suspected deep vein thrombosis." *Oxford Journals, Medicine, QJM: An International Journal of Medicine* 2005;98(7):513-527.

12. Dempfle CE, Korte W, Schwab M, Zerback R, Huisman MV; CARDIM study group "Sensitivity and specificity of a quantitative point of care D-dimer assay using heparinized whole blood, in patients with clinically suspected deep vein thrombosis." *Thromb Haemost*. 2006 Jul;96(1):79-83.
 13. Bates SM, Grand'Maison A, Johnston M, Naguit I, Kovacs MJ, Ginsberg JS. A latex D-dimer reliably excludes venous thromboembolism. *Arch Intern Med* 2001;161:447-53.
 14. Chan, Wee-Shian; Chunilal, Sanjeev; Lee, Agnes; Crowther, Mark; Ginsberg, Jeffrey S. "A Red Blood Cell Agglutination d-Dimer Test to Exclude Deep Venous Thrombosis in Pregnancy." *Obstetrical & Gynecological Survey*: January 2008;63(1):1-2
 15. Lennox AF, Delis KT, Serunkuma S, Zarka ZA, Daskalopoulou SE, Nicolaidis AN. Combination of a clinical risk assessment score and rapid whole blood D dimer testing in the diagnosis of deep vein thrombosis in symptomatic patients. *J Vasc Surg* 1999;30:794-803.
 16. Janes S, Ashford N. Use of a simplified clinical scoring system and D-dimer testing can reduce the requirement for radiology in the exclusion of deep vein thrombosis by over 20%. *Br J Haematol* 2001; 112:1079-82. [Erratum, *Br J Haematol* 2001;114:738.].
 17. Aguilar C, Martinez A, Martinez A, Del Rio C, Vazquez M, Rodriguez FJ. Diagnostic value of d-dimer in patients with a moderate pretest probability of deep venous thrombosis. *Br J Haematol* 2002;118:275-7.
 18. Anderson DR, Wells PS, Stiell I, et al. Management of patients with suspected deep vein thrombosis in the emergency department: combining use of a clinical diagnosis model with D-dimer testing. *J Emerg Med* 2000;19:225-30.
 19. Hiroshi Matsuo. Evaluation of D-Dimer in Screening Deep Vein Thrombosis in Hospitalized Japanese Patients with Acute Medical Diseases/Episodes. *Ann Vasc Dis* 2016;9(3):193-200.
 20. Philip C Hawley, Miles P Hawley. Difficulties in diagnosing pulmonary embolism in the obese patient: A literature review *Vascular Medicine* 2011; 16(6):444-451.
 21. Kanis J, Hall CL, Pike J, et al Diagnostic accuracy of the D-dimer in children *Archives of Disease in Childhood* Published Online First: 08 November 2017. doi: 10.1136/archdischild-2017-313315.
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