Correlation Between Oxygen Consumption Calculated Using Fick's Method and Measured with Indirect Calorimetry in Critically Ill Patients

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Objective *- To compare the oxygen consumption index measured by using indirect calorimetry (VO_2I_{Delta}) with a portable metabolic cart and calculated according to Fick's principle (VO_2I_{Fick}) in critically ill patients.*

Methods *- Fourteen patients (10 men and 4 women, mean age 39.4 ± 5.4 years) were analyzed, 5 of them trauma victims and 9 sepsis victims. The following mean scores were obtained for these patients: APACHE II = 21.3±1.8, ISS = 24.8±6, and sepsis score = 19.6±2.3. The mortality risk (odds ratio), calculated from APACHE II, was 41.9±7.1%. All patients underwent mechanical ventilation and invasive hemodynamic monitoring with a Swan-Ganz catheter. VO_2 was obtained using the 2 methods (VO_2I_{Delta} and VO_2I_{Fick}) at 4 different times (T_1-T_4).*

Results *- A good correlation was found between the 2 methods (r=0.77) for the mean of the 4 serial measurements. No statistically significant differences were observed between indirect calorimetry and Fick's equation at T_1 (VO_2I_{Delta} = 138±28 and VO_2I_{Fick} = 59±38 $mL.min^{-2}.m^{-2}$, P=0.10) and T_3 (VO_2I_{Delta} = 144±26 and VO_2I_{Fick} = 158±35 $mL.min^{-2}.m^{-2}$, P=0.14), but a significant difference was observed at T_2 (VO_2I_{Delta} = 141±27 and VO_2I_{Fick} = 155±26 $mL.min^{-2}.m^{-2}$, P=0.03) and T_4 (VO_2I_{Delta} = 145±24 and VO_2I_{Fick} = 162±26 $mL.min^{-2}.m^{-2}$, P=0.01).*

Conclusion *- We may state that indirect calorimetry can be used for oxygen consumption analysis in critically ill patients and is as efficient as Fick's reverse equation, with the benefit of being a noninvasive and risk-free procedure.*

Keywords: oxygen consumption, trauma, sepsis

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Received 12/2/02
Accepted 6/5/03

Serial determination of oxygen consumption (VO_2) is useful for monitoring the dysfunction of the circulatory system and its response to certain therapeutic interventions. Even though oxygen transport (DO_2) to tissues may be adequate, this does not guarantee oxygen utilization by the cell because microcirculation disorders such as those observed in septic or poly-traumatized patients may impair its uptake [1].

Although the analysis of various parameters obtained by invasive hemodynamic monitoring (Swan-Ganz catheter) is useful for more complex cases, the determination of VO_2 depends on analysis of arterial blood and central venous gases, on the measurement of serum hemoglobin concentration and on hemoglobin oxygen saturation. Thus, VO_2 is calculated by the arteriovenous difference in oxygen content multiplied by cardiac output. Another way to calculate VO_2 is with indirect calorimetry, whereby consumption is quantified by the analysis of respiratory gas exchanges in a noninvasive, serial manner. The objective of the present study was to correlate oxygen consumption obtained by using the Fick method and indirect calorimetry in critically ill patients.

Methods

The Research Ethics Committee of the University Hospital, Ribeirão Preto Medical School, University of São Paulo, approved the present study.

A prospective study was conducted on critically ill patients of both sexes, victims of trauma or sepsis who required prolonged, mechanical ventilation (more than 3 days) and invasive hemodynamic monitoring (IHM) admitted to the intensive care unit (ICU) of the above hospital. Exclusion criteria were the following: clinically contraindicated IHM, age >80 and <15 years, the need for FiO_2 (oxygen fraction of inspired air) >0.6, mean arterial pressure (MAP) <50 mmHg, heart rate (HR) <50 or >140 bpm, presence of a bronchopleural air fistula, irreversible circulatory shock, brain death, and finally refusal to participate in the study by the patient or the person legally responsible. The indications for IHM were as follows: assessment of hemodynamic instability, monitoring of blood volume replacement in patients with cardiopulmonary or renal disease, and monitoring during mechanical ventilation with positive end-expiratory pressure (PEEP) values higher than 10 cm H_2O. IHM was performed by inserting a Swan-Ganz catheter into the pulmonary artery by puncture of the internal jugular vein or subclavian vein, preferably on the right side. When respiratory and hemodynamic stabilization occurred within 3 days of admission to the intensive care unit (ICU), the patients were included in the study.

All patients were stratified according to the Acute Physiologic and Chronic Health Evaluation II (APACHE II) system [2]. Victims of trauma were also classified by the injury severity score (ISS) [3] and patients with sepsis by the sepsis score (SS) system [4] on the first day of admission to the ICU. The criteria used to determine the presence of sepsis/septic shock followed the model defined by the Consensus Conference promoted by the members of the American College of Chest Physicians (ACCP) in association with the Society of Critical Care Medicine (SCCM) [5] in 1992, ie, (a) systemic response to infection demonstrated by 2 or more of the following data: temperature >38°C or <36°C, heart rate >90 beats per minute, respiratory frequency >20 breaths per minute or $PaCO_2$ <32 mmHg, leukocytes >12,000 cells/mm^3 or <4,000 cells/mm^3, or the presence of more than 10% young forms (rods); (b) hypotension with systolic arterial pressure <90 mmHg or a reduction of >40 mmHg compared with basal levels despite adequate volume repletion, together with abnormalities in peripheral perfusion, such as lactic acidosis, oliguria, or acute alteration of consciousness. The Trauma and Injury Severity Score (TRISS) [6] was also calculated for victims of trauma to estimate the probability of survival based on the anatomical and physiological characteristics of the patient. Patient weight was estimated based on body mass index according to age.

We studied 14 patients, 10 men and 4 women, average age 39.4±5.4 years. Among the patients with sepsis (n=9 or 64.3% of the total), 5 (55.6%) were males and SS was 19.6±2.3. All the patients who were victims of trauma were males and corresponded to 35.7% of the total. ISS was 24.8±6.0. The mean body weight of the entire series was 65.6±1.7 kg, and height was 167.1±2.2 cm. The mean APACHE II index for all patients on the day of admission to the ICU was 21.3±1.8. The overall death risk calculated from the APACHE II was 41.9±7.1%.

All patients were mechanically ventilated with a microprocessed mechanical ventilator (BIRD 8400ST*i*® - Bird Prod. Corp., USA, or SERVO 900C®, Siemens Elema, Sweden). The patients were ventilated in the controlled-volume mode, with a tidal volume of 8 to 10 mL.kg^{-1}, at a frequency of 12 to 16 breaths per minute, with an FiO_2 of less than 0.6. Air leakage in the respirator's circuit or through the endotracheal tube was detected by rigorous visual and auditory observation and by observation of the respiratory quotient values provided by the calorimeter. When these values were outside the 0.5 to 1 range, they represented a possibility of air leakage in the internal or external circuit.

Oxygen consumption measurements were obtained for all patients by using a portable calorimeter (Deltatrac II® Metabolic Monitor - Datex-Ohmeda, Finland). An initial calibration was performed before the study protocol by using the alcohol-burning test according to the manufacturer's specifications. Before each study, the calorimeter was heated for 30 minutes and then calibrated with a known mixture of gases containing 5% carbon dioxide (CO_2) and 95% oxygen (O_2). The line for inspiratory gas collection was positioned in the outlet of the humidifying and heating system of the respirator. All expired air was collected from the expiratory pathway (purging) of the respirator. All the procedures described were performed according to the manufacturer's specifications.

With the patient in stable condition in a calm environment, with no manipulation of the upper airways or of the parameters of the respirator for at least 30 minutes, minute to minute VO_2 measurements (mL.min^{-1}) were made. At the end of each 30-minute period, the mean and standard deviation of VO_2 were calculated. The 4 series of hemodynamic measurements were started immediately after each period of study by indirect calorimetry. The design of the study is schematically illustrated in figure 1.

Arterial peripheral pressure and arterial pulmonary and central venous pressure were monitored with invasive pressure modules (Dixtal 2010 - Biomédica Ind. e Com. Ltda., Brazil). The invasive pressure transducers were positioned at the level of the middle axillary line in the fourth intercostal space.

Invasive hemodynamic monitoring was performed by inserting a Swan-Ganz catheter (Baxter Healthcare Corp., USA) caliber 7 French into the pulmonary artery. The proper positioning of the Swan-Ganz catheter was confirmed by a chest X-ray of anteroposterior incidence.

Cardiac output was measured by the thermodilution technique using a computer (Dixtal 2010 - Biomédica Ind. e Com. Ltda., Brazil). Four consecutive injections of ice-cold 0.9% saline solution, varying in temperature from 0 to 5°C, were performed within less than 4 seconds during the expiratory phase of the respiratory cycle. The value obtained is reported as liters per minute related to total body surface (cardiac index in L.min^{-1}.m^{-2}).

On the basis of cardiac index, hemoglobin (Hb) concentration in g.dL^{-1} and other variables of the Fick equation obtained by arterial and mixed venous gas measurements, such as partial pressure of arterial oxygen, arterial oxygen saturation, partial pressure of mixed venous oxygen, and saturation of mixed venous oxygen (PaO_2, SaO_2, PvO_2, and SvO_2, respectively), we calculated VO_2I (mL.min^{-1}.m^{-2}). Partial gas pressure was expressed as mmHg and oxygen saturation as a percentage (%).

Four comparative measurements of oxygen consumption index were made using indirect calorimetry (VO_2I_{Delta}) and the Fick method (VO_2I_{Fick}).

Data were analyzed statistically considering the mean values of 4 serial measurements of oxygen consumption index obtained for all patients by the 2 methods (indirect calorimetry and Fick's equation). The 2 methods were compared

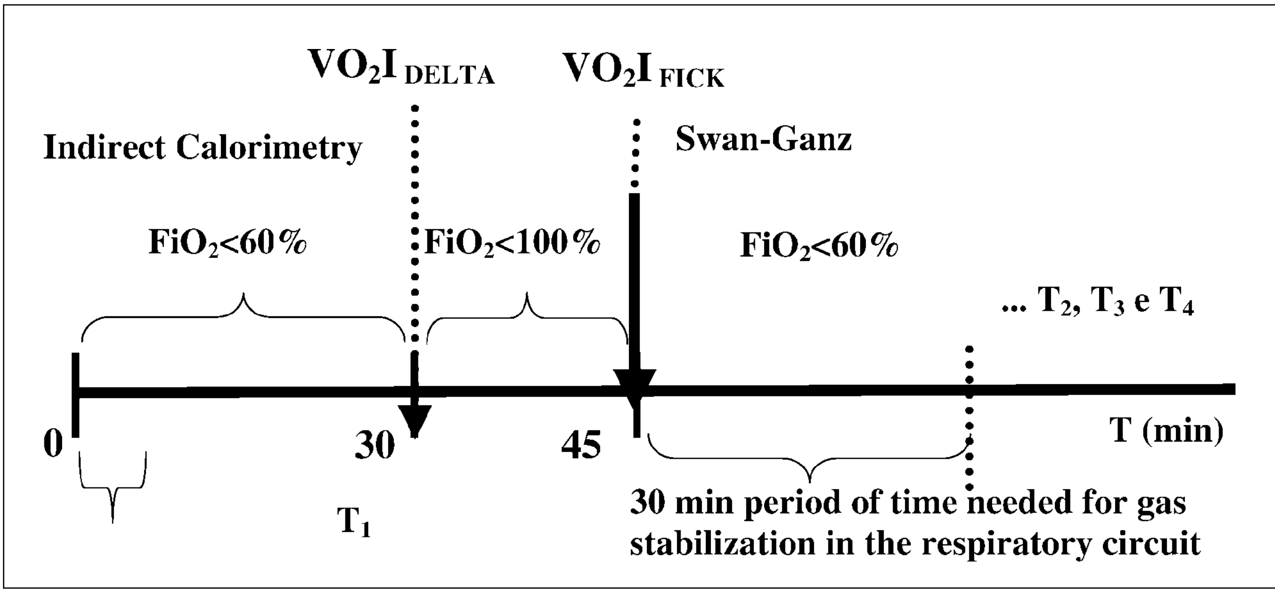

Fig. 1 - Design of the comparative study of determination of oxygen consumption by indirect calorimetry and the Fick method.

by using the nonparametric Wilcoxon test based on the null hypothesis (Vo_2I_{Delta} equal to VO_2I_{Fick}) and with a 95% confidence interval ($\alpha = 0.05$). Differences were considered significant when $P < 0.05$.

Results

A good correlation existed between the 2 methods (r=0.77), as can be seen in figure 2.

In patients with sepsis, mortality was 55.6% versus a death risk of 51.8±8.6% calculated from APACHE II. In traumatized patients, mortality was zero (APACHE II risk of 24.8±6 % and TRISS of 68.3 ± 13.3%). Overall mortality was 35.7% (APACHE II risk of 41.9 ± 7.1%).

No significant difference was noted in VO_2I measurements between the 2 methods at times T_1 and T_3 (P = 0.10 and P = 0.14, respectively). However, at times T_2 and T_4, the difference between methods was significant (P = 0.03 at T_2 and P = 0.01 at T_4). The mean difference between the measurements at times T_1 to T_4 ($T_{1Fick} - T_{1Delta}$, $T_{2Fick} - T_{2Delta}$, $T_{3Fick} - T_{3Delta}$, and $T_{4Fick} - T_{4Delta}$) was 17 ± 4 $mL.min^{-1}.m^{-2}$ (10 ± 2 %). The VO_2I values obtained by indirect calorimetry and by Fick's method at times T_1 to T_4 are shown in table I.

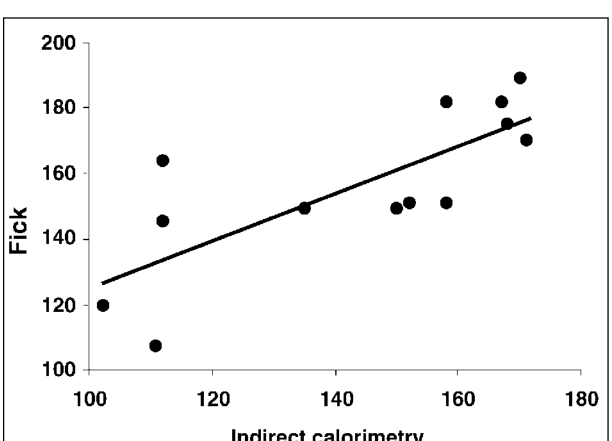

Fig. 2 - Correlation between the mean serial values of oxygen consumption rate measured by indirect calorimetry and by the Fick method (r = 0.77). Values are reported as $mL.min^{-1}.m^{-2}$.

Discussion

The objective of the present study was to compare the VO_2 obtained by the Fick method and by indirect calorimetry in critically ill patients who were victims of multiple trauma or sepsis. The Fick method for VO_2 monitoring continues to be the procedure most frequently used in intensive care. However, it is invasive because it requires the insertion of a Swan-Ganz catheter into the pulmonary artery through a central venous access and is associated with several well-documented complications [6].

Indirect calorimetry is another method available for VO_2 measurement, which is noninvasive and free of complications and requiring the use of a portable calorimeter connected to a respirator. However, in addition to involving expensive equipment, this method requires trained profes-

Table I - Oxygen consumption indices (VO_2I) obtained by the different methods at times T_1 to T_4 (SD = standard deviation) and difference between means

VO_2I ($mL.min^{-1}.m^{-2}$)	Time 1	Time 2	Time 3	Time 4
Indirect calorimetry				
Mean ± SD	138 ± 28	141 ± 27	144 ± 26	145 ± 24
Range	91 - 176	94 - 174	102 - 183	112 - 170
Fick's method				
Mean ± SD	159 ± 38	155 ± 26	158 ± 35	162 ± 26
Range	102 - 211	108 - 185	94 - 240	117 - 207
$VO_2I_{FICK} - VO_2I_{DELTA}$	21	14	14	17

sionals in order to obtain adequate calorimetric measurements as well as several precautions, such as appropriate calibration of the equipment before each use, careful analysis of the results, and the periodic execution of *in vitro* tests with alcohol burning [7].

The correlation between the mean of the 4 serial measurements was r = - 0.77. However, in the analysis according to time periods, no significant differences were detected between the 2 methods at T_1 and T_3. At T_2 and T_4, a small, significant difference existed between the 2 methods, ranging from 14 to 17 $mL.min^{-1}.m^{-2}$, which may mean very little in clinical practice. In the present study, some factors may have interfered with the accuracy of the indirect calorimetry measurements, such as the use of 2 different models of mechanical ventilators, even though the models were similar in terms of available resources and demonstrated the stability of the FiO_2 and minute volume parameters throughout the study. It is possible that the differences detected at 2 measuring time points (T_2 and T_4) reflect only a perfectly normal and temporal variation observed in studies of short duration. This is the reason why most studies continue to perform these comparative tests over a period lasting not less than 2 hours or 2 measurements, in order to reduce the discrepancies in certain measurements that might occur for the reasons mentioned above but that do not invalidate either method [8-12] (tab. II) [13-15].

Although the overall mortality rate for the series was very close to that predicted by the APACHE II index, it was not possible to associate greater mortality with the low ability to extract oxygen (low VO_2I) in either method. Although several studies have been conducted on critically ill patients, there still is no clear definition of the use of calorimetry in these cases, although this method has been defended as a more appropriate way of monitoring oxygen consumption and the adequacy of the caloric needs of the patient. In this respect, comparative studies of the 2 methods in different clinical situations have shown that indirect calorimetry is reliable for the determination of VO_2 (tab. II).

However, it is not our intention, with these results, to replace a more traditional and more routinely used (Swan-Ganz catheter) technique with indirect calorimetry. Some hemodynamic parameters are highly useful for the evaluation of the cardiocirculatory conditions of critically ill patients and can only be determined by introducing a catheter into the pulmonary artery, as is the case, for example, for the occlusion pressure of the pulmonary artery. The need for greater familiarity with, and training for this new high-cost equipment, is definitely a limiting factor for its routine use. Nevertheless, it is fundamental for more in-depth research and technical validation of the use of indirect calorimetry in Brazil, since this is equipment of relatively recent use, whereas invasive hemodynamic monitoring is a procedure that has been well standardized in ICUs since the 1970s.

Another point to be considered is that the Fick method is based on an equation using several measured parameters such as CO determined by thermodilution and the arterial and mixed venous blood O_2 content, leading to cumulative mathematical errors. Some of these parameters are also used to calculate oxygen supply. Thus, VO_2 calculated with the Fick method can have a coefficient of variation of up to 15%[16]. This variation justifies the general recommendation that calculated VO_2 should show at least a 15% alteration to be considered a significant physiological change.

Important differences of 32 ± 2% (P<0.001) were detected between VO_{2DELTA} and $VO_{2\,Fick}$ values [7]. However, after rigorous reinspection of methods and equipment, the authors detected an internal leakage in the calorimeter. In the present study, 1 patient was excluded after a leak was detected, although in the external circuit of the respirator (the fault was detected only at the end of the study). In patients undergoing heart surgery, greater precision was found in the VO_2 value obtained by indirect calorimetry than in the value obtained by the Fick method. The variations obtained, however, were mainly related to the method for CO measurement, ie, the greatest variations occurred due to the temperature of the injected fluid and to the phase of the respiratory cycle during which the measurements were made.

Closely similar errors have been observed for $VO_{2\,Fick}$ and $VO_{2\,Delta}$ (5% and 4%, respectively) [17], with the difference being that a continuous CO monitor was used, which is still not easily available in Brazil. However, another study [10] compared the 2 methods in patients who were victims of multiple trauma and detected significantly higher VO_{2Delta} values and concluded that indirect calorimetry should be the preferential method for VO_2 measurement in severely traumatized patients.

Septic complications after surgery or trauma are associated with higher metabolic rates. In patients with sepsis or septic shock, VO_2 values, contrary to what might be expected, are relatively reduced in the presence of greater metabolic necessities by the activation of the defense mechanisms of the organism and also by fever. Gas exchange measurements should be sufficiently long to ensure a correct interpretation of the results obtained, avoiding periods of unstable conditions, such as alterations of parameters of the mechanical ventilator and tracheal aspiration. In this respect, the number and duration of the measurements necessary to reach estimates of daily energy expenditure are very important. Although thus far, no standardization has occurred of the duration or the number of daily measurements by indirect calorimetry, some studies have indicated the convenience of measurements of short duration ranging from 5 to 30 minutes [18,19]. Two daily measurements of 15 minutes are sufficient to estimate 24-hour energy expenditure with a 4% error. For clinical purposes, it is acceptable to extrapolate 24-hour energy expenditure from measurements made over a period of 30 minutes [19]. Another study [20] suggested that shorter measurements over a period of 5 minutes are sufficient to measure energy expenditure when their variation is less than 5%. The major advantage of measurements of short duration is the possibility of daily monitoring of several critically ill patients, with a consequent reduction in equipment costs. In the present study, we decided to use 4 intervals of measurements of indirect calorimetry in order to minimize possible errors caused by lack of experience with

Table II - Summary of data obtained in studies that compared oxygen consumption measured by indirect calorimetry and the Fick method (* VO_2 in mL.min^{-1}), including the present study

Study	Number of patients	Type of patients	$VO_2I_{Calorimetry}$ (mL.min^{-1}.m^{-2})	VO_2I_{FICK} (mL.min^{-1}.m^{-2})	Difference between the 2 methods (%)
Bizouarn,1992[8]	10	After heart surgery	153 ± 17	120 ± 27	22
Brandi, 1992[13]	26	Critically ill	151 ± 26	145 ± 29	4
Myburgh, 1992[14]	20	Critically ill	308 ± 64*	284 ± 72*	8
Hanique, 1994[15]	73	Critically ill	153,9 ± 1,7	154.2 ± 2.3	0
	98	Critically ill	149,0 ± 1,4	146.8 ± 1.5	1
Cheong, 1997[9]	30	Heart surgery	129 ± 26	126 ± 16	2
	20	Critically ill	163 ± 33	145 ± 47	11
Epstein, 2000[10]	38	Polytrauma	170 ± 30	129 ± 46	24
Presente estudo	14	Polytrauma or Sepsis	142 ± 26	158 ± 24	- 11

the use of the calorimeter and interference by the environment (temperature, pressure, and humidity). However, unfortunately, no method for the assessment of oxygen supply and consumption in critically ill patients is free from limitations and criticisms.

In conclusion, the present results indicate the existence of a good correlation between VO_2 obtained by indirect calorimetry and by the Fick method, with the possibility of using indirect calorimetry as a method for the assessment of this parameter in critically ill patients as effectively as when using the reverse Fick equation, with the advantage that calorimetry is a noninvasive method free of complications.

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