Effectiveness of Laser Doppler Perfusion Monitoring in the Assessment of Microvascular Function in Patients Undergoing On-Pump Coronary Artery Bypass Grafting

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Objectives: **To evaluate the effectiveness of single-point laser Doppler perfusion monitoring (LDPM) in the assessment of microvascular reactivity in the skin during cardiopulmonary bypass (CPB).**

Design: **Cross-sectional observational study.**

Setting: **Government-affiliated teaching hospital.**

Participants: **Twenty male patients aged 60 ± 2 years who underwent coronary artery bypass grafting under CPB.**

Interventions: **The authors assessed the endothelium-dependent vasodilation of the skin microcirculation at the forehead and forearm using LDPM coupled with thermal hyperemia. This measurement was performed before and after the induction of anesthesia, during and after CPB, and 24 h after the end of the surgical procedure.**

Results: **The basal values of microvascular flow before the induction of anesthesia were significantly higher in the skin of the forehead compared with that of the forearm. There were no significant alterations in microvascular reactivity throughout the recording periods for both recording sites, as assessed by the vasodilation range expressed as cutaneous vascular conductance (arbitrary perfusion units / mean arterial pressure).**

Conclusions: **Using LDPM, the authors showed that the microcirculatory bed of the skin of the forehead, which is readily accessible during cardiac surgery, is a suitable model for the study of microvascular reactivity and tissue perfusion in cardiovascular surgical procedures using CPB. This technique could, thus, be suitable for evaluating the effects of drugs or technical procedures on tissue perfusion during cardiac surgery under cardiopulmonary bypass.**

KEY WORDS: laser Doppler, skin microvascular reactivity, cardiopulmonary bypass, perfusion monitoring

CARDIOPULMONARY BYPASS (CPB) is an essential technique for most cardiac surgical procedures. Nevertheless, CPB induces a complex systemic inflammatory response and coagulation system activation, and the subsequent organ dysfunction can result in various postoperative complications.[1–3] The involvement of systemic microcirculatory dysfunction in this response is well recognized, emphasizing the importance of an adequate microcirculatory blood flow and appropriate organ perfusion and oxygen delivery to the tissues.[4,5]

Cutaneous microcirculation currently is regarded as a model of generalized microvascular reactivity, mainly because of its accessibility in the clinical setting and its correlation with microvascular function in different vascular beds.[6,7] Because the skin's microvascular bed may mirror generalized systemic vascular function in both magnitude and underlying mechanisms,[8,9] this vascular bed has been used to investigate microvascular function in a variety of cardiometabolic diseases, including hypercholesterolemia,[10] hypertension,[11,12] diabetes,[13,14] coronary artery disease,[15,16] congestive heart failure[17] and metabolic syndrome.[18]

Laser Doppler perfusion monitoring (LDPM), coupled with physiologic or pharmacologic stimuli, is a noninvasive methodology used in the clinical evaluation of systemic and local microvascular endothelial function.[19] Although LDPM does not provide an absolute measure of blood flow in volume per time, the existence of a linear relationship between the laser Doppler signal and the skin microvascular blood flow already has been demonstrated.[20] For that reason, LDPM commonly is coupled with reactivity tests, such as thermal provocation.[6] Local heating of the skin induces a microvascular response known as "local thermal hyperemia" (LTH), which is useful in the evaluation of systemic microvascular endothelial function.[19,21] This methodology currently is used to evaluate microvascular reactivity in several clinical situations such as diabetes,[22,23] advanced age,[24,25] and renal failure.[26,27] Furthermore, thermal hyperemia has been used as a clinical surrogate marker in various diseases, such as Raynaud's phenomenon and systemic sclerosis.[28,29] Nevertheless, LDPM coupled with LTH has never been used to evaluate microvascular reactivity during surgery. Moreover, the use of CPB during cardiac surgery could preclude the use of skin LDPM in this situation because of the marked alterations in hemodynamic and biochemical parameters.

Thus, the aim of the present study was to evaluate the usefulness of LDPM to assess microvascular reactivity in the skin during CPB. LDPM could be suitable for evaluating systemic microvascular perfusion and reactivity during cardiac surgical procedures.

METHODS

This cross-sectional observational study, conducted at a tertiary healthcare center, included 20 consecutive male patients aged 60 ± 2 years with multivessel coronary artery disease who underwent coronary artery bypass grafting using cardiopulmonary bypass (CPB) at the National Institute of Cardiology, Rio de Janeiro, Brazil. Microvascular

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Table 1. The demographic and perioperative characteristics of study patients.

Characteristics	
Age (years)	60 ± 2
Weight (kg)	82 ± 3
Height (cm)	172 ± 9
Body mass index	27 ± 4
Arterial hypertension n (%)	16 (80)
Diabetes n (%)	9 (45)
Chronic renal failure n (%)	2 (10)
Central temperature before CPB (°C)	36 (35.1-36.4)
Central temperature during CPB (°C)	35 (34.9-35.5)##
Total CPB time (min)	92 ± 5
CPB flow (L/min/m2)	2.7 ± 0.1
Hemoglobin before CPB (g/dL)	13.2 ± 0.3
Hemoglobin during CPB (g/dL)	9.2 ± 0.3###
Hematocrit before CPB (%)	40.4 ± 0.9
Hematocrit during CPB (%)	28.5 ± 0.9###
Plasma lactate levels before CPB (mmol/L)	1 (0.7-1.4)
Plasma lactate levels during CPB (mmol/L)	3.4 (2.5-3.8) ###
MAP before anesthesia induction (mmHg)	91.5 ± 3.5
MAP after anesthesia induction (mmHg)	85.8 ± 3.4
MAP during CPB (mmHg)	54.7 ± 3.9***
MAP after CPB (mmHg)	71.5 ± 2.3***
MAP 24 h after end of surgery (mmHg)	74.3 ± 2.4***

The results are presented as the means ± SEM or as the medians (interquartile intervals).
CPB: cardiopulmonary bypass; MAP: mean arterial pressure.
***p < 0.0001 vs. before induction.
##p < 0.001.
###P < 0.0001 vs. before CPB.

blood flow was evaluated before and after the induction of anesthesia, during and after CPB and 24 hours after the end of the surgical procedure. The perioperative characteristics of the patients are described in Table 1. The present study was undertaken in accordance with the Helsinki Declaration of 1975 as revised in 2000. The study was approved by the Institutional Review Board (IRB) of the National Institute of Cardiology under protocol number # 0362/14-12-2011 and registered with the U.S. National Institutes of Health (ClinicalTrials.gov) with identifier NCT01616069.

Exclusion criteria included indications for emergency surgery, unstable angina and recent acute myocardial infarction (less than three months), plasma creatinine levels higher than 2.0 mg/dL, severe chronic obstructive pulmonary disease (predicted FEV_1 – forced expiratory volume <40%), the presence of active infection, class IV congestive heart failure (CHF) or EF < 30%, malignancy or immunosuppressive diseases, recent stroke (less than 1 year) and coagulation disorders. Once they were considered eligible, all prospective subjects were provided with an IRB-approved consent form, which they then signed upon their agreement to participate in the study.

The endothelium-dependent vasodilation of skin microcirculation was evaluated using a double-channel single-point LDPM system (Periflux 5001, Perimed, Järfälla, Sweden) for noninvasive and continuous measurements of skin microvascular perfusion changes (arbitrary perfusion units [APU] = 10 mV). After measuring the resting microvascular flow for five minutes using two heating laser probes (PF 457, Perimed) that were positioned on the skin of the forehead and forearm at the beginning of the anesthetic procedures (Fig 1), the authors investigated the maximal microvascular vasodilation using prolonged (20 minutes) local heating of the laser probe to 44 °C, as previously described.[30] The use of the area under the blood flow/time curve (AUC, expressed as APU/s) to assess skin microvascular reactivity using LDPM previously has been validated[31–33] and was calculated using PeriSoft for Windows 2.5 (Perimed, Järfälla, Sweden). Skin microvascular flow also was evaluated using the difference from the peak to baseline (P – B) cutaneous vascular conductance (CVC, expressed as APU/mean arterial pressure).

Patient care during surgery was standardized and included invasive arterial pressure monitoring, pulse oximetry and end-tidal carbon dioxide monitoring, urine output, electrocardiogram, central venous pressure, nasopharyngeal temperature monitoring and transesophageal echocardiography (GE Vivid®, Helsinki, Finland). All patients received the same anesthetic regimen, which included midazolam, etomidate, fentanyl and isoflurane for anesthesia and cisatracurium for neuromuscular relaxation. General anesthesia was induced with midazolam (0.05-0.1 mg/kg), etomidate (0.3 mg/kg) and fentanyl (10 μg/kg). Endotracheal intubation was facilitated with intravenously administered cisatracurium (0.2 mg/kg). The patients' lungs were mechanically ventilated with a tidal volume of 6-8 mL/kg and a respiratory rate of 12 breaths/min with a mixture of air and oxygen at a ratio of 50:50 and a positive end-expiratory pressure of 3 mmHg. The ventilator parameters were adjusted to attain a $PaCO_2$ of 35-40 mmHg. Anesthesia was maintained using continuous intravenous infusions of fentanyl (1-5 μg/kg/h) and cisatracurium (2.0 μg/kg/min) and 1-2 MAC isoflurane. CPB was established with a nonpulsatile flow between 2.5 and 3.5 L/min/m^2 using a membrane oxygenator and a 27-μm arterial line filter. During CPB, anesthesia was maintained with an intravenous infusion of propofol (50-75 μg/kg/min). Each patient's esophageal temperature was monitored continuously and maintained at 36 ± 1 ºC during CPB. CPB performed under temperatures of approximately 36 °C usually is considered CPB under normothermic conditions. The

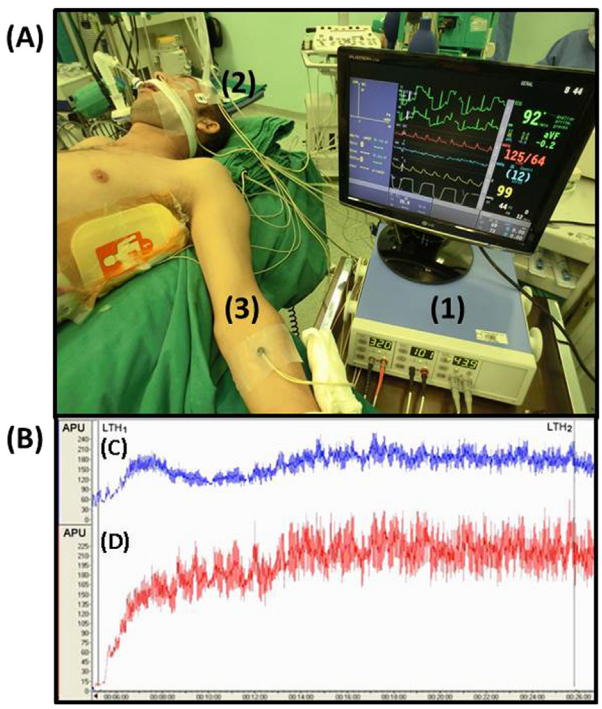

Fig 1. Picture of the experimental setup used to assess skin microvascular perfusion using laser Doppler perfusion monitoring (A). A representative example of the effects of heating on skin microvascular blood flow (B) in the forearm (C) and the forehead (D). (1) Laser Doppler unit, (2) forehead heating probe, (3) forearm heating probe (see methods). APU, arbitrary perfusion units; LTH_1: start of local thermal hyperemia; LTH_2: end of local thermal hyperemia.