Rapid quantitative POC assay for D-dimer in whole blood

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D-dimer assays have become an essential part of diagnosis in patients with clinically suspected deep vein thrombosis (DVT) or pulmonary embolism (PE). It has been shown, using several quantitative D-dimer assays, that a D-dimer concentration below an assay-specific threshold reliably excludes acute DVT and PE. In symptomatic outpatients without severe concomitant disease, D-dimer concentrations below the threshold are typically found in 20-30% of cases. Management studies performed with several D-dimer assays have shown that in patients whose risk of DVT or PE based on clinical criteria is not elevated, it is safe to withhold further technical diagnostic procedures, such as compression ultrasound (CUS) for DVT or spiral CT for PE, when D-dimer concentration is below the threshold.

For routine clinical use it is important that results of D-dimer assays are available within minutes rather than hours. Analysis time can be reduced by using point of care assay technology, and whole blood rather than centrifuged plasma as the sample material. D-dimer measurement, as well as measurement of troponin T, myoglobin, and other cardiovascular parameters, can be carried out using the Roche Cardiac reader [1, 2]. This compact semi-automated reflectometer unit uses heparinised whole blood and dedicated test strips. The time between blood sampling and the assay result is approximately 12 minutes, and specific steps for sample preparation are not necessary. In contrast to other point of care assays, quantitative results are provided. The CARDIAC D-Dimer assay has been optimised for reliable performance in the cutoff range for exclusion of DVT and PE. The CVs of the within-series and the day-to-day imprecision with blood samples and control materials were between 7% and 13% [3]. The assay showed a good correlation and accuracy (n=353; r=0.91; y=1.06x-0.03) when compared with the Tinaquant D-Dimer. No interference was detected in investigations with different haematocrit values (16% to 51%) and with haemoglobin levels up to 0.13 mmol/L, bilirubin levels up to 30 μmol/L, transaminase levels up to 75 U/L, and the major advantage of this assay is that it brings a quantitative and validated test system to the emergency room, vascular outpatient clinic or angiology practice. The only additional equipment needed apart from the compact stand-alone reader unit is a refrigerator for storage of the assay strips, and a pipette for transfer of a drop of heparinised whole blood to the assay strip. No centrifuge or other laboratory equipment is necessary. Use of the reader requires no specific laboratory skills since the assay procedure (after addition of the blood to the assay strip) is automated.

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Results from clinical studies

Three clinical studies have been published on the use of the CARDIAC D-Dimer assay for the diagnosis of DVT. In 85 patients with clinically suspected DVT, a sensitivity of 100% was found for proximal DVT at a cutoff value of 0.5 μg/mL [4]. A study of 87 consecutive outpatients with suspected DVT, using a cutoff value of 0.4 μg/mL, found the sensitivity for DVT was 100%, specificity 50%, negative predictive value (NPV) 100%, and positive predictive value (PPV) 57.1% [5]. The third study was recently presented at the XXth Congress of the International Society on Thrombosis & Haemostasis (ISTH) in Sydney. In this study of 563 patients with clinically suspected DVT, the condition was diagnosed in 223 patients by Duplex ultrasound examination. The diagnostic performance of the assay was evaluated for a pre-specified D-dimer cutoff level of 0.5 μg/mL. Seven of the 213 patients (3.3%) with a D-dimer value =0.5 μg/mL were diagnosed as DVT. Of 350 patients with D-dimer values >0.5 μg/mL, 216 (61.7%) were classified as DVT patients. The assay showed a sensitivity of 96.9% for the diagnosis of DVT and a high specificity of 60.6%.

The results indicate that the assay is a reliable tool for exclusion of DVT, with a diagnostic performance similar to reference automated laboratory assays. Additional data evaluations are needed to optimise the threshold values used for DVT exclusion. Currently there are no specific studies on the exclusion of PE, but for other D-dimer assays it has been shown that the cutoff levels determined for DVT exclusion also apply to PE exclusion.

References