



Case Report

Pragmatic classification of the causes of high D-dimer

Abstract

Venous thromboembolism (VTE) remains the most common preventable cause of in-hospital death and D-dimer (DD) is one of the essential diagnostic tools for it. Each risk factor for VTE can raise DD and they are numerous: 24 listed in 2008 European Guidelines. Acute coronary syndrome and stroke increase DD concentration, too. Thus, all three most important causes of cardiovascular death are capable of raising DD. Recent evidence suggests DD as a sensitive marker also for acute aortic dissection.

Many other processes may raise DD concentration: atrial fibrillation, congestive heart failure, disseminated intravascular coagulation, etc. The adequate DD interpretation is additionally important due to the frequent usage of the test (probably millions of times a year in the world). Simple and concise classification is much easier to remember and such one is suggested.

Venous thromboembolism (VTE) remains the most common preventable cause of in-hospital death [1]. Venous thromboembolism should be high on the list of priorities of medicine because of high number of patients diagnosed [2], which is getting even higher [3], much higher number of individuals suspected and evaluated for possible VTE, high number of persons on prophylaxis [4], high number of analyses needed for the diagnosis [5], high chances for misdiagnosis [6,7], high mortality rates if VTE remains undiagnosed or untreated [8], unacceptably high mortality even if treated [2], high recurrence rate and morbidity rate due to residual right ventricle dysfunction or postthrombotic syndrome [2,5], high workup and therapy costs, and so on.

Thus, VTE has been very important, and D-dimer (DD) is one of the essential diagnostic tools for VTE, widely and increasingly used [9,10]. In recent years, new clinical decision models based on patient characteristics and quantitative DD (dimerized plasmin fragment D) testing have become commonplace and have revolutionized the evaluation of suspected pulmonary thromboembolism. The first step in safely using the DD is to determine the patient's risk of pulmonary thromboembolism [11].

Table 1 Straightforward and necessarily simplified classification of high DD

Cause	Including (among others)
1. Bleedings [15-17]	
2. Thrombosis	
2a. VENOUS thrombosis (VTE) [5,13]	Predisposing factors: strong, moderate or weak [5]
2b. ARTERIAL thrombosis [18-21].	AMI, stroke, PAD, arterial thromboembolism
2c. MICROVASCULAR thrombosis [22] and [23]	DIC
2d. INTRAVASCULAR thrombosis due to foreign material [24-27]	Catheters, pace-makers, artificial valves
3. Aortic dissection [28-31]	
4. Cardiologic, renal and liver diseases [15,32-39]	Atrial fibrillation, LV aneurysm, heart failure, heart thrombus
5. False positives [40,41]	

AMI indicates acute myocardial infarction; PAD, peripheral arterial disease; DIC, disseminated intravascular coagulation; LV, left ventricle.

To interpret DD properly, physicians ought to know at least the main currently recognized causes of increased DD. Here we approach the problem: many processes may raise DD concentration, and usually up to 10 causes have been mentioned [12-14]. Elevation of DD may be caused by each risk factor for VTE and they are numerous: 24 listed in most recent guidelines [5]. Many colleagues perhaps think what one physician said: "Everything may increase DD." This point out that the list of factors capable of rising DD concentration is respectably long.

Of course, simple and concise classifications are much easier to remember, and we suggest one (Table 1).

Combination of causes may also exist. Indeed, this classification does not pretend to be complete, but it seems logical and practical enough to become useful in everyday work. It may be used as a "starting point"; suggestions for improvement are needed and welcome.

In addition to causes given in table, DD might reflect other environmental risk factors for thrombosis [42], including, for example, cigarette smoking [43] and intravenous drug use [44,45]. There are reports about raised DD in

chronic urticaria [46], but knowledge about it is more important to dermatologists than to emergency medicine physicians and cardiologists.

In addition to clinical usefulness of the DD, underlined in European Society of Cardiology 2008 Guidelines [5], the importance of adequate DD interpretation rises also with the frequency of the test applied (probably millions of times a year in the world). A great number of physicians evaluate patients with a few mostly nonspecific symptoms but in life-threatening situation (like many of VTE patients are). Physicians who experienced this pressure to manage such patients promptly and properly realize the importance of practical guidelines and classifications.

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doi:10.1016/j.ajem.2008.11.017

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