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DETERMINATION OF ACTIVATED FACTOR VII LEVELS DURING CARDIOPULMONARY BYPASS

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Introduction: The tissue factor pathway plays a significant role in initiating coagulation during cardiopulmonary bypass (CPB) (1-3). Measurements of activated factor VII (FVIIa) may have underestimated the contribution of this pathway in the presence of heparin (4). We show that when FVIIa is measured with a clot based assay during CPB, failure to account for inhibition by tissue factor pathway inhibitor (TFPI) will lead to erroneously low values for FVIIa.

Methods: Following IRB approval, we performed clot-based assays of FVIIa on plasma drawn from 9 elective adult cardiac surgery patients at the following times: beginning of surgery (Baseline), 10 min after initiation of CPB (On CPB), one hour after initiation of CPB (CPB 1 Hr), 10 min after protamine (Off CPB), and 24 hours after ICU arrival (Next Day). Heparin was neutralized using hexadimethrine bromide. Antibodies to inhibit TFPI were provided by Dr George Broze (Washington Univ, St Louis). A modified prothrombin time (mPT) was developed, where plasma was diluted with normal saline to produce a PT of about 30 sec, yielding a time that was sensitive to the inhibition of TFPI. Effect of the anti-TFPI antibody on mPT during CPB was evaluated using paired t-test with Bonferroni correction for multiple comparisons.

Results: Without inhibitory antibodies, a decrease in FVIIa level was observed upon initiation of CPB, more than could be explained by dilution (Figure 1; $p<0.001$). When TFPI was inhibited, an increase in FVIIa level was observed. Patients undergoing CPB exhibited antibody-corrected FVIIa levels which increased mildly at the start of CPB, and then fell throughout CPB (Figure 2). During CPB, mPT decreased with TFPI inhibition, showing that TFPI contributes measurably to anticoagulation during CPB ($p<0.05$; Figure 3).

Discussion: FVIIa measurements during CPB are likely to be underestimated if not accounting for TFPI in a clot-based assay. TFPI contributes toward anticoagulation during CPB (5).

References:

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