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Influence of Ventilatory Settings on Indirect Calorimetry in Mechanically Ventilated Patients

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***Abstract*— With the aim to assess metabolic monitor's suitability to the use in mechanically ventilated patients, a method, based on the comparison between the measurements performed by the monitor and the ventilator, is here described. In particular, the effects of positive end-expiratory pressure and oxygen inspiratory fraction (FiO_2) on the metabolic measurements in presence of bias flow are investigated.**

In this study a metabolic monitor is used to estimate the energy expenditure of 10 mechanically ventilated cardiosurgical patients at different positive end-expiratory pressure, FiO_2 and two different modes of ventilation, with bias flow. The influence of the ventilatory settings on the parameters measured by the monitor is here quantified: a slight decrease of respiratory quotient and a slight increase of resting energy expenditure are observed with the increase of FiO_2.

This study shows a good agreement between the measurements of the two devices: FiO_2, expiratory volume (mean difference lower than 3%), and respiratory frequency (mean difference lower than 1%). This also demonstrates the capability of the metabolic monitor to reject the effect of the bias flow.

I. Introduction

THE introduction of advanced technology into the area of patient monitoring in Intensive Care Unit has made available many important measurements [1]. Among these, the resting energy expenditure (REE) is the preferred assessment of energy balance to provide appropriate energy supply to patients [2]-[5].

Indirect calorimetry allows the estimation of REE and respiratory ratio (R), in a non-invasive way, through the measurement of oxygen consumption (VO_2) and carbon dioxide production (VCO_2). A monitor for indirect calorimetry is normally equipped with sensors (i.e. O_2, CO_2, airflow) and a software dedicated to the elaboration of sensors' output, calculation of non-directly measured parameters, and segmentation of the whole respiratory trend into acts and, in particular, inspiration and expiration phases.

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Some issues have been addressed in the metabolic monitoring of patients subject to mechanical ventilation. Among them, one important issue is related to high values of positive end-expiratory pressure (PEEP) that results critical for the correct functioning of the sensors [6]. Secondly, accurate measurements of inspiratory fraction of O_2 (FiO_2) are essential in measuring VO_2. This requires that a stable FiO_2 is delivered to the patient throughout each breath and between breaths [7]. Stability thresholds of FiO_2 become narrower with the decrease of inspired-expired oxygen difference [1]: this generally happens increasing the FiO_2. Therefore, the higher the FiO_2 the greater the potential error in measuring VO_2 [8], [9].

Another issue is related to the bias flow (φ): a minimum continuous flow useful for patient triggering conveyed through the patient circuit, which does not participate to the pulmonary gas exchange. The accuracy loss in metabolism assessment, caused by φ, is still subject of debate [6], [9], [10]. Moreover, the interaction of φ with the breath identification algorithm needs further investigation.

The novelty of this work is investigating the effect of varying PEEP and FiO_2 on the metabolic measurements (REE and R) in presence of bias flow. The accuracy of the metabolic monitor in measuring O_2 concentration is also analyzed through a comparison with the FiO_2 delivered by the ventilator. Considerations about the potential effects of φ on the act segmentation algorithm and the calculation of the expired gas volume (V_E) are also reported.

II. Theoretical Background

According to an algorithm implemented into the majority of commercially available metabolic monitors, VO_2 is calculated by the following equation [11]:

$$VO_2\left[\frac{mL}{\min}\right] = V_I \cdot FiO_2 - V_E \cdot FeO_2 \tag{1}$$

and VCO_2 by a similar equation:

$$VCO_2\left[\frac{mL}{\min}\right] = V_E \cdot FeCO_2 - V_I \cdot FiCO_2 \tag{2}$$

where FeO_2 [%], $FeCO_2$ [%] and $FiCO_2$ [%] are the mean expiratory fraction of O_2 and CO_2, and the mean inspiratory fraction of CO_2 respectively. V_I [mL] and V_E [mL] are the inspired and expired gas volume respectively.

The two parameters, R and REE, object of a detailed analysis in this work, are computed through the following expressions:

$$R = \frac{VCO_2}{VO_2} \tag{3}$$

and the Weir equation [11]:

$$REE\left[\frac{kcal}{die}\right] = \left(3.94 \cdot VO_2 + 1.11 \cdot VCO_2\right) \cdot 1.44 \tag{4}$$

Ventilatory parameters are measured by both the metabolic monitor and the mechanical ventilator: expiratory volume (V_E), breathing frequency (f), and FiO_2.

The robustness of the metabolic monitor to the introduction of potential errors on the estimation of f and V_E, caused by φ, is assessed through a direct comparison with the ventilator's measurements.

III. Experimental Setup and Clinical Protocol

The experimental setup is described as follows. A paramagnetic oxygen sensor is the standard for measuring oxygen concentrations in modern metabolic monitors; analyzers based on infrared absorption are used for carbon dioxide measurements. Gases are generally sampled at fixed flow-rate from the ventilator circuit and drawn into the device [6]. In this study the Quark RMR (Cosmed srl, Italy) metabolic monitor has been utilized. With reference to figure 1, a turbine flow-meter is placed at the ventilator outlet (Fig. 1-E) and the gas sampling port is inserted in line with the breathing circuit downstream the 'Y-piece' (Fig. 1-A): this way makes possible to sample both inspiratory and expiratory gases.

All data are elaborated by the software, which is also able to detect breaths and recognize inspiration and expiration phases on the base of flow measurements and gas concentration trends. The estimation of φ is performed through the measurement of the continuous flow detectable after the end of the patient's expiration.

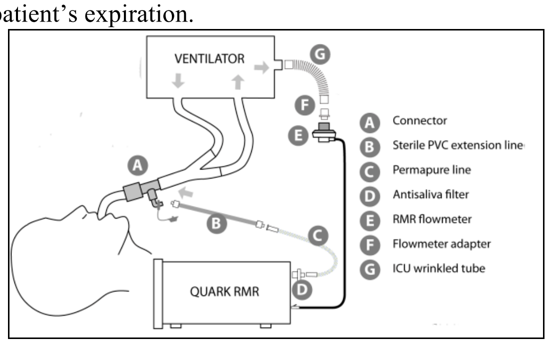


Fig. 1. Schematic representation of the measurement setup.

Before the test, the metabolic monitor needs a calibration: for the gas analyzers a certified mixture composed of 5 % of CO_2 and 15 % of O_2 is sampled, whilst the turbine flow-meter is calibrated through a syringe of 3 L.

Patients, who underwent cardiac surgery under general anesthesia, were recruited in this study. During a deep sedation, the subjects were ventilated by Servo-i ventilator (Maquet Gmbh & Co. KG, Germany) and their metabolic expenditure was monitored by the Quark RMR, using the setup showed in Fig. 1.

The patients were divided into two groups of 5 subjects each. Both groups were ventilated in Pressure Control (PC) and Synchronized Intermittent Mandatory Ventilation (SIMV) modes. For Group 1 the PEEP level was fixed to 5 cmH_2O, whilst the FiO_2 was set to the following levels: 21 %, 40 % and 50 %. For Group 2 the FiO_2 level was fixed to 50 %, whilst the PEEP was varied: 0 cmH_2O, 2 cmH_2O and 5 cmH_2O. All the ventilatory setting combinations, covering the range typically used during the intensive care, were repeated in both ventilation modes. φ was constant and equal to 2 L/min in every test [12].

Patients were given a resting period of at least 60 min between the surgery and the test, and a pause of 5 min between each test, for the reaching of a steady ventilation after the setting modification.

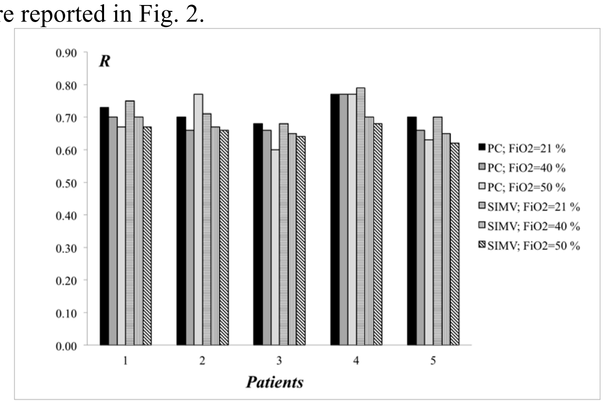
Before the test, the Quark RMR was calibrated and the procedure for φ detection was executed.

Each test had a duration of about 15 min, during which the ventilatory setting remained unchanged and the breath-by-breath data were collected by the Quark RMR. At the end of the test a report showed the averages and the ranges of variation of each parameter of interest (R, REE, VO_2, f, V_E and FiO_2).

The study was approved by the ethics committee of the University Campus Bio-Medico of Rome and the recruited patients expressed their informed consent for the clinical protocol-based treatment and data collection.

IV. Results and Discussion

REE (4) and R (3) values for patients belonging to Group 1 are reported in Fig. 2.



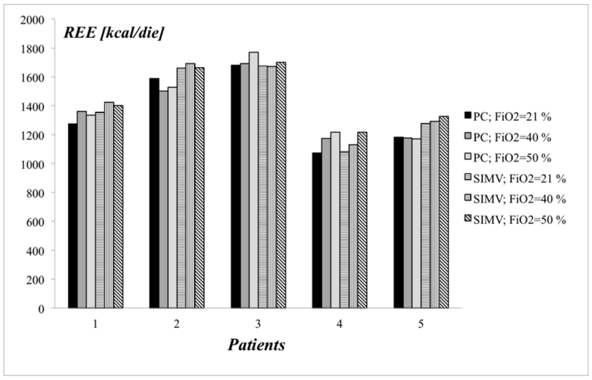


Fig. 2. R and REE values for Group 1 patients, ventilated using both PC and SIMV modes, at the three different FiO_2 values (21 %, 40 % and 50 %) and PEEP=5 cmH_2O.

REE and R values of Group 2 are shown in Fig. 3.

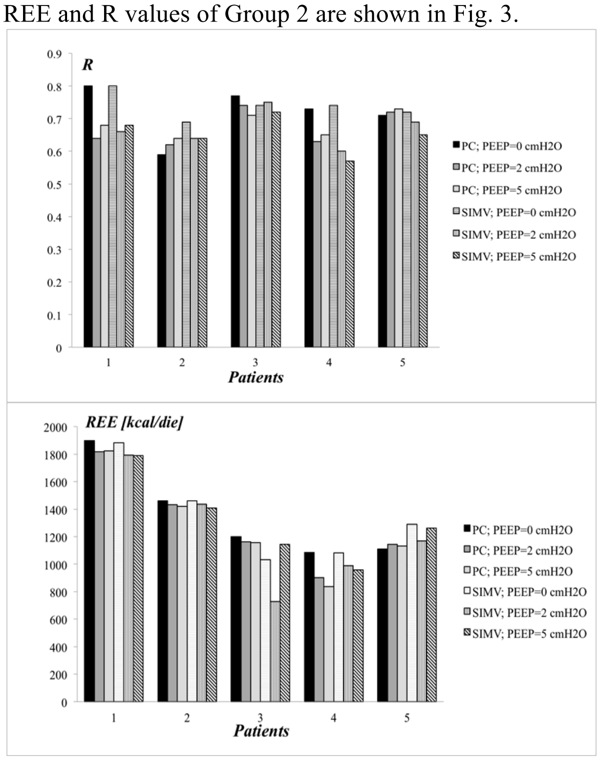


Fig. 3. R and REE values for Group 2 patients, ventilated using both PC and SIMV modes, at the three different PEEP values (0 cmH_2O, 2 cmH_2O, 5 cmH_2O) and FiO_2=50 %.

Tables I and II report R and REE mean values and standard deviations (SD) for both ventilation modes and at different FiO_2 and PEEP values: the means of REE and R in a group do not show significant variations with PEEP and FiO_2. However a slight variation as a function of FiO_2 is deducible if an intra-patient analysis is conducted: i.e. changing FiO_2 from 21 % to 40 % the value of R decreases in 9 trials out 10, the only one left reports the same value of R, and changing FiO_2 from 40 % to 50 % the value of R decreases in 8 trials out 10. These trends could be explained by the experimentally estimated increase of VO_2 with FiO_2 (+3.3 % from FiO_2=21 % to FiO_2=40 %, and +5.9 % from FiO_2=21 % to FiO_2=50 %), causing an increase of REE and a decrease of R. These results appear to confirm the observations reported in [13], [14].

From an intra-patient analysis, PEEP does not seem to have a net influence on the values of R and REE.

TABLE I
MEAN (SD) VALUES OF REE AND R FOR BOTH GROUPS

Group 1-SIMV	REE_{mean} (SD) [kcal/die]	R_{mean} (SD)
FiO_2=21 %	1411 (260)	0.726 (0.044)
FiO_2=40 %	1442 (242)	0.674 (0.025)
FiO_2=50 %	1462 (212)	0.654 (0.024)
Group 1-PC		
FiO_2=21 %	1360 (262)	0.716 (0.035)
FiO_2=40 %	1381 (221)	0.690 (0.048)
FiO_2=50 %	1404 (246)	0.688 (0.079)
Group 2-SIMV		
PEEP=0 cmH_2O	1349 (344)	0.738 (0.040)
PEEP=2 cmH_2O	1223 (409)	0.668 (0.056)
PEEP=5 cmH_2O	1312 (313)	0.652 (0.055)
Group 2-PC		
PEEP=0 cmH_2O	1350 (340)	0.720 (0.081)
PEEP=2 cmH_2O	1292 (348)	0.670 (0.056)
PEEP=5 cmH_2O	1274 (370)	0.682 (0.038)

The dependence of metabolic measurements as a function of φ has also been performed.

The breath identification algorithm seems to be effective: the mean difference between the measurements of f, considering all the 60 trials, results lower than 1 %. The mean difference, obtained during the trials performed at PEEP=5 cmH_2O, is lower than the mean difference at the two other PEEP values (about 0.4 % and 1.4 %).

Considering that the patients were deeply sedated, i.e. no spontaneous breathings were detected, these data show that the algorithm for the segmentation of respiratory trend is able to reject the influence of φ: in particular the procedure of φ detection allows the system to shift the threshold, used in the act recognition, of the quantity needed to segment the patient's breathing with good results.

The measurements of V_E, performed by the turbine flow-meter, sufficiently agree with the values reported by the mechanical ventilator: the mean percentage difference considering all the tests is lower than 3 %. The trials performed at a PEEP equal to 5 cmH_2O seem to show a better agreement between the two devices (difference lower than 1.5 %) than the trials performed at 50 % of fixed FiO_2 (difference of about 4 %).

A Bland-Altman plot is used to illustrate the differences between the values of V_E (Fig. 4) and FiO_2 (Fig. 5) obtained by the metabolic monitor and the ventilator: the means and the differences are reported on the x-axis and the y-axis, respectively. The differences, contained into the range defined for the ventilator's accuracy, confirm the agreement between the two devices.

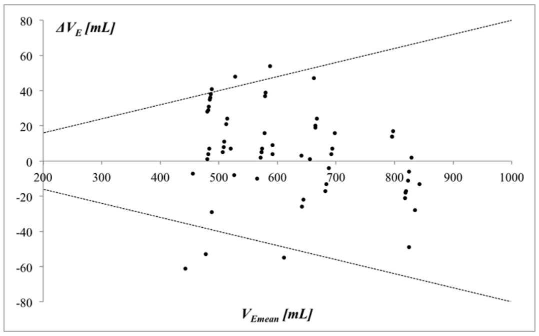


Fig. 4. Bland-Altman plot for the comparison between the values of V_E measured through the metabolic monitor and the ventilator respectively. The two dashed lines represent the accuracy of the ventilator in the V_E measurement [12].

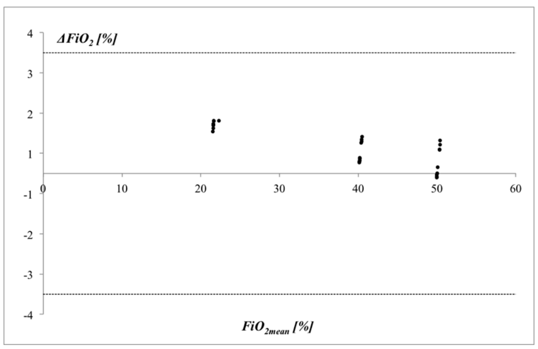


Fig. 5. Bland-Altman plot for the comparison between the values of FiO_2 measured through the metabolic monitor and the values set by ventilator. The two dashed lines represent the accuracy of the ventilator in the FiO_2 delivering [12].

Experimental data show that the metabolic monitor, used in this study, performs well in the act identification, in the FiO_2 and V_E measurements even using ventilator with φ.

The described approach, in which some measurements of metabolic monitor are compared to other obtained by the pulmonary ventilator, could give a method to assess the correct functioning of the monitor, when used in mechanically ventilated patients, in presence of φ, as also reported *in vitro* [10].

Therefore, the agreement of FiO_2, V_E, and f values is necessary condition to obtain a correct estimation of derived parameters, such as REE and R.

V. Conclusions

In vivo tests are performed to investigate some of the limitations addressed in literature [1], [6]-[8], related to the indirect calorimetry in mechanically ventilated patients. Tests are performed at different ventilatory settings, i.e. by varying PEEP, FiO_2 and ventilation mode. In this research, a slight dependence of R and REE on FiO_2 is evidenced, as also reported in [13], [14], whilst PEEP value seems not to show an influence.

Thanks to the comparison with the ventilatory parameters, the metabolic monitor appears not to be sensitive to the presence of φ on act recognition and measurement of expiratory volume; it also shows accurate measurements of FiO_2. This agreement guarantees the reliability of the monitor's measurements when it is coupled with a mechanical ventilator.

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