Microcirculatory perfusion disturbances and endothelial hyperpermeability following cardiopulmonary bypass persist in the early postoperative period

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Introduction

Increased endothelial permeability following cardiopulmonary bypass (CPB) is an important contributor to microcirculatory perfusion disturbances and postoperative organ dysfunction. We therefore hypothesised that microcirculatory perfusion disturbances remain altered after surgery and are paralleled by prolonged impairment of endothelial barrier function.

Methods

Microcirculatory perfusion was assessed in 17 patients undergoing cardiac surgery with CPB using sublingual sidestream dark-field imaging from which red blood cell filling, percentage of perfused vessels, and perfused boundary region (glycocalyx permeability) was calculated. **Plasma** was obtained before connection to CPB (pre-CPB), during CPB, after weaning from CPB (post-CPB) and 1, 24 and 72 hours after weaning from CPB. Using electric cell-substrate impedance sensing (ECIS) of human pulmonary and renal microvascular endothelial cells (MVECs), the effect of plasma exposure for 3 hours on *in vitro* endothelial barrier was measured. **Endothelial gap formation** of pulmonary MVECs after plasma exposure was visualized using **immunofluorescence** (IF). Plasma syndecan-1 levels were studied with ELISA as marker for **glycocalyx degradation**.

Results

Patient characteristics

<i>n</i> = 17	
Age (years)	68 ± 7
Males (%)	88
Body mass index (kg/m ²)	29 ± 4
Surgery time (min)	239 ± 38
Cross-clamp time (min)	70 ± 14
Packed red blood cell transfusion (% patients)	12
Thrombocytes (5-donor concentrate; % patients)	18
Cell saver retransfusion (ml)	491 ± 119

Table 1. Values represent frequencies, means ± standard deviation or median with interquartile range. *CPB, cardiopulmonary bypass.

Prolonged impairment of microcirculatory parameters

Fig. 1: Haematocrit levels (A), capillary red blood cell filling (B), proportion of perfused vessels (C) and perfused boundary region (D) during the perioperative period. * $P < 0.05$ RM ANOVA, # $P < 0.05$ vs. Pre-CPB.

Prolonged endothelial hyperpermeability and gap formation

Fig. 2: Effect of plasma exposure obtained before and after CPB on pulmonary (A) and renal (B) microvascular endothelial barrier measured with ECIS and IF staining of PMVECs exposed to pre-CPB (C) and post-CPB (D) plasma; VE-cadherin (green), DAPI (blue), F-actin (white); scale bar 50 μ m. Endothelial gaps are indicated with red arrows * $P < 0.05$ RM ANOVA.

Glycocalyx shedding is associated with microcirculatory perfusion disturbances and pulmonary endothelial hyperpermeability

Fig. 3: Association between plasma glycocalyx shedding molecule syndecan-1 and proportion of perfused vessels (A) and pulmonary endothelial barrier (B). Pearson correlation. Values are presented with 95% confidence intervals.

Conclusion

Microcirculatory perfusion disturbances in patients undergoing cardiac surgery with CPB **persist** in the **first postoperative days** and are **paralleled by prolonged endothelial hyperpermeability** and **shedding of endothelial glycocalyx** constituents.