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EDITORIAL

The diagnosis of disseminated intravascular coagulation made easy

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Disseminated intravascular coagulation (DIC) is a complication of many disorders that are associated with a systemic inflammatory response and is increasingly appreciated as a pathogenetic pathway contributing to organ dysfunction, for example in sepsis, severe trauma or other conditions.[1-3] Any form of systemic inflammation will virtually always be associated with activation of coagulation, ranging from changes in molecular markers in coagulation factors with equivocal clinical significance to its most full-blown variant, known as disseminated intravascular coagulation (DIC).[4] Until recently, a diagnosis of DIC in routine clinical practice was hampered by the limited availability of reliable and simple tools with sufficient diagnostic accuracy. Indeed, no single clinical or laboratory test has an adequate sensitivity and specificity to confirm or reject a diagnosis of DIC. However, combinations of several readily available coagulation tests may be helpful to establish this diagnosis. Following a previously developed Japanese scheme, the subcommittee on DIC of the International Society of Haemostasis and Thrombosis has proposed a simple scoring algorithm using the platelet count, a prolongation of the prothrombin time, a decreased fibrinogen, and plasma levels of a fibrin-related marker, such as D-dimer or other fibrin degradation products.[5] Importantly, the score can only be used if the patient has been diagnosed with an underlying condition known to be associated with DIC. The various components of the scoring algorithm are assigned points and based on retrospective data a score of ≥5 is compatible with DIC. Prospective validation of this system in consecutive patients with a clinical suspicion of DIC confirmed a high sensitivity and specificity of this scoring system.[6-8] Moreover, application of the score in large databases of patients with severe sepsis has revealed that the DIC score is a strong and independent predictor of mortality and that the scoring system may select patients who will have a relatively large benefit from interventions in the coagulation/inflammatory cascades, such as the administration of recombinant human activated protein C.[9] Based on these observations, the DIC scoring system may be a helpful tool in clinical practice but also in the design and execution of trials aimed at improving the clinical management of patients with DIC and associated conditions.[10]

However, although the diagnosis of DIC is greatly facilitated by this scoring algorithm, some problems remain. One of these problems is well illustrated by the case report by Constantineacu *et al*. in this issue of the Netherlands Journal of Medicine.[11] The scoring system uses a 'fibrin-related marker', which in most institutions will be an assay for fibrin degradation products. Many routine laboratories are now employing D-dimer assays around the clock to enable the exclusion of venous thromboembolism (VTE) in low-risk patients and indeed the D-dimer assay has been found serviceable for the DIC score. However, we need to realise that there are a large number of different D-dimer assays, each with different sensitivities and specificities for various conditions.[12,13] In fact, the case by Constatinescu *et al*. clearly illustrates that the initially used D-dimer assay apparently had a much lower sensitivity for the diagnosis of DIC than the alternative, more commonly used assay. We need to learn from this observation that each different D-dimer assay needs to be validated before it can be used for a specific clinical question, such as the exclusion of VTE or the diagnosis of DIC.[14] The optimal cut-off for the D-dimer assay in the DIC score needs to be determined as well. A previous study showed that for each different D-dimer assay optimal cut-off points for the DIC score can be defined.[15] Most prospective studies on the international DIC score now use values above the upper limit of normal of a given D-dimer test as a 'moderately increased' test result, whereas a value that is five times higher than the upper limit of normal would qualify for a 'strongly increased' test result.[7]

Another difficulty of the current international system may be its static nature, thereby not taking into account dynamic

changes in the respective parameters over a certain period of time. In fact, in the report by Constantinescu *et al.* the patient had a normal, albeit relatively low, platelet count.[11] However, if we assume that the pre-existent platelet count in this patient with extensive malignancy was 400 x 10^9/l, it would mean that more than one trillion platelets would have been consumed in a short time span as a result of coagulation activation. Hence, more dynamic measurements may yield a more sensitive measure of ongoing activation of coagulation. In fact, previous reports on a simplified DIC score, solely based on evolvement of the platelet count and the prothrombin time over time, confirm this notion.[16] A prospective exploration of this system in patients with severe sepsis showed a good correlation with organ failure and provided useful information as to the evolvement of the clinical condition of the patient. These observations are in line with a recent report, demonstrating that a composite dynamic coagulopathy score was quite accurate in identifying patients who would progress to multiple organ failure and who would not survive.[17] Taking these two reports together, it seems that adding dynamic changes to scoring systems for DIC may result in valuable improvement in the predictive power of the scoring systems for DIC, although the accuracy of both systems remains to be established in prospective studies.

In conclusion, simple scoring systems for DIC employing readily available laboratory tests seem to be useful for confirming or rejecting a diagnosis of this condition. Prospective validation studies show that these algorithms are quite accurate and recent studies indicate that small modifications may improve their diagnostic accuracy even further. A caveat in the scoring algorithm is the fact that the test that is used as fibrin-related marker, which is mostly a D-dimer test, should be validated for its use in the diagnosis scoring system for DIC. The new international scoring system for DIC is a simple tool that may be helpful at the bedside but also for the use in clinical studies aimed at the improvement of the clinical management of patients with conditions known to be associated with DIC.

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