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Relationship between Oxygen Uptake and Mixed Venous Oxygen Saturation in the Immediate Postoperative Period

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Background: During muscular exercise, a negative correlation has been demonstrated between the value of mixed venous oxygen saturation ($S\bar{v}_{O_2}$) and the level of muscular work, expressed at each level as the ratio of oxygen uptake ($\dot{V}_{O_2}$) to each subject's maximal oxygen uptake ($\dot{V}_{O_2}$max). Because the immediate postoperative period is associated with an increase in whole body oxygen demand, and in this regard resembles the effects of muscular exercise, a similar correlation may exist during this period.

Methods: $\dot{V}_{O_2}$max was determined in 11 patients 3–5 days before coronary artery bypass surgery. During the first 2 postoperative h, $\dot{V}_{O_2}$ and $S\bar{v}_{O_2}$ were monitored. $\dot{V}_{O_2}$ was measured by indirect calorimetry and $S\bar{v}_{O_2}$ by a fiberoptic pulmonary arterial catheter.

Results: The highest postoperative value of $\dot{V}_{O_2}$ was most often associated with visible shivering and ranged among patients from 19% to 53% of preoperatively measured $\dot{V}_{O_2}$max. There was a highly significant negative correlation between $S\bar{v}_{O_2}$ and the ratio $\dot{V}_{O_2}/\dot{V}_{O_2}$max. This correlation was observed when data were examined collectively (136 simultaneous determinations of the two variables) and at the individual level (10–18 determinations for each patient). The slopes and the y intercepts of individual lines of correlation were within a narrow range.

Conclusions: During the first 2 postoperative h after coronary artery bypass surgery, $\dot{V}_{O_2}$ rarely exceeds 50% of preoperative $\dot{V}_{O_2}$max. Assuming a stable state of myocardial function, $S\bar{v}_{O_2}$ measurement may provide an indirect means of assessment of the "exercise test" imposed on patients recovering from general anesthesia. (Key words: Measurement technique: oximetry. Monitoring: mixed venous oxygen saturation; oxygen uptake; postoperative period. Surgery: cardiac.)

THE immediate postoperative period is associated with an increase in whole body oxygen demand and is therefore often regarded as a form of "exercise test." Indeed, in both circumstances, there is a simultaneous increase in cardiac output and tissue oxygen extraction to satisfy the increase in body oxygen requirements.[1,2]

Tissue oxygen extraction during muscular exercise has been studied extensively by Weber *et al.*[3] in patients with cardiac failure of various classes of severity. Weber and Janicki[4] found that, whatever the patient's functional cardiac status, a close positive correlation was observed between the value of tissue oxygen extraction and the level of muscular work, expressed at each level as the ratio of oxygen uptake ($\dot{V}_{O_2}$) to each subject's maximal oxygen uptake ($\dot{V}_{O_2}$max). As expected, a close negative correlation was found when mixed venous oxygen saturation ($S\bar{v}_{O_2}$) was plotted against the level of muscular exercise.[4] Indeed, provided that arterial hemoglobin oxygen saturation is close to 100%, $S\bar{v}_{O_2}$ may be expressed as 1-extraction.[5]

The objective of the present study was to answer the following questions: (1) What is the intensity of the exercise test, expressed as $\dot{V}_{O_2}/\dot{V}_{O_2}$max, which is imposed on patients recovering from general anesthesia? (2) Does a correlation between $S\bar{v}_{O_2}$ and $\dot{V}_{O_2}/\dot{V}_{O_2}$max exist during this period, similar to that previously observed by Weber *et al.* during muscular exercise?

Materials and Methods

Eleven patients scheduled to undergo coronary artery bypass surgery were enrolled in the study after obtain-

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ing institutional approval and informed consent. Three of them had a history of myocardial infarction. Preoperatively, angiographic left ventricular ejection fraction was measured according to the area-length method of Sandler and Dodge.[6] Regional wall motion was analyzed according to the method of Herman and Gorlin.[7] No patient had significant left ventricular dyssynergia. Doses of antianginal medications were constant throughout the study. Clinical data are given in table 1.

Three to five days before surgery, the patients' $\dot{V}_{O_2}$max was determined by exercise testing. The exercise protocol consisted of a symptom-limited ramp exercise testing[8] with an electromagnetically controlled cycle ergometer (Siemens Elema 930 B, Solna, Sweden). After a 5-min warm up period at 20 W and 60 rpm, the work rate was increased by 10 W every 60 s. Heart rate and electrocardiogram were monitored continuously, and blood pressure was measured every minute. $\dot{V}_{O_2}$, carbon dioxide pulmonary elimination ($\dot{V}_{CO_2}$), minute ventilation ($\dot{V}E$), and respiratory quotient were measured breath by breath using a metabolic cart (Metasys Brainware, La Valette Du Var, France) and displayed on a monitor. The endpoint of exercise was exhaustion, judged as an inability to continue pedalling at 60 rpm and a rapidly rising respiratory quotient greater than 1. During exercise, the anaerobic threshold point was determined visually using the following criteria: (1) an increase in the ventilatory equivalent for oxygen ($\dot{V}E/\dot{V}_{O_2}$) without an increase in the ventilatory equivalent for carbon dioxide ($\dot{V}E/\dot{V}_{CO_2}$) and (2) a steep increase in the respiratory quotient[9] (fig. 1). All patients were exercised beyond the work rate corresponding to the anaerobic threshold to ensure that maximal levels of exercise were achieved.[3] $\dot{V}_{O_2}$max was defined as the average $\dot{V}_{O_2}$ of the last 30 s of exercise. No patient experienced chest pain during exercise testing.

Coronary artery bypass surgery was performed by the same surgical and anesthetic team, under normothermic cardiopulmonary bypass. Patients were premedicated with orally administered hydroxyzine (1.5 mg/kg) and midazolam (80 μg/kg). Anesthesia was induced with intravenous midazolam (150 μg/kg), alfentanil (100 μg/kg), and pancuronium (100 μg/kg). After tracheal intubation, anesthesia was maintained with midazolam (150 $\mu g \cdot kg^{-1} \cdot h^{-1}$), alfentanil (100 $\mu g \cdot kg^{-1} \cdot h^{-1}$), and pancuronium (2–4 mg when required). Ventilation was controlled with an inspired fractional concentration of oxygen (F_{IO_2}) of 100%.

Upon arrival in the recovery room, 100 μg/kg of morphine was administered subcutaneously. Subsequent patient management decisions, including volume loading and supplemental doses of opioids or sedatives, were made independently of the study investigators by primary-care physicians. Then, during the first 2 postoperative h of mechanical ventilation in the assist-control mode (F_{IO_2} 40%), blood pressure, core temperature, arterial hemoglobin oxygen saturation (Sp_{O_2}), $S\bar{v}_{O_2}$, and $\dot{V}_{O_2}$ were monitored. Values of measured variables were noted every 15 min, and whenever a marked change in $\dot{V}_{O_2}$ or $S\bar{v}_{O_2}$ was observed, cardiac output was simultaneously measured by the thermodilution technique. The results of three end-expiratory injections were averaged. Hemoglobin and blood gas analysis were assessed serially. Pulse oximetry was used to measure Sp_{O_2}. Core temperature, cardiac output (expressed as cardiac index), and $S\bar{v}_{O_2}$ were measured using a fiberoptic pulmonary arterial catheter (Oxymetrix Abbott, Mountain View, CA) inserted before induction of anesthesia. The catheter was calibrated before insertion using a reflective standard provided by the manufacturer. The accuracy of the system was assessed after insertion and upon arrival in the recovery room by comparing the $S\bar{v}_{O_2}$ value of a mixed venous sample (Instrumentation co-oximeter, Ciba Corning, Medfield, MA) with the value displayed by the oximetric system 1 min before sampling. $\dot{V}_{O_2}$ was measured every minute using an indirect calorimetry system (Deltatrac Datex, Helsinki, Finland) calibrated before each study.[10]

All data are expressed as mean ± SE. Data obtained at different periods during the first 2 postoperative h were analyzed by analysis of variance (Statgraphics SGS, Rockville, MD) for repeated measurements with Duncan's multiple range follow-up tests.[11] Correlations between $S\bar{v}_{O_2}$ or cardiac index and $\dot{V}_{O_2}$ (expressed as the percentage of the preoperative measured $\dot{V}_{O_2}$max, $\dot{V}_{O_2}/\dot{V}_{O_2}$max) were investigated by regression analysis. Correlation coefficients were compared after Fischer Z transformation.[12]

Results

Preoperatively measured $\dot{V}_{O_2}$max ranged among patients from 12.5 to 27.8 $ml \cdot kg^{-1} \cdot min^{-1}$ (mean 20.1 $ml \cdot kg^{-1} \cdot min^{-1}$). During the exercise test, $\dot{V}_{O_2}$ at the anaerobic threshold was 67.9 ± 2.7% of $\dot{V}_{O_2}$max.

Table 2 shows the mean values of some selected physiologic parameters at three characteristic periods

Table 1. Patient Characteristics

Patient	Age (yr)	Sex	Weight (kg)	Treatment	LVEF (%)	Number of Grafts	Duration of CPB (min)
1	60	M	65	N-CB	64	1	20
2	56	M	90	N-BB	56	3	101
3	75	M	74	N	70	1	23
4	58	M	76	BB	60	1	22
5	51	M	76	N-CB	51	2	54
6	66	M	91	CB-BB	71	2	59
7	67	M	63	CB-Digox	51	3	66
8	64	F	64	N-CB	70	3	108
9	65	M	75	N-CB-BB	77	1	33
10	61	M	85	CB	55	2	71
11	77	M	80	N-BB	64	1	30

LVEF = Angiographic left ventricular ejection fraction; N = long-acting nitrates; CB = calcium channel blockers; BB = β adrenergic blockers; Digox = digoxin; CPB = cardiopulmonary bypass.

during the first 2 postoperative h: upon arrival in the recovery room, at the moment of the highest $\dot{V}_{O_2}$, and finally at the end of the study period. Upon arrival in the recovery room, the $\dot{V}_{O_2}$ value was lower than that measured at rest preoperatively before beginning the exercise test (135 ± 11 *vs.* 186 ± 15 ml · min^{-1} · m^{-2}, $P < 0.05$). The highest $\dot{V}_{O_2}$ value most often was associated with visible shivering and ranged among patients from 19% to 53% of preoperative $\dot{V}_{O_2}$max. This was observed in four patients between the 30th and 60th minutes of the study period, and in the seven other patients between the 75th and 110th minutes. As expected, it also was associated with a marked increase in cardiac index and a marked decrease in $S\bar{v}_{O_2}$. At the end of the study period, a moderate increase in core temperature was observed, whereas all other parameters returned to values similar to that observed upon arrival in the recovery room. Throughout the study time, Sp_{O_2} remained greater than 95% and hemoglobin concentration between 100 and 120 g/l. Plasma lactate concentration was unchanged. No postoperative complications occurred, and all patients survived.

Figure 2 shows the correlation between $S\bar{v}_{O_2}$ and $\dot{V}_{O_2}/\dot{V}_{O_2}$max. This correlation was found highly significant collectively (136 simultaneous determinations of $S\bar{v}_{O_2}$ and $\dot{V}_{O_2}/\dot{V}_{O_2}$max) and at the individual level (10–18 determinations of the two variables for each patient). The slopes and the y intercepts of individual lines of correlation were within a narrow range, with coefficients of variation 13% and 6%, respectively.

Figure 2 also depicts the relation between cardiac index and $\dot{V}_{O_2}/\dot{V}_{O_2}$max (n = 98). The relationship was weak, with an absolute value of correlation coefficient significantly less than the one found between $S\bar{v}_{O_2}$ and $\dot{V}_{O_2}/\dot{V}_{O_2}$max (0.40 *vs.* 0.82, $P < 0.05$). The slopes and the y intercepts of individual lines of correlation were scattered, with coefficients of variation 57% and 79%, respectively.

Discussion

To our knowledge, the present study is the first in which, using an approach similar to that used in exercise physiology, $\dot{V}_{O_2}$ measured in the immediate postoperative period was expressed as a percentage of $\dot{V}_{O_2}$max. The two majors findings were that $\dot{V}_{O_2}$ may increase to 19–53% of preoperatively measured $\dot{V}_{O_2}$max and that there is a close negative correlation between $S\bar{v}_{O_2}$ and $\dot{V}_{O_2}/\dot{V}_{O_2}$max.

Measuring $\dot{V}_{O_2}$max by exercise testing in our patients scheduled for coronary surgery posed two major problems. The first was that these patients were receiving antianginal medication, most often β-adrenergic or calcium channel blockers and long-acting nitrates, which might interfere with the exercise response. However, it has been demonstrated in hypertensive patients that β-adrenergic blockade does not significantly alter $\dot{V}_{O_2}$max.[13] It can be assumed that other antianginal drugs have no major effects on $\dot{V}_{O_2}$max determination. The second problem dealt with the criteria used to define $\dot{V}_{O_2}$max during incremental exercise. From a physiologic point of view, $\dot{V}_{O_2}$max is the level of $\dot{V}_{O_2}$ remaining invariant despite

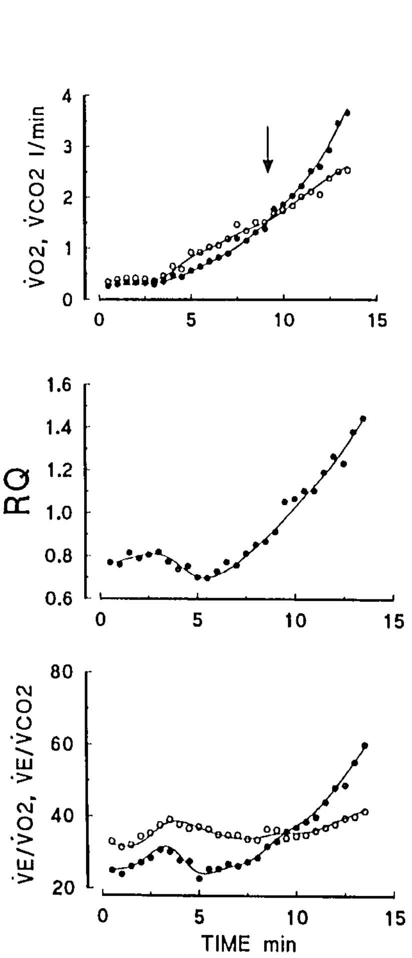

Fig. 1. A typical individual example (patient 2) of exercise testing, performed 4 days before surgery. The exercise is started at the 3rd minute of the recording. (*Top*) Time course evolution of oxygen consumption ($\dot{V}_{O_2}$, open circles) and carbon dioxide pulmonary elimination ($\dot{V}_{CO_2}$, closed circles). (*Middle*) Time course evolution of respiratory quotient (RQ). (*Bottom*) Time course evolution of ventilatory equivalent for oxygen ($\dot{V}E/\dot{V}_{O_2}$, open circles) and for carbon dioxide ($\dot{V}E/\dot{V}_{CO_2}$, closed circles). Arrow indicates the anaerobic threshold point.

an increment in workload sustained for 30 s or more.[14] Thus, true $\dot{V}_{O_2}$max is rarely obtained in patients. We measured symptom-limited $\dot{V}_{O_2}$max, with the subjective endpoint being dyspnea, exhaustion, and leg discomfort.[15] During exercise, special attention was paid to the measurement of the $\dot{V}_{O_2}$ corresponding to the anaerobic threshold, an objective variable that reflects lactic acid buffering by bicarbonate when oxygen availability to the muscles becomes inadequate.[16] Several authors have shown in various groups of patients that the anaerobic threshold point occurs at 60% or more of $\dot{V}_{O_2}$max,[8] which is consistent with the 67.9 ± 2.7% value found in our patients. Thus, it appears that they had exercised at close to their maximal effort. The values of their $\dot{V}_{O_2}$max were low compared to those measured in normal subjects of similar age (about 30 ml · min^{-1} · kg^{-1}),[15] but were close to those measured by Weber *et al.* in patients who were considered as having little or no impairment in aerobic capacity.[3]

The extent to which the preoperatively determined $\dot{V}_{O_2}$max is a relevant measure for the early postoperative period needs to be discussed. It is well established that cardiac function is the major determinant of the ability of the cardiopulmonary and metabolic systems to increase oxygen uptake.[17] In the immediate postoperative period after coronary artery bypass surgery, two main opposite factors may affect cardiac function, and thus $\dot{V}_{O_2}$max. On the one hand, deterioration of ventricular contractility may occur because of direct myocardial damage secondary to surgical manipulation of the heart and cardiopulmonary bypass. On the other hand, improved coronary perfusion, and thus oxygen supply to the myocardium, is an important factor in improving ventricular function. Beyond the 2nd hour after bypass, severe and persisting impairment in ventricular

Table 2. Evolution of Selected Physiologic Parameters in the 11 Studied Patients upon Arrival in the Recovery Room, at the Moment of the Highest $\dot{V}_{O_2}$, and at the End of the 2nd Postoperative H

	Arrival in Recovery Room	Peak $\dot{V}_{O_2}$ in Recovery Room	2 h after Arrival in Recovery Room
Temperature (° C)	35.0 ± 0.2	36.8 ± 0.3*	37.8 ± 0.2*
Mean arterial pressure (mmHg)	90.5 ± 5.1	94.5 ± 5.8	85.1 ± 3.5
Pulmonary wedge pressure (mmHg)	10.1 ± 1.2	11.5 ± 1.7	9.5 ± 1.6
Cardiac index (l · min^{-1} · m^{-2})	3.1 ± 0.3	4.6 ± 0.5*	3.2 ± 0.3
$\dot{V}_{O_2}$ (ml · min^{-1} · m^{-2})	135 ± 11	259 ± 14*	145 ± 6
$\dot{V}_{O_2}/\dot{V}_{O_2max}$ (%)	17.9 ± 2.7	34.3 ± 3.2*	18.9 ± 1.3
Sp_{O_2} (%)	97.5 ± 0.4	97.0 ± 0.4	97.8 ± 0.4
$S\bar{v}_{O_2}$ (%)	68.5 ± 3.0	52.5 ± 2.9*	69.3 ± 1.7
Plasma lactate (mM · l^{-1})	1.9 ± 0.2	2.3 ± 0.3	1.9 ± 0.1

Data are mean ± SEM.

$\dot{V}_{O_2}$ = oxygen uptake; $\dot{V}_{O_2max}$ = preoperative maximal oxygen uptake; Sp_{O_2} = arterial oxygen saturation measured by pulse oximeter; $S\bar{v}_{O_2}$ = mixed venous oxygen saturation.

* $P < 0.05$ by comparison with values measured upon arrival in the recovery room.

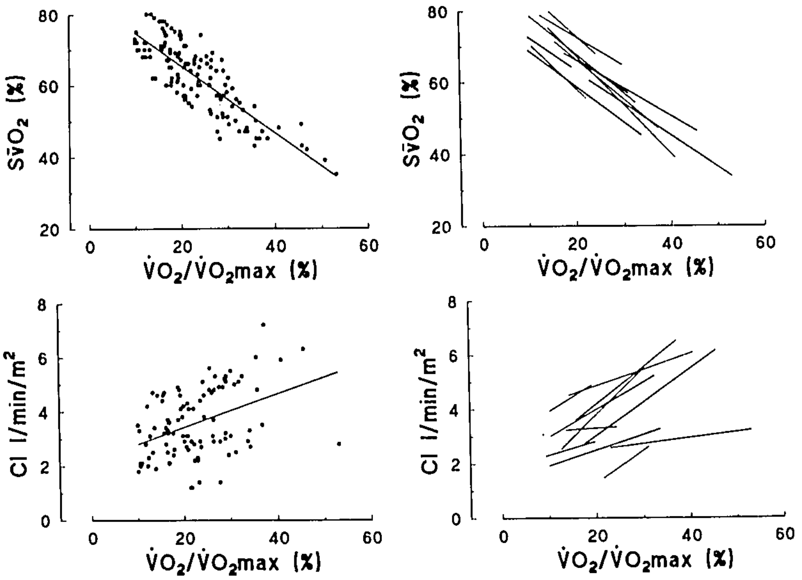

Fig. 2. (*Top*) Correlation between mixed venous oxygen saturation ($S\bar{v}_{O_2}$) and oxygen uptake expressed as the percentage of preoperatively measured maximal oxygen uptake ($\dot{V}_{O_2}/\dot{V}_{O_2}max$, %) (*Top left*) All data points are shown (n = 136), r = −0.82 ($P < 0.0001$). (*Top right*) Individual lines of correlation are shown. Correlation coefficients ranged among patients from −0.67 to −0.99. Slopes and y intercepts ranged from −0.78 to −1.3 and from 79.2 to 96.9, respectively. (*Bottom*) Correlation between cardiac index (CI) and $\dot{V}_{O_2}/\dot{V}_{O_2}max$ (%). (*Bottom left*) All data points are shown (n = 98), r = 0.40 ($P < 0.05$). (*Bottom right*) Individual lines of correlation are shown. Correlation coefficients ranged among patients from 0.24 to 0.98. Slopes and y intercepts ranged from 0.01 to 0.17 and from −1.1 to 3.7, respectively.

function has been shown to be related to preoperatively existing low ejection fraction or wall motion abnormalities.[18] In the present study, all patients had a preoperative ejection fraction of greater than 50% with no evidence of dyssynergia. However, postoperative cardiac dysfunction cannot be excluded, which could conceivably lead to a $\dot{V}_{O_2}max$ lower than that measured preoperatively. The intensity of the postoperative exercise test imposed on these subjects was expressed as the ratio of $\dot{V}_{O_2}$ to the preoperatively evaluated $\dot{V}_{O_2}max$ and, therefore, might have been underestimated. However, considering the low value of the coefficient of variation of the slopes of the individual lines of correlation between $S\bar{v}_{O_2}$ and $\dot{V}_{O_2}/\dot{V}_{O_2}max$, this underestimation was either moderate or consistent among all the patients.

Changes in metabolic rate associated with the perioperative period have been studied extensively. During general anesthesia, $\dot{V}_{O_2}$ decreases an average of 25–30%.[2,19] Postoperatively, the stress associated with return to consciousness and recovery of pain sensation, the work of breathing, shivering, and the thermogenesis needed to correct the temperature fall occurring during surgery are the main factors known to increase $\dot{V}_{O_2}$.[19] We found that, during the first 2 postoperative h, $\dot{V}_{O_2}$ almost never exceeded 50% of preoperatively measured $\dot{V}_{O_2}max$. Therefore, the preoperative anaerobic threshold level never was reached, and blood lactate remained unchanged. This value of 50% of $V_{O_2}max$ can be considered as equivalent to a moderate level of exercise; for example, a normal adult during a 4-mph walk on a flat road.[15] Our patients were mechanically ventilated and still had the benefit of the large doses of narcotics administered during the operation. These conditions may explain the relatively low energetic cost of their recovery period.

As expected, the increase in $\dot{V}_{O_2}$ during the postoperative period was associated in our patients with an increase in cardiac index and a decrease in $S\bar{v}_{O_2}$, a pattern similar to that observed during muscular exercise. We found the relationship between cardiac index and $\dot{V}_{O_2}/\dot{V}_{O_2}max$ to be quite variable. In patients with chronic heart failure, Weber *et al.* observed that the slope of the cardiac index response to exercise decreased as the severity of heart failure increased.[3] Thus, the most likely explanation for the variability of the cardiac index-$\dot{V}_{O_2}/\dot{V}_{O_2}max$ relationship among our patients was differences in functional cardiac status that were likely to exist before the operation. Preoperative ejection fraction measured under resting conditions was higher than 50% in all patients. However, this did not preclude differences in ventricular performance during exercise as evidenced by variability of preoperative $\dot{V}_{O_2}max$.[17] By contrast, the relationship between $S\bar{v}_{O_2}$ and $\dot{V}_{O_2}/\dot{V}_{O_2}max$ was similar among our patients. As Sp_{O_2} remained close to 100%, this suggested an appropriate adaptation of global tissue oxygen extraction at the whole body level to incremental value of $\dot{V}_{O_2}/\dot{V}_{O_2}max$, regardless of myocardial function.

Our data may be significant for the postoperative management of patients. As shown in figure 2, an $S\bar{v}_{O_2}$ measured at 60% corresponds to a low level of exercise, of about 25% of $\dot{V}_{O_2}max$. An $S\bar{v}_{O_2}$ measured at 40% corresponds to a higher level of exercise, of about 50% of $\dot{V}_{O_2}max$. In patients recovering from cardiac surgery, maintaining $\dot{V}_{O_2}$ lower than 60% of $\dot{V}_{O_2}max$, *i.e.*, lower than the threshold beyond which anaerobiosis and lactic acidosis took place preoperatively appears a logical therapeutic objective. From a practical point of view, our data indicate that this can be achieved by maintaining $S\bar{v}_{O_2}$ greater than 40%. In this regard, limitation or correction of heat loss during the surgical procedure and/or use of therapeutic interventions known to reduce the incidence or the intensity of postoperative shivering may be of great value.[20-22]

In conclusion, this study was carried out in the early postoperative period after coronary artery bypass surgery, in patients who preoperatively had left ventricular ejection fraction greater than 0.5 and no signs of ventricular dyssynergia. We found $\dot{V}_{O_2}$ to be most often less than 50% of the preoperatively measured $\dot{V}_{O_2}max$. In addition, the $S\bar{v}_{O_2}$ value was inversely related to the ratio of $\dot{V}_{O_2}$ to the preoperatively measured $\dot{V}_{O_2}max$, and thus was representative of the intensity of the exercise test imposed on them. However, before generalization of these observations to other patient groups and clinical conditions, some limitations of the present study should be considered. First, our observations were limited to the first 2 postoperative h and assume that no deterioration of cardiac function occurred during this period. Second, before interpreting a decrease in $S\bar{v}_{O_2}$ during the early postoperative period as an index of an increase in $\dot{V}_{O_2}$, other factors of variation of this multifactorial variable have to be eliminated: a decrease in arterial oxygen saturation or hemoglobin concentration and, most of all in the context of cardiac surgery, a decrease in cardiac output.

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