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Cardiac output estimation in mechanically ventilated patients: a comparison between prolonged expiration method and thermodilution

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Abstract— **A non-invasive method to estimate cardiac output (CO) in mechanically ventilated patients, based on prolonged expiration, has been previously described. With the aim to assess its performances, we prospectively enrolled fifteen cardiac surgery patients, and compared the results obtained with the non-invasive method with the ones obtained using two invasive approaches based on thermodilution. The correlations between the prolonged expiration method with both the thermodilution-based ones show high values (ρ^2>0.77 and ρ^2>0.89). This encouraging agreement is also confirmed by the closeness between the measured values of CO: the mean differences considering all patients and the two reference invasive techniques are -0.8 % and -7.5 %. These values show the slight underestimation of CO by the proposed non-invasive method with respect to the gold standard. On the other hand the described method could represent a good compromise between accuracy and non-invasiveness, which fosters the implementation of a new monitoring tool suitable for a semi-continuous CO assessment.**

I. Introduction

Cardiac output monitoring provides an indication of the ventricular function, representing the blood volume pumped by one ventricle per unit of time; therefore, it is considered an important parameter in the treatment of patients with cardiovascular diseases [1] and results crucial in the therapy management to maintain adequate tissue perfusion [2]. The two gold standards for CO measurements, i.e., the Fick method [3] and pulmonary artery thermodilution [4], are both invasive methods, requiring the use of central venous catheter and Swan-Ganz catheter, respectively. With the aim to reduce the risks for the patient, a big research effort has been made to investigate minimally invasive or non-invasive methods: transthoracic bioimpedance, Doppler ultrasound, and dye-dilution among others. The high costs of the devices and the use of disposable tools, together with the operator-dependent accuracy, have prevented the widespread use of these new methods in favor of the two gold standards.

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The pulmonary blood flow (PBF), which is the volume of blood that actively participates in the gas exchange per unit of time, is the directly estimated variable that some techniques employ to calculate CO. These involve the gas analysis at the subject's mouth and they are based on the application of the Fick method in two different phases: the former takes into account measurements during the steady state, whilst the second starts when a sudden perturbation into the CO_2 elimination process is introduced. Several approaches have been used to create such perturbation including: breath-holding [5], changing the minute ventilation [6] or the respiratory rate [7], and partial rebreathing of the expired gas [8].

In a previous study [9] we presented a prolonged expiration-based method to estimate CO in mechanically ventilated patients using the algorithm proposed by Kim *et al.* [10]. This technique provides a non-invasive estimation of the artero-venous content of CO_2, and consequently allows the calculation of PBF according to the Fick method.

Moreover, we compared the results obtained using our non-invasive approach with thermodilution on twenty mechanically ventilated patients, which underwent cardiac surgery. According to this first investigation, our method slightly underestimates the CO values obtained by thermodilution, but shows a precision and a percentage error slightly lower than other minimally invasive techniques [11].

In the present study the newly proposed method is tested on fifteen mechanically ventilated cardiac surgery patients and its outcome is compared to the values obtained from two invasive measurement systems based on thermodilution (i.e., the traditional intermittent bolus thermodilution, and the semi-continuous mode). This study aims to evaluate the performances of the prolonged expiration method on mechanically ventilated patients, and extends the validity of the method through the comparison with a further invasive technique.

In the following section a brief description of the theoretical background, at the base of the prolonged expiration method, is reported.

II. Principle of Measurement

The method used to perform the non-invasive estimation of CO, based on a prolonged expiration [9], involves a modified version of the Fick equation [3]:

$$PBF = \frac{\dot{V}_{CO_2}}{CvCO_2 - CaCO_2} \quad (1)$$

where $\dot{V}_{CO_2}$ is the amount of carbon dioxide produced by the patient per unit of time, $CvCO_2$ and $CaCO_2$ are the venous and the arterial concentration of carbon dioxide, respectively.

Considering the simplifying hypothesis of linear dissociation curve of CO_2, (1) can be expressed as follows:

$$PBF = \frac{\dot{V}_{CO_2}}{S \cdot \left(PvCO_2 - PaCO_2\right)} \quad (2)$$

where S is the slope of the carbon dioxide dissociation curve in the blood (solubility of carbon dioxide in blood), $PvCO_2$ and $PaCO_2$ are the venous and the arterial partial pressure of carbon dioxide, respectively.

$PvCO_2$ and $PaCO_2$ values are calculated using the method introduced by Kim *et al.* [10] based on the analysis of the gas exchange during both normal breathing and prolonged expiration. Their estimation is performed through the introduction of the instantaneous exchange ratio (R):

$$R = \frac{s - F_I O_2 \cdot s - F_I CO_2}{1 - F_I O_2 \cdot s - F_I CO_2} \quad (3)$$

where F_IO_2 and F_ICO_2 are the inspiratory fraction of oxygen and carbon dioxide, respectively, s is the slope of the parabolic curve obtained from the quadratic regression of P_ACO_2 vs. P_AO_2 data, registered during a prolonged expiration [10], P_ACO_2 and P_AO_2 are the alveolar partial pressure of carbon dioxide and oxygen, respectively.

In calculating the mentioned quadratic regression, only the last part of the prolonged expiration waveform (one third) is considered, as the first part contains the sampling of gas coming predominantly from dead-space. The elaboration consists of two steps: the former is a preliminary parabolic regression of P_ACO_2 as a function of P_AO_2 data (Fig. 1); in the second step, the points having a P_ACO_2 within the range 0-0.7 mmHg, from the related points on the first calculated curve, are considered for the elaboration of a further parabolic regression.

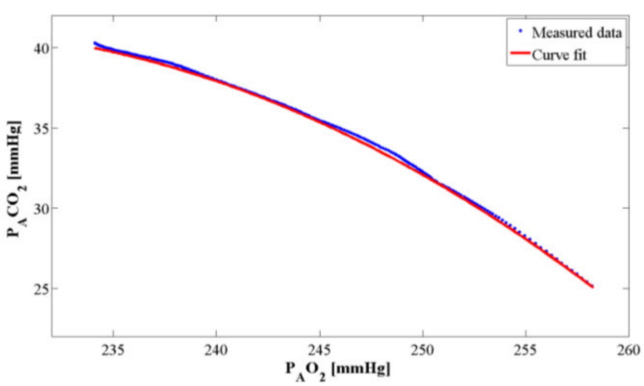

Figure 1. P_ACO_2 vs. P_AO_2 during a prolonged expiration performed by a mechanically ventilated patient. Measured data (•) and parabolic curve fitting (-).

The obtained function is used to calculate s and R (3). PBF is estimated using (2) on the base of three simplifying hypotheses: 1) in agreement with Kim *et al.*, we consider that R linearly diminishes with P_ACO_2 increase; 2) we also consider P_ACO_2 and P_AO_2 instantaneously equal to $PaCO_2$ and PaO_2 (arterial partial pressure of oxygen); 3) we assume that $PaCO_2$ is equal to the P_ACO_2 value corresponding to R value equal to the mean exchange ratio $RQ = \dot{V}_{CO_2} / \dot{V}_{O_2}$ within the minute preceding the prolonged expiration and that P_VCO_2 corresponds to the P_ACO_2 value at R=0.32 (magnitude of the Haldane effect [10]), as shown in Fig. 2.

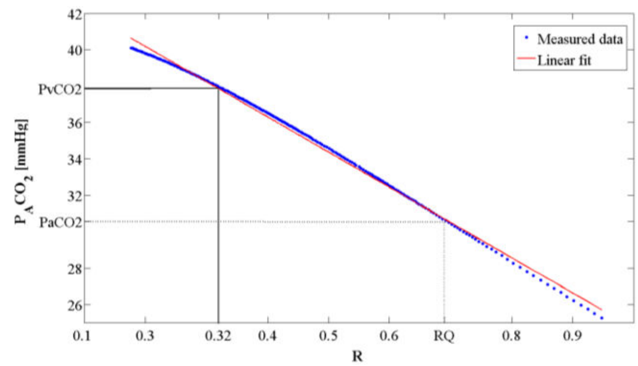

Figure 2. P_ACO_2 vs. R during a prolonged expiration performed by a mechanically ventilated patient. Measured data (•) and linear fitting (-). $PaCO_2$ and $PvCO_2$ are obtained in correspondence of R=0.32 and R=RQ, respectively.

Assumed S constant (4.7 $mL \cdot L^{-1} \cdot mmHg^{-1}$), the measurements of $\dot{V}_{CO2}$, during normal breathing, allow obtaining PBF from (2).

Finally, CO is calculated as follows [8]:

$$CO = \frac{PBF}{1 - F} \quad (4)$$

where F is the shunting fraction: i.e., the ratio between the amount of blood which does not participate to the alveolar gas exchange and the amount of blood pumped by the left ventricle during heart contraction. F can be estimated according the iso-shunt plots [8].

III. Patients and Methods

In this prospective study fifteen patients were recruited: they all underwent cardiac surgery and needed to be mechanically ventilated after procedure. The study was approved by the local Institute Ethical Committee, and the patients expressed their informed consent for the clinical protocol-based treatment and data collection (Prot. N. 19/2011 ComEt CBM). All patients were ventilated by Servo-I ventilators (Maquet GbmH & Co. KG) and neither spontaneous muscular activity nor spontaneous respiratory effort was registered during the procedure. Monitoring of the clinical and therapeutic courses of all recruited patients needed the introduction of a Swan-Ganz catheter.

CO estimation was performed with three different approaches. 1) the Swan-Ganz, previously introduced for intra-operative management, was interfaced to the CO module of the patient's monitor (MP70 IntelliVue, Philips Healthcare, Inc.) to obtain a CO estimation using a gold standard method, the thermodilution (CO_T). This estimation was performed ten times using injections of 10 mL of a solution (0.9 % NaCl) at room temperature. 2) The Swan-Ganz was interfaced to a monitor (Vigilance II, Edwards Lifesciences), which provided a semi-continuous calculation of CO: twenty values were recorded (CO_V). 3) The algorithm for the non-invasive estimation of CO described in the previous section was performed twenty times (CO_K). At this purpose, a metabolic monitor (Quark RMR, Cosmed s.r.l.), previously tested *in vitro* and *in vivo* on mechanically ventilated patients [12,13], was used (Fig. 3): it sampled gas from the "Y" piece of the breathing circuit through a suction pump. Gas sample was used to continuously record RQ, expired (F_EO_2, and F_ECO_2) and inspired (F_IO_2, and F_ICO_2) O_2 and CO_2 fraction in steady state conditions. Airflow was measured by a turbine flowmeter placed at the ventilator outlet. The whole data were elaborated by a custom made application implemented in LabView environment allowing to detect breathing acts, recognize inspiration and expiration phases and gas concentration trends, calculate the mean values of RQ and $\dot{V}_{CO2}$ in a time interval of 1 min preceding the prolonged expiration.

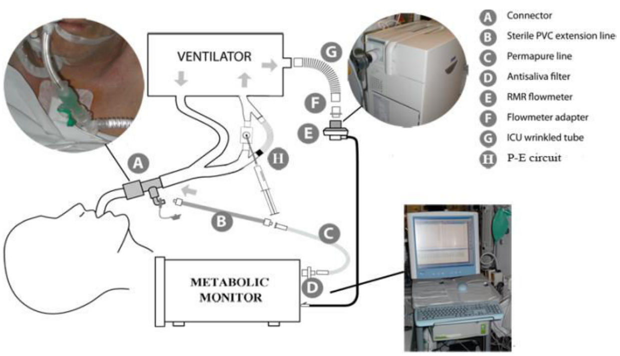

Figure 3. Schematic representation of the measurement set-up.

In order to obtain the prolonged expiration, a custom developed element with two branches was added in the expiratory limb of the breathing circuit. In one of these, an orifice pneumatic resistance, having a diameter of 1.2 mm and a mean pneumatic resistance of 5 $cmH_2O \cdot L^{-1} \cdot min$, was inserted to increase the expiratory time. In the other branch a balloon valve was used to deviate the airflow (Fig. 4).

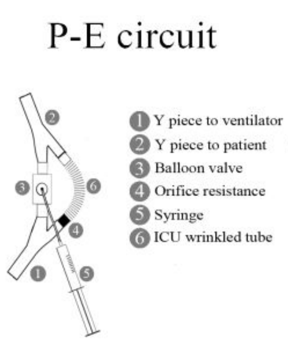

Figure 4. Schematic circuit for the induction of prolonged expiration.

When the balloon valve was opened, the majority of the expired flow went through it. When the valve was closed, the whole expiratory flow went through the orifice resistance: this made the patient expire with a higher time constant. Experimental data of CO_2 and O_2 concentration were recorded and processed after the measurement session thanks to an *ad hoc* developed LabView application, which converted the gas fractions into partial pressures, segmented the trends, executed the data-reduction and, after obtaining the values of $PvCO_2$ and $PaCO_2$ as described, it calculated the CO value using the above mentioned algorithms.

IV. Results and Discussion

CO mean values estimated with all three methods for each patient are reported in Table I.

TABLE I. Mean values and standard deviation of CO for each patient using the three methods.

Patients	CO_T [$L \cdot min^{-1}$]	CO_K [$L \cdot min^{-1}$]	CO_V [$L \cdot min^{-1}$]
1	4.8 (0.75)	4.7 (0.76)	5.9 (0.09)
2	3.8 (0.40)	3.3 (0.48)	3.8 (0.22)
3	3.1 (0.21)	3.0 (0.34)	3.2 (0.08)
4	3.1 (0.21)	3.3 (0.41)	3.2 (0.26)
5	3.5 (0.31)	3.7 (0.56)	3.8 (0.11)
6	4.4 (0.70)	4.3 (0.43)	4.4 (0.06)
7	6.4 (0.59)	5.1 (0.60)	6.4 (0.14)
8	3.2 (0.17)	3.6 (0.52)	4.0 (0.38)
9	5.1 (0.42)	6.4 (0.71)	6.6 (0.34)
10	4.2 (0.23)	4.3 (0.62)	4.1 (0.20)
11	2.5 (0.04)	2.4 (0.27)	2.8 (0.02)
12	3.6 (0.28)	3.5 (0.28)	3.5 (0.09)
13	2.5 (0.18)	2.3 (0.28)	2.4 (0.15)
14	4.4 (0.43)	4.1 (0.36)	4.4 (0.04)
15	3.0 (0.23)	3.0 (0.29)	3.1 (0.06)

CO_T: cardiac output estimated by thermodilution
CO_K: cardiac output estimated by prolonged expiration
CO_V: cardiac output estimated using the Vigilance II

In order to compare the agreement between the three methods, the percentage differences between CO values estimated using different approaches are calculated as follows:

$$\Delta CO_{1\to 2}\% = \frac{CO_1 - CO_2}{CO_1} \cdot 100 \tag{5}$$

where CO_1 and CO_2 are the mean estimated values of CO for the same patient using two different methods. Fig. 5 shows these differences calculated considering all the three pairs of methods for each patient.

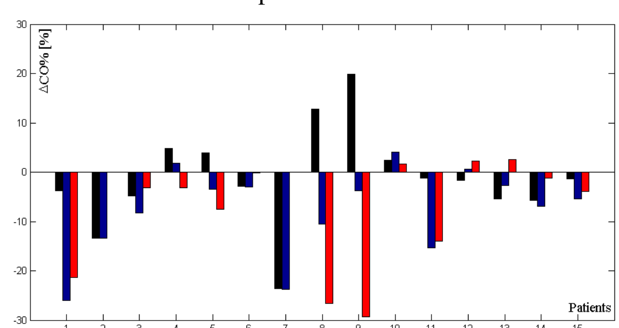

Figure 5. $\Delta CO_{1\to 2}\%$ for each patient considering all methods. Black bars: $\Delta CO_{K\to T}\%$; blue bars: $\Delta CO_{K\to V}\%$; red bars: $\Delta CO_{T\to V}\%$.

Fig. 5 clearly shows that the CO differences estimated between our non-invasive method and the two invasive approaches are comparable to the differences between the values obtained with the two invasive methods. This is confirmed by the closeness of agreement between mean CO differences calculated considering all patients: $\Delta\overline{CO}_{K\to T}\% = -0.8\%$; $\Delta\overline{CO}_{K\to V}\% = -7.5\%$; $\Delta\overline{CO}_{T\to V}\% = -7.2\%$.

These data also show that: 1) the proposed non-invasive method only slightly underestimates the gold standard method [9], 2) the use of an invasive method does not guarantee an improved precision of the estimation, as demonstrated by the discrepancy between CO_T and CO_V, which results of the same order of magnitude of those reported also in previous studies.

The regression between CO values estimated with different techniques is performed using the minimization of least square error, as shown in Fig. 6. In all three pairs high correlation coefficient are obtained (i.e., ρ^2=0.77, 0.89, and 0.87 for CO_K vs. CO_T, CO_K vs. CO_V and CO_V vs. CO_T respectively). The good correlation and the slight underestimation, when the non-invasive method is used, are underlined also by the simple regression analysis: in both CO_K vs. CO_T and CO_K vs. CO_V the slope of the best fitting line is slightly lower than 1 (0.98 and 0.92, respectively).

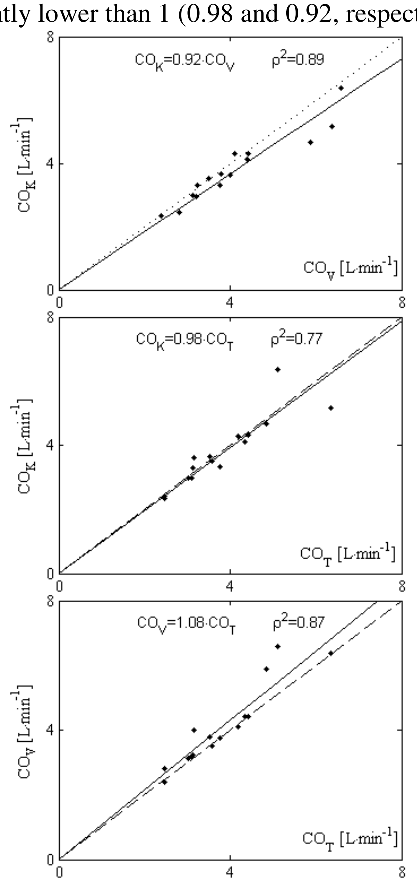

Figure 6. Correlation between CO values obtained with two different methods: experimental data (black dots), simple regression (continuous line) and line of equality (dotted line).

The agreement between the proposed non-invasive method and the gold standard in the CO assessment, is in line, or even better, with the findings of Peyton *et al.* [11] about the accuracy of other minimally invasive methods.

V. Conclusions

In this prospective study a non-invasive method for CO estimation is applied on fifteen patients. The good agreement between the results obtained using this method and the ones obtained by two invasive measuring approaches strengthens the results of our earlier investigations [9].

Several advantages can be introduced by the prolonged expiration technique: non-invasive measurement, easy implementation, independency from operator ability among others. All these aspects encourage further clinical studies and further effort towards the automation of the procedure.

These results could promote the development of a new monitoring device or a tool to be integrated in an existing medical system, which executes the non-invasive estimation of CO with a reduced risk for the patient.

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References

[1] P. Christensen, and J. Grønlund, “Repeatability of the single-breath method for estimation of pulmonary bloodflow: comparison among four data-reduction procedures,” *Clin. Physiol.*, vol. 6, pp. 221–234, 1986.

[2] T.G. Sanderland, and P. do Nascimiento, “Maintaining tissue perfusion in high-risk surgical patients: a systematic review of randomized clinical trials,” *Anesth. Analg.*, vol. 112, pp. 1384–1391, 2011.

[3] A. Fick, “Über die messung des blutquantums in den hertzventrikeln,” *Sitzungsberichte der Physiologisch- Medizinosche Gesellschaft zu Wuerzburg*, vol. 2, 1870.

[4] R.A. Norman, R.W. Johnson, J.E. Messinger, and B. Sohrab, “A continuous cardiac output computer based on thermodilution principle,” *Ann. Biomed. Eng.*, vol. 17, pp. 61–73, 1989.

[5] A. Gedeon, P. Krill, and B. Österlund, “Pulmonary blood flow (cardiac output) and the effective lung volume determined from a short breath hold using the differential Fick method,” *J. Clin. Monit. Comp.*, vol. 17, pp. 313-321, 2002.

[6] A. Gedeon, L. Forslund, G. Hedenstierna, and E. Romano, “A new method for noninvasive bedside determination of pulmonary blood flow,” *Med. Bio. Eng. Comput.*, vol. 18, pp. 411–418, 1980.

[7] P.J. Peyton, D. Thompson, and P. Junor, “Non-invasive automated measurement of cardiac output during stable cardiac surgery using a fully integrated differential CO2 Fick method,” *J. Clin. Monit. Comp.*, vol. 22, pp. 285–292, 2008.

[8] M.B. Jaffe, “Partial CO2 rebreathing cardiac output–operating principles of the NICO™ system,” *J. Clin. Monit. Comp.*, vol. 15, pp. 387-401, 1999.

[9] S. Cecchini, E. Schena, M. Notaro, M. Carassiti, and S. Silvestri, “Non-invasive estimation of cardiac output in mechanically ventilated patients: a prolonged expiration method,” *Ann. Biomed. Eng.*, DOI: 10.1007/s10439-012-0534-3, Published online.

[10] T.S. Kim, H. Rahn, and L.E. Fahri, “Estimation of true venous and arterial PCO2 by gas analysis of a single breath,” *J. Appl. Physiol.*, vol. 21, pp. 1338-1344, 1966.

[11] P.J. Peyton, and S.W. Chong, “Minimally invasive measurement of cardiac output during surgery and critical care: a meta-analysis of accuracy and precision,” *Anesthesiology,* vol. 113, pp. 1220–1235, 2010.

[12] S. Cecchini, E. Schena, R. Cuttone, M. Carassiti, and S. Silvestri, “Influence of ventilatory settings on indirect calorimetry in mechanically ventilated patients,” in *Proc. 33rd Annu. International Conf. IEEE Eng Med Biol Soc*, Boston, 2011, pp. 1245–1248.

[13] S. Cecchini, E. Schena, M.N. Di Sabatino, and S. Silvestri, “Uncertainty evaluation of a calibration method for metabolic analyzer in mechanical ventilation,” in: *Proc. 6th IEEE International Symposium on Medical Measurements and Applications (MeMeA 2011)*, Bari (Italy), 2011, pp. 143–147.