Pump Flow Changes Do Not Impair Sublingual Microcirculation During Cardiopulmonary Bypass

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Objective: **The flow rate of the cardiopulmonary bypass (CPB) pump used in cardiac surgery often undergoes inherent fluctuations ranging from 10% to 20% of its theoretic value. However, the effects of such alterations remain unknown. In the present study, the authors investigated whether such variations could induce changes in the microvascular flow, which is considered a primary indicator of poor perfusion.**

Design: **A prospective, observational, clinical study.**

Setting: **A university-affiliated teaching hospital.**

Participants: **Thirty adult patients undergoing elective cardiac surgery with CPB.**

Interventions: **Analysis of the sublingual microcirculation during CPB using a pump flow rate of 80% or 100% of the theoretic value.**

Measurements and Main Results: **Sidestream dark field (SDF) imaging was used to record 2 video clips of the sublingual microcirculation in each patient. The videos were recorded at the same site at 80% and 100% of the theoretic flow rate. Microvascular analysis displaying the De Backer score, the microvascular flow index, the total vessel density, the perfused vessel density, and the proportion of perfused vessels was performed. Moreover, the mean arterial pressure (MAP), SvO_2, and $PaCO_2$ were evaluated. No significant changes in the measured parameters were noted at the 2 different flow rates.**

Conclusions: **Changes in the CPB pump flow rate within 20% (80%-100%) of its theoretic value do not alter the sublingual microcirculation. Thereafter, it is conceivable that during perioperative adjustments of the CPB pump rate, blood flow autoregulation mechanisms are activated so that limited changes in the pump flow can be considered safe not only at the sublingual site but also for the entire microcirculation.**

KEY WORDS: cardiopulmonary bypass, sidestream dark field imaging, microcirculation, pump flow, autoregulation

CARDIOPULMONARY BYPASS (CPB), a technique introduced for cardiac surgery in the early 1950s, has proved to be essential for most cardiac operations. Nevertheless, CPB leads to the formation of microemboli and the development of a complex systemic inflammatory response that is associated with several postoperative complications including neurologic dysfunction, respiratory failure, renal dysfunction, altered liver function, and, ultimately, multiple organ failure.[1-3] Organ dysfunction after cardiac surgery is known to be related to a prolonged intensive care unit (ICU) stay and long-term mortality.[4] Although the mechanism inducing such a clinical state may include global hemodynamic alterations, mitochondrial dysfunction, and regional blood flow modifications, in the last few years the impact of microcirculatory abnormalities has proved to be of major importance.[5] In fact, the microcirculation plays an essential role in tissue perfusion and organ activity by transporting oxygen and nutrients, eliminating cellular waste products, and ensuring adequate immunologic function[6]; and its aberration is related to a variety of systemic proinflammatory and shock states, such as septic shock, cardiogenic shock, and ischemia/reperfusion injury.[7-9] Thus, an adequate microcirculatory blood flow rate is a basic requisite for proper perfusion and, hence, sufficient oxygen delivery to tissues.

The use of CPB causes nonphysiologic blood distribution in tissues whereby cerebral perfusion is maintained over that of the gastric mucosa, pancreas, small bowel, and skeletal muscle.[10,11] Moreover, during CPB, the blood flow rate, determined by the mechanical pump, may decrease by about 20% of its full theoretic arterial value (calculated as the product of the patient's Dubois body surface area and the cardiac index, corresponding to 2.4 L/min/m^2 in an adult patient) as evidenced by clinical reports about CPB-assisted cardiac surgery in the last 25 years. Such a decrease may be related to mechanical, technical, or physiologic causes.[10] The effects of unsatisfactory perfusion are particularly serious at the splanchnic level where prolonged ischemia can lead to changes in intestinal permeability; the release of endotoxins into the circulation; and, finally, systemic inflammatory response syndrome.[3,12,13] The need to analyze the microcirculation during CPB, particularly in the splanchnic region, is thus clear.

Microcirculatory analysis can be performed using several methods, but the sidestream dark field (SDF) imaging system (Fig 1) represents the most advanced validated technique for imaging at the bedside[14] when studying the human microcirculation in exposed organs and at the tissue surface. The areas of investigation concern only organs covered by a thin epithelial layer such as the skin, conjunctiva, gingival, ileostomies, colostomies, rectal mucosa, and, as the site of choice, the sublingual area. During surgery, these areas also can be extended to the brain, lungs, tongue, liver, and gut.[15] Although essentially the same as its forerunner, the orthogonal polarization spectral system, SDF imaging does not use polarized light, but rather side illumination of the area under investigation provided by a surrounding ring of light-emitting stroboscopic diodes located at the tip of the gear. The lens in the core of the device is optically isolated from the outer diodes, and, thus, at the target site, the light reflected by superficial layers, perpendicular to the light source, is discarded, whereas the light reflected from deeper layers reaches the center of the machine where it is imaged onto a charge-coupled device camera.[15,16] The incident light emitted by the light-emitting diodes has a central wavelength of 530 nm corresponding to the optimal optical absorption point of the hemoglobin contained in the red

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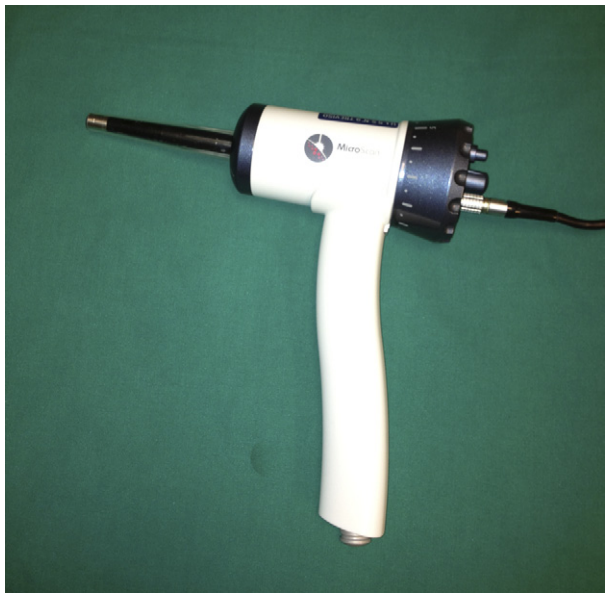

Fig 1. The SDF device. (Color version of figure is available online.)

blood cells (RBCs) regardless of its oxygenation state, so the resulting images display dark globules, the RBCs, moving against a white background.[14] As a result, vessels can be detected only when they enclose RBCs, and, because the vascular wall cannot be directly visualized by SDF imaging, empty vessels are ignored. Thanks to the optical isolation of the lens system and the stroboscopic lights synchronized with the charge-coupled device frame rate, the SDF method provides good-quality images of microvascular vessels filled with RBCs, both in terms of contrast and sharpness.[14,15]

The aim of the present study was to evaluate the effects of oscillations of the theoretic CPB pump flow on the microcirculation by monitoring one area of the sublingual mucosa using the SDF system at different flow rates. This target tissue was chosen because it is easily accessible; it shares the same embryologic origin with the gastrointestinal tract[17]; and it shows analogous alterations to those in the splanchnic area after the induction of modified states, such as sepsis, as revealed by previous experimental observations.[18-23] Thus, the sublingual area can be used as a proxy for the splanchnic bed, which is the real region of interest. The current analysis could shed light on the effects of CPB on the perfusion of organs that are at risk during cardiac surgery and, in turn, improve their perfusion and limit the pathophysiologic consequences of microcirculation abnormalities.

METHODS

After approval from the local ethics committee and obtaining written informed consent, 30 consecutive patients were enrolled in the study. The inclusion criteria were age >18 years of age, and cardiac surgery involving CPB. The exclusion criteria were emergency surgery, sublingual mucosal laceration, and active bleeding.

All patients received fentanyl, 1 μg/kg, and midazolam, 0.07 mg/kg intramuscularly, 25 minutes before admission to the operating room. Anesthetic induction was performed with fentanyl, 5 μg/kg; propofol with a target-controlled infusion of 3 μg/mL at the target site; sufentanil with a target-controlled infusion of 0.3 ng/mL at the target site; and rocuronium, 0.6 mg/kg. Anesthesia was maintained using propofol, 2.4 to 3 μg/mL, at the target site and sufentanil, 1.5 ng/mL, before the sternotomy and sufentanil, 1 ng/mL, 0.75 ng/mL, and 0.5 ng/mL, respectively, before cannulation, during CPB, and before skin suture. Mechanical ventilation was performed using a volume-controlled mode, with a tidal volume in the range of 6 to 8 mL/kg and a positive end-expiratory pressure of 4 to 6 cmH_2O to achieve a PaO_2 >75 mmHg and a $PaCO_2$ in the range of 35 to 43 mmHg. All patients were monitored routinely by measuring invasive arterial pressure, and their mean arterial pressure was maintained at values ≥60 mmHg. Cardiac surgery was performed through a median sternotomy. Heparin dosage was calculated using a hemostasis management system (HMS; Medtronics, Inc, Minneapolis, MN). The target activated coagulation time was 480 seconds. Patients with a hematocrit value ≤30% received blood transfusion (18/30 patients). Moderate systemic hypothermia (32°C) was induced during CPB. The central aorta and the vena cava were cannulated, an arterial filter of 40 μm and a disposable membrane oxygenator (Maxima Forte, Medtronics, Inc) were used with a continuous flow of 2.4 L/min/m^2. Pump priming was performed with 1,300 mL of a crystalloid solution (Baxter, Lessines, Belgium). When mechanical ventilation was stopped, continuous positive airway pressure of 10 cmH_2O was maintained. Myocardial protection was achieved using a combination of anterograde and retrograde cold blood cardioplegia.

When moderate systemic hypothermia was achieved, 2 videos of the sublingual mucosa were recorded using an SDF camera (Microscan; MicrovisionMedical, Amsterdam, The Netherlands). After the removal of saliva by gauze, the tip of the SDF device was applied onto the sublingual mucosa as gently as possible to prevent pressure artifacts. An optical magnification of 5× was used for the acquisition of the images. Once blood vessels were discernible, the selected area was manually focused, and 2 sequences of 10 seconds each were recorded on a disk using a personal computer. As previously described,[24] the contact pressure of the probe was minimized to the point at which the small vessels remained in focus and showed maximum flow according to the online image depicted on the monitor. The 1st clip was acquired with a CPB pump flow value of 80%, whereas the 2nd image was recorded after increasing and maintaining the pump flow to a stable rate of 100% (or vice versa) for at least 2 minutes so the 2 clips related to the same area but differed for the pump flow value applied (80% or 100%). After cardiac surgery, all patients were transferred to the dedicated ICU, intubated, and mechanically ventilated.

Video sequences were analyzed blindly in a random order. Microcirculatory image analysis focused on vessels with a diameter <20 μm because they are acknowledged as the primary determinants of tissue perfusion.[25] Moreover, previous studies have revealed that most of the alterations of the microcirculation in cardiac surgery patients occur in small rather than medium or large vessels.[5,19] Semiquantitative analyses were performed using the dedicated software AVA3.0 (Automated Vascular Analysis, MicroVision Medical) developed by Dobbe et al.[26] As established in the consensus conference on the evaluation of the microcirculation,[25] the following parameters were considered: the De Backer score (DBS), the total vessel density (TVD), the microvascular flow index (MFI), the perfused vessel density (PVD), and the proportion of perfused vessels (PPV). The DBS and the TVD concern vessel density, the MFI is correlated with the type of flow in perfused vessels, and the PVD and the PPV provide information on capillary functionality and on the heterogeneity of perfusion. Each image was divided by a network made up of 3 equidistant horizontal lines crossing 3 equidistant vertical lines (the De Backer grid). The ratio between the number of times the vessels crossed the De Backer grid, and the total length of the grid gave a pure value corresponding to the DBS. The ratio between the total length of the analyzed vessels and the area of the image provided the TVD (mm/mm^2). Considering only the central lines