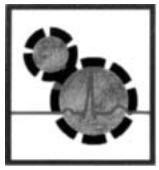

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Abstracts

OXYGENATOR TYPE AND BLOOD CELL TRAUMA IN CARDIAC SURGERY

Objective: Blood cell trauma in cardiac surgery is mainly attributed to the use of the heart lung machine and the oxygenator. The optimization of oxygenator design and membrane technology (e.g., chemical properties of surface material), aiming at reducing the blood cell alterations, is an objective of current developments. Clinical evaluation of different oxygenators concerning alterations of blood cells and markers of organ function provide an appropriate level of complexity because various patient characteristics and operative data are involved. Our clinical research database enables us to study the impact of different oxygenator types on blood cells and markers of organ function in the homogenous group of elective coronary artery bypass grafting (CABG) patients.

Materials and Methods: Prospective data from 4847 patients who underwent isolated CABG were collected, of which 282 had off-pump coronary artery bypass grafting (OPCAB). The blood cell parameters white blood cell (WBC) counts, platelet (PLT) counts, and red blood cell counts and the marker of organ function lactate dehydrogenase (LDH) and creatinine clearance (CC) were determined pre- and postoperatively. The changes of these parameters were analyzed among the 13-oxygenator type groups and compared with the OPCAB group. To account for individual differences in blood volume, flow rate, and bypass time, we introduced a formula to normalize blood alterations per transfer cycle across the oxygenator.

Results: We could observe significant different blood cell alterations between the various oxygenator groups. The increase of WBC was positive correlated with LDH and negative with CC. The oxygenators with the least decrease in PLT had the highest WBC increase. Two manufacturer's modifications in oxygenator surface material are observed to result in a trade off between induced WBC and PLT blood alterations.

Conclusion: Cardiotomy suction blood separation had a clear effect on blood activation parameters. The cardiotomy suction blood separation enabled us to separate a main part of blood activation and prevent its negative effects. Further studies should prove whether retransfusion of cardiotomy suction blood without cell saver is indicated at all in routine CABG.

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INFLUENCE OF CARDIOTOMY SUCTION BLOOD SEPARATION DURING CPB

Introduction: The circumstances of cardiopulmonary bypass (CPB) during cardiac surgery mandate a complex blood management to economize on allogenic blood transfusion. In traditional CPB systems mediastinal and pleural shed blood as well as pericardial suction blood is drained to a reservoir and returned to CPB. This intraoperative retransfusion is critically considered under the aspect of the biocompatibility of the CPB. Mainly, activation of biological systems is expected through blood to air contact and retransfusion of pericardio-pleural fluids as well as through mechanical trauma caused by the blood suction.

Methods: Thirty-four patients selected from April until September 2002 (26 males 64 ± 6 years, 8 female 63 ± 9 years) undergoing elective coronary artery bypass grafting surgery (CABG) were involved in this prospective randomized study. During the operation suctioned blood was collected separately. Then it was retransfused to the patient at the end of the operation (group A, $n = 14$), or it was retained (group B, $n = 20$). Inflammatory and hemolytic indicators such as PMN elastase, P-selectin, IL-6, β-thromboglobulin, blood biochemistry, free Hb, LDH, haptoglobin, CK, CK-MB, and CRP were determined before and after the 90-min CPB.

Results: Preoperative clinical data did not differ between groups. Systemic IL-6 level (A: 21 ± 9 vs. B: 14 ± 10, $p < 0.01$), PMN-elastase (A: 188 ± 120 vs. B: 110 ± 19, $p < 0.05$), CRP (A: 24 ± 29 vs. B: 6 ± 6, $p < 0.05$), CK-MB (A: 41 ± 16 vs. B: 29 ± 16, $p < 0.05$) at 90 min after surgery were significantly increased in the group A. Obviously the cardiotomy suction blood separation (CSBS) during CPB also can have an advantage to save platelets (A: 158 ± 57 vs. B: 232 ± 45 , $p < 0.01$) and Hb (A: 8 ± 1 vs. B: 9 ± 1, $p < 0.05$). Thus CSBS resulted in reduced platelet loss and inflammatory response together with a decrease in hemolysis in the CSBS treated groups. In all other parameters measured, no differences between the two groups were observed.

Conclusion: CSBS had a clear positive effect on blood activation parameters. Further studies should prove whether retransfusion of cardiotomy suction blood without cell saver is indicated in routine CABG.

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OFF-PUMP CABG REVEALS LESS PRONOUNCED EFFECT ON MARKERS OF CONTACT ACTIVATION, INFLAMMATORY RESPONSE, COAGULATION, AND CEREBRAL ISCHEMIA COMPARED WITH ON-PUMP CABG

Objectives: Off-pump coronary artery bypass (OPCAB) is still not widely used. However, a beneficial effect on the results in a subgroup of patients with poor left ventricular function, acute myocardial infarction, or high risk for cerebral ischemia could recently be demonstrated. Nevertheless, the pathophysiologic mechanisms on which the improved outcome is based are not clearly identified.

Methods: We investigated in 10 patients undergoing off-pump coronary revascularization intra- and postoperatively the change in markers of contact activation (FXII, C3a), coagulation (FXIII, Fab 1/2), inflammatory response (elastase, IL-6, procalcitonin), astroglial damage (S-100b, MMST), and myocardial ischemia (CK, CK-MB, TropT) and compared the data with 10 on-pump CABG patients.

Results: Most interestingly we found no group differences in FXII, which plays a major role in contact activation after exposition of blood to foreign surfaces of the extracorporeal circuit. C3a as representative of the alternative pathway of complement activation showed only weak statistical difference. Coagulation and cerebral markers remained nearly unaffected with at least a more concise increase of Fab 1/2 after on-pump surgery. Inflammatory response could not be detected by IL-6, but elastase was elevated moderately in on-pump patients. As expected, myocardial ischemia markers were significant lower in OPCAB patients.

Conclusion: The focus on this study was not the potential improvement of clinical results in patients after off-pump revascularization; we instead attempted to examine the pathophysiological correlate. Considering the fundamental differentiation of the groups with the missing extracorporeal circuit and its proved biochemical consequences, the nearly nonexistent statistical differences are difficult to explain.

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SIMULATION OF CRITICAL SITUATIONS DURING EXTRACORPOREAL PERFUSION

The importance of simulators for the training of qualified staff in sensitive biomedical areas is increasing steadily. Medical fields such as emergency care, minimally invasive surgery, endoscopy, and anesthesia already use highly sophisticated simulators.

To cover the part of cardiovascular technique the heart-lung-machine (HLM) hardware simulator "CardioSim" is being developed by professors and students at the Medical Engineering Faculty of FH Furtwangen, Germany. Designed in an almost-real operating room environment, cardiovascular engineers can receive training in standard situations on the HLM linked to an artificial patient. In a control room beside the "operating room," all clinically relevant data of HLM, anesthesia, and perfusion equipment are displayed on a computer terminal and can be supervised and manipulated there by a trainer.

Now, with the development of a system called GREENBOX, the cardiovascular engineer can also receive training in some special critical situations that can emerge during extracorporeal perfusion. Basically, the system consists of a combination of pipes, electrical valves, stepper-motors and pumps, and a water reservoir. All electrical parts are computer-controlled. Connected to the heart-lung-machine GREENBOX simulates realistic blood pressures and flows that can be changed by the trainer on the control terminal. That way, the HLM display for the MAP can be altered or an obstruction of the arterial reflow simulated. Additionally, by pressing virtual buttons on the terminal, the trainer can pump air into the pipes that then will be detected by the bubble sensor and make the arterial pump stop; he can also simulate the occlusion of the arterial filter.

Additional features that were realized and that the cardiovascular engineer has to cope with are technical problems of the HLM itself. With virtual switches on the computer terminal, the trainer can turn off the displays of the HLM. With the HLM still running, the trainee then no longer has any information about pressures, flows, and pump ratings. Another one is the interruption of the CAN connection of the arterial pump that leaves the trainee without control of the system. Finally, the cardiovascular engineer even can find himself winding the pump manually when the trainer switches of the power supply entirely.

As a certified trainings center of the EBCP, "CardioSim" intends to become a center of education, training, and recertification for cardioanesthesiologists and perfusionists.

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INDICATORS OF BRAIN DAMAGE DURING CONTROLLED HYPOPERFUSION AND HYPOTHERMIA IN THE PIGLET MODEL

Objective: We sough to evaluate specific markers of cerebral ischemia/reperfusion damage (heat shock protein [HSP] 70 and malondialdehyde [MDA]) in relation to controlled hypoperfusion and hypothermia.

Methods: Female piglets (n = 55, 7–10 kg, 3–4 weeks old) received extracorporal circulation (ECC) at 25, 50, or 100% of the standard flow rate for 60 min of cardioplegic cardiac arrest. Body temperature was kept at 18, 25, and 37°C. Routine hemodynamic and functional parameters were measured online until 4 h of reperfusion. Immunohistology was used to quantify HSP70 levels in cortex, thalamus, cerebellum, pons, and hippocampus; high-performance liquid chromatography was used to quantify jugular venous blood MDA levels.

Results: Measurements were performed successfully in all animals, intracranial pressure remained stable during the entire study. Reduced ECC flow led to significant reduction of mean arterial pressure by 79%, reduction of jugular venous oxygen saturation by 47%, reduction of carotid blood flow by 92%, and an increase of serum lactate by 350%. All these changes were significantly enhanced in the 38°C versus the 25°C and the 18°C groups. Tissue oxygenation index was reduced by 25% in the 38°C low-flow groups ($p < 0.05$). There was a significant increase in HSP70 (predominantly in the hippocampus) and MDA in the 25 and 50% flow groups.

Conclusion: Reduction in global blood flow during ECC leads to significant biochemical changes in certain areas of the brain. HSP70, lactate, and MDA may be important parameters to evaluate the efficacy of further anti-ischemic therapies during surgical corrections.

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EXTRACORPOREAL PRESERVATION OF CARDIAC FUNCTION IN ISOLATED PIG HEART

Objective: The clinically accepted ischemic time for donor hearts is 4 h. The objective of this study was to develop a working heart perfusion system to allow for prolonged donor heart preservation up to 24 h in a metabolic equilibrium.

Methods: After cardioplegic arrest (500 mL of Bretschneider solution) donor hearts of 30-kg pigs were explanted and connected to a recirculating constant pressure-modified Langendorff perfusion system, consisting of a hollow fiber oxygenator and a centrifugal pump. The perfusion system was filled 1000 mL of leukocyte-depleted pig blood. Electrolytes, buffers, glucose, insulin, and antibiotics were supplemented. Via an adjustable occluder, the left atrium was permanently filled. Hemodynamics (left atrial pressure [LAP], aortic root pressure [ARP], flow) and ECG were recorded. LAP and ARP were kept constant by a microprocessor-based closed-loop control. Cardiac function was assessed by direct measurement of left ventricular pressure. Hemofiltration was performed continuously.

Results: Twenty-three pig hearts were perfused up to 24 h maintaining adequate cardiac function throughout. Based on a time-discrete proportional plus integral plus derivative controller LAP and ARP could be kept constant. Acid-base balance (pH, pCO_2, and pO_2), electrolytes, hemoglobin, and lactate levels in the perfusate were also kept constant without difficulties. There was no increase of lactate in the perfusate, indicating ATP production by an aerobic metabolism of the perfused heart.

Conclusion: The described working heart perfusion system allows for long-term preservation of explanted hearts. This may enable expansion of recruitable organs and could facilitate further evaluation of the donor heart. Besides, the setup could be used for surgical training or trials requiring isolated working hearts.

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EXTRA CORPOREAL SYSTEMS WITH SURFACE-MODIFIYING ADDITIVES DO NOT IMPROVE CLINICAL OUTCOME AFTER CABG

Background: The interaction between foreign surface from cardiopulmonary bypass (CPB) circuits and human blood induces activation of coagulation cascade and cellular blood elements during extra corporeal circulation (ECC). Fully systemic heparinization, alone or in combination with heparin- or albumen-coated circuits, cannot completely inhibit this material-associated reaction. Blending materials with thromboresistant copolymers (surface-modifying additives [SMA]) have been adapted for CPB circuits. Th aim of this prospective, randomized, and partially blinded study, approved by the MLU Human Ethics Committee, was to compare a tip-to-tip SMA-treated CPB circuit (SMARxT™, COBE® Cardiovascular, Sorin Group) with an identical, but unmodified circuit regarding global parameters for clinical outcome.

Patients and Method: Adult patients (n = 150) undergoing elective first-time coronary artery bypass grafting (CABG) were randomized into either the SMA (n = 72) or the control group (n = 78). Exclusion criteria were renal insufficiency, liver disease, stroke, coagulopathy, coumarin therapy, current inflammation, balloon counterpulsation therapy, or revision. Anesthesia, surgery, and ECC were performed in a standardized manner. The CPB circuit consisted of a flat sheet membrane oxygenator (COBE® CML Duo™), 43-μ arterial filter (Sentry™), hard shell venous and cardiotomy reservoir, PVC tubing, and silicon tubing in the pump heads. The circuit was primed with 1000 mL of electrolyte solution, 500 mL of hetastarch 6%, 250 mL of mannitol M15, 50 mL of sodium bicarbonate, 5000 U heparin, and 1×10^6 U aprotinin. Including anesthesia, total dose of heparin was 300 U/kg, and of aprotinin 3×10^6 U. Arterial pump flow was kept between 2.4 and 3.0 L/min/sqm. The study was designed to detect a significant difference in mean postoperative blood loss 24 h after arrival on intensive care unit. Two-tailed t-test or Mann--Whitney U test were used to analyze on difference between the two groups. A p value < 0.05 was considered statistically significant.

Results: Patients received 3.4 ± 0.7 Grafts in (SMA vs. control) 56 ± 16 versus 57 ± 17 min X-clamp time and 104 ± 30 versus 102 ± 26 min bypass time. Bleeding was 387 ± 254 versus 399 ± 197 mL 24 h postoperatively and 844 ± 496 versus 780 ± 413 mL total (mean values). Transfusion was necessary in 47 versus 41% of patients. Intubation time was 16.5 versus 14 h, intensive care time was 41 versus 25 h, and total hospital stay 10 days in the both groups (median values).

Conclusion: Using "open" CPS circuits with common venous and drain reservoir and roller pump, SMA-treated surfaces show no clinical advantages. Neither postoperative blood loss nor transfusion units, intensive care unit stay, or hospital stay showed significant differences compared with identical, but untreated circuits. Published studies with positive hematologic, hemodynamic, and clinical effects were all performed without use of kallikrein inhibitors. The only published work without positive results was based on use of aprotinin as kallikrein inhibitor, as well as in our study. It is possible that aprotinin covers the antifibrinolytic effects of SMA surfaces and their expected benefit on clinical outcome. Larger studies with and without pharmaceutical platelet-protective agents should be able to give an answer. However, because the use of aprotinin is currently state-of-the-art in cardiac surgery during ECC, it is difficult to perform such a study without use of aprotinin.

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