Microcirculatory Perfusion Is Preserved During Off-Pump but Not On-Pump Cardiac Surgery

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Objective: **This study investigated the perioperative course of microcirculatory perfusion in off-pump compared with on-pump surgery. Additionally, the impact of changes in systemic hemodynamics, hematocrit, and body temperature was studied.**

Design: **Prospective, nonrandomized, observational study.**

Setting: **Tertiary university hospital.**

Participants: **Patients undergoing coronary artery bypass grafting with (n = 13) or without (n = 13) use of cardiopulmonary bypass.**

Interventions: **Microcirculatory measurements were obtained at 5 time points ranging from induction of anesthesia to ICU admission.**

Measurements and Main Results: **Microcirculatory recordings were performed with sublingual sidestream dark field imaging. Despite a comparable reduction in intraoperative blood pressure between groups, the perfused vessel density decreased more than 20% after onset of extracorporeal circulation but remained stable in the off-pump group. The reduction in microvascular perfusion in the on-pump group was further paralleled by decreased hematocrit and temperature. Although postbypass hematocrit levels and body temperature were restored to similar levels as in the off-pump group, the median microvascular flow index remained reduced after bypass (2.4 [2.3-2.7]) compared with baseline (2.8 [2.7-2.9]; p = 0.021).**

Conclusions: **Microcirculatory perfusion remained unaltered throughout off-pump surgery. In contrast, microvascular perfusion declined after initiation of cardiopulmonary bypass and did not recover in the early postoperative phase.**

KEY WORDS: cardiopulmonary bypass, coronary artery bypass, off-pump cardiac surgery, microcirculation

CARDIOPULMONARY BYPASS during cardiac artery bypass surgery (OPCAB) is associated with disturbances in microcirculatory perfusion and oxygenation.[1–4] In addition to the primary microcirculatory injury related to contact activation by extracorporeal circulation and absence of pulsatile flow, on-pump procedures result in hemodilution, which independently deteriorates microvascular function.[2,5–8]

In contrast, off-pump coronary artery bypass surgery (OPCAB) is associated with preserved hematocrit levels and pulsatile flow generated by the beating heart, contributing to preservation and maintenance of microcirculatory perfusion.[9] Moreover, extracorporeal contact activation is absent in off-pump surgery. On the other hand, cardiac positioning during OPCAB procedures is associated with short-lasting cessation of microcirculatory flow.[3] Whether multiple positioning events during off-pump surgery lead to more enduring disturbances in microvascular perfusion is still unknown.

Current literature is limited regarding microcirculatory perfusion dissimilarities between on-pump and off-pump procedures, in particular with respect to the course throughout the intraoperative period.[1,3,10] The authors previously showed that patients undergoing on-pump coronary artery bypass surgery (CABG) develop a decrease in microcirculatory perfusion after the onset of cardiopulmonary bypass (CPB), irrespective of pulsatile or nonpulsatile perfusion.[4] Although De Backer et al suggested that microcirculatory alterations are most pronounced during surgery with CPB, they have not performed intraoperative measurements in off-pump patients, prohibiting a close comparison between groups.[1] In the present study, the authors, therefore, compared intra- and early postoperative microcirculatory perfusion in patients undergoing on-pump and off-pump coronary artery surgery. Additionally, the relationship between microcirculatory alterations during both surgical modalities and intraoperative hematocrit or body temperature was examined. It was hypothesized that use of CPB during on-pump surgery induces more severe and enduring disturbances of microcirculatory perfusion compared with off-pump surgery, which are not fully explained by systemic hemodynamics, hematocrit, and body temperature.

METHODS

This single center, nonrandomized clinical study was approved by the local Human Subjects Committee of this university medical center, and written informed consent was obtained from all participants. The 2 study groups consisted of patients undergoing coronary artery surgery with nonpulsatile cardiopulmonary bypass (CPB; n = 13) or off-pump beating heart OPCAB procedures (OPCAB; n = 13) in the period March 2010 to March 2012. Exclusion criteria were previous heart surgery, emergency surgery, insulin-dependent diabetes mellitus, and a body mass index over 30 kg/m^2. Assignment to OPCAB procedures was based on the operating schedule. OPCAB surgery was performed by a single surgeon specializing in this type of procedure (EKJ). Surgery with CPB was performed randomly by 1 of the 4 other surgeons in the cardiosurgical department.

The anesthesia protocol for CPB and OPCAB procedures was similar and earlier described by this group [4]. Briefly, platelet inhibitors were continued until 5 (clopidogrel) and 1 (acetylsalicylic acid) days preceding surgery. After lorazepam administration (5 mg),

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The present study was supported by the European Association for Cardiothoracic Anesthesiologists.

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1053-0770/2601-0001$36.00/0

http://dx.doi.org/10.1053/j.jvca.2013.05.026.

anesthesia was induced using sufentanil (3-7 μg/kg), pancuronium bromide (0.1 mg/kg), and midazolam (0.1 mg/kg) and maintained by continuous propofol infusion (200-400 mg per hour). Ventilation parameters consisted of 10 mL/kg tidal volume, 4% to 5% end-tidal CO_2, 45% inspiratory O_2, and positive end-expiratory pressure of 5 cm H_2O. After anesthesia induction, patients received dexamethasone (1 mg/kg) and cefazolin (1 g). In patients undergoing CPB surgery, cardiac output was monitored intermittently using a thermodilution pulmonary artery catheter. For OPCAB surgery, all patients received a pulmonary artery catheter for continuous cardiac output monitoring (Vigilance monitor, Edwards Lifesciences, Irvine, CA). In all patients, a cell saving device was used for retransfusion of pericardial shed blood. At the end of surgery, heparin was reversed with protamine, and tranexamic acid (2 g) was administered as antifibrinolytic therapy.

Cardiopulmonary bypass (CPB) was performed with an S5 heart-lung machine with a heater-cooler device (Stöckert Instrumente GMBH, Munich, Germany) and centrifugal pump (Sarns, Terumo Europe NV, Leuven, Belgium), combined with a heparin-coated polyvinyl tubing system with a hollow-fiber oxygenator and arterial line filter (Affinity, Medtronic, Minneapolis, MN). Priming of the circuit was performed with 1,000 mL of modified fluid gelatin (Braun Melsungen AG, Germany), 250 mL of lactated Ringer's solution (Baxter BV, Utrecht, The Netherlands), 100 mL of mannitol (20%, Baxter BV), and 50 mL of sodium bicarbonate (8.4% Braun Melsungen AG), 1000 mg of cefalozin (Eli Lilly Nederland BV, Nieuwegein, The Netherlands), and 5000 IU of porcine heparin. Nonpulsatile CPB (34°C; 2.2-3.0 L/min/m^2) started after heparin administration (300 IU/kg) when the activated coagulation time (ACT) exceeded 480 seconds. Cardiac arrest was induced by 4°C crystalloid cardioplegia solution (St. Thomas, VU University Medical Center, Amsterdam, The Netherlands). Patients were weaned from CPB when rectal temperature was above 36°C.

In OPCAB surgery, an initial heparin dose of 300 IU/kg was administered. During grafting, the ACT was maintained above 380 seconds. Patients were kept normothermic throughout surgery. OPCAB procedures were performed with 2 deep pericardial stitches and a mechanical stabilizer (Ultima, Maquet, Hilversum, The Netherlands). To avoid systemic hypoperfusion, cardiac repositioning was performed when systolic blood pressure dropped under 70 mmHg or when venous oxygen saturation declined under 60% [11].

Sublingual mucosal microcirculation measurements were performed during surgery and in the intensive care unit (ICU) using side dark field (SDF) imaging (MicroScan, Microvision Medical, Amsterdam, The Netherlands), as previously described.[3,4] During CPB surgery, images were made after induction of anesthesia (T1), 10 minutes after cross-clamping the aorta during CPB (T2), 10 minutes before removing the aortic cross-clamp during CPB (T3), after weaning from CPB, in the operating room (T4), and in the first hour in ICU, while on mechanical ventilation (T5). In the OPCAB group, measurements were performed after induction of anesthesia (T1), during the grafting of the first and second anastomoses (T2 and T3, respectively), at the end of surgery (T4), and in the first hour in ICU, while on mechanical ventilation (T5). To be able to perform comparisons of changes in perioperative microcirculatory perfusion, measurement time points for both CPB and OPCAB groups were named according to CPB surgical events. At each time point, 3 sequences of 10 seconds were recorded.

Analysis was performed blinded for each study group as described earlier.[4] In brief, automatic vascular analysis software (AVA 3.0, Microvision Medical, Amsterdam, The Netherlands) was used to determine parameters of relevance, according to general consensus.[12] All vessels were identified manually for total vessel density (TVD). Subsequently, each vessel was scored individually for its flow character to obtain perfused vessel density (PVD). Finally, videos were analyzed for microvascular flow index (MFI). This is a semiquantitative score, in which the flow score (no flow, sluggish flow, intermittent flow, and continuous flow) that is demonstrated by most small vessels is assigned to a quadrant of the video screen. Scores of the 4 quadrants were averaged per video. All scores were calculated for small vessels (diameter <20 μm) to enable specific focus on the microvasculature important for oxygen exchange.

From all patients, intra- and early postoperative hematocrit levels, administered vasoactive medication and systemic variables, including temperature, mean arterial pressure, and cardiac index, were recorded. Moreover, lactate levels in arterial blood gases were determined at baseline (T1) and at the end of surgery (T4).

The study sample size was based on previous findings of the group, showing a 23% reduction in perfused small vessel density during cardiopulmonary bypass with a standard deviation of up to 15%.[3] A power of 90% and an alpha of 0.01 were used in the sample size calculation. The primary outcome parameter was sublingual perfused small vessel density. Data were analyzed using SPSS statistical software package (17.0; IBM, New York, NY). All values are expressed as mean ± standard deviation or median with interquartile range (IQR). Repeated-measures (RM) ANOVA was performed to analyze time-dependent differences between groups. Differences between groups at individual time points were analyzed by Student's *t* test for parametric data or Mann-Whitney U tests for nonparametric data. Within-group differences were tested with paired *t* test or Wilcoxon test for parametric and nonparametric data, respectively. Correlations between changes in hemodynamic variables, hematocrit, or temperature and alterations in microcirculatory variables during onset of CPB or weaning from CPB were tested with Pearson correlations tests; $p < 0.05$ was considered statistically significant.

RESULTS

Group characteristics are presented in Table 1. Overall, patient demographic characteristics were similar among groups; however, patients undergoing OPCAB surgery received less heparin and protamine throughout the procedure compared with CPB surgical patients.

Perioperative values of hematocrit (panel A) and temperature (panel B) are shown in Fig 1 for CPB and OPCAB groups. Cardiopulmonary bypass was associated with an intraoperative reduction in temperature, but no alterations were observed during OPCAB surgery (ANOVA RM: $p = 0.001$). Hematocrit declined after onset of extracorporeal circulation compared with baseline ($p < 0.001$) and was lower than in the OPCAB group after weaning from CPB (0.28 ± 0.04 *v* 0.38 ± 0.05, respectively; $p < 0.001$). In the ICU, hematocrit levels in the CPB group restored toward hematocrit levels as observed in the OPCAB group (0.33 ± 0.03 *v* 0.35 ± 0.04, respectively; $p = 0.223$). The courses of cardiac index (panel C) and mean arterial pressure (panel D) did not reveal differences between groups over the course of the study. Dopamine or nitroglycerin infusion was not different between groups (Table 2).

Figure 2 represents the median microvascular flow index and average total vessel density and perfused vessel density of the sublingual mucosal microvasculature with a diameter <20 μm. The microvascular flow index (panel A) remained unaltered throughout the study period in the OPCAB group. The MFI score tended to decrease after initiation of extracorporeal circulation from 2.8 (2.7-2.9) to 2.7 (2.4-2.7, $p = 0.241$). On ICU admission, the MFI-score in CPB patients was decreased compared with baseline levels (2.4 [2.3-2.7], $p = 0.021$ *v* baseline).