ORIGINAL ARTICLE

# Oxygen Consumption – A Comparison Between Calculation by Fick's Principle and Measurement by Indirect Calorimetry

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## Summary

Oxygen consumption values calculated by Fick's principle ($cVO_2$) were compared to simultaneously obtained values measured by indirect calorimetry ($mVO_2$) in two groups of patients; post-coronary artery bypass graft (post-CABG) and septic shock. In both groups of patients, oxygen consumption values derived using indirect calorimetry were higher than that from Fick's principle. Whilst the bias obtained between the two methods of measurement were of acceptable amount clinically, the limits of agreement were wide: -57 to 51 $ml.min^{-1}.m^{-2}$ in the post-CABG group and -101 to 67 $ml.min^{-1}.m^{-2}$ in the group of septic patients; indicating that significant differences exist between paired individual values such that $cVO_2$ and $mVO_2$ were not interchangeable in this study.

*Key Words:* Oxygen consumption, Thermodilution, Fick principle, Indirect calorimetry, Critical illness, Cardiopulmonary bypass

## Introduction

The determination of oxygen consumption ($VO_2$) and oxygen delivery ($DO_2$) have assumed a more important role in the management of critically ill patients. Potential uses include the study of oxygen debt as an indicator of the severity of illness[1], as an end-point during resuscitation in the critically ill[2,3], the evaluation of pulmonary oxygen consumption[4,5], and the assessment of the daily caloric needs[6].

In clinical practice, oxygen consumption can be determined by two means. Firstly, it could be measured with an indirect calorimeter by analysis of respiratory gases[7]. Secondly, it can be calculated using the Fick method from the product of the arteriovenous oxygen content difference and the cardiac output. The aim of this study is to investigate if these two methods provide similar and interchangeable results in two groups of surgical patients with different pathological processes and metabolic states – postcoronary artery bypass grafting (post-CABG) and in patients with septic shock.

## Methods

Two groups of mechanically ventilated patients, who for clinical reasons were monitored with flow-directed pulmonary artery and arterial catheters, were studied. Group I consisted of 30 patients after uncomplicated CABG operations. Group II consisted of 20 patients with septic shock. The study was approved by the institutional ethics committee and informed consent obtained prior to surgery from the patients in Group I or their relatives or, when not available, from the attending primary physicians for patients in Group II. It was completed in the intensive care unit as part of the clinical management of the patients.

Patients with any one of the following conditions were excluded from the study : (a) air leakage from either endotracheal tube or thoracic drain, (b) active bleeding, or (c) inspired oxygen greater than 60%.

### Group I

Thirty patients who underwent CABG operation under moderate hypothermic cardiopulmonary bypass were studied. All these patients were clinically stable and were not in cardiac failure prior to surgery. Patients were induced with fentanyl 50 $\mu g.kg^{-1}$ and pancuronium bromide 0.1 $mg.kg^{-1}$ was used to facilitate endotracheal intubation. Anaesthesia was maintained with 50% oxygen in nitrous oxide. Additional doses of fentanyl and pancuronium were given intraoperatively as required. Cardiopulmonary bypass was instituted with a membrane oxygenator (COBE Laboratories Inc. Arvada, C080004 USA) with a pump flow rate of 2.2 $l.mim^{-1}.m^{-2}$. Moderate hypothermia (blood temparature 28°C) was achieved using a heat exchanger.

Postoperatively, all patients received mechanical ventilation (Siemens Elema, 900C) with tidal volumes 7-10 $ml.kg^{-1}$ at a rate of 10-15 $breaths.min^{-1}$ with a fraction of inspired oxygen 0.4, keeping the $PaCO_2$ at 35-45 mmHg. Intravenous morphine and diazepam or midazolam were used to provide sedation and nitroprusside used to control blood pressure.

Measurements in this study were performed in patients 12 to 16 hours postoperatively when they were cardiovascularly stable, free from pain and the core temperature was normothermic. Ventilatory support was maintained during the study period using synchronised intermittent mandatory ventilation.

### Group II

Twenty patients with septic shock were studied. The diagnosis of septic shock was made according to the criteria of the ACCP/SCCM Consensus Conference[8] : (1) a systemic response to infection as evidenced by two or more of the following : temperature >38°C or <36°C, heart rate >90$beat.minute^{-1}$, respiratory rate >20 $breaths.minute^{-1}$ or $PaCO_2$ <32 mmHg, WBC count >12000 $cells.mm^{-3}$, <4000 $cells.mm^{-3}$ or greater than 10% immature form. (2) hypotension with systolic blood pressure <90 mmHg or a reduction of greater than 40 mmHg from baseline despite adequate fluid resuscitation, along with presence of perfusion abnormalities that may include lactic acidosis, oliguria, or an acute alteration in mental status.

Patients were treated conventionally with fluids, catecholamines, vasodilators, sedatives, muscle relaxants and other support measures according to their haemodynamic and respiratory status. Mechanical ventilation were effected (Siemens Elema, 900C) with a minute volume and a fraction of inspired oxygen between 0.4 to 0.6 to maintain $PaO_2$ > 60 mmHg and the $PaCO_2$ at 35-45 mmHg.

### Measurement protocol

The study in each patient consisted of serial measurements of the haemodynamics parameters and oxygen-related indices after the patient had been left undisturbed for at least 30 minutes prior to the test period. Two different but simultaneously applied methods were used to determine oxygen consumption ($VO_2$) : (1) $cVO_2$, calculated from the product of cardiac index and the arteriovenous oxygen content difference, (2) $mVO_2$, measurement by analysis of respired gas.

All patients had a pulmonary artery catheter inserted (Opticath ® catheter P7110-EH, 7.5F Heparin coated, Abbott, USA). Cardiac output (CO) was determined by standard thermodilution technique and the use of a cardiac output computer (Oximetric 3, $SO_2$ and CO computer, Abbott, USA). Measurements were performed in triplicate using 10 ml room temperature normal saline. The morphology of the thermodilution curves were monitored. The results of three end-expiratory injections were averaged. Thereafter, arterial and pulmonary artery (mixed venous) blood sampling were performed simultaneously. Arterial and mixed venous oxygen saturation, partial pressure of oxygen ($SaO_2$, $S\bar{v}O_2$, $PaO_2$, $P\bar{v}O_2$, mmHg) were determined with a blood gas machine, Statprofile 5. Haemoglobin was measured by spectrophotometry (Tehnicon, Bayer, U.S.A). Arterial and mixed venous oxygen content ($CaO_2$, $C\bar{v}O_2$, $ml.dl^{-1}$) were calculated from the following equations:

$$CaO_2 = SaO_2 \bullet Hb \bullet 1.39 + 0.0031 \bullet PaO_2$$
$$C\bar{v}O_2 = S\bar{v}O_2 \bullet Hb \bullet 1.39 + 0.0031 \bullet P\bar{v}O_2$$

Oxygen consumption ($cVO_2$,$ml.min^{-1}$) was calculated by the reverse Fick equation:

$$cVO_2 = CO \bullet (CaO_2\text{-}C\bar{v}O_2) \bullet 10$$

Oxygen consumption was measured simultaneously from continuous respiratory gas analysis with an open circuit indirect calorimeter (Deltatrac, Datex Instrumentarium, Helsinki, Finland). Each reported value, $mVO_2$, was the mean of 10 successive measurements obtained immediately after determination of cardiac output by the thermodilution technique and blood sampling. The use of the monitor has been validated in previous clinical studies using similar patient groups[9,10]. The monitor is calibrated with a known concentration of oxygen and carbon dioxide prior to the study period according to the manufacturer's instructions. No changes of therapy occurred during the period of evaluation.

### Statistical method

Differences of values obtained between methods were analysed by using Student's t-test for paired samples. The agreement between the two methods used to obtain the same parameter, $VO_2$, was analysed according to the method of Altman and Bland[11]. The differences between paired $VO_2$ measurements by the two methods is the error, and the average error is the bias. Limits of agreement were calculated as bias ± 2 X standard deviation. A $p$ value of <0.05 is regarded as statistically significant.

## Results

### Group I

Of the 30 patients, 25 were males and five were females. The mean age was 55.8 ± 10.3 years; mean weight was 65.5 ± 9.4 kg; and mean body surface area was 1.69 ± 0.15 $m^2$. The mean $cVO_2$ determined by the Fick principle was 126 ± 16 $ml.min^{-1}.m^{-2}$ and the mean $mVO_2$ was 129 ± 26 $ml.min^{-1}.m^{-2}$ by respired gas analysis (Table I). The difference was not statistically significant (p=0.49, *t*-test). Bias between the two methods was -3.0 ± 27 $ml.min^{-1}.m^{-2}$. The limits of agreement obtained between the measured and calculated values were from -57 to 51 $ml.min^{-1}.m^{-2}$.

### Group II

The demographic and clinical data of the patients are presented in Table II. The mean APACHE II score for the group was 22 ± 7 and only 5 out of the twenty patients survived. The mean $cVO_2$ was 145 ± 47 $ml.min^{-1}.m^{-2}$ and the mean $mVO_2$ was 163 ± 33 $ml.min^{-1}.m^{-2}$, the difference between the two was not statistically significant (p=0.07, *t*-test) (Table II). The study of the individual paired differences between the measured and the calculated values showed that the magnitudes of the differences were substantial. The bias was -18$ml.min^{-1}.m^{-2}$ with standard deviation of 42 $ml.min^{-1}.m^{-2}$ with the limits of agreement were -101 to 67 $ml.min^{-1}.m^{-2}$ (Table I).

## Discussion

This study compared two different methods of clinical measurement of oxygen consumption applied simultaneously in two distinct groups of patients; after routine cardiopulmonary bypass graft surgery and those in septic shock. We found that in both groups of patients, $mVO_2$ as determined by analysis of respiratory

**Table I**
**Measured and calculated $VO_2$ values in Group I (post-CABG) and Group II (septic) patients**

| | Group I | | Group II | |
|---|---|---|---|---|
| | $cVO_2$ | $mVO_2$ | $cVO_2$ | $mVO_2$ |
| patients (n) | 30 | | 20 | |
| mean ± SD ($ml.min^{-1}.m^{-2}$) | 126 ± 29 | 129 ± 26 | 145 ± 47 | 163 ± 33 |
| bias ($ml.min^{-1}.m^{-2}$) | -3.0 ± 27 | | -18 ± 42 | |
| limits of agreement ($ml.min^{-1}.m^{-2}$) | -57 to 51 | | -101 to 67 | |

**Table II**
**Demographic data and clinical diagnoses of Group II patients**

| Sex | Age | Clinical diagnosis | Positive cultures |
|---|---|---|---|
| F | 81 | Aortoduodenal fistula | blood, tracheal aspirate |
| F | 68 | Empyema gallbladder | blood, bile |
| F | 51 | Ileal perforation | blood, intraabdominal pus |
| M | 63 | Colonic perforation | intraabdominal pus |
| F | 89 | Postgastrectomy anastomotic leakage | blood, intraabdominal pus |
| M | 57 | Perforation of diverticulitis | blood, intraabdominal pus |
| M | 75 | Postcholecystectomy bronchopneumonia | tracheal aspirate |
| M | 66 | Postcolectomy anastomotic leakage | intraabdominal pus |
| F | 20 | Colonic perforation | blood, intraabdominal pus tracheal aspirate |
| F | 36 | Acute pancreatitis | blood, tracheal aspirate |
| F | 66 | Postcholecystectomy bronchopneumonia | tracheal aspirate |
| M | 36 | Fournier's gangrene | blood |
| M | 66 | Postcolectomy bronchopneumonia | tracheal aspirate |
| M | 29 | Fractured pelvis, infected intraabdominal clots | tracheal aspirate, intraabdominal pus |
| M | 29 | Subhepatic abscess | tracheal aspirate, intraabdominal pus |
| M | 73 | Colonic perforation | abdominal drainage |
| F | 53 | Acute pancreatitis | abdominal drainage |
| M | 28 | Acute pancreatitis | intraabdominal pus, blood tracheal aspirate |
| F | 68 | Colonic perforation | intraabdominal pus, blood |
| M | 58 | Colonic perforation | tracheal aspirate, intraabdominal pus |

gases is higher than $cVO_2$, obtained using the reverse Fick method. In addition, the $VO_2$ values, bias and limits of agreement were of greater magnitude in Group II septic patients compared to Group I patients after CABG.

While $cVO_2$ and $mVO_2$ should be identical, various clinical studies that compared the two have consistently reported a difference between paired observations obtained by the two methods of measurement (Table III). This difference was observed in patients populations not unlike those in our present study, *viz.* after routine postcardiopulmonary bypass cardiac surgery as well as in critically ill patients. This difference was postulated to be due mainly to the oxygen consumption of the lungs themselves. Intrapulmonary $VO_2$ is not measured by the reverse Fick method as the pulmonary circulation is bypassed in the calculation of thermodilution-derived cardiac output. Under normal conditions, lung $VO_2$ is less than 5% of the total $VO_2$ however, it may rise to as high as 15% during inflammatory processes involving the lungs[16]. The value of 3 $ml.min^{-1}.m^{-2}$ in Group 1 and 18 $ml.min^{-1}.m^{-2}$ in Group 2 – the difference between $VO_2$ measured by indirect calorimetry and by the reverse Fick method – represented 2.4% and 11.6% of total body $VO_2$ and might be due to intrapulmonary

**Table III**
**Summary of similar studies**

| Study | No. & type of patients | $mVO_2$ | $cVO_2$ | bias |
|---|---|---|---|---|
| 1. Takala *et al*[9] | 20 post-CABG | 294 ± 59 | 247 ± 58 | 49 ± 25 $ml.min^{-1}$ |
| 2. Bizouarn *et al*[12] | 10 post-cardiac | 153 ± 17 | 120 ± 27 | 34 ± 27 $ml.min^{-1}.m^{-2}$ |
| 3. Hanique *et al*[13] | 73 critically ill | 153.9 ± 1.7 | 154.2 ± 2.3 | 0.3 ± 70 $ml.min^{-1}.m^{-2}$ |
| | 98 critically ill | 149.0 ± 1.4 | 146.8 ± 1.5 | 2.2 ± 52 $ml.min^{-1}.m^{-2}$ |
| 4. Brandi *et al*[14] | 26 critically ill | 151 ± 26 | 145 ± 29 | 5.2 ± 8 $ml.min^{-1}.m^{-2}$ |
| 5. Myburgh *et al*[15] | 20 critically ill | 308 ± 64 | 284 ± 72 | 24 ± 47 $ml.min^{-1}$ |

*Results are expressed as mean ± SD*

$VO_2$. Other explanations for these between-method differences may reflect the amount of bronchial blood supply that drains back into the pulmonary veins or coronary blood flow that returns directly into the left ventricle via the Thebesian veins both of which would not be detected by the Fick method. However, left-sided Thebesian flow is only a small fraction of total coronary artery blood flow (<1%) and is thus unlikely to account for any great degree of the observed differences, even if myocardial oxygen consumption is increased. In addition, the cumulative effects of the errors of measurements of the numerous primary variables entering the Fick equation introduce another potential source of error[17,18].

The mean $VO_2$ of 145 $ml.min^{-1}.m^{-2}$ obtained by Fick method and 163 $ml.min^{-1}.m^{-2}$ determined via indirect calorimetry are comparable to the figures obtained in other studies of $VO_2$ in septic patients[19,20]. The higher metabolic state of the septic patients as compared to those patients with uneventful cardiopulmonary bypass is evident from the higher mean oxygen consumption values. This is not unexpected as the septic patients are often in a hypermetabolic state while the patients after uneventful open heart surgery are neither hypermetabolic or hypercatabolic when compared with their baseline state preoperatively[21].

The bias and standard deviation was of a larger magnitude for the group of septic patients (18 ± 42 $ml.min^{-1}.m^{-2}$) as compared to the group of patients who had undergone cardiopulmonary bypass surgery (3.0 ± 27 $ml.min^{-1}.m^{-2}$). As discussed previously, the increase in oxygen usage by the pulmonary tissues might account for the larger bias. This is not unexpected as the latter group of patients is more homogenous and were free from any significant pulmonary pathology preoperatively. The former group had developed septic shock from a variety of infective foci and 10 of the 20 patients had chest infection with positive cultures and a varied degree of pulmonary involvement. The relative nonhomogeneity of this group of patients gave rise to the greater variability in repeated measurements as compared to the more stable group of Group I patients after routine CABG.

We have carried out simultaneous measurements and calculations of $VO_2$ in two distinct groups of patients: after uncomplicated postcoronary artery bypass graft surgery and those in septic shock. Our results demonstrated that these 2 methods of measurement did not provide results which were interchangeable in clinical practice. Measurement of $VO_2$ using analysis of respiratory gases by a metabolic monitor should be preferred because of the better reproducibility as compared to calculated results obtained via the reverse Fick method.

## Acknowledgement

We would like to thank Mrs Koh Bee Choo of the Biostatistics Consultancy Unit, Clinical Research Centre for her help in the statistical analysis.

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