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**TITLE:** MODIFICATION OF HEMOSTATIC PARAMETERS DURING CARDIOPULMONARY BYPASS (CPB): EFFECTS OF HIGH DOSE APROTININ.

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Previous studies have demonstrated that the administration of high dose aprotinin (A) to patients undergoing open heart surgery significantly reduced intra- and postoperative blood loss (1,2). The precise mode of action has not yet been elucidated (2). The aim of this double blind placebo-controlled study was to obtain further information about high-dose A on coagulation patterns in patients undergoing myocardial revascularisation.

**Methods:** With the approval of the Ethical Committee and informed consent, 40 patients without medication known to affect coagulation prior to surgery were studied. Upon skin incision, patients received either a loading dose of A 250 mg over 30 min, a further 250 mg into the oxygenator prime and a continuous infusion of 50 mg/hr during the whole time of surgery (gr A, n=20) or a corresponding amount of placebo (gr P, n=20). Anesthetic management was identical in all patients with fentanyl, pancuronium, air/oxygen and controlled ventilation. Surgery and CPB were performed with membrane oxygenators and a crystalloid prime under standard flow rate, moderate hypothermia and myocardial preservation with cold cardioplegic solution. During bypass, the activated clotting time was maintained at >400 sec with heparin (H) which was neutralized after completion of CPB with protamine chloride. Arterial blood samples were obtained 5 min after H administration (T1), 15 and 75 min after the start of CPB (T2, T3), 15 min after H neutralization (T4) and 4 h postoperatively (T5). These were assayed for plasmatic levels of platelet factor 4 (PF4), β-thromboglobulin (BtG), D-dimers, plasminogen activator inhibitor (PAI-1), tissue-type plasminogen activator (t-PA) and its inhibitor (t-PA-I).

1. Platelet membrane GP IIb/IIIa, GP IIb/IIIa and GMP-140 were measured by fluorescence flow cytometry. Statistical analysis was performed using non-parametric tests (Kruskal-Wallis and Wilcoxon) after correction of plasma protein concentrations for the hematocrit.

**Results:** A was well tolerated by all patients without any adverse effects. In gr A, intra- and postoperative blood losses were respectively 59 and 52% lower than in gr P. With the exception of GMP-140, the platelet's proteins changed significantly and similarly in both groups during CPB. GP IIb/IIIa and GP IIb/IIIa decreased at T2 in gr A by 36 and 47%, respectively (p<0.05) and in gr P by 41 and 45% (p<0.05) from their starting values. They remained low during CPB. PF4 and BTG increased to reach a maximal value at T3 and tended to normalise at T5. The activation of coagulation is demonstrated by elevated levels of F1+2 at T2, T3, and T4. PAI-1, PAP and D-dimers showed increased levels (p<0.001) during CPB in gr P without decrease at T5. Aprotinin did not affect significantly the kinetics of most parameters. PAP however remained stable during CPB in gr A and D-dimers which rose from 0.01 to 0.07 at T1 to 5.03 ng/ml at T5 (p<0.001) in gr P, attained a maximal value of 60 ng/ml only at T3.

**Conclusion:** As fibrin degradation products, reflected by D-dimers, possess platelet antiaggregating activity, the impairment of their formation by aprotinin could explain the reduction of bleeding after administration of this platelet inhibitor.

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**TITLE:** REPERFUSION SYNDROME DURING ORTHOTOPIC LIVER TRANSPLANTATION: ECHOCARDIOGRAPHIC ANALYSIS OF VENTRICULAR DYNAMICS

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Reperfusion of ischemic tissue is not only associated with transient systemic hypotension but also with pulmonary hypertension. This is well documented for declamping of the abdominal aorta during aneurysmectomy (1), as well as for termination of cardiopulmonary bypass (2). Pulmonary hypertension also occurs during reperfusion of the liver graft during orthotopic transplantation without institution of venovenous bypass. The goal of this study was to determine whether reperfusion causes transient right or left ventricular dysfunction and to evaluate the magnitude of simultaneous pulmonary vasoconstriction.

**Material and Methods:** 23 patients scheduled for OLT (49 ± 11 yrs) were studied. A thermocatheter was floated into the pulmonary artery to measure cardiac output, right ventricular volumes, and right ventricular ejection fraction. For echocardiographic measurements a 5 MHz transducer was advanced into the esophagus. Informed consent and institutional approval were obtained. Statistical methods included analysis of variance for repeated measurements. Values are represented as means ± SEM.

**Results:** Transesophageal 2-dimensional echocardiography revealed right ventricular enlargement during reperfusion, which could be ascertained by the thermocatheter technique while the enddiastolic volumes of the left ventricle did not change (Fig). Both right and left ventricular ejection fractions, which had been depressed during the anhepatic time (-31 ± 4% vs. -16 ± 8%), rose to prehepatic levels. Mean pulmonary artery pressure was increased significantly (43 ± 12% reaching a peak within 15 minutes after reperfusion. This was paralleled by an increase of the diastolic-pulmonary-artery-to-wedge-pressure gradient from 3.7 ± 0.4 mmHg to 7.1 ± 1.2 mmHg.

**Conclusion:** Reperfusion is associated with an enlargement of the right ventricle together with an increase in right ventricular afterload, however, without respective changes of the left ventricle. Thus, alterations in right ventricular wall stress are not only caused by an enlargement of venous return upon declamping of the inferior cava but also due to elevated levels for right ventricular outflow resistance. These changes are an integrated part of the reperfusion syndrome and may precipitate right ventricular ischemia or right ventricular failure.

References: