

Editorial / Editöryal Yorum

Using the D-dimer test in infective endocarditis

D-dimer testinin enfektif endokarditte kullanımı

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D-dimer is used as a global indicator of coagulation activation and fibrinolysis in clinical practice.^[1] Three D-dimer assays, by using monoclonal antibodies, have been developed and are currently on the market. These are the enzyme-linked immunosorbent assay (ELISA), the whole-blood agglutination assay and the latex agglutination assay. Their sensitivity and specificity in venous thromboembolism are shown in Table 1.^[1] The gold standard method of D-dimer measurement is ELISA, which is a quantitative and highly sensitive method; however, it is time-consuming. The immunoturbidimetric latex agglutination assay is less sensitive than the ELISA, but more fully automated and rapid (in <15 mins).^[2] It has been difficult to standardize D-dimer testing and, at present, the results of each assay should be considered method-specific.^[3] Therefore, clinicians need to be aware of the variability in the D-dimer assay performance and the characteristics of their institution's test while making clinical decisions.^[2]

Levels of D-dimer are typically elevated in acute venous thromboembolism. However, elevated levels are also present in a wide variety of inflammatory and prothrombotic conditions (Table 2). In certain types of assays, false-positive results may also be seen with high levels of rheumatoid factor, lipemia, hyperbilirubinemia, and hemolysis.^[1,2] The higher baseline values of D-dimer in hospitalized patients may reflect any one of several underlying disease processes that initiate

intravascular fibrin formation but do not necessarily result in overt thrombosis. Because fibrin may be cross-linked before it gels, D-dimer antigen may be generated in the absence of overt thrombosis.^[4]

Abbreviations:

CRP	C-reactive protein
ELISA	Enzyme-linked immunosorbent assay
IE	Infective endocarditis
MPV	Mean platelet volume

Previous reports have stated that the levels of cytokines, interleukin-1, tumor necrosis factor, plasminogen activator inhibitor-1, β -thromboglobulin, and platelet factor 4, all of which play a role in the activation of inflammation and the coagulation cascade such as platelet aggregation, were significantly increased in patients with infective endocarditis (IE).^[5] Coagulation activation, enhanced platelet activity/damage, and impaired fibrinolysis, to some extent, were established in patients with IE.^[6] Activation of coagulation also occurs in severe infections and sepsis and may contribute to the development of thrombosis. Activation of the coagulation cascade is often promoted by inflammatory responses, resulting in elevated plasma D-dimer antigen levels.^[7]

A variety of complications, the majority of which usually result from the embolism of vegetations, occur in most patients with IE. Although risk prediction models, showing which patients have increased risk of embolism, have not evolved thus far, it has been demonstrated that age, large vegetation, C-reactive protein (CRP), and mean platelet volume (MPV) are

Table 1. The results of D-dimer assay methods in venous thromboembolism^[1]

	ELISAs ^a	ELFAs ^b	Latex agglutination			Whole-blood assay
			Immuno-turbidimetric	Semi-quantitative	Qualitative	
Deep vein thrombosis						
Sensitivity (%)	94	96	93	85	69	83
Specificity (%)	53	46	53	68	99	71
Pulmonary embolism						
Sensitivity (%)	95	97	95	88	75	87
Specificity (%)	50	43	50	66	99	69

a: ELISAs ¼ Enzyme-linked immunosorbent assays; data restricted to microplate assay format; b: ELFAs ¼ Enzyme-linked fluorescent assays.

predictors of embolism in IE.^[8,9] In the study conducted by Bakal et al.,^[10] D-dimer assays were also suggested in the prediction of embolism in patients with IE. D-dimer levels in the study were evaluated

using latex agglutination assays. That study showed increased plasma D-dimer levels in patients with IE who suffered from clinically significant systemic embolism. D-dimer levels of >425 ng/dl demonstrated a sensitivity of 77% and specificity of 62% for the prediction of clinical embolism.^[10]

Clinicians should be aware of the possibility of systemic embolism in IE patients with elevated D-dimer levels. However, it is necessary to keep in mind the variability and reliability of D-dimer assay methods before clinical decision-making. A comprehensive evaluation of patients, consisting of clinical risk assessment in combination with measurement of D-dimer level and other suggested risk parameters for embolism, such as CRP and MPV, should be performed in predicting emboli in IE. Further prospective, randomized studies are needed to recommend with certainty routine measurements of D-dimer level and to clearly confirm the clinical effectiveness of this assay in the prediction of embolism in IE patients.

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Table 2. Conditions associated with elevated D-dimer levels

• Venous thromboembolism (deep vein thrombosis and pulmonary embolism)
• Hemolysis
• Thrombolytic therapy
• Disseminated intravascular coagulation
• Myocardial infarction
• Atrial fibrillation
• Aortic dissection
• Aneurysm
• Peripheral arteriopathy
• Congestive cardiac failure
• Ischemic cardiomyopathy
• Surgery
• Trauma
• Burns
• Infection
• Pregnancy and the puerperium
• Cancer
• Stroke
• Connective tissue disorders
• Inflammatory bowel disease
• Advanced age
• Acute respiratory distress syndrome
• Liver or renal disease

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