Are the point-of-care diagnostics MULTIPLATE and ROTEM valid in the setting of high concentrations of heparin and its reversal with protamine?

Abstract: To evaluate the in vitro effects of high concentrations of heparin and its reversal with protamine on routine laboratory parameters as well as on modified thromboelastogram (ROTEM; TEM International, Munich, Germany) and impedance aggregometry (MULTIPLATE; Dynabyte, Munich, Germany). An observational, nonrandomized in vitro study. A single-center, university hospital. Ten healthy volunteers. Heparinization of whole blood to levels of 2, 4, 6, and 8 IU/mL of heparin and reversal with protamine. For MULTIPLATE measurements, heparin levels up to 20 IU/mL were tested. The present results show that the prothrombin time (PT) and fibrinogen measurements are altered significantly by heparin concentrations above 2 IU/mL. Protamine reversal also affected coagulation tests except for the fibrinogen. The INTEM test using the ROTEM system was influenced significantly by heparin concentrations of 2 IU/mL or higher, whereas EXTEM measurements remained stable up to 4 IU/mL. The findings for the FIBTEM test were stable up to 6 IU/mL but then declined to values less than 50% of baseline at 8 IU/mL. HEPTEM results remained valid under all concentrations of heparin tested. The effect of protamine on ROTEM was seen mainly in the INTEM and HEPTEM measurements. Heparin concentrations up to a level of 20
U/mL had no effect on MULTIPLATE measurements. Effects of protamine on MULTIPLATE became significant at heparin-to-protamine ratios below 1:1 and were more pronounced for adenosine diphosphate than for thrombin receptor-activated protein testing. Neither fibrinogen (Clauss) nor derived fibrinogen or FIBTEM testing is valid in the setting of high concentrations of heparin unless antagonized by heparinase. Reversal of heparin with protamine worsens platelet function at all ratios as detected by aggregometry (MULTIPLATE) and thromboelastography (ROTEM), starting at a 1:1 ratio. Therefore, appropriate coagulation testing under cardiopulmonary bypass conditions should be selected carefully according to heparin levels. In particular, fibrinogen values are falsely low at heparin levels of 2 IU/mL and above. Therefore, newer algorithms promoting the correction of fibrinogen levels on cardiopulmonary bypass should be based on appropriate testing.