

Harshika Lekkala, Atul Laddu, and Jawed Fareed, Global Thrombosis Forum, Suwanee, GA, and Loyola University, Chicago, IL, U.S.A.

INTRODUCTION

D-dimer (DD, Figure 1) is a protein fragment in every person's blood. It is a soluble fibrin degradation product resulting from the fibrinolytic system's breakdown of thrombi. DD serves as a valuable marker of coagulation and fibrinolysis activation. Elevated DD levels may indicate an increased risk of blood clotting or a recent clot. A degradation product of cross-linked fibrin, which is the protein that forms the meshwork of a blood clot. Normal DD level is considered less than 0.50 µg/mL. DD has also been evaluated to determine the optimal duration of anticoagulation in VTE patients, to diagnose and monitor disseminated intravascular coagulation, and to aid in the identification of medical patients at high risk for VTE. The quantification of DD levels thus serves a vital role in guiding therapy.

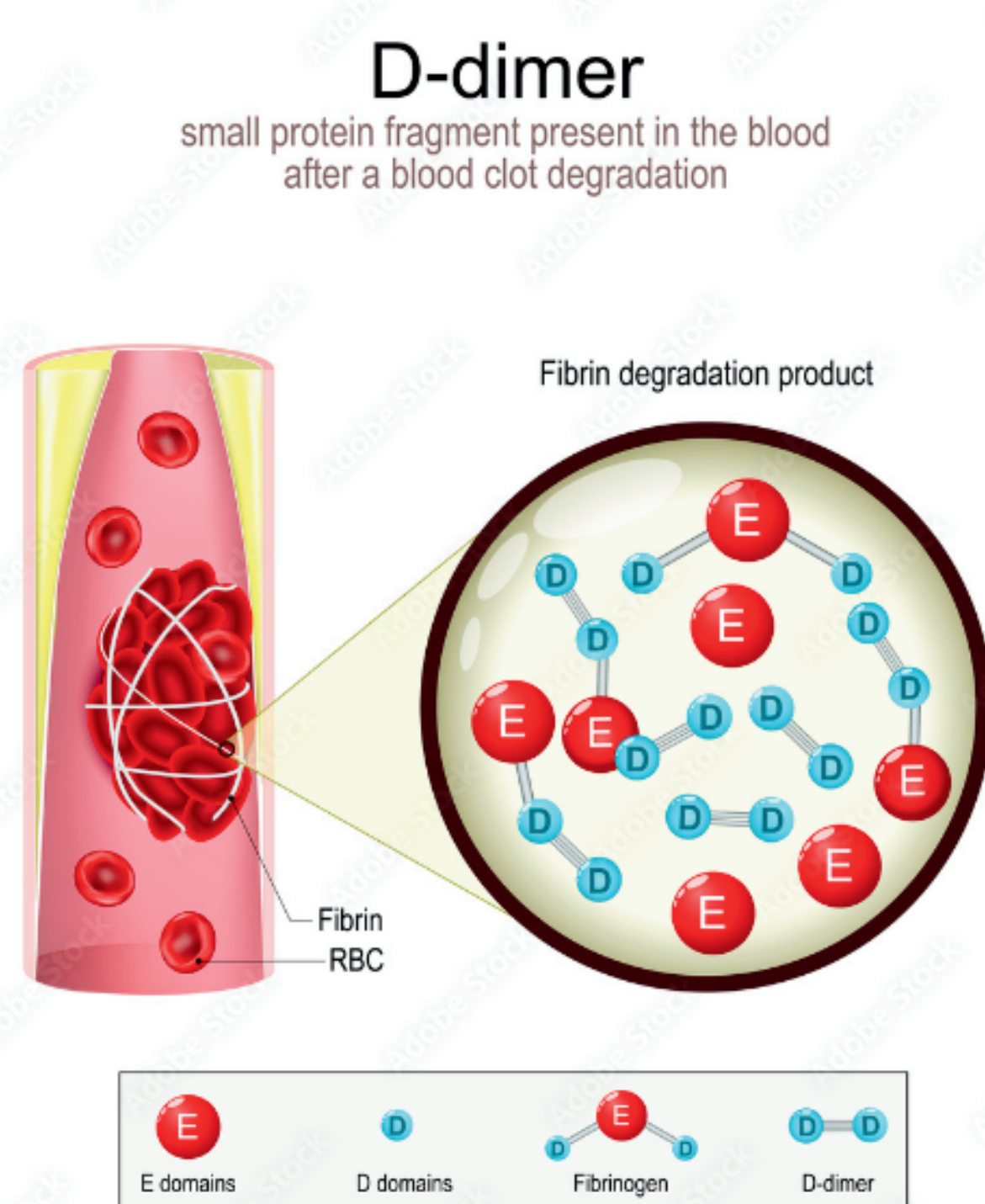


Figure 1: DD

The role of DD in patients with other conditions, such as predicting the risk of stroke in atrial fibrillation, identifying patients with coronary artery disease or human immunodeficiency virus (HIV) infection at risk for cardiovascular events, or for ruling out acute aortic dissection, is uncertain.

ELEVATION OF DD

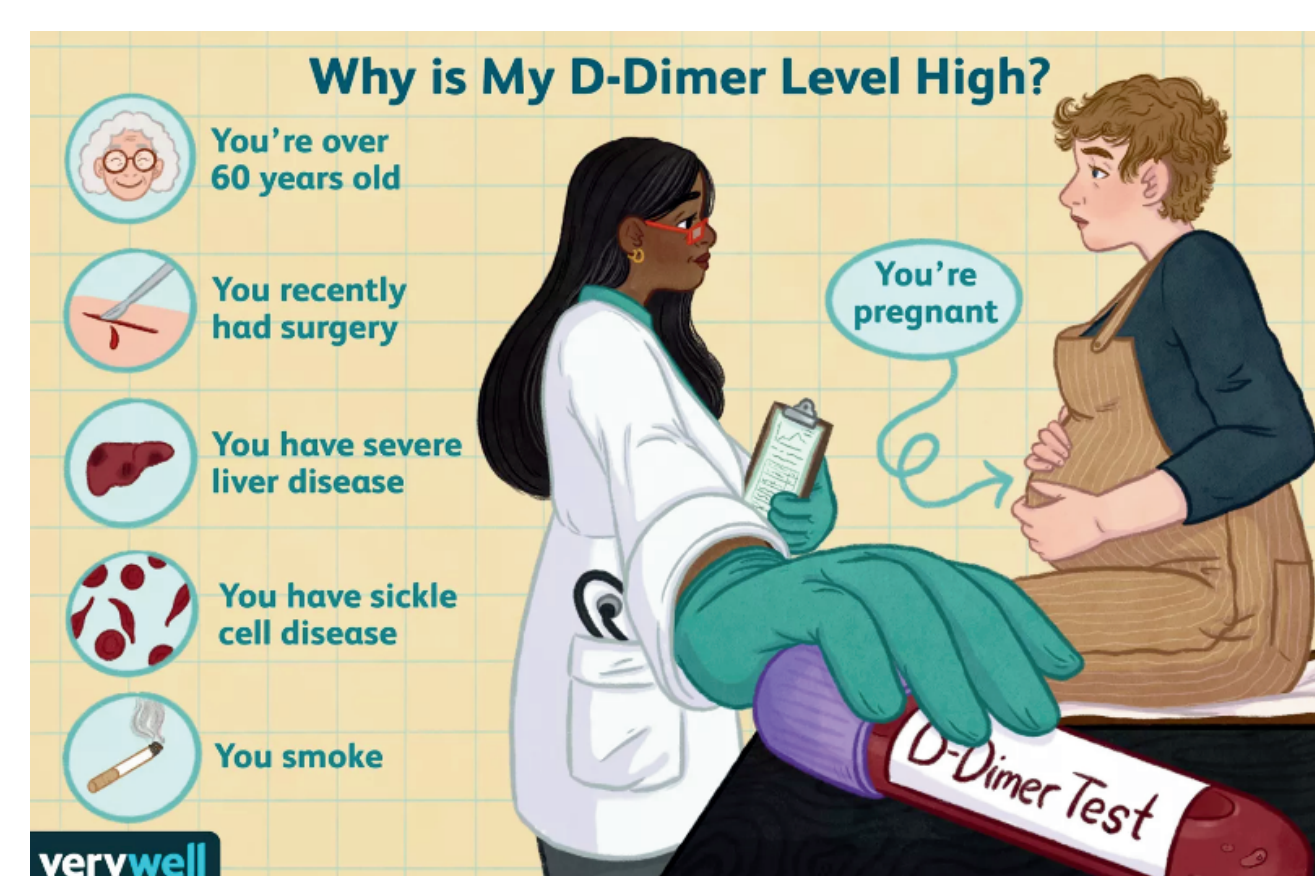


Figure 2: Why Is My DD Level High?

CAUSES OF ELEVATED DD

- PE
- DVT
- Stroke
- Pregnancy
- Recent surgery
- Infection
- Cancer
- Myocardial ischemia
- Ischemic stroke
- Disseminated Intravascular Coagulation
- Trauma
- Liver disease
- Inflammatory conditions

DIAGNOSTIC ASSAYS FOR DD

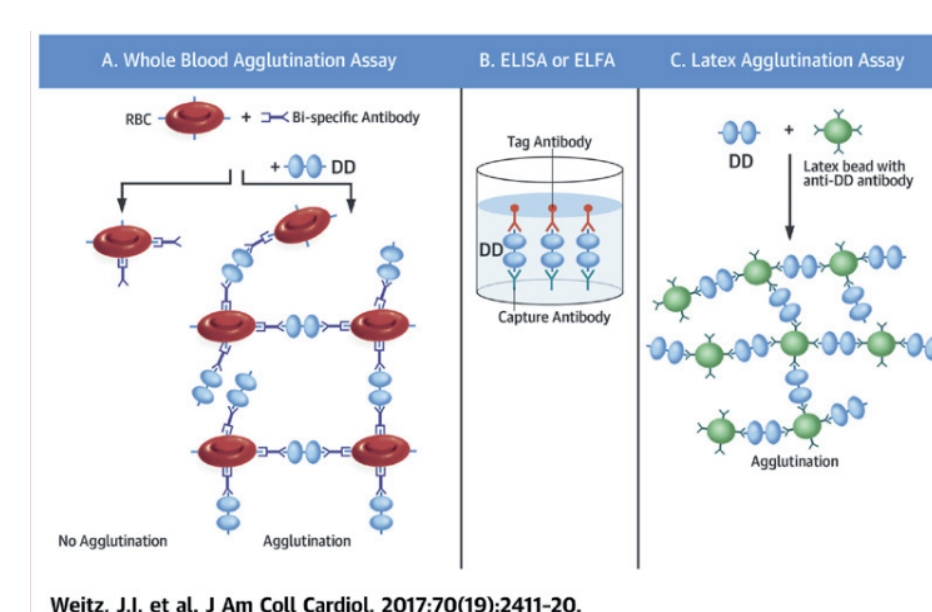


Figure 3: Assays for D-Dimer

QUESTION

Can DD be elevated without any evidence of DVT/PE?

Yes, DD can be elevated without evidence of DVT/PE.

OUR CASE

- An 85 years old male had mild pain on the right side of the chest, a slight cough, and a mild temperature.
- Upon ER admission, the DD was 3200.
- The patient may have either DVT/PE.
- The routine CT scan and angiogram indicated no blood clot and Venous Thromboembolism (VTE).

MEANING

- The DD is not a very specific test for VTE.
- If the DD is negative, one can reasonably conclude that the patient has no element of VTE.
- If the DD is elevated, further testing is needed to diagnose or exclude VTE.

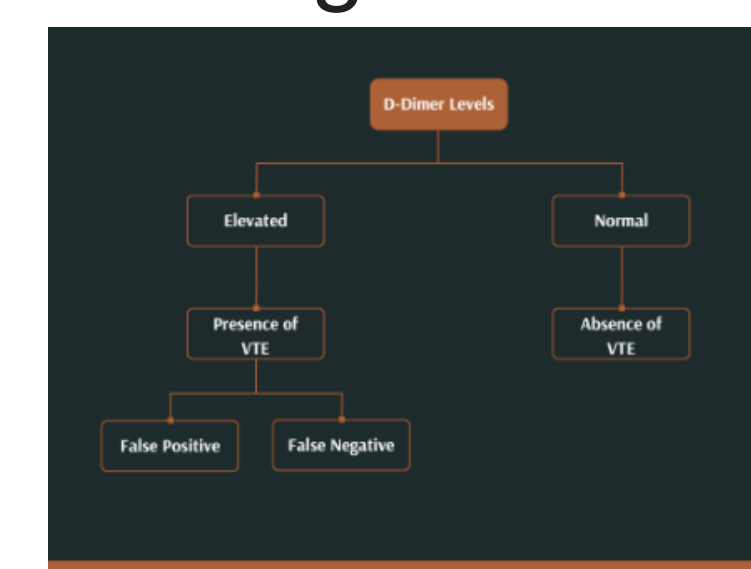


Figure 4

Understanding changes in DD levels

DD is a very valuable marker for patients with VTE. However, elevation of DD does not always mean the presence of VTE.

ORIGIN OF DD

DD is a plasmin-derived soluble degradation product of cross-linked fibrin. Generation of DD requires the sequential activity of thrombin, activated factor XIII (factor XIIIa), and plasmin. Thrombin converts soluble fibrinogen to fibrin monomers. Each fibrinogen molecule is a dimer composed of 3 pairs of polypeptide chains, α, β, and γ held together by disulfide bonds, with a central E domain linked by coiled-coil regions to 2 peripheral D domains. Thrombin cleaves peptides from the α- and β-chains to expose "knobs" in the E domains that insert into "holes" in the D domains, allowing fibrin monomers to polymerize in a half-staggered manner into double-stranded protofibrils, which associate into fibrils. Factor XIIIa, activated by thrombin, cross-links the D domains of adjacent fibrin monomers and the γ-chains of opposing monomers to form DD and γ-polymers. Plasminogen, activated by tissue plasminogen activator (tPA) on the fibrin surface, is converted to plasmin, which cleaves cross-linked fibrin between the D and E domains, generating the (DD)E complex DD noncovalently bound to fragment E. Further proteolysis releases fragment E, and DD circulates in plasma with an ~8-hour half-life before clearance. Because DD forms only from degraded cross-linked fibrin, it serves as a marker of coagulation and fibrinolytic activity.

CONCLUSION

DD helps detect abnormal blood clotting and is reliable for ruling out conditions like DVT and PE when results are negative. However, elevated levels are non-specific and can occur with many conditions such as stroke, pregnancy, recent surgery, infection, cancer, myocardial ischemia, trauma, liver disease, and inflammatory disorders. Further tests are needed to confirm a diagnosis. While DD itself can not be controlled, a healthy lifestyle may reduce the risk of clotting.