Microcirculatory Alterations in Cardiac Surgery: Effects of Cardiopulmonary Bypass and Anesthesia

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Background. **Heterogeneity in microvascular perfusion is associated with impaired tissue oxygenation. We hypothesized that cardiac surgery with or without cardiopulmonary bypass (CPB) could induce microvascular alterations.**

Methods. **We used an orthogonal polarization spectral imaging technique to evaluate the sublingual microcirculation in patients undergoing cardiac surgery with (n = 9) or without (n = 6) CPB. We also included, as a control group, 7 patients undergoing thyroidectomy with the same anesthetic procedure. Hemodynamic and microcirculatory variables were obtained the day before surgery, after induction of anesthesia, during CPB, on admission to the intensive care unit or the recovery room, and 6 and 24 hours after the end of the surgical procedure. Data are presented as median (25th to 75th percentile).**

Results. **No differences in hemodynamic variables were observed between the two cardiac surgery groups. The proportion of perfused vessels was similar in all three groups at baseline (89% [87% to 90%]), and decreased similarly after induction of anesthesia to 71% (69% to 74%). It decreased further during CPB to 53% (50% to 56%). On admission to the intensive care unit or recovery room, alterations were more severe in CPB than in off-pump patients (60% [59% to 62%] versus 64% [61% to 65%]; $p = 0.03$), whereas they had already normalized in thyroidectomy patients (89% [86% to 90%]; $p = 0.0005$ versus cardiac surgery). In both cardiac surgery groups these microcirculatory alterations decreased with time, but persisted at 24 hours. The severity of microvascular alterations correlated with peak lactate levels after cardiac surgery ($y = 11.5 - 0.15x$; $r^2 = 0.65$; $p < 0.05$).**

Conclusions. **Microcirculatory alterations are observed in cardiac surgery patients whether or not CPB is used. Anesthesia contributes to these alterations, but its effects are transient.**

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Cardiac surgery is sometimes associated with organ dysfunction, and the severity of postoperative organ dysfunction is associated with intensive care unit (ICU) length of stay and mortality [1]. The mechanisms leading to organ dysfunction may include global hemodynamic alterations, regional blood flow alterations, mitochondrial dysfunction, and microcirculatory alterations.

Skin and gut microvascular blood flows may be altered in cardiac surgery patients [2, 3] whereas skin reactive hyperemia was preserved after surgery with cardiopulmonary bypass (CPB) [4]. However, the techniques used in these studies do not assess the heterogeneity of microvascular blood flow. New techniques such as orthogonal polarization spectral imaging allow the direct visualization of the microcirculation at bedside [5, 6]. Bauer and colleagues [7] reported that functional capillary density decreased slightly and transiently during CPB, but baseline values were obtained after induction of anesthesia and patients were monitored for only 1 hour after CPB discontinuation. Similarly, microvascular alterations were observed in 6 patients admitted to the ICU after cardiac surgery [8]. In both studies, all measurements were obtained while patients were anesthetized. As anesthetic agents impair the microcirculation [9], these observations may underestimate the severity of the microvascular alterations.

Cardiac surgery, with or without CPB, is associated with an inflammatory reaction that may promote microcirculatory alterations. Cardiopulmonary bypass is associated with release of mediators [10] that seem to be involved in the alterations in tissue permeability [11]. The inflammatory reaction may be less significant when CPB is not used [12], even though this was challenged [13]. The role of CPB on microvascular alterations remains thus poorly defined.

The goal of this study was to investigate the microcirculation perioperatively in patients undergoing cardiac surgery with or without CPB. We hypothesized that microvascular alterations may be present after cardiac surgery, especially in the presence of CPB. To separate

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the effects of cardiac surgery from those of anesthesia, we also studied patients scheduled for elective thyroidectomy in whom the same anesthesia was used.

Material and Methods

The study was approved by the institutional ethics committee, and each patient gave written informed consent before inclusion. We enrolled 15 adult patients scheduled for elective cardiac surgery (coronary artery bypass and or valvular surgery) with (n = 9) or without (n = 6) CPB and 7 patients undergoing thyroidectomy (localized thyroid cancer).

Exclusion criteria were as follows: pregnancy, cirrhosis, infection, diabetes or hypertension with significant vascular complications, redo operation, left ventricular ejection fraction less than 0.40, advanced chronic lung disease, and stomatologic diseases.

Anesthetic Procedures

All cardiac surgery patients received the same anesthetic regimen. Induction was performed with propofol and remifentanil and paralysis with cisatracurium. The maintenance regimen was propofol and remifentanil at doses adjusted according to a desired target-controlled infusion.

In CPB patients, no active hypothermia was induced but body temperature was allowed to drift, usually resulting in a minimal temperature of 34° to 35°C. Patients were actively rewarmed to 36°C at the end of CPB. In the other patients, temperature was maintained with warm forced-air convection.

In CPB patients, heparin was adapted to maintain an activated clotting time longer than 450 seconds. These patients also received aprotinin up to the end of CPB. Pump priming was performed with 1000 mL of a gelatin solution (Geloplasma, Fresenius, Germany), 200 mL of Hartmann solution (Baxter, Lessines, Belgium), and 0.3 g/kg of mannitol 20% solution (Baxter). Cardiac arrest was induced with Hartman/KCl solution (retrograde or anterograde). All CPB patients received 1 g intravenous bolus of methylprednisolone at induction. The CPB pump uses a continuous flow of 2.4 L/m^2, maintaining a pressure between 60 and 90 mm Hg.

Patients undergoing cardiac surgery without CPB also received heparin to achieve an activated clotting time longer than 300 seconds during the surgical procedure. These patients did not receive aprotinin or methylprednisolone. In all cardiac surgery patients, anticoagulation was reversed at the end of surgery using protamine to achieve a normal activated clotting time.

On arrival in the ICU, sedation with propofol and analgesia with remifentanil were continued for 4 to 6 hours until achievement of normothermia, bleeding control, and hemodynamic stabilization. At that time, the patient was weaned from mechanical ventilation.

Patients undergoing thyroidectomy were anesthetized with propofol and remifentanil using the same target-controlled infusion as for patients undergoing cardiac surgery. These patients were extubated at the end of the surgical procedure.

All patients undergoing cardiac surgery had arterial and central venous lines placed. All but 2 patients (both in the off-pump group) were also monitored with a

Table 1. Baseline Characteristics and Type of Surgery

	Type of Surgery		
	Cardiac Surgery		
Characteristic	CPB CABG (n = 6) CABG + valve (n = 3)	Off-pump CABG (n = 6)	Thyroidectomy for Thyroid Cancer (n = 7)
Number of grafts	2 grafts (n = 4) 3 grafts (n = 3) 4 grafts (n = 2)	1 graft (n = 1) 2 grafts (n = 4) 4 grafts (n = 1)	NA
Heart exposure	Sternotomy (n = 9)	Sternotomy (n = 4) Lateral thoracotomy (n = 2)	NA
Patients	(n = 9)	(n = 6)	(n = 7)
Age (y)	66 (55–75)[a]	66 (65–70)[a]	59 (55–65)
Male/female sex	6/3[a]	6/0[a]	3/4
Diabetes (no. of patients)	4	3	2
Hypertension (no. of patients)	5	3	3
MAP (mm Hg)	96 (83–100)	87 (82–93)	82 (78–88)
HR (beats/min)	69 (60–77)	60 (59–61)	70 (64–77)
RR (breath/min)	16 (15–19)	17 (15–19)	17 (16–19)
Hemoglobin concentration (g/dL)	14.4 (13.3–15.7)	14.9 (14.0–15.3)	14.0 (13.1–14.9)
SOFA score	1 (0–1)	1 (0–1)	1 (0–1)

[a] $p < 0.05$ versus thyroid surgery.

CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; HR = heart rate; MAP = mean arterial pressure; NA = not applicable; RR = respiratory rate; SOFA = sequential organ failure assessment.

Table 2. Evolution of Global Hemodynamic and Microcirculatory Variables in the Three Groups[a]

Variable	Baseline	Induction	CPB	End Surgery	6 h After Surgery	24 h After Surgery	ANOVA		
							G × T	G	T
Macrocirculatory variables									
Mean arterial pressure (mm Hg)									
CPB	96 (83–100)	76 (72–77)	59 (56–67)[c]	81 (77–85)	77 (74–80)	78 (75–79)			
Off-pump	87 (82–93)	75 (63–80)	NA	79 (70–85)	75 (69–77)	79 (71–79)	0.10	0.02	0.0001
Thyroidectomy	82 (78–88)	76 (71–81)	NA	77 (66–82)	79 (72–84)	76 (74–84)			
Cardiac index ($L \cdot min^{-1} \cdot m^{-2}$)									
CPB	NA	4.2 (4.0–5.1)	2.1 (2.0–2.3)[d]	4.5 (3.8–5.3)	4.0 (3.5–4.6)	3.5 (3.1–3.9)			
Off-pump	NA	4.5 (3.9–5.2)	NA	4.6 (3.8–5.3)	4.0 (3.3–4.6)	3.6 (3.1–4.1)	0.85	0.88	0.04
Thyroidectomy	NA	NA	NA	NA	NA	NA			
Microcirculatory variables									
Vessel density (all vessels; n/mm)									
CPB	7.5 (6.4–7.7)	7.4 (6.7–7.7)	7.2 (6.8–7.6)	7.6 (7.0–8.2)	7.7 (6.7–8.3)	7.9 (6.9–8.1)			
Off-pump	6.8 (6.5–7.7)	7.1 (6.3–8.2)	NA	7.7 (7.0–8.1)	7.4 (7.1–8.4)	7.8 (6.9–8.2)	0.99	0.91	0.33
Thyroidectomy	7.2 (7.0–7.7)	7.6 (7.1–8.1)	NA	7.7 (7.6–7.8)	7.6 (6.9–7.9)	7.8 (7.6–8.0)			
Perfused small vessel density (n/mm)[b]									
CPB	4.3 (3.8–5.1)	3.4 (3.1–4.1)[e]	2.8 (2.5–3.0)[f]	3.1 (2.8–3.6)[gh]	3.8 (2.8–4.4)[ij]	4.4 (3.9–4.7)[k]			
Off-pump	4.6 (4.4–5.1)	3.8 (3.3–4.9)	NA	3.7 (3.2–4.1)[lm]	4.0 (3.8–4.7)[n]	4.8 (3.9–5.1)	0.31	0.03	0.006
Thyroidectomy	4.5 (4.4–4.9)	3.9 (3.5–4.1)[o]	NA	5.0 (4.8–5.1)	5.0 (4.3–5.3)	5.1 (4.9–5.4)			
Vasopressor and inotropic requirement, n (dose range in $\mu g \cdot kg^{-1} \cdot min^{-1}$)									
CPB			NE, 4 (0.05–0.12)	NE, 1 (0.04) DB, 5 (3–5)	DB, 1 (5)	DB, 1 (5)			
Off-pump				NE, 1 (0.11)			NA	NA	NA
Thyroidectomy				DB, 1 (5)					

[a] Number of patients per group: cardiac surgery with CPB (n = 9), cardiac surgery off-pump (n = 6), and thyroidectomy (n = 7). [b] Small vessels are defined by a diameter <20 μm.

Post-hoc statistical comparisons: [c] $p = 0.012$; [d] $p = 0.012$; [e] $p = 0.038$; [f] $p = 0.012$; [g] $p = 0.028$; [i] $p = 0.028$; [l] $p = 0.043$; [n] $p = 0.043$; [o] $p = 0.021$ compared with baseline; and [h] $p = 0.047$; [j] $p = 0.013$; [k] $p = 0.013$; [m] $p = 0.007$ versus thyroid surgery.

ANOVA = two-way analysis of variance for group × time interaction (G × T), groups (G), and time (T); CPB = cardiopulmonary bypass; DB = dobutamine; NA = not available (insufficient observations); NE = norepinephrine.

pulmonary artery catheter (Edwards Lifesciences, Irvine, CA). In thyroidectomy patients, blood pressure was monitored noninvasively and a central venous catheter was not used.

Study Periods

The study of the microcirculation and the collection of data were performed at baseline preoperatively (the day before surgery), after the induction of anesthesia, 30 to 45 minutes after the start of CPB in patients undergoing CPB, on admission to the ICU (cardiac surgery) or recovery room (thyroidectomy) (end surgery period), and 6 and 24 hours after the end of the surgical procedure.

Study of the Microcirculation

We studied the sublingual microcirculation using the Cytoscan A/RII (Cytometrics, Philadelphia, PA) with a 5× objective (167× magnification) using standard operating procedures [5, 14].

After gentle removal of secretions, the device was applied to the lateral side of the tongue at 2 cm from the tip of the tongue. Five sequences of 20 seconds each were recorded on a computer using a video card (MicroVideo, Pinnacle Systems), stored under a random number, and later analyzed semiquantitatively [5] by an investigator (Marc-Jacques Dubois) blinded to the origin of the sequence. To ensure consistency in the readings, 10% of the images were reviewed by the senior investigator (Daniel De Backer).

Three horizontal and three vertical lines were drawn over the video screen. Vessel density was calculated as the number of vessels crossing these lines divided by the total length of the lines. The type of flow was defined as continuous, intermittent, or absent (nonperfused). The proportion of perfused vessels (%) was calculated as the number of continuously perfused vessels divided by the total number of vessels. Perfused vessel density (n/mm) was calculated as vascular density times the proportion of perfused vessels. The vessels were separated according to their diameter into large and small vessels using a cutoff of 20 μm (vessels smaller than 20 μm mostly represent capillaries and vessels larger than 20 μm mostly venules; arterioles are not visualized as these are located in deeper layers). In each patient, the values of the five areas were averaged.

With this methodology, we previously reported intraobserver variability close to 5% [5] and a repeatability coefficient of 5% between successive measurements [14]. Accordingly, changes greater than 10% can be considered significant.

Data Collection

Age, sex, type of planned surgery, significant past medical history, left ventricular ejection fraction, and current therapy were collected at baseline. Mean arterial pressure, heart rate, respiratory rate, and pulse oximetry were obtained at each time period. In patients undergoing cardiac surgery, mean pulmonary artery pressure, pulmonary artery occlusion pressure, central venous pressure, cardiac index, and mixed venous oxygen saturation were also measured. Blood gas values, hemoglobin, and blood lactate concentrations were measured using a blood gas analyzer (ABL4; Radiometer, Copenhagen, Denmark). Pump pressure and flow levels were measured at the time of microvascular examination during CPB. Acute Physiology and Chronic Health Evaluation II [15] and Sequential Organ Failure Assessment (SOFA) [16] scores were also calculated for the cardiac surgery patients.

Statistical Analysis

We anticipated that cardiac surgery could lead to a 20% decrease in the proportion of perfused vessels. As the proportion of perfused vessels is expected to be close to 95% at baseline, we calculated that 13 patients should be included to achieve 80% power with an alpha error level of 5%. We increased this number to 15 patients to account for a variable magnitude of the effect.

To ensure coherence in image reading, the interobserver agreement was assessed with Kappa statistics for ordinal data in the 10% of sample images that were analyzed by 2 investigators.

As the data were not normally distributed (Kolmogorov-Smirnov test), nonparametric tests were used. Data were analyzed by a two-way analysis of variance (time, n = 6, and group, n = 3) to evaluate the difference in the evolution of microvascular blood flow in the different groups. Statistical differences among the different periods were assessed by a Friedman test followed by a Wilcoxon test with Bonferroni adjustment for multiple comparisons.

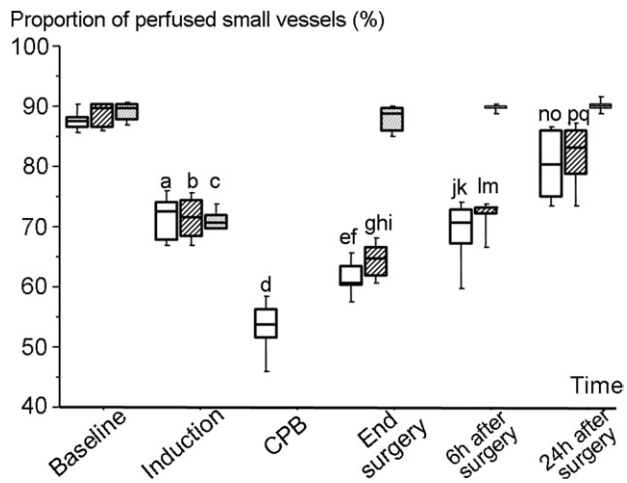

Fig 1. Evolution of the proportion of perfused small vessels in patients undergoing cardiac surgery with (white boxes, n = 9) and without (hatched boxes, n = 6) cardiopulmonary bypass (CPB), and in patients undergoing thyroid surgery (dotted boxes, n = 7). Analysis of variance: group × time interaction $p < 0.0001$, group comparisons $p < 0.0001$, and time effect $p < 0.0001$. Post-hoc comparisons: $^{a}p = 0.008$; $^{b}p = 0.03$; $^{c}p = 0.04$; $^{d}p = 0.002$; $^{e}p = 0.008$; $^{g}p = 0.03$; $^{j}p = 0.012$; $^{l}p = 0.03$; $^{n}p = 0.008$; $^{p}p = 0.04$, compared with baseline; $^{h}p = 0.03$, without versus with CPB; and $^{f}p = 0.0015$; $^{i}p = 0.004$; $^{k}p = 0.0019$; $^{m}p = 0.004$; $^{o}p = 0.0015$; $^{q}p = 0.004$, versus thyroid surgery.

Table 3. Evolution of Lactate Levels in the Cardiac Surgery Groups[a]

Sample time	Lactate Levels (mEq/L)				Difference Between Groups, *p* Value
	CPB (n = 9)	*p* Value versus Induction	Off-Pump (n = 6)	*p* Value versus Induction	
Induction	1.1 (0.8–1.4)	. . .	0.9 (0.7–1.0)	. . .	0.45
Peak lactate level	3.6 (3.3–4.6)	0.008	1.4 (1.2–2.2)	0.04	0.007
24 h after surgery	1.8 (1.2–2.5)	0.04	1.1 (1.0–1.2)	0.07	0.02

[a] Lactate levels were not available in thyroidectomy patients.

CPB = cardiopulmonary bypass.

Linear regression was also used to assess relationships between microcirculatory alterations and temperature, pH, hemoglobin concentration, arterial oxygen saturation, arterial partial pressure of oxygen, pump pressure, and flow levels during CPB.

Data are expressed as median (25th and 75th percentiles). A probability value less than 0.05 was considered as statistically significant. All analyses were performed with the StatView program (StatView for Windows, version 5.0; SAS Institute, Cary, NC).

Results

Baseline Characteristics

The baseline data and the type of surgery are presented in Table 1. There were no differences among the three groups except for a younger age and a larger proportion of female patients in the thyroidectomy group.

Study of the Microcirculation

Agreement between the 2 investigators was excellent with a Kendall W coefficient of concordance of 0.93 ($p < 0.001$). The mean difference in evaluating the proportion of perfused vessels was 3% ± 2%.

In all groups, total vessel density did not change with time (Table 2). The proportion of perfused large vessels was 100% (100% to 100%) at baseline in the three groups and remained unaltered (data not shown).

In the CPB group, the proportion of perfused small vessels decreased significantly after induction of anesthesia (Fig 1). This decrease was more pronounced during CPB; it improved slightly thereafter but failed to return to baseline value and persisted after 24 hours. The off-pump cardiac surgery patients exhibited less severe microcirculatory alterations in the immediate postoperative period (Table 2, Fig 1); these alterations improved slightly thereafter but also persisted after 24 hours. As a result, microvascular perfusion was altered similarly in CPB and off-pump patients 6 and 24 hours after ICU admission. In thyroidectomy patients, significant microcirculatory alterations were present after induction of anesthesia, but these changes reversed rapidly in the postoperative period.

In all groups, the decreased perfusion of small vessels was attributable to an increase in both intermittently perfused and nonperfused vessels (data not shown).

Hemodynamic and Laboratory Data

There were no differences at baseline in heart rate, mean arterial pressure, or respiratory rate among the groups (Table 1). After induction of anesthesia, mean arterial pressure was similar in the three groups (Table 2), and cardiac index was similar in the CPB and off-pump groups. During CPB, pump blood flow and arterial pressure were lower than corresponding variables during anesthesia alone. On ICU admission, mean arterial pressure and cardiac index were similar in both cardiac surgery groups and did not differ compared with values at induction of anesthesia. Low doses of dobutamine and norepinephrine were used in a few patients during surgery and at the end of surgery, with rapid weaning after ICU admission (Table 2). None of the thyroidectomy patients required vasopressors agents.

Core temperature decreased during cardiac surgery especially during CPB, but there was no difference in temperature in the cardiac surgery groups at any other time (data not shown). There were no differences in mean pulmonary arterial pressure, pulmonary artery occlusion pressure, central venous pressure, mixed venous oxygen saturation, oxygen delivery, oxygen consumption, oxygen extraction ratio, and blood gas and hemoglobin concentrations in the two groups of cardiac surgery patients (data not shown). Peak lactate value was higher in CPB than in off-pump patients; lactate levels remained

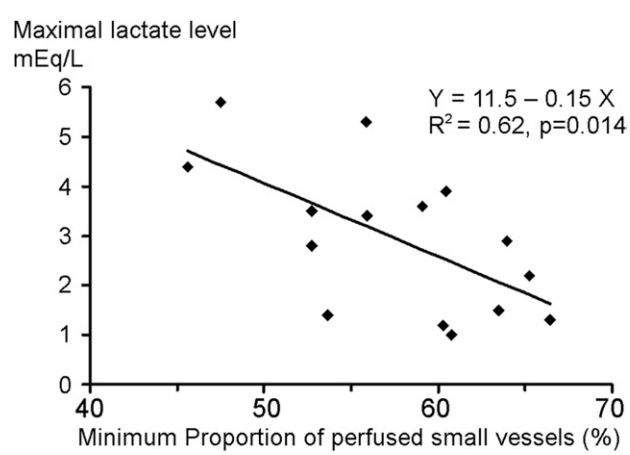

Fig 2. Relationship between minimum proportion of perfused small vessels and peak lactate level in patients undergoing cardiac surgery ($y = 11.5 - 0.15x$; $r^2 = 0.62$; $p = 0.014$).

slightly higher at the time of ICU discharge in the CPB group (Table 3).

Postoperative Course and Organ Function

The postoperative course was uneventful in all patients. At baseline, all groups had a SOFA score of 1 (0 to 1) but at 24 hours there was an increase in the SOFA score in the cardiac surgery patients (to 3 [3 to 3] in the CPB group and 2 [2 to 2] in the off-pump surgery group, both $p < 0.05$ compared with baseline), although it remained stable at 1 (0 to 1) in the thyroidectomy group. A proportion of perfused small vessels less than 60% predicted a change in SOFA score of greater than 2 points with a sensitivity of 0.78 and a specificity of 0.92. A proportion of perfused small vessels less than 60% predicted a peak lactate level of greater than 3.0 mEq/L with a sensitivity of 0.86 and a specificity of 0.75.

Relationship Between Microvascular Perfusion and Other Variables

There was no relationship between microcirculatory and systemic hemodynamic and blood gas variables (data not shown). During CPB, there was no relationship between the proportion of perfused small vessels and pump pressure or flow ($r^2 = 0.07$ for both; $p = 0.53$), core temperature ($r^2 = 0.05$; $p = 0.91$), or hemoglobin concentration ($r^2 = 0.26$; $p = 0.20$). There was a significant relation between the minimum proportion of perfused small vessels and the peak lactate level in the cardiac surgery patients (Fig 2).

There was a significant relationship between changes in the SOFA score and maximal change in small vessel perfusion ($y = -0.06x - 0.26$; $r^2 = 0.38$; $p = 0.004$) or minimum proportion of perfused small vessels ($y = -0.06x + 5$; $r^2 = 0.38$; $p = 0.004$).

Comment

This study indicates that cardiac surgery is associated with significant microcirculatory alterations, characterized by a decrease in proportion of perfused small vessels and a decreased density of perfused small vessels. These alterations were more severe and less transient than in another type of surgery using the same anesthetic technique. Cardiopulmonary bypass induced a further transient alteration in microvascular perfusion.

These microvascular alterations were characterized by a marked heterogeneity of perfusion reflected by the decreased proportion of perfused small vessels [17]. As in septic patients [5, 18], the alterations were independent of global hemodynamic variables. Importantly, distribution of perfusion is more critical for tissue oxygenation than total blood flow to the area because heterogeneity of perfusion is more poorly tolerated than a homogeneous decrease in organ perfusion [19, 20].

One may expect these alterations to be more severe after CPB, because this procedure is associated with endothelial injury [21] and impaired red blood cell deformability [22]. Cardiopulmonary bypass was associated with further deterioration in microvascular perfusion, but this was minor and transient, as reported by others [7]. Importantly, our study design allowed us to identify long-lasting microcirculatory alterations specifically related to cardiac surgery, as they were not observed in another type of surgery using the same anesthesia.

What could explain these alterations specific to cardiac surgery, even in the absence of CPB? First, the inflammatory response may not be less in cardiac surgery patients not undergoing CPB [13]. Second, these patients also undergo ischemia-reperfusion injury, related to transient decreases in global perfusion during manipulation of the myocardium and clamping of the coronary arteries. Of note, corticosteroids were given before CPB, which may affect the inflammatory response induced by CPB [23]. As steroids may also improve the sublingual microcirculation [9], the differences between the two groups may have been more pronounced without corticosteroids.

General anesthesia can contribute to these microvascular alterations. Numerous experimental studies have shown important effects of different anesthetic agents on the microcirculation [24, 25]. In humans, the hyperemic response to an occlusion test is altered not only during midazolam and sufentanil administration [26] but also during propofol administration [27], suggesting that these agents may alter the human microcirculation. We recently showed that propofol alters the sublingual microcirculation during brief anesthetic procedures [9]. As it is impossible to study a control group of patients without anesthesia, we included a group of patients undergoing a less invasive procedure but with the same anesthetic agents given at similar doses. Anesthesia induced similar alterations in the three groups, but these were further exacerbated and prolonged only in cardiac surgery patients. Of note our study cannot discriminate between a direct effect of one of these agents and an indirect effect (ie, caused by release of endogenous catecholamines). Anesthesia may, therefore, contribute to microvascular alterations, but is not a major player.

Other factors may have influenced the microcirculation, including the decrease in core temperature. However, the influence of moderate hypothermia on the microcirculation is questionable and disappears with rewarming [28]. We observed no relationship between the severity of microvascular alterations and core temperature. Hemodilution and acidosis may also play a role, but we failed to observe any relationship between microvascular alterations and hemoglobin levels or pH. The type of blood flow during CPB may also influence the microcirculation. We used continuous blood flow; pulsatile flow may be associated with less severe microvascular alterations [29], although other investigators failed to identify differences in microcirculatory effects of pulsatile and nonpulsatile flows [30].

It is unlikely that the microvascular alterations we observed were related to the decreased metabolism as it should be accompanied by a homogeneous decrease in capillary density whereas we observed the opposite. In addition, the relationship between the severity of microvascular alterations and peak lactate levels suggests that

the microvascular alterations were associated with impaired cellular oxygenation.

Finally, cardiac surgery patients were more frequently treated with vasoactive agents than thyroidectomy patients. Norepinephrine administration is associated with an impairment in microvascular perfusion in control conditions [31] but not when this agent is used to restore blood pressure in shock [32]. Several studies have shown that dobutamine can improve the diseased microcirculation [18, 33]. Thus the more frequent use of norepinephrine and dobutamine in the cardiac surgery patients is unlikely to explain these microvascular alterations.

What are the implications of these findings? At 24 hours, cardiac surgery patients still showed some degree of microvascular alterations and had a small increase in the SOFA score. These observations are in line with recent findings in septic patients showing that the evolution of microvascular perfusion is inversely related to changes in organ function [34] and that persistent microvascular alterations are associated with a poor outcome [35]. Recently, Jhanji and associates [36] reported that microvascular alterations were associated with development of perioperative complications after major abdominal surgery.

Our study has some limitations. First, the number of patients was relatively small and not powered for subgroup analysis between cardiac surgery patients, so that we may have missed minor differences attributable to CPB. However, these data, obtained in a homogeneous group of patients studied during a relevant time interval, already show that some important microvascular derangements occur during cardiac surgery, and the study was powered for this purpose. Second, the sublingual area may not be representative of other vascular beds [37]. Nevertheless, multiple studies have shown that the severity and persistence of sublingual microvascular alterations are associated with a poor outcome in patients with severe sepsis [5, 34, 35], cardiac failure [6], or abdominal surgery [36]. This suggests that sublingual microvascular alterations reflect a generalized microvascular dysfunction, although more severe alterations may occur in other organs because of their specific anatomy or alterations in regional perfusion. Finally, it should be noted that differences between CPB and off-pump groups are not only related to the use of CPB but include other factors related to surgical approach (ie, thoracotomy versus sternotomy, number of grafts, associated procedures), and these may also influence the microcirculation. Finally, we assessed the microcirculation using a semiquantitative analysis. Although manually driven, the determination of vessel density is quantitative; only determination of flow may be considered as subjective. We [5, 14] and others [38] have previously reported the excellent reproducibility of this semiquantitative analysis. Agreement in this study was also excellent. In addition, the magnitude of the changes was similar to those observed using a computer-aided microvascular assessment [7, 8].

In conclusion, microcirculatory alterations are observed in patients undergoing cardiac surgery; CPB plays a minor role in these changes. Anesthesia partially contributed to these alterations, directly or indirectly, but could not by itself explain the severity of the lesions and their persistence up to 24 hours after the surgical procedure.

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