Commentary

Is coagulopathy a contraindication for thromboprophylaxis?

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In recent years, there is a heightened awareness of the risks of thrombosis in hospital patients. Considerable efforts in ensuring thromboprophylaxis for these inpatients have translated to significant reduction in thrombosis-related events in hospitals. In this regard, the National Institute of Clinical Excellence (NICE) has produced documents which guide physicians to prepare local protocols and implement these measures strictly.1 However, one of the caveats of these protocols, and indeed the NICE guidance, is the statement—‘thromboprophylaxis should be avoided in patients with an acquired bleeding disorder or coagulopathy’. Is this entirely true?

In this context, it is important to examine the term ‘coagulopathy’. Most physicians consider clinical situations like liver disease and sepsis with or without disseminated intravascular coagulation as common causes of acquired bleeding disorder or coagulopathy. There is also a common habit among junior physicians of calling patients who have abnormal coagulation screen to include prothrombin time (PT) and activated partial thromboplastin time (APTT) as having coagulopathy. Although the term ‘coagulopathy’ literally means pathology of the coagulation system, it is important to bear in mind that it does not always imply a bleeding tendency, but can also mean an increased clotting or thrombotic risk, which also is a pathology of the coagulation system. Indeed, both liver disease and disseminated intravascular coagulation are conditions with increased thromboembolic risk. Also, patients with abnormal clotting screens are not immune to thrombotic problems for reasons discussed below.

Patients with liver disease have been considered to be auto-anticoagulated, a myth which still exists in medical textbooks, despite evidence to the contrary. This myth probably arose from the fact that liver is the organ which synthesizes coagulation factors and as such, moderate to severe liver disease is a risk factor for bleeding from reduced coagulation factor production.2 Also, this reduced synthesis is reflected in the clotting screen, which is most often prolonged in patients with liver disease and is considered as a prognostic marker in Child-Pugh scoring system and the Model for End-Stage Liver disease score.2 However, what is often not understood is that liver disease patients also synthesize the endogenous anticoagulant factors. In physiological states, a balance exists between the procoagulant and the anticoagulant factors. In liver disease patients, this balance is maintained due to the simultaneous decrease in synthesis of both these components. This would mean that although the procoagulant factors are decreased, the anticoagulant factors are simultaneously decreased, and a balance exists which is similar to the normal individuals.3

So, why do the patients with liver impairment bleed? As often observed, the bleeding occurs from variceal sites, which may be compared to an open blood vessel which needs ‘closure’ by endoscopic methods rather than replacing clotting factors with fresh frozen plasma. The other contributory factors to bleeding in liver disease are associated renal failure with haemostatic problems known to occur with kidney injury and sepsis.3 Anaemia due to its effect of rheology can also contribute to the bleeding tendency of liver patients. In other words, the prolonged clotting screen is of no value in determining the liver disease patients who are at risk of bleeding. Most importantly, the coagulopathy of
liver disease does not protect these patients from venous thromboembolic disease. Recent reports confirm this fact by stressing the need for thromboprophylaxis in patients with liver function abnormalities despite the abnormal coagulation screen, unless the patient is actively bleeding.4

What about the other patients with abnormal clotting tests? In this context, it needs to be borne in mind that both the components of the clotting screen, the PT and APTT, were ‘created’ to identify patients with haemophilia or single coagulation factor deficiency and not bleeding risk in people who may need to undergo surgery or an interventional procedure.5 When we consider the intensive care patients who are the other major group of patients who is noted to have abnormal clotting screen, it is not often that they bleed like patients with haemophilia or coagulation factor deficiency, but from skin and mucosal surfaces. This bleeding pattern is not characteristic of coagulation factor deficiencies. So why do they have the abnormal laboratory result?

A decrease in individual clotting factor levels to less than the normal range is only necessary to prolong the clotting screen. However, studies performed in large number of patients with individual clotting factor deficiency have identified that in most cases, a factor level of 15–20% is only necessary for haemostatic purposes.6 However, the normal ranges for most of these clotting factors are in the order of 60% or more, the threshold below which the laboratory tests will start becoming abnormal. This would mean that a mild to moderate abnormality in a patient’s clotting screen just reflects the reduction in factor level to less than the normal range but certainly not less than the haemostatic level. Also, in patients who may have sepsis, or liver disease, multiple clotting factors tend to decrease to lower than normal range reflecting in much bigger prolongation of the screening tests.7 These individuals are unlikely to bleed from the reduction of these factors but could however bleed from other reasons including thrombocytopenia, platelet dysfunction, or vascular abnormalities. At the same time, the patients in the intensive care are highly prothrombotic for various reasons including their severely ill state, being immobile, sepsis itself being a prothrombotic state, the presence of central venous lines and many hyper-viscous drugs.8

So how should we change our practise? First of all, there is the question of when should clotting screens be ordered? There is definite evidence that it is not at all helpful in predicting bleeding before surgery or interventional procedures. It has already been discussed that these tests are not helpful in identifying bleeding risk in individuals without an inherited bleeding disorder. However, in a person with a strong personal or family bleeding history, it may be helpful as a screening test. Also in patients with massive bleeding, it may be useful to determine the need for clotting factor replacement. For the same reasons, in the cases of disseminated intravascular coagulation, unless there is active bleeding, it is not recommended to give coagulation factors in the form of fresh frozen plasma, despite abnormal clotting screens.9

What about thromboprophylaxis? This should be strongly encouraged in anyone who has additional risk factors for thrombosis despite abnormal clotting screens, if at all, they have been ordered. The coagulopathy which qualifies for exclusion in these circumstances should only be active bleeding. This would maximize the benefit in patients who are wrongly denied thromboprophylaxis from a poor understanding of the coagulation system.

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References