

LETTER TO THE EDITORS

Evaluation of the diagnostic yield of D-dimer testing in suspected venous thromboembolism in primary care: a 2-year retrospective analysis

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Dear Sirs,

Venous thromboembolism is a common, sometimes fatal, disease.¹ It is important to recognise a possible case of pulmonary embolism (PE), since clinical manifestations vary from asymptomatic or mild unspecific features to sudden death. The diagnostic strategy to rule out the disorder by combining clinical assessment, laboratory studies, and imaging techniques has proven its use in multiple studies.²⁻⁶ The Achilles heel of this diagnostic work-up is the low specificity of D-dimer testing.⁷

Recently the first multi-centre prospective study was performed with a dichotomous decision rule for suspected deep venous thrombosis (DVT) in primary care.⁸ The patients referred had DVT in 25% and only 1.4% of D-dimer negative patients had thrombosis during follow up. The authors concluded that referral for suspected DVT could be reduced by 50%. These results are promising for reducing unnecessary medical investigations. Nevertheless, no study has yet been performed concerning PE. Furthermore, in clinical practice we felt that in many cases D-dimer testing is done early in the differential diagnosis and given the dichotomous decision rules, this often leads to referral.

Therefore we retrospectively analysed the charts of patients from whom D-dimer tests were requested by primary care physicians. The main purpose of this study was to evaluate the diagnostic yield of further investigation after abnormal D-dimer testing in primary care.

All patients with D-dimer measurements performed in the haematological laboratory of Maastricht University Medical Centre (MUMC+, in Maastricht the Netherlands) and requested by general practitioners (GPs) in the region of MUMC+ from January 1st 2007 to December 31st 2008 were collected. The D-dimer test used is a particle-enhanced immunoturbidimetric assay Innovance DDIMER (Siemens Medical Solutions) with cut off value 500 ng/ml, issued on an automated coagulation analyser Sysmex CA-7000. This test on this analyser has been validated.⁷

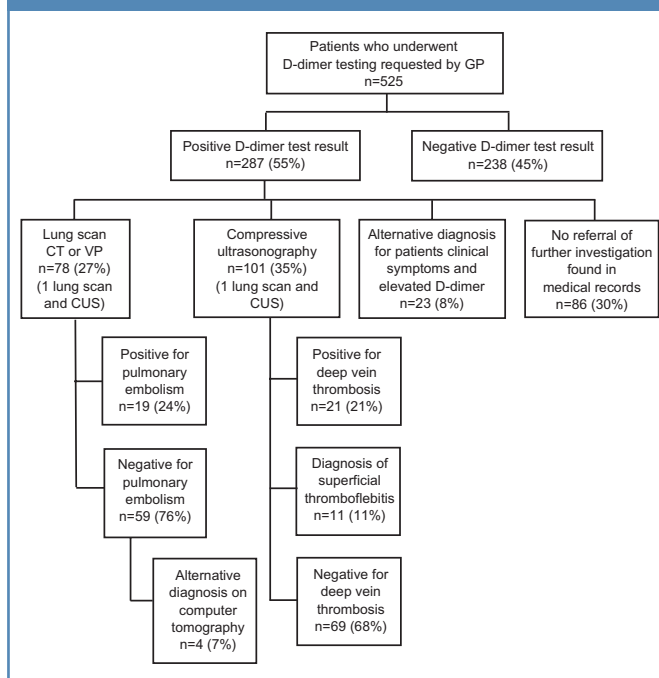
Retrospectively revising the hospital charts, we analysed how many patients with positive D-dimer levels subsequently underwent further investigation – computer tomography (CT) pulmonary angiography, ventilation-perfusion scintigraphy, and/or venous compression ultrasonography of the limb veins – and how often in percentage terms this resulted in a diagnosis.

A total of 525 patients with D-dimer tests were collected and 287 (55%) of the tests were positive. Of those, 78 (27%) patients underwent CT pulmonary angiography or ventilation perfusion scintigraphy, and 101 (35%) underwent compressive ultrasonography. We found that CT pulmonary angiography/ventilation perfusion scintigraphy for suspected pulmonary embolism and venous compression ultrasonography for suspected DVT in patients with positive GP-requested D-dimer tests gave a diagnostic yield of 24% and 21%, respectively (see Figure 1). In 23 cases (8%), no further investigation for venous thromboembolism was performed after referral because an alternative diagnosis could be established for the patient's clinical symptoms and elevated D-dimer levels (see Table 1).

In 4 of 58 (7%) patients in whom PE was excluded with CT angiography/ventilation perfusion scintigraphy, an alternative diagnosis could be established on the CT images.

We are aware of the fact that this study is a retrospective analysis with potential bias. Yet the diagnostic yield of the radiologic investigation that follows D-dimer testing is an

Figure 1. Flow chart with test results. CT, computer tomographic (pulmonary angiography); VP, ventilation perfusion scintigraphy; CUS, compression ultrasonography; PE, pulmonary embolism; DVT, deep venous thrombosis; GP, general practitioner.



important finding. Since this is a retrospective analysis it is not possible to explain the fact that in 86 patients (30%) with a positive D-dimer test no further test results could be found in the medical records. Possibly the general physician established an alternative diagnosis or perhaps patients were referred to other hospitals, but given the location of Maastricht surrounded by country borders and the fact that our hospital is exclusive in the region we consider this to be unlikely. Given the yield of CT pulmonary angiography and venous compression ultrasonography in patients referred by GPs in this study it is possible that in several cases further investigation was indicated while it was not performed.

In conclusion, therefore, we believe that D-dimer testing in primary care is a useful tool in suspected venous thromboembolism and that abnormal findings should lead to referral for additional testing. CT pulmonary angiography/ventilation perfusion scintigraphy and venous compression ultrasonography performed in our hospital in 2007 and 2008 in patients with abnormal D-dimer testing requested by GPs gave a diagnostic yield of 24% and 21%, respectively.

Conflict of interest declaration

No conflict of interest to declare.

Table 1. Alternative diagnoses established for patients symptoms and elevated D-dimer levels.

Pneumonia (4)
Upper respiratory tract infection (2)
Emphyema
Left heart failure (2)
Thoracic chest pain due to lung cancer (2)
Mediastinal tumor
Postoperative chest pain after thoracic surgery
Musculoskeletal pain (2)
Anemia in colitis ulcerosa
Anemia in occult gastro-intestinal blood loss
Pancreatitis
Erysipelas
Cellulitis
Thoracic vertebral collapse
Acute renal failure with metabolic acidosis
Exclusion of thromboembolic disease on clinical grounds after referral

References

1. Cohen AT, Agnelli G, Anderson FA, et al. VTE Impact Assessment Group in Europe (VITAE). Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. *Thromb Haemost* 2007;**98**(4):756-64.
2. Wells PS, Anderson DR, Rodger M, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. *Ann Intern Med* 2001;**135**(2):98-107.
3. van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. *JAMA* 2006;**295**(2):172-9.
4. Righini M, Le Gal G, Aujesky D, et al. Diagnosis of pulmonary embolism by multidetector CT alone or combined with venous ultrasonography of the leg: a randomised non-inferiority trial. *Lancet* 2008;**371**(9621):1343-52. [http://dx.doi.org/10.1016/S0140-6736\(08\)60594-2](http://dx.doi.org/10.1016/S0140-6736(08)60594-2)
5. Mos IC, Klok FA, Kroft LJ, de Roos A, Dekkers OM, Huisman MV. Safety of ruling out acute pulmonary embolism by normal CT pulmonary angiography in patients with an indication for CT: systematic review and meta-analysis. *J Thromb Haemost* 2009 Jun 22. [Epub ahead of print]
6. Klok FA, Kruisman E, Spaan J, et al. Comparison of the revised Geneva score with the Wells rule for assessing clinical probability of pulmonary embolism. *J Thromb Haemost* 2008;**6**(1):40-4. <http://dx.doi.org/10.1111/j.1538-7836.2007.02820.x>
7. de Moerloose P, Palareti G, Aguilar C, Legnani C, Reber G, Peetz D. A multicenter evaluation of a new quantitative highly sensitive D-dimer assay for exclusion of venous thromboembolism. *Thromb Haemost* 2008;**100**(3):505-12.
8. Buller HR, Ten Cate-Hoek AJ, Hoes AW, et al. Safely ruling out deep venous thrombosis in primary care. *Ann Intern Med* 2009;**150**(4):229-35.

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