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Different dosages of dobutamine in septic shock patients: determining oxygen consumption with a metabolic monitor integrated in a ventilator

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Abstract *Objective*: Oxygen consumption (VO_2) obtained from respiratory gases by indirect calorimetry ($VO_{2,IC}$) with a metabolic monitor integrated in a ventilator were to be compared to VO_2 obtained by the Fick principle ($VO_{2,Fick}$) in septic patients following an increase in oxygen delivery (DO_2) induced by positive inotropic support.
Design: Prospective clinical study.
Setting: University Hospital, Surgical Intensive Care Unit (ICU).
Patients: Thirty patients suffering from sepsis.
Interventions: DO_2 was increased by dobutamine infusion, starting with an initial dosage of 5 μg·kg·min, increased to a maximum of 10 μg·kg·min.
Measurements and main results: Dobutamine infusion induced a dosage-related increase in DO_2 (from 577 ± 192 to 752 ± 202 ml·min·m^2, $p < 0.01$), which was associated with a statistically significant increase in $VO_{2,IC}$ (from 173 ± 30 to 188 ± 28 ml·min·m^2, $p < 0.01$) and in $VO_{2,Fick}$ (from 140 ± 25 to 156 ± 24 ml·min·m^2, $p < 0.01$). The comparison between $VO_{2,IC}$ and $VO_{2,Fick}$ revealed differences (bias and precision – 33 ± 32 ml·min·m^2).
Conclusions: With a metabolic monitor integrated in a ventilator it was possible to carry out continuous monitoring of calorimetric data under clinical conditions. In contrast to previous studies using indirect calorimetry, this study showed a moderate correlation between VO_2 and DO_2 in septic patients using either method. The clinical relevance of this finding requires further investigation. Different factors (e. g. injectant temperature, pulmonary VO_2) produced substantial differences between $VO_{2,IC}$ and $VO_{2,Fick}$ as previously shown.

Key words Dobutamine · Indirect calorimetry · Oxygen consumption · Oxygen delivery · Sepsis

Introduction

The relationship between oxygen consumption (VO_2) and oxygen delivery (DO_2) has been studied frequently, but oxygen supply dependency in the critically ill remains controversial [1]. Under physiological conditions, VO_2 does not depend on DO_2 over a wide range. In situations when DO_2 drops below a critical value, VO_2 does become dependent on this. This leads to anaerobic metabolism with an accumulation of lactate. In the critically ill this oxygen supply dependency was found over a wider range of VO_2. This fact has been considered to be a major risk factor in the development of multiple organ failure (MOF) [2].

Several studies have demonstrated this oxygen supply dependency in sepsis and ARDS, especially when VO_2 was determined using the Fick principle ($VO_{2,Fick}$) [3, 4]. Investigators could not confirm this oxygen supply dependency by determining VO_2 in respiratory gases [5, 6]. One explanation for the discrepancy may be

the mathematical coupling of measurement errors in shared variables for the determination of VO_2 [7]. The determination of $VO_{2,Fick}$ requires invasive measurements and does not allow continuous reading of VO_2. The determination of $VO_{2,Fick}$ contains the potential risk of measurement errors when determining cardiac output (CO), oxygen and hemoglobin concentration and oxygen(O_2) saturation of hemoglobin [8]. In hypodynamic and hyperdynamic shock the measurement error using this technique may be above 10% [9]. Factors like volume and temperature of injectant in the process of obtaining CO may also influence the accuracy of this method [10].

Indirect calorimetry (IC) is an appropriate non-invasive tool which can be used to determine $VO_{2,IC}$, carbon dioxide (CO_2) production ($VCO_{2,IC}$) and respiratory quotient (RQ_{IC}) continuously [11]. In healthy spontaneously breathing volunteers IC is the gold standard for monitoring VO_2. Several systems designed to use IC have been validated in the laboratory. Those validations have demonstrated a high degree of accuracy and precision [12, 13]. These results were confirmed under clinical conditions [14, 15]. In critically ill patients requiring mechanical ventilation, this method has some limitations: results can be affected by changes of the inspired oxygen fraction (FIO_2), by changes of pressure or by gas leaks in the ventilatory system [16, 17]. A high FIO_2 may lead to errors due to the limited ability of O_2 sensors to discriminate high O_2 concentrations [15, 18].

A metabolic monitor, synchronized with a conventional mechanical ventilator, has been designed for continuous reading of VO_2. Integrated algorithms of the monitor using ventilatory parameters offer the opportunity to determine variables of respiratory gas exchange in critically ill patients. Weissman et al. validated a monitor of this kind in the laboratory by simulating various conditions of mechanical ventilation [19]. In their study, VO_2 and VCO_2 were within 7% of the predicted values.

The aim of this study was to determine VO_2 and VCO_2 in septic patients by IC and the Fick principle with dobutamine-induced changes in DO_2.

Materials and methods

Patients

The study was approved by the ethics committee of the Free University of Berlin. As required by the ethics committee, the patient's wishes to participate in the study were confirmed by their relatives in a written statement. Thirty patients with septic shock were studied in a surgical intensive care unit. All patients fulfilled the criteria of septic shock as defined by the American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference [20].

Only septic shock patients hemodynamically stabilized with vasopressor therapy were included in this study. Prior to beginning the study, an optimal left atrial filling pressure was reached, using the pulmonary artery occlusion pressure at the plateau value for left ventricular stroke work. The hematocrit was maintained above 30%. A vasopressor (norepinephrine 0.6 ± 0.4 μg·kg·min) was infused continuously to maintain mean arterial blood pressure above 70 mmHg. The dosage of the vasopressor remained constant throughout the study. The patients were mechanically ventilated in a volume- or pressure-controlled mode which was not changed throughout the study (Ventilator 7250, Nellcor Puritan Bennett, Carlsbad, Calif.), sedated (fentanyl, midazolam) and paralyzed (pancuronium) to prevent spontaneous breathing. The depth of sedation was checked using the Ramsay score (target ≥5) before the administration of the neuromuscular blocking agent. The occurrence of spontaneous breathing was monitored by continuous capnography. *Patients were on parenteral nutrition prior to the onset of the study (1.5–3 g glucoses/kg, 0.3–0.8 g lipids/kg). The parenteral nutrition remained unchanged throughout the study.*

Patients with unstable hemodynamic conditions and changes in body temperature of more than ± 0.5 °C within 120 min of the start of the dobutamine infusion or during the course of the study were excluded. Those with respiratory failure (FIO_2 above 0.6) or with airway gas leaks were not included in the study. The respiratory circuit was checked for airway gas leaks before the onset of the study and immediately after completion of the final measurement following the operating requirements of the manufacturer.

Protocol

Three sets of hemodynamic and metabolic parameters, $VO_{2,Fick}$ and DO_2 were obtained at baseline, after the stabilization of each intervention and postinfusion. Baseline data prior to dobutamine infusion were taken as the average of the data obtained at 90, 60 and 30 min prior to the start of the dobutamine infusion.

With respect to $VO_{2,IC}$ and $VCO_{2,IC}$, the reported data are the averages of all the values obtained breath-by-breath during a 15-min cycle. After baseline measurements were completed, dobutamine infusion was started at a dosage of 5 μg·kg·min and maintained over a period of 2 h. Thereafter, the dosage was increased to 10 μg·kg·min and maintained for another 2 h. After 4 h the dobutamine infusion was discontinued. The final measurements were taken 2 h after the catecholamine infusion had been discontinued (postinfusion). Dobutamine infusion was stopped earlier if clinical signs of intolerance appeared (heart rate above 140 beats/min, arrhythmias).

The instruments were calibrated before starting each series of measurements. The gas analyzers of the metabolic monitor were calibrated using a defined mixture of 95% O_2 and 4% CO_2 as required by the manufacturer.

Pulmonary artery catheter

Routine cardiovascular monitoring in septic shock patients was performed using a pulmonary artery catheter (Swan-Ganz Oximetry, TD-Catheter, Baxter Edwards Critical Care, Irvine, Calif.) and an arterial catheter (A. radialis, A. dorsalis pedis, A. femoralis). The pressure waveform and the necessity of inflating at least 1 ml of air into the catheter balloon to achieve pulmonary artery occlusion confirmed the correct position of the pulmonary artery catheter tip.

Measurements

Measurements included hemodynamics and blood gas analyses. Hemodynamics consisted of heart rate, systemic and pulmonary artery pressures and pulmonary capillary wedge pressure. Cardiac output (CO) was determined using the thermodilution technique (SAT-2 Oximeter, Cardiac Output Computer, Baxter Edwards Critical Care, Irvine, Calif.) using three aliquots (10 ml) of a cold solution (below 10 °C) and expressed as the mean of three end-expiratory measurements (variation between measurements below 10 %). In cases of a variation above 10 %, measurements were repeated.

After completion of CO measurements, arterial and mixed venous blood samples were analyzed immediately for O_2 and CO_2 concentrations (ABL 300, Radiometer, Copenhagen, Denmark), hemoglobin concentration and oxygen saturation (SO_2) (OSM 3 Hemoximeter, Radiometer, Copenhagen, Denmark). Arterial lactate concentrations [a(La^-)] were measured both at baseline and postinfusion (enzymatic method, normal range 0.5–2.2 mmol/l).

Indirect calorimetry

Indirect calorimetry was obtained continuously using the Metabolic Monitor 7250 integrated in the Ventilator 7200 (Nellcor Puritan Bennett, Carlsbad, Calif.). This monitor is an indirect calorimeter which uses the open gas circuit principle. Inspired and expired oxygen fractions are measured simultaneously by a chemical O_2 cell and a paramagnetic sensor. Concentrations of CO_2 are measured by an infrared analyzer. Pressure transducers are located in parallel to the gas analyzers. Expired tidal volume was measured by an anemometer located in the ventilator.

Calculations

The Fick principle was used to calculate the $VO_{2,Fick}$. $VO_{2,IC}$ and $VCO_{2,IC}$ were calculated by a microprocessor on a breath-by-breath basis using the following equations:

$$VO_{2,IC}\ (ml/min) = (V_T \times [F(I\text{-}E)O_2\text{-}FIO_2 \times FECO_2\ ]) \times f/(1\text{-}FIO_2)$$

$$VCO_{2,IC}\ (ml/min) = (V_T \times [FECO_2\text{-}FICO_2]) \times f$$

where V_T is tidal volume, $F(I\text{-}E)O_2$ is difference between inspired and expired oxygen concentrations, $FECO_2$ is expired fraction of CO_2, f is respiratory frequency, $FICO_2$ is inspired fraction of CO_2.

Statistical analysis

All data were expressed as means ± standard deviation. The Pearson correlation coefficient between $VO_{2,IC}$ and $VO_{2,Fick}$ was calculated. According to Bland and Altmann, the agreement between the two methods was expressed as bias and precision [21]. The slope of the VO_2-DO_2 relationship was determined by regression for each patient. The Wilcoxon matched paired signed-rank test was used to compare the variables before and after each intervention. A p equal to or below 0.05 was considered statistically significant. The SPSS statistical package was used for statistical evaluation.

Results

The basic characteristics are listed in Table 1 (mean age 61 ± 19 years, mean APACHE II 24 ± 6, mean MOF score 9 ± 1 [20], mortality rate 60 %). There were no changes in hemodynamic parameters and vasoactive support within 120 min of the start of the dobutamine infusion. The FIO_2 was 0.43 ± 0.06. Body temperature remained stable throughout the study (difference below 0.5 °C).

Out of thirty patients the source of sepsis was pneumonia in 16 patients and peritonitis in 11 patients. The three remaining sources were sinusitis (1), mediastinitis (1) and necrotic fasciitis (1). The correlation coefficient between $VO_{2,IC}$ and $VO_{2,Fick}$ was found to be 0.83 (Fig. 1). The comparison between the two methods revealed a bias of 33 ml·min·m^2 and a precision of 32 ml·min·m^2 (Fig. 2). The coefficient of variation of $VO_{2,IC}$ was 4.4 % and of $VO_{2,Fick}$ 6.8 % (CO 7.0, SaO_2 6.5, SvO_2 8.2).

Dobutamine induced a significant dosage-related increase in cardiac index due to a combined increase in heart rate (from 105 ± 19 to 125 ± 16 beats·min) and stroke index (from 42.6 ± 12.7 to 46.5 ± 12.9 ml·m^2). In general, intravascular pressures remained stable (Table 1). There was a slight, but statistically significant, increase in mixed venous partial pressure of O_2 (PvO_2) (from 5.2 ± 0.7 to 5.6 ± 0.8 kPa) while arterial partial pressure of O_2 (PaO_2) decreased statistically significantly (from 13.7 ± 2.6 to 12.5 ± 2.2 kPa).

Dobutamine led to a progressive dosage-related increase in DO_2 (from 577 ± 192 to 752 ± 202 ml·min·m^2) which was associated with a moderate and statistically significant increase in both $VO_{2,IC}$ and $VO_{2,Fick}$ (from 173 ± 30 to 188 ± 28 ml·min·m^2 and from 140 ± 25 to 156 ± 24 ml·min·m^2). The changes in oxygen transport-related variables are paralleled by a statistically significant decrease in oxygen extraction ratio determined by either method (from 30 ± 1 % to 26 ± 1 % and from 26 ± 1 % to 23 ± 1 %). A significant increase of $VCO_{2,IC}$ during dobutamine infusion was determined (from 139 ± 24 to 147 ± 18 ml·min·m^2), while RQ_{IC} and body temperature remained unaffected. The three patients for whom dobutamine infusion had to be discontinued at the dosage of 10 μg·kg·min due to tachycardia or tachyarrhythmia recovered quickly. These patients were excluded from further analysis.

Individual VO_2/DO_2 slopes during dobutamine infusion were calculated for $VO_{2,Fick}$ (r = 0.68, Fig. 3) and $VO_{2,IC}$ (r = 0.55, Fig. 4). The mean VO_2/DO_2 slopes were 8.6 % $VO_{2,IC}$ and 9.1 % for $VO_{2,Fick}$ (Fig. 5). The only difference in the parameters between baseline and postinfusion was the a[La^-] (Table 1). The mean a[La^-] was normal in 22 of 30 patients (73.3 %) before starting the intervention. During dobutamine infusion there was a slight, but statistically significant, decrease in a[La^-] (from 2.0 ± 1.2 to 1.8 ± 1.0 mmol/l; $p < 0.01$).

Table 1 Hemodynamics, blood gas and metabolic parameters before, during and after dobutamine infusion. Results are expressed as means ± SD (*HR* heart rate, *MAP* mean arterial pressure, *mPAP* mean pulmonary artery pressure, *PCWP* pulmonary capillary wedge pressure, *CI* cardiac index, *SI* stroke index, PaO_2 arterial partial pressure of O_2, SaO_2 arterial saturation of oxygen, PvO_2 mixed venous partial pressure of O_2, *SvO2* venous saturation of oxygen, DO_2 oxygen delivery, $VO_{2,IC}$ oxygen consumption determined by indirect calorimetry, $VO_{2,Fick}$ oxygen consumption determined by Fick principle, $EO_{2,Fick}$ oxygen extraction ratio determined by Fick principle, $EO_{2,IC}$ oxygen extraction ratio determined by indirect calorimetry, VCO_2 carbon dioxide production, V_E minute ventilation, *RQ* respiratory quotient, aLa^- arterial lactate concentrations)

HR (beats/min)	Baseline	Dobutamine		Postinfusion
		5 μg·kg·min	10 μg·kg·min	
	105 ± 19	117 ± 18**	125 ± 17**	106 ± 18
MAP (mmHg)	92 ± 10	91 ± 10	88 ± 11**	91 ± 10
mPAP (mmHg)	28 ± 6	28 ± 6	28 ± 5	28 ± 6
PCWP (mmHg)	14 ± 3	14 ± 3	14 ± 2	14 ± 3
CI ($l \cdot min \cdot m^2$)	4.6 ± 1.5	5.2 ± 1.5**	5.7 ± 1.6**	4.7 ± 1.5
SI ($ml \cdot m^2$)	42.6 ± 12.7	45.4 ± 12.7**	46.5 ± 12.9**	42.9 ± 12.8
V_E (l·min)	8.2 ± 2.4	8.2 ± 2.4	8.1 ± 2.5	8.2 ± 2.3
PaO_2 (kPa)	13.7 ± 2.6	13.2 ± 2.6**	12.5 ± 2.7**	13.5 ± 2.5
SaO_2 (%)	95.2 ± 1.2	94.7 ± 1.3**	94.3 ± 1.5**	95.0 ± 1.2
PvO_2 (kPa)	5.2 ± 0,7	5.4 ± 0.7*	5.6 ± 0.8*	5.3 ± 0.7
SvO_2 (%)	71.0 ± 6.2	73.1 ± 5.2**	74.1 ± 5.0**	71.4 ± 6.0
DO_2 ($ml \cdot min \cdot m^2$)	577 ± 192	675 ± 195**	752 ± 202**	592 ± 197
$VO_{2,Fick}$ ($ml \cdot min \cdot m^2$)	140 ± 25	147 ± 24**	156 ± 24**	141 ± 24
$VO_{2,IC}$ ($ml \cdot min \cdot m^2$)	173 ± 30	182 ± 29**	188 ± 28**	174 ± 29
$VCO_{2,IC}$ ($ml \cdot min \cdot m^2$)	139 ± 24	145 ± 26**	147 ± 25**	140 ± 25
RQ_{IC}	0.80 ± 0.05	0.80 ± 0.05	0.79 ± 0.05	0.80 ± 0.05
$EO_{2,Fick}$ (%)	24 ± 1	22 ± 1**	21 ± 1**	24 ± 1
$EO_{2,IC}$ (%)	30 ± 1	27 ± 1**	26 ± 1**	30 ± 1
$a[La^-]$ (mmol/l)	2.0 ± 1.2			1.8 ± 1.0**

* $p < 0.05$ versus baseline, ** $p < 0.01$ versus baseline

Discussion

In this prospective study dobutamine infusion was used to increase DO_2 in our patients with septic shock in order to assess the VO_2-DO_2 relationship. The study was limited to patients with stable hemodynamic and metabolic conditions who showed no sign of severe respiratory failure (FIO_2 below 0.6). Dobutamine induced a dose-related increase in cardiac index and DO_2. VO_2 was determined simultaneously by indirect calorimetry and Fick principle and showed a moderate, but statistically significant, increase using either method, which resulted in a parallel positive slope in the VO_2-DO_2 relationship (Fig. 5). The positive slope in the VO_2-DO_2 relationship was associated with a statistically significant decrease in $a[La^-]$ and the oxygen extraction ratio.

The correlation coefficient between the two methods was satisfactory, but comparison between $VO_{2,IC}$ and $VO_{2,Fick}$ revealed substantial differences in our study. The mean value of $VO_{2,IC}$ was 20 % higher than $VO_{2,Fick}$. Intra-individual differences reached 86 $ml \cdot min \cdot m^2$ (52 % of the global means). Moreover, $VO_{2,IC}$ and $VO_{2,Fick}$ did not run parallel over the full range of VO_2 levels. At higher levels, these deviations were much more pronounced (Fig. 2).

There are numerous studies that compare $VO_{2,IC}$ and $VO_{2,Fick}$. While some investigators demonstrated good agreement between the two methods [18, 22], others noticed distinct differences [23, 24]. Discrepancies between the two methods may be attributed to several factors. The VO_2 of the lung can not be assessed by $VO_{2,Fick}$ [25]. In healthy individuals there is no difference between $VO_{2,IC}$ and $VO_{2,Fick}$. In cases of pulmonary disorders, VO_2 discrepancies can amount to as much as 19 % [26]. Pulmonary disorders such as pneumonia were present in all of the septic patients under study, probably explaining most of the discrepancies in our study. Unfortunately, there is no correlation between the difference of $VO_{2,IC}$ and $VO_{2,Fick}$ with indices of the ventilation-perfusion ratio [27].

In a methodological study, Chioléro et al. looked at the influence of injectant temperature on the reliability of CO measurement [28]. They ascertained no difference between $VO_{2,IC}$ and $VO_{2,Fick}$ if injectant at room temperature was used. When using ice cold injectant, however, the levels of $VO_{2,Fick}$ were statistically significantly lower than $VO_{2,IC}$. There were also substantial differences, of up to 25 %, between $VO_{2,IC}$ and $VO_{2,Fick}$ in earlier studies if cold injectant was used for CO determination [15, 29, 30]. These differences were below 10 % when using room temperature injectant [22, 23, 24]. In the present study cold injectant was used to determine CO, which may explain some of the differences. Another potential source of error is due to the mathe-

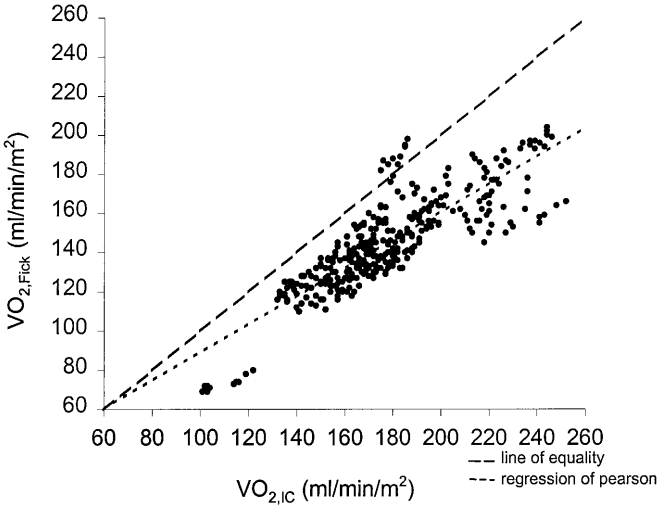

Fig. 1 Correlation between oxygen consumption determined by indirect calorimetry and by the Fick principle ($n = 342$, $r = 0.84$)

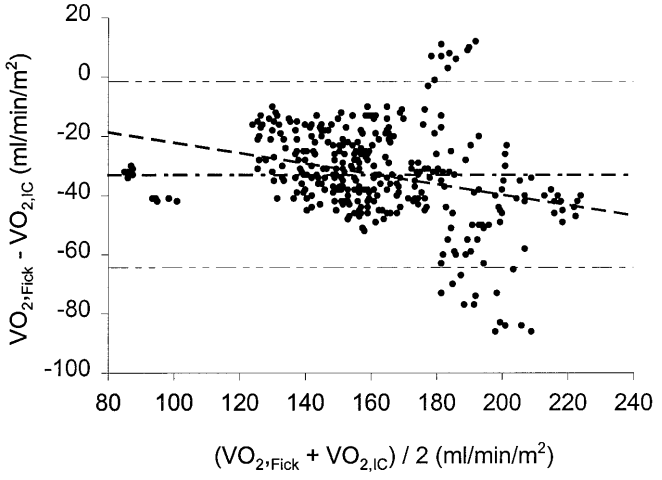

Fig. 2 Bias and precision between the determination of oxygen consumption by indirect calorimetry and by the Fick principle ($n = 342$)

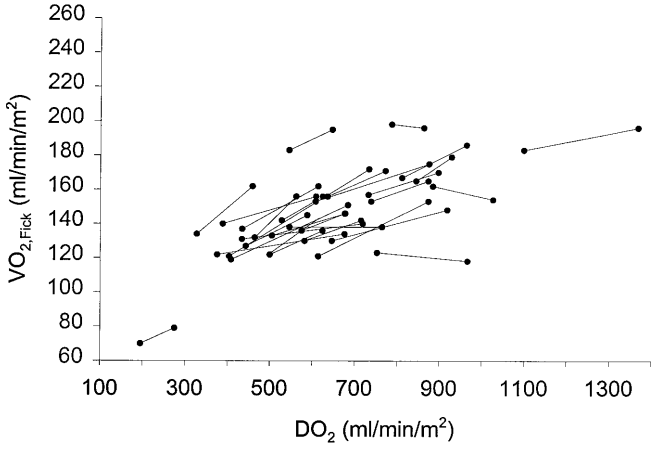

Fig. 3 Individual oxygen consumption determined by the Fick principle/oxygen delivery slopes during catecholamine infusion ($r = 0.56$)

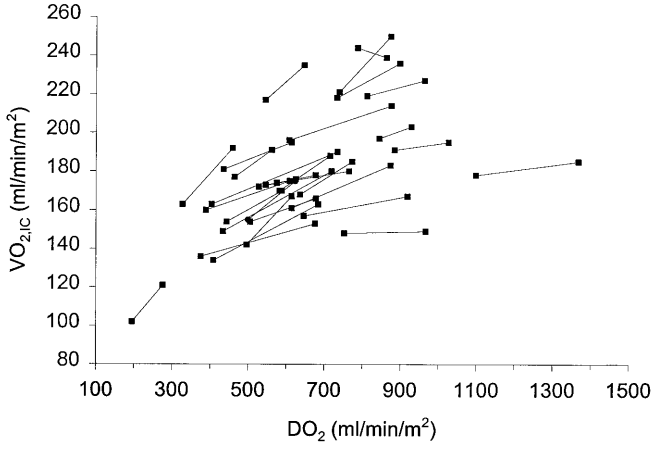

Fig. 4 Individual oxygen consumption determined by indirect calorimetry/oxygen delivery slopes during catecholamine infusion ($r = 0.55$)

matical coupling of shared variables used to calculate $VO_{2,Fick}$ and DO_2 [7, 29]. The phenomenon of increased scatter of data in our study at the low and high values (Fig. 2) could be caused by a greater variability of CO measurements at these levels of CO [9].

The effects of intervention (fluid loading catecholamine support) on DO_2 and VO_2 were studied in critically ill patients. Ronco et al. investigated the effects of volume loading on O_2 transport variables in patients with ARDS with normal $a[La^-]$ [6]. The increase in $VO_{2,IC}$ they documented was statistically not significant, though, since the mean slope of the VO_2-DO_2 relationship was 4.3% for $VO_{2,IC}$ and 8.6% for $VO_{2,Fick}$. This clinical investigation was repeated by the same study group in ARDS patients with different $a[La^-]$ where catecholamines were administered [29]. In this study a positive correlation between $VO_{2,Fick}$ and DO_2 was documented, while there was no correlation between $VO_{2,IC}$ and DO_2. The results of these two studies show that volume loading and catecholamine infusion increases $VO_{2,Fick}$ but not $VO_{2,IC}$ [6, 29].

Critically ill patients with ARDS, sepsis or hepatic failure, most of them with a normal $a[La^-]$, were investigated by Hanique et al. [30]. In this study, colloid infusion was used to increase DO_2, resulting in a significant correlation between $VO_{2,Fick}$ and DO_2. $VO_{2,IC}$ did not change significantly in any patients, but an individual O_2 supply dependency was detected in nearly 20% of them. De Backer et al. and Ronco et al. applied dobutamine infusion in septic patients [31, 32]. De Backer

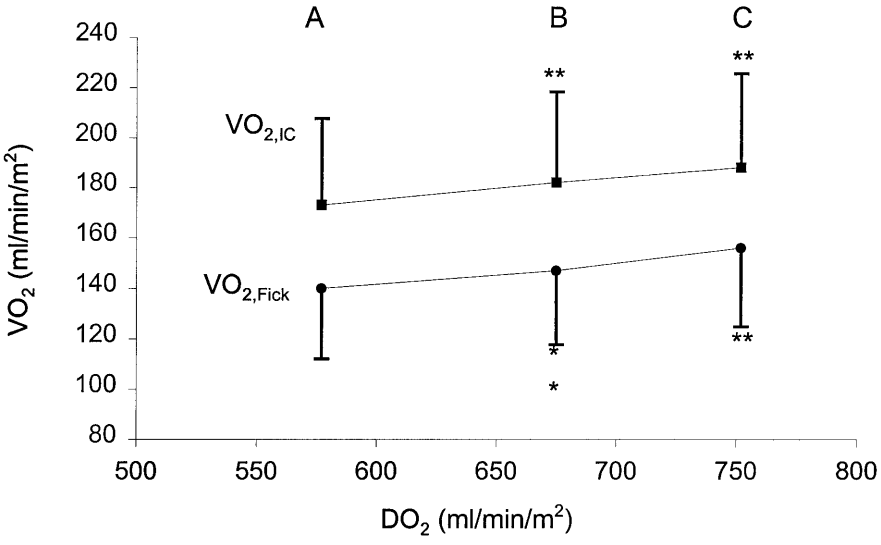

Fig. 5 Evolution of oxygen consumption as determined by indirect calorimetry and by the Fick principle during catecholamine infusion (*A* baseline, *B* 5 μg·kg·min dobutamine, *C* 10 μg·kg·min dobutamine) ** $p < 0.01$, * $p < 0.05$

and colleagues noted an increase in DO_2 in their patients, which was associated with a moderate, but statistically significant, increase in $VO_{2,IC}$ and $VO_{2,Fick}$. All patients had normal a[La^-]. The mean slope of the relationship was 8.8% for $VO_{2,IC}$ and 10.5% for $VO_{2,Fick}$ [31]. Ronco et al. increased DO_2 in septic patients with an infusion of different dosages of dobutamine from 5 to 15 μg·kg·min [32]. The authors found that VO_2 remained relatively constant despite large increases in DO_2. This occurred no matter whether the patients had normal or elevated lactate levels.

Dobutamine infusion induced a dosage-related increase in DO_2 due to β_1 cardiac stimulation [33]. In healthy volunteers administration of catecholamines resulted also in a persistent increase in VO_2 due to elevated myocardial VO_2 and stimulation of β_2 receptors with increased gluconeogenesis and lipolysis [34]. The influence of exogenous catecholamines on VO_2 in septic patients is controversial and may be due to different dosage regimens. When studying septic patients, Gilbert et al. demonstrated an increase in $VO_{2,IC}$ after volume expansion or blood transfusion only in patients with elevated plasma lactate concentrations [35]. Catecholamines also led to an increase in $VO_{2,IC}$, even in patients with no elevated lactate concentrations. However, the data on the metabolic effects of catecholamines in critically ill patients are controversially discussed in the literature. After infusion of dobutamine, Silverman and Tuma have shown an increase in $VO_{2,IC}$ in septic patients with elevated plasma lactate concentrations only [36], Gilbert et al. demonstrated this effect in patients with normal lactate concentrations, too [35].

Various factors may be responsible for a positive slope in the VO_2-DO_2 relationship during changes in DO_2 caused by an infusion of dobutamine. One factor could be the stimulation of β_2 adrenoceptors by the drug. Furthermore, in experimental conditions a small positive slope was also observed in the VO_2-DO_2 relationship during changes in DO_2 induced by hemorrhage or tamponade [37, 38].

We conclude that the ventilator-integrated Metabolic Monitor 7250 provides accurate, continuous and non-invasive determination of O_2 supply and other metabolic data in critically ill patients. Dobutamine infusion led to an increase in DO_2 in our septic patients, which was associated with a moderate increase in both $VO_{2,IC}$ and $VO_{2,Fick}$. IC with the Metabolic Monitor may be a helpful tool to guide therapy with catecholamines in septic shock patients.

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