

# D-Dimer as an Applicable Test for Detection of Posttraumatic Deep Vein Thrombosis in Lower Limb Fracture

Hooman Bakhshi, MD, Mostafa Alavi-Moghaddam, MD, Karin C. Wu, BS, Mohammad Imami, MD, and Mohammad Banasiri, MD

## Abstract

Measuring the plasma levels of D-dimer is an accurate and easy modality to detect deep vein thrombosis (DVT) in nontraumatic settings. However, the diagnostic reliability of D-dimer assays in detecting posttraumatic DVT among patients with lower limb fracture undergoing orthopedic surgery is not validated.

In this study, 141 patients with lower limb fracture admitted through the emergency department and undergoing orthopedic surgery were enrolled. Postoperative venous blood samples for D-dimer assay were taken on the 1st, 7th, and 28th postoperative days. Color Doppler sonography examination of both lower limbs was performed at the same time as a standard test.

Eight out of the 141 patients (6%) had acute DVT based on Color Doppler sonography. Mean D-dimer was 2160 ng/mL in DVT positive patients and 864 in DVT negative patients. D-dimer levels greater than 1000 ng/mL were 100% sensitive and 71% specific for detecting postoperative DVT.

D-dimer assay is a useful and sensitive test for detecting posttraumatic DVT.

**V**enous thromboembolism is the major cause of morbidity and mortality in posttraumatic patients who have undergone orthopedic surgery. Although the condition is often asymptomatic, fatal pulmonary embolism is the first clinical manifestation of posttraumatic deep vein thrombosis

(DVT) of the lower limb in many patients.<sup>1</sup> Posttraumatic DVT is also associated with clinical morbidity in the form of the postthrombotic syndrome.<sup>2,3</sup> There are multiple diagnostic modalities currently available for detecting DVT. Compared with other tests, D-dimer assay is relatively easy to perform, has high sensitivity and low negative predictive value.<sup>4</sup> In recent years, studies have evaluated the role of D-dimer assay in diagnosing DVT among posttraumatic patients.<sup>5-6</sup>

D-dimers are released as a result of fibrinolysis, and thus, serve as a circulating marker of the presence of endovascular thrombus. A raise in D-dimer is also seen in other instances such as postsurgery, major trauma, inflammatory arthritis, cancer, and infection.

There are 5 different methods to measure D-dimer: enzyme-linked immunosorbent assay (ELISA), latex agglutination assay, whole blood assay, turbidimetric assay, and immunofiltration assay. Of these, turbidimetric assay is a rapid and quantitative test.<sup>7-10</sup> All of these assays have been validated in nontraumatic patients, but to our knowledge, their sensitivity and reliability to detect DVT among posttraumatic patients have yet to be validated.<sup>11-14</sup>

The present study evaluated the diagnostic reliability of D-dimer using the turbidimetric assay to detect posttraumatic DVT in patients with lower limb fracture undergoing orthopedic surgery.

## METHODS

This study was performed at the orthopedic surgery department of Imam Hossein Teaching Hospital (Tehran, Iran) between January 2008 and June 2008. Of a total of 1401 patients, 141 patients who were admitted through the emergency department and underwent general anesthesia/surgery (ie, open reduction and internal fixation) with lower limb fracture, without prior history of thromboembolic event, or any known DVT risk factors based on Well's criteria were enrolled in the study. All patients received similar prophylactic anticoagulant and analgesic agents.

Postoperative venous blood samples were analyzed for plasma D-dimer levels at the 1st, 7th, and 28th postoperative days and Color Doppler sonography (CDS) examination of both lower limbs was performed at the same time as a standard test. Patients were also evaluated clinically for signs of DVT in the immediate postoperative period and

Dr. Bakhshi is Assistant Professor, Department of Orthopaedic Surgery, and Dr. Alavi-Moghaddam is Associate Professor, Department of Emergency Medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Ms. Wu is Medical Student, Keck School of Medicine, University of Southern California, Los Angeles, California. Dr. Imami and Dr. Banasiri are Assistant Professors, Department of Orthopaedic Surgery, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences.

Address correspondence to: Mostafa Alavi-Moghaddam, MD, Associate Professor, Emergency Medicine Department, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran (fax +982177556970; e-mail, mosalavi@yahoo.com).

*Am J Orthop.* 2012;41(6):E78-E80. Copyright Quadrant HealthCom Inc. 2012. All rights reserved.

**Table. Sensitivity and Specificity of D-dimer to Detect DVT Cut Off Points.**

Plasma D-dimer (ng/ml)	Sensitivity (95% CI)	Specificity (95% CI)
2000	100 (67-100)	34 (26-42)
3000	88 (53-98)	98 (94-99)
4000	63 (31-86)	98 (94-99)

1 month after discharge. In order to minimize bias, all qualified radiologists and laboratory technologists interpreting the results of CDS and D-dimer assays were unaware of the patient's clinical presentation or the results of other objective tests. D-dimer assay was performed using semiquantitative latex monoclonal antibody-based immunoassay (Immuno turbidometry) and levels less than 500 ng/mL were considered negative. Finally, all data were entered in to an Excel database and analyzed using SPSS statistical software version 16 (SPSS Inc., Chicago, Illinois).<sup>16</sup>

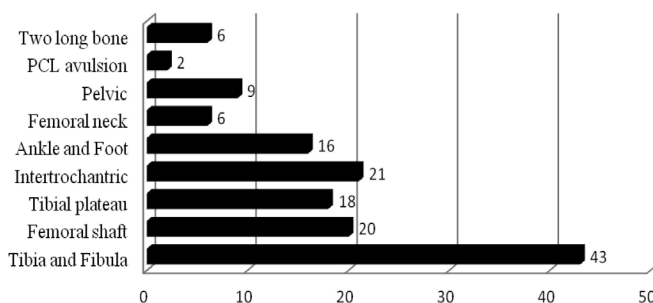
## RESULTS

One hundred forty one patients with mean age of  $37.7 \pm 18.5$  years (range, 14 to 80 years) were enrolled; 85% were male. The Figure shows the type of lower limb fracture in the study patients population. Based on CDS results, 8 patients (6%; 6 female) were found to have DVT, 7 of them at day 7 and 1 at day 28 (4 patients with tibiofibular fracture, 2 tibial plateau, 1 femoral neck, and 1 femoral shaft). D-dimer test was positive in all of these patients. Mean D-dimer values were 2160 ng/mL in DVT-positive and 864 ng/mL in DVT-negative patients. The Table shows the sensitivity and specificity of D-dimer in different plasma level cut off points. Comparing the results of CDS and D-dimer in DVT positive patients, the sensitivity, specificity, and accuracy of D-dimer greater than 1000 ng/mL was 100%, 71.4%, and 92.5%, respectively.

## DISCUSSION

In this study, we evaluated the accuracy of D-dimer assay in detecting DVT in posttraumatic patients. In line with other studies, the sensitivity, specificity, and positive and negative predictive value of D-dimer greater than 1000 ng/mL in our study to detect DVT among posttraumatic patients were as high as 100%, 71.4%, 2.5%, and 100%, respectively.<sup>15,16</sup>

The high sensitivity and specificity of CDS in detecting DVT of the lower extremity allows early diagnosis and subsequent treatment of the condition.<sup>17,18</sup> However, this technique is operator dependant and sonographer's skill can affect the result of this diagnostic modality in detecting DVT. Further, a single lower-extremity CDS for detection of DVT in patients with no symptoms may not be very successful.<sup>13</sup> Thus, we



**Figure.** Type of lower limb fractures observed in the study population.

used repeated CDS as gold standard test for detection of DVT to prevent spectrum bias in our study.

Previous studies have suggested that a normal (<500 mg/L) D-dimer concentration, measured by turbidimetric<sup>19</sup> or ELISA techniques<sup>20</sup> in a patient with a low-risk pre-test probability, has less than a 1% post-test probability of DVT. Therefore, we considered this value as the cut-off to define normal D-dimer in our study.

It is important to note that the normal level of D-dimer in posttraumatic patients has not been determined. In fact, postoperative elevation of D-dimer for 48 hours may be a normal event as increased levels of D-dimers are seen in critically injured patients.<sup>21,22</sup> Hauchand and colleagues<sup>23</sup> have previously shown that the concentrations of D-dimer rise to 1800 ng/mL immediately postoperatively, and to 480 ng/mL 7 days after the operation. Therefore, we repeated our D-dimer measurements in our patients to further validate the findings of our study.

In a study conducted by Levy and colleagues,<sup>24</sup> 2 cut-off values were significant for the detection of DVT among posttraumatic patients, with levels less than 2500 ng/mL having a negative predictive value of 100% in detecting DVT, values greater than 2500 ng/mL needed further evaluation. However, in the present study, we found that plasma D-dimer levels higher than 1000 ng/mL at day 7 had sensitivity of 100% in detecting DVT. Our results showed that the measurement of D-dimer using the turbidometry assay is an applicable preliminary test to detect DVT in posttraumatic patients. This method has an acceptable accuracy and it is easy to apply, making it an ideal option for screening posttraumatic patients with clinical suspicion of having DVT. The efficacy of negative D-dimer test in ruling out DVT among posttraumatic patients merits further studies.

## CONCLUSION

D-dimer assay is a useful and sensitive test to detect posttraumatic DVT in patients with lower limb fracture undergoing orthopedic surgery. However, interpretation of negative D-dimer test to rule out DVT among these patients should be evaluated in the future studies.

## AUTHORS' DISCLOSURE STATEMENT AND ACKNOWLEDGEMENTS

The authors report no actual or potential conflict of interest in relation to this article. The contribution of Dr. Mehdi Yaseri at varying phases of the project is acknowledged and greatly appreciated.

## REFERENCES

1. Anand SS, Wells PS, Hunt D, Brill-Edwards P, Cook D, Ginsberg JS. Does this patient have deep vein thrombosis? [published correction appears in JAMA. 1998;280(4):328. *JAMA*. 279(20):1614]. *JAMA*. 1998;279(14):1094-1099.
2. Agnelli G. Prevention of venous thromboembolism in surgical patients. *Circulation*. 2004; 110(24 Suppl 1): IV4-12.
3. Prandoni P, Lensing AW, Cogo A, et al. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med*. 1996;125(1):1-7.
4. Perrier A, Desmarais S, Miron MJ, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet*. 1999;353(9148):190-195.
5. Agarwala S, Bhagwat AS, Modhe J. Deep vein thrombosis in Indian patients undergoing major lower limb surgery. *Indian J Surg*. 2003;65(2):159-162.
6. Johna S, Cemaj S, O'Callaghan T, Catalano R. Effect of tissue injury on D-Dimer levels: a prospective study in trauma patients. *Med Sci Monit*. 2002;8(1):CR5-8.
7. Schutgens RJ, Esseboom EU, Haas FJ, Nieuwenhuis HK, Blesma DH. Usefulness of a semiquantitative D-dimer test for the exclusion of deep venous thrombosis in outpatients. *Am J Med*. 2002;112(8):617-621.
8. Gosselin RC, Owings JT, Utter GH, Jacoby RC, Larkin EC. A new method for measuring D-dimer using immunoturbidometry: a study of 255 patients with suspected pulmonary embolism and deep vein thrombosis. *Blood Coagul Fibrinolysis*. 2000; 11(8):715-721.
9. Knecht MF, Heinrich F. Clinical evaluation of an immunoturbidimetric D-dimer assay in the diagnostic procedure of deep vein thrombosis and pulmonary embolism. *Thromb Res*. 1997;88(5):413-417.
10. Brown MD, Rowe BH, Reeves MJ, Birmingham JM, Goldhaber SZ. The accuracy of the enzyme-linked immunosorbent assay D-dimer test in the diagnosis of pulmonary embolism: a meta-analysis. *Ann Emerg Med*. 2002;40(2):133-144.
11. Janssen MC, Heebels AE, de Metz M, et al. Reliability of five rapid D-dimer assays compared to ELISA in the exclusion of deep venous thrombosis. *Thromb Haemost*. 1997;77(2): 262-266.
12. Dale S, Gogstad GO, Brosstad F, et al. Comparison of three D-dimer assays for the diagnosis of DVT: ELISA, latex and an immunofiltration assay (NycoCard D-Dimer). *Thromb Haemost*. 1994;71(3):270-274.
13. American College of Emergency Physician (ACEP) Clinical Policies Committee; ACEP Clinical Policies Subcommittee on Suspected Lower-Extremity Deep Venous Thrombosis. Clinical policy: critical issues in the evaluation and management of adult patients presenting with suspected lower-extremity deep vein thrombosis. *Ann Emerg Med*. 2003;42(1):124-135.
14. Kearon C, Ginsberg JS, Douketis J, et al. Management of suspected deep venous thrombosis in outpatients by using clinical assessment and D-dimer testing. *Ann Intern Med*. 2001;135(2): 108-111.
15. Bucek RA, Quehenberger P, Feliks I, Handler S, Reiter M, Minar E. Results of new rapid d-dimer assay (cardiac-d-dimer) in the diagnosis of deep vein thrombosis. *Thromb Res*. 2001; 103(1):17-23.
16. 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(3):447-453.
17. Kearon C, Ginsberg JS, Hirsh J. The role of venous ultrasonography in the diagnosis of suspected deep venous thrombosis and pulmonary embolism. *Ann Intern Med*. 1998;129(12):1044-1049.
18. Goodacre S, Sampson F, Thomas S, van Beek E, Sutton A. Systematic review and meta-analysis of the diagnostic accuracy of ultrasonography for deep vein . *BMC Med Imaging*. 2005 Oct 3;5:6.
19. Duet M, Benelhadj S, Kedra W, et al. A new quantitative D-dimer assay appropriate in emergency: reliability of the assay for pulmonary embolism exclusion diagnosis. *Thromb Res*. 1998;91(1):1-5.
20. Legnani C, Pancani C, Palareti G, Guazzaloca G, Coccheri S. Contribution of a new, rapid, quantitative and automated method for D-dimer measurement to exclude deep vein thrombosis in symptomatic outpatients. *Blood Coagul Fibrinolysis*. 1999;10(2):69-74.
21. Kearon C, Julian JA, Newman TE, Ginsberg JS. Noninvasive diagnosis of deep venous thrombosis. McMaster Diagnostic Imaging Practice Guidelines Initiative. *Ann Intern Med*. 1998; 128(8):663-677.
22. Owings JT, Gosselin RC, Anderson JT, Battistella FD, Bagley M, Larkin EC. Practical utility of the D-dimer assay for excluding thromboembolism in severely injured trauma patients. *J Trauma*. 2001; 51(3):425-429.
23. Hauch O, Jørgensen LN, Kølbe TR, Wille-Jørgensen P, Nerstrøm H, Neerstrand HS. Plasma cross-linked fibrin degradation products fraction D in patients undergoing elective abdominal surgery. *Thromb Res*. 1988;51(4):385-389.
24. Levy G, Levy PY, Hessmann J, Monin P. Diagnosis of post-operative venous thrombosis using determination of plasma D-dimer [in French]. *J Mal Vasc*. 1998;23(4):269-267