Cardiopulmonary Bypass and Forearm Blood Flow*

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Study objective: To assess the effect of cardiopulmonary bypass (CPB) on muscle blood flow (MBF) when measured in the forearm by venous occlusion plethysmography.

Design: This was a prospective study.

Setting: Operating room area of a tertiary care university medical center.

Participants: Twenty-seven patients (25 men and 2 women), aged 62 ± 1.5 years, undergoing elective coronary bypass grafting.

Interventions: Measurements were made during the surgical procedure: before, during cold and warm, and after discontinuation of CPB.

Measurements and results: Changes in forearm blood flow (FFB), derived forearm vascular resistance (FVR), mean arterial pressure (MAP), and cardiac output (CO) were evaluated by repeated measures analysis of variance. The control FBF (measured before CPB) was found to be approximately 50 percent lower than that previously reported for awake volunteers and patients.

The FVR was similarly higher. From these low values, the FBF increased significantly (p<0.001) during normothermic bypass and after CPB. Forearm vascular resistance decreased significantly (p<0.001) throughout the cold, warm, and postbypass periods. Only during the warm and the postbypass periods did FBF and FVR reach normal values. Mean arterial pressure decreased significantly (p<0.01) throughout. There was no statistically significant association between any of the variables and FBF or FVR. After correcting for patient and surgical phase variability, only MAP had a statistically significant effect (p=0.042) on FVR; blood temperature, skin temperature, hematocrit level, PaCO2, serum potassium, and systemic vascular resistance (SVR) had no effect on either FBF or FVR when tested singly or in combination.

Conclusion: These findings indicate that the increase in MBF seen during warm and the post-CPB periods is only a recovery toward normal blood flow. The role of this change in the low SVR that usually accompanies CPB is equivocal.

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Key words: blood pressure; cardiac surgery; cardiopulmonary bypass; muscle blood flow

deincreases, because MVR represents 40 percent of the SVR, such a decrease could force a decline in SVR, producing systemic hypotension. This potential effect of CPB on MBF has not previously been evaluated in man. The object of this study was to assess the effect of CPB on MVR as estimated by simultaneous measurement of forearm blood flow (FBF) and radial intra-arterial pressure in patients undergoing CPB.

METHODS

After this study was approved by the Institution’s Clinical Research Practices Committee, written consent was obtained from 27 patients, 25 male and 2 female, 62 ± 1.5 (SEM) years old, who were undergoing scheduled coronary bypass grafting. Those with symptoms of peripheral artery disease (ie, claudication), history of heart failure, atrial fibrillation, or ejection fraction less than 50 percent were excluded.

Radial artery pressure and FBF were measured on the left arm. Preanesthetic medication consisted of lorazepam, 0.05 mg/kg, administered by mouth and morphine, 0.1 mg/kg, given intramuscularly. Fentanyl (50 to 100 µg/kg) and midazolam (250 to 350 µg/kg) were the primary anesthetics, and pancuronium, the muscle relaxant. No nitrous oxide or volatile anesthetics were used.
Patients were ventilated with a mixture of O₂ and air, having an inspired O₂ concentration of 50 to 80 percent. Through capnography, the PaCO₂ level was maintained between 35 and 42 mm Hg by adjusting ventilation to a suitable end-tidal PCO₂. Monitoring included electrocardiography, radial and pulmonary artery pressure, and finger pulse oximetry (Satlite Datex Medical Instrumentation, Inc., Tewksbury, Mass).

Core and skin (Mallinckrodt) temperatures were measured rectally and on the distal part of the forearm under study. Blood temperature was measured in the pulmonary artery before and after CPB and in the blood returning to the oxygenator during CPB.

Radial pressure was measured through a 5-cm, 20-gauge catheter made of synthetic fluorine-containing resins (Teflon) attached to a 91-cm long, high-pressure tube, and a transducer (model T36AD-R, Spectromed, Inc., Oxnard, Calif). The system was calibrated statically to a mercury standard, and its natural frequency and damping coefficient were determined after each comparison by the flash method.²

No vasodilator or vasoactive support was used except phenylephrine, 50 ug/min, or less during normothermic CPB in two and after cessation of CPB in three patients. The FBF was measured by a mercury-in-rubber strain-gauge on the mid-forearm. The pressure of the venous occlusion cuff, placed above the elbow, was set at 20 mm Hg below the prevalent radial MAP. This was done after the circulation to the hand had been excluded at the wrist for 1 min by a cuff 4 cm wide inflated to 200 to 250 mm Hg. Changes in girth measured by the strain-gauge were equated with changes in volume of the forearm.²

Each observation consisted of 8 flow traces taken within 2 min and averaged. Only those series of tracings in which all individual flows remained within the 95 percent confidence interval for the series were included. They were secured before cannulation for bypass, 18 min after crossclamping of the aorta during mild hypothermia to 26 to 28 °C blood temperature as well as 10 min before and 10 min after discontinuation of CPB. The flows were recorded with the patient in the neutral horizontal position and the arm under study maintained at sternal level. The MAP was obtained by electronic integration and recorded during the FBF measurement. Vascular resistance was calculated as:

$$[[\text{MAP-central venous pressure}]/\text{CO}] \times 80 \text{ (dyne-s-cm}^{-5})$$

Forearm vascular resistance (FVR), expressed in arbitrary units, was the quotient of MAP and FBF. Cardiac output was measured in duplicate by thermodilution using iced saline solution. Cardiac index (CI) was derived from the CO or the oxygenator blood flow and body surface area. Additional data included heart rate, blood temperature, hematocrit value, PaCO₂, PaO₂, pH, serum potassium, and duration of CPB. The membrane oxygenator was primed with 1.5 L of Ringer’s lactate solution. Blood cardioplegia was suitably cooled and potassium loaded to 10 to 24 mEq/L, and buffered to 7.8 pH.

**Figure 1.** Behavior of FBF (a), FVR (b), SVR (c), and comparison of the decrease in SVR and FVR (d) as a percentage of the control resistance. The FVR decreased more than the SVR, and both changed in a similar direction; however, statistically they were not related.
Using repeated measures analysis of variance, we tested MAP, FBF, FVR, SVR, CI, blood temperature, skin temperature, hematocrit level, PaCO\(_2\), PaO\(_2\), pH, and serum potassium value for significant (p<0.05) variability during the surgical phases of CPB (pre-CPB, cold-CPB, normothermic-CPB, and post-CPB). When a significant difference for any of these variables was found, contrasts were performed to determine in which surgical phases the values were different from the pre-CPB baseline. The contrasts' alpha (probability values) levels were adjusted for multiple comparisons using the Bonferroni method. The effect of the aforementioned variables on FBF and FVR was tested using a repeated measures analysis of variance design with the covariate values changing with each surgical phase. The covariates were tested singly, as a group, and in combinations formed by stepwise elimination of the least significant covariates. Covariates tested were MAP, blood temperature, skin temperature, hematocrit level, PaCO\(_2\), and SVR. We also tested for associations between combinations of the previously noted variables and FBF or FVR using multivariate (canonical) correlation analysis with adjustments for the surgical phase. All results are expressed as mean ±SEM.

RESULTS

There were 25 male and 2 female patients, 62 ±1.5 years of age, and the frequency response and damping coefficient of the blood pressure measuring system were 23 ±0.6 and 0.3 ± 0.0 Hz, respectively. The MAP decreased significantly (p<0.001) during both periods of bypass and the postbypass period (Table 1). The FBF was 1.6 ±0.1 mmol/100 mmol tissue/min during the prebypass period and increased slightly to 1.8 ±0.1 during cold bypass, and to 3.7 ±0.3 and 3.6 ±0.3 during the warm and the postbypass periods, respectively. The PaCO\(_2\) (uncorrected for body temperature), PaO\(_2\), and pH were similar during the four study periods. Rectal temperature remained within ±0.7°C of the blood temperature except during cold-CPB when it was 31.2 ±1.0°C. The serum potassium level varied between 3.4 mEq/L during the prebypass period and 5.8 mEq/L during cold-CPB. It was kept between 3.8 and 5.5 mEq/L by replacement during normothermic CPB and the postbypass period. No blood transfusions were required during the study.

By repeated measures analysis of variance, it was found that MAP, FVR, SVR, blood temperature, skin temperature, and hematocrit value changed significantly (p<0.001) from the prebypass to the three subsequent periods, even when the probability value levels were adjusted for multiple comparisons (Bonferroni method). Similar changes were reached by FBF and CI only during the warm-CPB and the post-CPB periods; serum potassium levels were higher (p<0.001) in the cold- and post-CPB than in the pre-CPB periods. Although FBF increased by 12 percent during cold-CPB, it did not reach statistical significance. It reached 126 percent and 121 percent, respectively, during normothermic- and post-CPB, respectively. For the whole group, both FVR and SVR changed in the same direction from the pre-CPB to the post-CPB phase; however, FVR decreased proportionately more than SVR: 31 vs 17 percent, 66 vs 47 percent, and 59 vs 33 percent during cold-, normothermic-, and the post-CPB periods. Additionally, the changes in FVR and SVR during progression from one surgical phase to the next offer some contrasts. Most noticeable is that from the warm- to the post-CPB period: FVR decreased in 13, did not change in 2, and increased in 12, while SVR decreased in 5, did not change in 2, and increased in 20. Additionally, these two variables changed in opposite directions in 12, while in another 5 one of them changed and the other did not. This may explain the lack of correlation between FVR and SVR.

There was no statistically significant association between any of the variables and FBF or FVR. After correcting for patient and surgical phase variability, only MAP had a statistically significant effect (p=0.042) on FVR; none of the other covariates

Table 1—Effect of Cardiopulmonary Bypass on Forearm Blood Flow, Systemic Vascular Resistance, and Other Observed Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-CPB</th>
<th>Cold-CPB</th>
<th>NormT°C-CPB</th>
<th>Post-CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP, mm Hg</td>
<td>84.5 ±2.0</td>
<td>65.2 ±1.6*</td>
<td>63.6 ±1.5*</td>
<td>78.4 ±1.5*</td>
</tr>
<tr>
<td>FBF, mmol/100 ml tissue/min</td>
<td>1.6 ±0.1</td>
<td>1.8 ±0.2*</td>
<td>3.7 ±0.3*</td>
<td>3.6 ±0.3*</td>
</tr>
<tr>
<td>FVR, MAP/FFB ratio</td>
<td>59.0 ±5.0</td>
<td>41.0 ±3.0*</td>
<td>20.0 ±1.0*</td>
<td>24.0 ±2.0*</td>
</tr>
<tr>
<td>% decrease in FVR</td>
<td>31.0</td>
<td>66.0</td>
<td>59.0</td>
<td>59.0</td>
</tr>
<tr>
<td>SVR, dynes s cm⁻²</td>
<td>1,607 ±78</td>
<td>1,335 ±50*</td>
<td>655 ±27*</td>
<td>1076 ±33*</td>
</tr>
<tr>
<td>% decrease in SVR</td>
<td>17.0</td>
<td>47.0</td>
<td>47.0</td>
<td>35.0</td>
</tr>
<tr>
<td>CI, L/m²</td>
<td>2.0 ±0.1</td>
<td>2.0 ±0.1*</td>
<td>2.0 ±0.1*</td>
<td>2.8 ±0.1*</td>
</tr>
<tr>
<td>Blood temperature, °C</td>
<td>35.0 ±0.1</td>
<td>27.7 ±0.3*</td>
<td>37.0 ±0.2*</td>
<td>36.3 ±0.1*</td>
</tr>
<tr>
<td>Skin temperature, °C</td>
<td>26.6 ±0.5</td>
<td>24.5 ±0.4*</td>
<td>29.4 ±0.8*</td>
<td>31.3 ±0.5*</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>36.6 ±0.7</td>
<td>22.8 ±0.5*</td>
<td>22.8 ±0.5*</td>
<td>22.9 ±0.5*</td>
</tr>
<tr>
<td>PaCO(_2), mm Hg</td>
<td>38.0 ±0.7</td>
<td>37.9 ±0.7*</td>
<td>37.9 ±0.5*</td>
<td>38.3 ±0.8*</td>
</tr>
<tr>
<td>PaO(_2), mm Hg</td>
<td>279 ±18.2</td>
<td>289 ±7.0</td>
<td>261 ±6.5</td>
<td>300 ±12.5</td>
</tr>
<tr>
<td>pH</td>
<td>7.39 ±0.1</td>
<td>7.41 ±0.01</td>
<td>7.45 ±0.01</td>
<td>7.39 ±0.01</td>
</tr>
<tr>
<td>Serum potassium level, mEq/L</td>
<td>3.4 ±0.05</td>
<td>5.4 ±0.08*</td>
<td>3.5 ±0.6</td>
<td>5.3 ±0.7*</td>
</tr>
</tbody>
</table>

*The decrease in FVR was greater than the decrease in SVR, but was not statistically significant.
†Probability less than 0.001 from pre-CPB.
tested (blood temperature, skin temperature, hematocrit level, PaCO₂, serum potassium value, and SVR) had an effect on either FBF or FVR when tested singly or in combination. When the Bonferroni correction for multiple comparisons was applied, the lowest probability value became greater than 0.25. Using multivariate (canonical) correlation analysis, we found no significant correlations between combinations of covariates and FBF or FVR after adjustments for the surgical phase of the study.

Two patients who were receiving phenylephrine during warm-CPB showed lower FBFs at this stage than during the post-CPB when they were not receiving phenylephrine; however, their respective low flows were 2.3 and 3.0 ml/100 ml of tissue/min, while 4 patients who were not receiving phenylephrine had even lower flows ranging from 1.6 to 2.0 ml/100 ml/min. The three patients receiving phenylephrine during the post-CPB period showed lower flows during this period than during the warm-CPB period. However, the decreases in relation to the previous period ranged from 17 to 36 percent, while patients receiving no phenylephrine showed similar decreases (17 to 48 percent). The range of FBFs at this stage was 1.8 to 4.0 ml/100 ml of tissue/min for patients receiving phenylephrine and from 1.8 to 5.9 ml/100 ml of tissue/min in those not receiving phenylephrine. Thus, it seems that phenylephrine at the doses used had no visible effect on FBF.

**DISCUSSION**

The decrease in FVR found in this study during CPB was significant. However, the FVR or ratio of radial MAP to FBF (an arbitrary but accepted way to express this variable is 18 to 30 in awake, unstressed subjects) in the control readings was 3 times higher in these patients than in awake subjects. This ratio decreased from 59 to 41 during cold bypass and to 20 and 24 during warm and the postbypass periods. Thus, FVR decreased during the first part of bypass, reaching a normal level only during warm and the postbypass periods. Stern et al. reported a lower FVR at discontinuation of CPB in relation to that before CPB. Unfortunately, these authors did not report the FBF in milliliters per 100 ml of tissue per minute, nor did they give the FVR as the ratio of MAP to the FBF. They only stated their findings as a percent decrease in FVR from the pre- to the post-CPB state; thus, we do not know if they found a real decrease in FVR or only a recovery toward normal. Lazenby et al. found, in dogs anesthetized with isoflurane, that blood flow in the femoral arteries increased significantly during hypothermic-CPB, while it decreased in other vascular beds (mesenteric, renal, etc.). These authors conclude that hypothermic-CPB increased MBF and decreased MVR. It is difficult to isolate the increase in MBF that these authors found from that produced by isoflurane anesthesia itself.

Whether the likely low MBF found before and during cold-CPB has any detectable metabolic effects is unlikely; the acid-base status of our patients was entirely PaCO₂-dependent, with a neutral and unchanged base excess. Furthermore, it has been found in men, that muscle intracellular metabolism is well preserved during CPB, even in the presence of low perfusion pressure.

Because the vasomotor control of skeletal muscle is uniform for all muscle groups, our findings would indicate that a decrease in vascular resistance toward normal, rather than below normal, had occurred in 40 percent of the total body mass. Thus, although it contributes to the prevalent decreased MAP seen during CPB, it does not seem to be the major factor in patients under the conditions of those studied.

In order to equitably evaluate the effect of CPB on FBF as measured in this study we have to address some factors that could undermine our conclusions: (a) Moderate hypercapnia can increase MBF or decrease MVR; therefore, great care was taken to keep PaCO₂ within 35 to 42 mm Hg. Likewise, hyperoxia (PaO₂ ≥ 500 mm Hg) can increase FVR, great care was taken to avoid such levels. (b) Inhalational anesthetics do not seem to affect MBF, although halothane decreases it, and isoflurane increases it; thus all were avoided. (c) Venous occlusion plethysmography has not been used in the presence of changing skin temperatures and during nonpulsatile blood flow. Therefore, we calibrated the strain gauges on the forearm before each measurement, and we accepted as true blood flow slopes, only those with straight-line pitch for a minimum of 3 s, equivalent to the first 3 pulsations accepted when using this method in subjects with pulsatile flow. (d) Because any form of stress will alter MBF and these patients were under different degrees of stress from the moment they learned of the need to have these operations, we discarded the possibility of obtaining true control blood flows. The pre-CPB blood flows were taken as control values, speculating that CPB would affect them sufficiently for changes to be discerned. (e) Mechanical ventilation during a closed, and then an open, chest would unevenly exaggerate the effect of positive intrathoracic pressure on FBF. Accordingly, all measurements were made with the chest opened since three of the four sets could not be done with the chest closed. (f) We considered excluding the two patients who received small doses of phenylephrine during warm-CPB and three following discontinuation of CPB. Phenylephrine, having similar effects to those of norepinephrine, should reduce FBF, and in fact, in the two patients re-
ceiving phenylephrine during warm-CPB, the FBF increased slightly when the infusion was discontinued, and in the three who began receiving the infusion in the post-CPB period, the FBF decreased slightly. However, the flow variability seen in these patients was well within that of those not so treated. This equivocal effect probably is due to the small doses given. (g) Reliable measurements of forearm or hand blood flow by venous-occlusion plethysmography requires that the tested arm be positioned at or above heart level with no interference to venous return and patient displacement be limited. If the flows are low, as they were in our study, patient displacement must be entirely avoided. Thus, the surgical procedure had to be interrupted for a few minutes every time a measurement was done. The side effect of this decision was the short duration of the observation periods. We also only analyzed flow traces in which all 8 tracings were within the 95 percent confidence interval of each sample.

The mild effect of CPB on MBF is not a surprise since FBF and FVR tend to remain stable in the presence of mild hypotension produced by thiopentone,15 propofol,11 nitrous oxide,15 methoxyflurane,21 and severe sepsis.22 In fact, halothane, while reducing MAP, increases FVR in patients4,12,13-23 and in dogs.24 Up to date, only isoflurane is known to decrease FVR significantly,16 and sedation with meperidine is known to produce a moderate decrease.12 The environment in which this clinical study was performed was unsuitable for establishing cause-effect relationships between changes in FBF and other assessed variables. The relationship, or rather the lack thereof, between the changes in FVR and SVR during the warm-post-CPB period illustrates the futility of trying to establish relationships by statistical methods. It seems that the small-vessel vascular system is too complex in its behavior to be analyzed during a clinical study. We should add to this observation the different ages of our patients and, very likely, the differing states of their vascular systems. However, examining the results in Table 1, one can relate the moderate decrease in FVR during cold-CPB to the interaction between a low hematocrit value, which would decrease viscosity and improve flow, and moderate hypothermia, which would decrease flow. During the warm- and the post-CPB periods, the effect of hemodilution would be unopposed, favoring the greater increase in FBF seen then. However, we found no statistical hint of a cause-effect relationship. Other speculative relationships to consider include nonpulsatile flow whose effect on the local and systemic vasomotor response is unknown, the level of circulating catecholamines, and other systemic25 and local vasoactive substances.26 The cause of the low flows during the prebypass period is not obvious, and the only factors that could intuitively be associated with this finding are the blood temperature of 35.0 ± 0.1°C, although there was no statistical association, and full muscle relaxation by pancuronium, which deserves further investigation.

In summary, in a group of 27 patients undergoing narcotic-midazolam anesthesia and mild hypothermia (blood temperature, 35 ± 0.1°C), the FVR was found to be conspicuously low before exposure to CPB. Introduction of CPB decreased the SVR significantly, reaching levels comparable to those of awake untrated men only during rewarming and in the first few minutes of the post-CPB period. Thus, a decrease in MVR plays a role in the reduction of SVR during the warm- and post-CPB periods. However, its importance is not clear, since it was found that the FBF did not really increase above normal values but recovered toward normal values during CPB and remained normal after discontinuation of bypass.

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