

Research

Comparison of bedside measurement of cardiac output with the thermodilution method and the Fick method in mechanically ventilated patientsJésus Gonzalez¹, Christian Delafosse², Muriel Fartoukh³, André Capderou⁴, Christian Straus⁵, Marc Zelter⁶, Jean-Philippe Derenne⁷ and Thomas Similowski⁸¹Senior Resident, Laboratoire de Physiopathologie Respiratoire et Unité de Réanimation, Service de Pneumologie, Groupe Hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France²Junior Consultant (Chef de Clinique), Réanimation Médicale, Groupement Hospitalier Eaubonne-Montmorency, Hôpital Simone Veil, Eaubonne, France³Junior Consultant (Chef de Clinique), Laboratoire de Physiopathologie Respiratoire et Unité de Réanimation, Service de Pneumologie, Groupe Hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France⁴Assistant Professor of Physiology, Centre Chirurgical Marie-Lannelongue, Le Plessis-Robinson, France⁵Assistant Professor of Physiology, Service Central d'Explorations Fonctionnelles Respiratoires, Groupe Hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France⁶Professor of Physiology, Head of the Pulmonary Function Tests, UPRES EA 2397, Université Paris VI Pierre and Marie Curie, Paris, France⁷Professor of Respiratory Medicine, Head of Respiratory Medicine, Groupe Hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Paris, France⁸Professor of Respiratory Medicine, UPRES EA 2397, Université Paris VI Pierre and Marie Curie, Paris, FranceCorrespondence: Thomas Similowski, thomas.similowski@psl.ap-hop-paris.fr

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Critical Care 2003, **7**:171-178 (DOI 10.1186/cc1848)This article is online at <http://ccforum.com/content/7/2/171>© 2003 Gonzalez *et al.*, licensee BioMed Central Ltd (Print ISSN 1364-8535; Online ISSN 1466-609X). This is an Open Access article: verbatim copying and redistribution of this article are permitted in all media for any purpose, provided this notice is preserved along with the article's original URL.**Abstract**

Introduction Bedside cardiac output determination is a common preoccupation in the critically ill. All available methods have drawbacks. We wished to re-examine the agreement between cardiac output determined using the thermodilution method (Q_{THERM}) and cardiac output determined using the metabolic (Fick) method (Q_{FICK}) in patients with extremely severe states, all the more so in the context of changing practices in the management of patients. Indeed, the interchangeability of the methods is a clinically relevant question; for instance, in view of the debate about the risk-benefit balance of right heart catheterization.

Patients and methods Eighteen mechanically ventilated passive patients with a right heart catheter in place were studied (six women, 12 men; age, 39–84 years; simplified acute physiology score II, 39–111). Q_{THERM} was obtained using a standard procedure. Q_{FICK} was measured from oxygen consumption, carbon dioxide production, and arterial and mixed venous oxygen contents. Forty-nine steady-state pairs of measurements were performed. The data were normalized for repeated measurements, and were tested for correlation and agreement.

Results The Q_{FICK} value was 5.2 ± 2.0 l/min whereas that of Q_{THERM} was 5.8 ± 1.9 l/min ($R = 0.840$, $P < 0.0001$; mean difference, -0.7 l/min; lower limit of agreement, -2.8 l/min; upper limit of agreement, 1.5 l/min). The agreement was excellent between the two techniques at Q_{THERM} values < 5 l/min but became too loose for clinical interchangeability above this value. Tricuspid regurgitation did not influence the results.

Discussion and conclusions No gold standard is established to measure cardiac output in critically ill patients. The thermodilution method has known limitations that can lead to inaccuracies. The metabolic method also has potential pitfalls in this context, particularly if there is increased oxygen consumption within the lungs. The concordance between the two methods for low cardiac output values suggests that they can both be relied upon for clinical decision making in this context. Conversely, a high cardiac output value is more difficult to rely on in absolute terms.

Keywords cardiac output, mechanical ventilation, oxygen consumption, thermodilution

Introduction

Estimating cardiac output at the bedside is a common pre-occupation in critically ill patients. Many methods are available; some invasive and others not, some operator dependent and others not. The thermodilution cardiac output obtained through right heart catheterization has been the clinical standard for decades [1–3]. However, various kinds of metrological limitations are the source of inaccuracies [4–6]. The direct Fick method, or metabolic method, relies on the calculation of cardiac output as the ratio of oxygen uptake ($V'O_2$) to the arteriovenous difference in oxygen content. It was originally used to validate the thermodilution method [7] and is often considered the 'physiological' gold standard. It cannot be taken as a clinical gold standard in intensive care practice because, although this has not been precisely assessed, there are possible causes of error specific to this setting, such as an increased oxygen consumption in the lungs in the presence of the acute respiratory distress syndrome or in the presence of pneumonia [8]. In addition, measuring $V'O_2$ is not easy when the inspired fraction of oxygen is high. Another means to estimate cardiac output at the bedside is the echocardiographic approach, particularly from the transesophageal route. By visualizing the heart directly, the echocardiographic approach alleviates several drawbacks of other methods, but it is strongly operator dependent and thus may not always be readily available.

Comparisons of thermodilution cardiac output and metabolic cardiac output have demonstrated statistically significant correlations [7,9–15], but this does not mean 'agreement' or 'clinical interchangeability'. More recently, a satisfactory agreement has been found between the two methods in stable children [16] and in stable patients with pulmonary hypertension [17]. Other studies, however, have suggested that discrepancies could appear in less stable situations such as exercise [18] or critical illness [19,20].

In the present study, we re-examined the concordance between thermodilution cardiac output and metabolic cardiac output, for several reasons. First, ventilatory management in the intensive care unit has evolved; low tidal volume strategies currently being much more common than a few years ago. The corresponding permissive hypercapnia can have hemodynamic effects [21,22] and can interfere with the

results of both the thermodilution and the metabolic methods. A second reason is that the controversy on the risk–benefit balance of right heart catheterization in critically ill patients [23,24] makes it important to gather knowledge about possible alternative methods. Finally, we wished to obtain data in a population of critically ill patients exhibiting indices of extreme severity, in whom cardiac output determination and manipulation are likely to be a more frequent issue than in other subsets of patients.

Materials and methods

Patients

Eighteen mechanically ventilated patients were studied (Table 1). Criteria for inclusion were: criteria 1, the presence of a flow-directed, balloon-tipped pulmonary artery catheter placed after the decision of the physician in charge of the patient; criteria 2, controlled mechanical ventilation without spontaneous respiratory activity; criteria 3, a stable level of inspired oxygen fraction and positive expiratory pressure when present; and criteria 4, spontaneous or drug-induced clinical unresponsiveness. Criteria 2–4 were set to minimize the risk of variations in oxygen consumption due to nonhemodynamic factors. When the patients received vascular expansion or when a change in the infusion rate of catecholamines was decided, a 10 min period of stability (<10% changes in cardiac frequency and arterial pressure) was required before the measurements were taken.

The patients were recruited on a consecutive basis. The study was a byproduct of another study, relying on the same methods, and that fulfilled the French legal criteria for patient studies. With approval of the appropriate authority, informed consent was not sought because the study-related intervention was noninvasive and bore no risk of interference with the clinical management of the patients.

Measurements and calculations

Metabolic method

Oxygen consumption was determined from the measurements of carbon dioxide and oxygen concentrations in the inspired and expired gases, using a standard portable metabolic monitor (Deltatrac Metabolic Monitor™; Datex Instrumentation Corp., Helsinki, Finland) calibrated prior to each set of measurements with a 96% oxygen–4% carbon dioxide

Table 1**Characteristics of the patients**

Patient	Age (years)	Sex	SAPS II score	Main diagnosis	Outcome
1	73	Male	41	Acute respiratory failure on chronic obstructive pulmonary disease	Discharged from ICU, returned home
2	76	Female	85	Cardiogenic shock	ICU death
3	74	Male	76	Acute respiratory distress syndrome Alveolar hemorrhage	ICU death
4	64	Female	67	Cardiogenic shock	ICU death
5	66	Female	111	Hemorrhagic shock	ICU death
6	74	Male	46	Cardiogenic shock Pulmonary edema	Discharged from ICU Returned home
7	69	Female	59	Sepsis syndrome	ICU death
8	84	Male	41	Acute respiratory distress syndrome Influenza	Discharged from ICU Hospital death
9	39	Female	56	Acute respiratory distress syndrome Septic shock	ICU death
10	51	Male	51	Septic shock	ICU death
11	84	Male	68	Cardiogenic shock Pulmonary edema	ICU death
12	77	Male	39	Acute respiratory failure on chronic obstructive pulmonary disease	ICU death
13	69	Male	69	Acute respiratory failure on chronic obstructive pulmonary disease	Discharged from ICU, returned home
14	65	Male	65	Acute respiratory distress syndrome Pneumonia	ICU death
15	68	Male	65	Cardiogenic shock Pulmonary edema	ICU death
16	79	Female	79	Cardiogenic shock	ICU death
17	69	Male	75	Acute respiratory failure on chronic obstructive pulmonary disease	Discharged from ICU, returned home
18	74	Male	65	Septic shock	ICU death

ICU, intensive care unit; SAPS, simplified acute physiology score.

gas mixture. This monitor has been validated for accuracy, sensitivity and reproducibility over a wide range of conditions [18,25]. To retain a given measure for analysis, a 10 min 'metabolic' steady state was required (<5% change in the respiratory quotient [R], in $\dot{V}O_2$, and in carbon dioxide production).

Blood gas analysis was performed on simultaneously drawn arterial and mixed venous samples (5 ml aliquots, with an AVL Omni9™ analyzer; AVL Medical Instruments, Shaffhausen, Switzerland). The hemoglobin concentration and oxygen saturation were measured using the corresponding co-oximeter, as well as arterial and mixed venous oxygen contents (CaO_2

and $C\dot{v}O_2$, respectively). Cardiac output determined using the metabolic (Fick) method (QT_{FICK}) was calculated as the ratio of $\dot{V}O_2$ to the $CaO_2 - C\dot{v}O_2$ difference. Each of the QT_{FICK} values used in the subsequent comparisons corresponded to 10 min measures of $\dot{V}O_2$.

Thermodilution

From a flow-directed, balloon-tipped pulmonary artery catheter positioned in a nondependent zone of the lung [26], the cardiac output determined using the thermodilution method (QT_{THERM}) was measured by fast injections of a 10 ml bolus of 5% dextrose solution, at room temperature. All the measurements were performed by the same operator. Each

injection was performed at end expiration. The thermal decay curve was visually inspected extemporaneously, and the data were rejected if the curves were obviously aberrant and in the presence of waveform irregularities suggesting technical artifacts. Each of the Q_{THERM} values used in the subsequent comparisons derives from three successive measures normalized according to Poon [27].

Tricuspid regurgitation

Pulsed Doppler echocardiography (parasternal short-axis view) was used to qualitatively detect a regurgitant signal in the right atrium.

Data analysis

Forty-nine paired measurements of Q_{FICK} and of Q_{THERM} were performed either at baseline or after a therapeutic intervention, with a minimum of two sets of measurements in each patient. The statistical association between Q_{FICK} and Q_{THERM} was expressed in terms of the Z coefficient of correlation with the 95% confidence interval. The agreement between the two techniques was studied using a graphical analysis according to Bland and Altman [28] and using the regression method described by Passing and Bablok [29]. This regression was first calculated using the whole data set. Data points lying far off the regression line were then tested for outlier status (data point considered outlier if value above mean + 3SD of the data set not including this data point). Outliers so defined were removed from the data set and the regression recomputed. The analysis was conducted in the whole study population (18 patients, 49 pairs of measurements), over restricted ranges of cardiac output, and after exclusion of the patients with tricuspid regurgitation (14 patients remaining, 41 pairs of measurements).

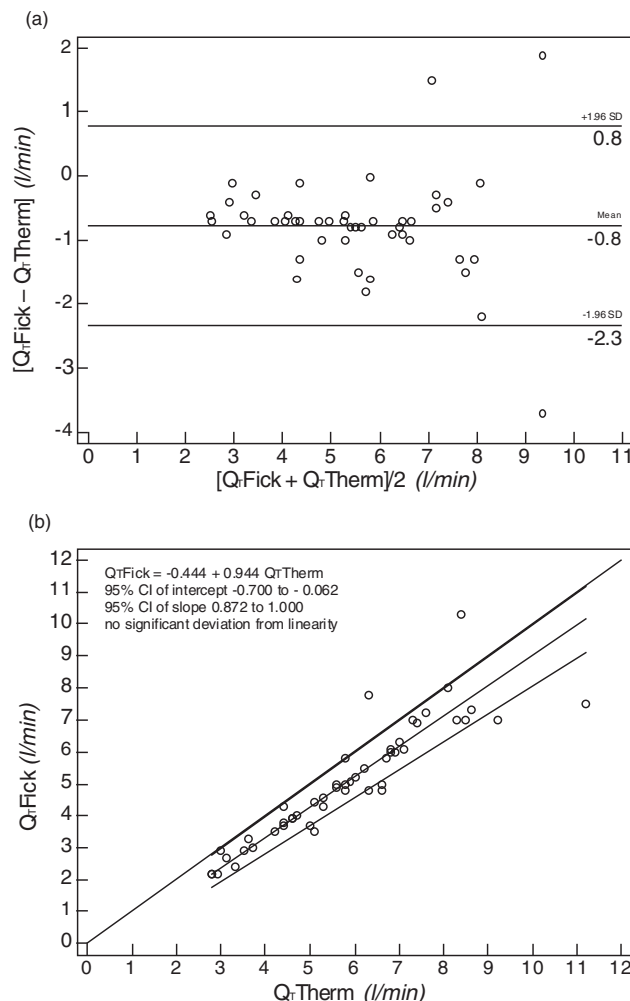
The data are expressed as the mean \pm SD.

Results

Whole population

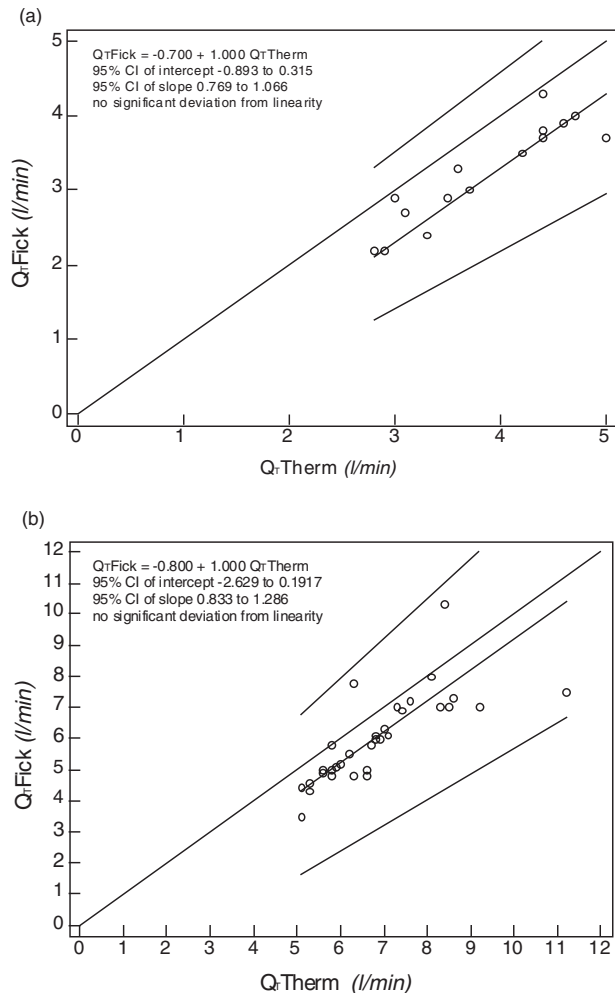
The values for Q_{FICK} ranged from 2.2 to 11 l/min (mean \pm SD = 5.2 ± 2.0 l/min), whereas the values for Q_{THERM} ranged from 2.8 to 11.2 l/min (mean \pm SD = 5.8 ± 1.9 l/min) ($R=0.84$, 95% confidence interval = 0.73–0.91, $P<0.0001$). After the removal of one data point meeting the outlier definition (see Materials and methods), the mean difference between Q_{FICK} and Q_{THERM} was -0.8 l/min, with a lower limit of agreement (magnitude of underestimation of Q_{FICK} by Q_{THERM}) at -2.3 l/min and an upper limit (magnitude of overestimation of Q_{FICK} by Q_{THERM}) at 0.8 l/min (Fig. 1a). The results of the Passing and Bablok regression of Q_{FICK} against Q_{THERM} are shown in Figure 1b. The 95% confidence interval of the intercept did not include 0 (-0.70 to -0.06) and the upper limit of the 95% confidence interval of the slope was equal to 1 (0.87 – 1.00), indicating the existence of a systematic difference between the two techniques [29].

Figure 1



Comparison of cardiac output determined using the thermodilution method (Q_{THERM}) and cardiac output determined using the metabolic (Fick) method (Q_{FICK}) according to (a) the Bland and Altman graphic method [28], and (b) the Passing and Bablok regression method [29]. Determined using the whole set of data after removal of one data point identified as an outlier (48 pairs obtained in the 18 patients), irrespective of the cardiac output value and of the presence of a tricuspid regurgitation. CI, confidence interval; SD, standard deviation.

For Q_{THERM} values ≤ 5 l/min ($n=17$, range = 2.8–5 l/min, mean \pm SD = 3.8 ± 0.7), the correlation between the two methods was extremely strong ($R=0.93$, 95% confidence interval = 0.81–0.97, $P<0.0001$). The mean difference between Q_{FICK} and Q_{THERM} was -0.6 l/min, with a lower limit of agreement at -1.2 l/min and an upper limit at -0.1 l/min. The 95% confidence interval of the Q_{THERM} versus Q_{FICK} regression intercept included 0 (-0.89 to 0.32) and the 95% confidence interval of the slope included 1 (0.77 – 1.07), indicating the absence of a systematic difference between the two techniques over that range of values (Fig. 2a) [29]. The Q_{FICK} values never exceeded the Q_{THERM} values.

Figure 2

Passing and Bablok regression of cardiac output determined using the metabolic (Fick) method (Q_{TFICK}) against cardiac output determined using the thermodilution method (Q_{TTHERM}) [29] restricted to (a) Q_{TTHERM} values < 5 l/min and (b) Q_{TTHERM} values > 5 l/min (after removal of one outlier). CI, confidence interval.

For Q_{TTHERM} values > 5 l/min ($n=34$, range = 5.1–11.2 l/min, mean \pm SD = 6.8 ± 1.3), the correlation between the two methods was weaker ($R=0.61$, 95% confidence interval = 0.34–0.79, $P<0.0001$) (Fig. 2b). After removal of the outlier, the mean difference between Q_{TFICK} and Q_{TTHERM} was -0.9 l/min, with a lower limit of agreement at -2.7 l/min and an upper limit at 1.0 l/min.

Population restricted to patients without tricuspid regurgitation ($n=14$)

The values for Q_{TFICK} ranged from 2.2 to 11 l/min (mean \pm SD = 5.0 ± 1.9 l/min), whereas the values for Q_{TTHERM} ranged from 2.8 to 11.2 l/min (mean \pm SD = 5.8 ± 1.8 l/min) ($R=0.83$, 95% confidence interval = 0.71–0.91, $P<0.0001$). The

mean difference between Q_{TFICK} and Q_{TTHERM} was -0.8 l/min, with a lower limit of agreement (magnitude of underestimation of Q_{TFICK} by Q_{TTHERM}) at -2.2 l/min and an upper limit (magnitude of overestimation of Q_{TFICK} by Q_{TTHERM}) at 0.7 l/min (Fig. 3a). The Passing and Bablok regression of Q_{TFICK} against Q_{TTHERM} (Fig. 3b) indicated a systematic difference between the techniques (confidence interval of the intercept = -0.70 to -0.21 ; confidence interval of the slope = 0.9 – 1.0). For Q_{TTHERM} values < 5 l/min, the mean difference between Q_{TFICK} and Q_{TTHERM} was -0.6 l/min (range, -1.2 to -0.02 l/min). For Q_{TTHERM} values > 5 l/min, the mean difference between Q_{TFICK} and Q_{TTHERM} was -0.8 l/min (-2.5 to 0.9 l/min).

Discussion

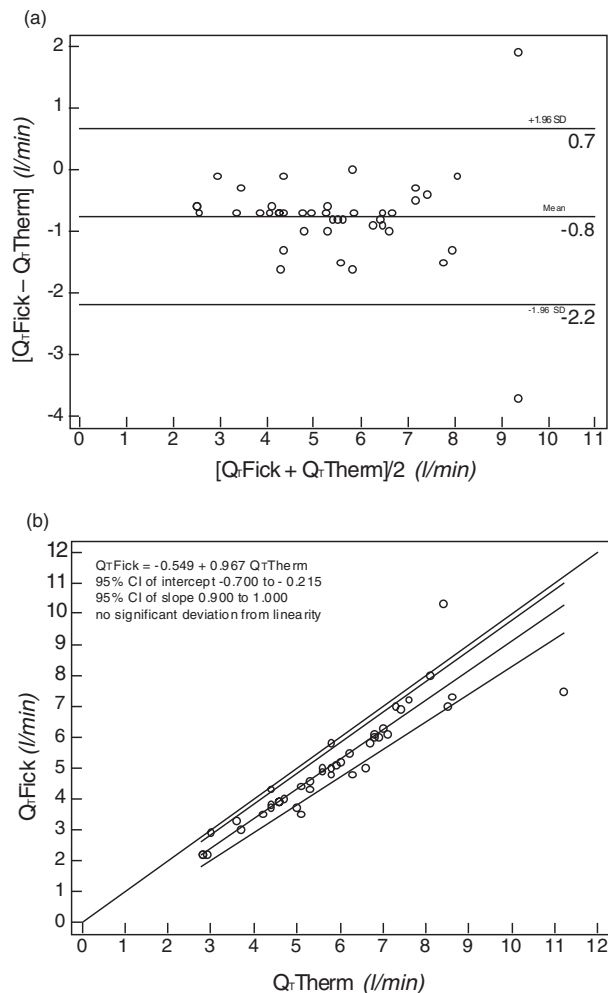
The present study, conducted in a pragmatic manner to stay close to the clinical practice, shows that the bolus thermodilution method and the metabolic method can provide clinically interchangeable measures of low cardiac output values in mechanically ventilated, critically ill patients. Conversely, there are marked discrepancies between the two approaches for high cardiac output values.

Divergences between methods to estimate cardiac output in critically ill patients have been reported. Sherman *et al.* [19] found in 10 septic patients (average Acute Physiology and Chronic Health Evaluation [APACHE] II score = 18), as opposed to 10 nonseptic patients (average APACHE II score = 12), that the thermodilution cardiac output could overestimate the metabolic cardiac output by more than 6 l, or underestimate it by more than 3 l. In the study of Sherman *et al.*, 17 out of 20 of the cardiac output values were > 5 l/min.

Axler *et al.* [20] compared 45 pairs of measurements obtained in 13 patients of moderate severity (10 discharged alive from the intensive care unit, 3 deceased). In this series, transesophageal echocardiography, bolus thermodilution and the Fick method provided substantially different results. Although the thermodilution cardiac output values and the metabolic cardiac output values were not statistically different, their limits of agreement ranged from -2.7 to 4.8 l/min. From this, the authors insisted on the notion that clinical decision making could not rely on a cardiac output measurement alone, whatever the technique used to obtain it. In this series, only six metabolic cardiac output data points were < 5 l/min.

The present study differs from the previous two studies by the extreme severity of the clinical status of the patients, as illustrated by high simplified acute physiology II scores and a calamitous outcome (Table 1). Such clinical contexts are generally associated with complex hemodynamical situations, which may serve as a justification to the decision of right heart catheterization. Preliminary data obtained in a cohort of about 600 such patients [30] suggest that this procedure is not associated with an increased mortality, as opposed to what has been suspected in less severe patients [23,24].

Figure 3



Comparison of cardiac output determined using the metabolic (Fick) method (Q_{TFICK}) and cardiac output determined using the thermodilution method (Q_{TTHERM}) according to (a) the Bland and Altman graphic method [28], and (b) the Passing and Bablok regression method [29]. Restricted to the patients in whom cardiac echography ruled out tricuspid regurgitation (14 patients, 40 pairs of measurements, after removal of one outlier). CI, confidence interval; SD, standard deviation.

Dhingra *et al.* [31] recently published a study similar to the present one regarding motives, design and methods. In 18 mechanically ventilated, critically ill patients with high APACHE II scores, these investigators showed that the thermodilution method and the metabolic method had limits of agreement ranging from -3.30 to 2.96 l/min. For cardiac output values >7 l/min, these limits were -5.67 to 1.87 l/min.

As compared with the data of Sherman *et al.* [19] and those of Axler *et al.* [20], the extreme severity of the patients' condition probably explains the relatively large proportion of low cardiac output values in the present data (Fig. 1) and in the data of Dhingra *et al.* [31]. Although splitting the data set in

two parts carries the risks inherent to all *post hoc* analyses, it can clearly be seen from Figures 1 and 2 that the discrepancies between Q_{TTHERM} and Q_{TFICK} become major only for high cardiac outputs. The agreement between Q_{TTHERM} and Q_{TFICK} at cardiac output values <5 l/min was almost as good as that reported by Capderou *et al.* in normal individuals [16] (range -0.8 to -0.3 l/min), and Q_{TTHERM} never underestimated Q_{TFICK} . In the study by Dhingra *et al.* [31], looking at the data suggests that the thermodilution method and the metabolic method were probably interchangeable up to 6 l/min. From a set of 105 measurements, among which 90 provided values <5 l/min, Hoepfer *et al.* [17] reported limits of agreement between -1 and 1.2 l/min.

It appears that, in severely ill patients and in stable patients, a thermodilution cardiac output value <5 l/min probably reflects 'adequately' what this value would have been with the metabolic method, and *vice versa*. It must be noted that the meaning of 'adequately' here is arbitrary. The Bland and Altman graphical approach to compare two methods of measurements of a given biological value does not determine whether the agreement found between these two methods is 'good'. This depends on the error magnitude that is, arbitrarily, considered clinically acceptable. It seems to us that the degree of agreement reported by ourselves and others is sufficient to render reasonable a decision making process relying on a low cardiac output value, whatever the method used to obtain it. This is clinically relevant because, as emphasized by Dhingra *et al.* [31], "cardiac output manipulation is likely to have the greatest impact on outcome when cardiac output is low". It must be borne in mind, however, that the thermodilution method is notoriously unreliable when the cardiac output is very low. van Grondelle *et al.* [15] reported overestimates of cardiac output, with the thermodilution method reaching 35% of the measured value when the cardiac output was <2.5 l/min. Of note, we did not observe such low values in the present patients (Fig. 2).

The situation is different regarding the higher values of the cardiac output range that we observed. The acceptable agreement found at low values is clearly lost (Fig. 2). This is in line with the data of Sherman *et al.* [19], of Axler *et al.* [20] and of Dhingra *et al.* [31]. This is also in line with the results reported for cardiac output values >5 l/min by Koobi *et al.* [32] in stable adults in the context of a coronary artery bypass, and in line with the observations of Hsia *et al.* [33] in dogs and of Espersen *et al.* [18] in healthy humans, who described a dramatic decrease in agreement between the thermodilution method and the metabolic method when going from rest to exercise. The discrepancies between the thermodilution method and the metabolic method may be due to metrological limitations affecting both techniques, particularly in the intensive care setting. Of note, the presence of tricuspid regurgitation did not seem to have a major impact on the present results (Fig. 3), but it was relatively rare in our series.

Key messages

- This study confirms that the method chosen to evaluate cardiac output in critically ill patients can influence the results, and that this metrological dimension must be taken into account when interpreting clinical data
- The good level of agreement between thermodilution measurement and metabolic measurement at low cardiac output suggests that such a value can be relied on to build a clinical decision, whatever the method used to determine it. This is novel information
- Conversely, the divergence between methods for high cardiac output values prompts caution in the presence of such results

We wish to emphasize that finding a low level of agreement between the thermodilution method and the metabolic method when the cardiac output is high does not necessarily mean that either of the two methods is closer than the other to the reality. Indeed, many sources of errors have been identified regarding the thermodilution method, and many publications have warned clinicians against them [6,15,34,35]. The metabolic method is also far from being free of criticism. In spite of the availability of easy-to-use metabolic carts, it remains difficult to use at the bedside. There is a risk to cumulate measurement errors (respiratory gas sampling and blood gas analysis). The reliability of the measurement of oxygen consumption can be decreased by metabolic instability, patient-ventilator dyssynchrony, high inspired oxygen fraction, circuit leaks, and so on. In addition, the metabolic method provides an accurate estimate of cardiac output only if the pulmonary artery flow, the mixed venous oxygen content, and the arterial oxygen content are reasonably constant [36], a condition that may not be fulfilled in hemodynamically compromised, mechanically ventilated patients. It is therefore not possible from the available data to designate a gold standard.

In summary, the present data concur with those of Dhingra *et al.* [31] to suggest that, in daily practice, a low thermodilution or metabolic cardiac output can reasonably be relied on to build a clinical decision, which is novel information. Conversely, both the present study and that of Dhingra *et al.* [31] confirm that, in critically ill patients, as in other types of patients, the methodological approach chosen to evaluate the cardiac output has an important influence on the result when cardiac output is high. High cardiac output values should thus be treated and used cautiously.

Competing interests

None declared.

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