Comparison of bedside measurement of cardiac output with the thermodilution method and the Fick method in mechanically ventilated patients

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Received: 3 July 2002
Revisions requested: 16 August 2002
Revisions received: 25 October 2002
Accepted: 8 November 2002
Published: 20 December 2002

Critical Care 2003, 7:171-178 (DOI 10.1186/cc1848)
This article is online at http://ccforum.com/content/7/2/171
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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 (QTHERM) and cardiac output determined using the metabolic (Fick) method (QTFICK) 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). QTHERM was obtained using a standard procedure. QTFICK 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 QTFICK value was 5.2 ± 2.0 l/min whereas that of QTHERM 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 QTHERM values < 5 l/min but became too loose for clinical interchangeability above this value. Tricuspid regurgitation did not influence the results.

APACHE = Acute Physiology and Chronic Health Evaluation; CaO2 = arterial oxygen content; CVO2 = mixed venous oxygen content; QTFICK = cardiac output determined using the metabolic (Fick) method; QTHERM = cardiac output determined using the thermodilution method; R = respiratory quotient; SD = standard deviation; VO2 = oxygen consumption.
Distress and can interfere with the agitated patient. The corresponding permissive hypercapnia can have implications currently being much more common than a few years ago. The intensive care unit has evolved; low tidal volume strategies, for several reasons. First, ventilatory management in the presence of pneumonia [8]. In addition, measuring VO₂ 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 subsets of patients.

Introduction

Estimating cardiac output at the bedside is a common preoccupation 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 (VO₂) 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 VO₂ 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 noninvasive respiratory distress syndrome or in the presence of pneumonia [8]. In addition, measuring VO₂ 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.

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

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
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 $V'\text{O}_2$, 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 ($\text{CaO}_2$ and $\text{CvO}_2$, respectively). Cardiac output determined using the metabolic (Fick) method ($Q_{\text{FICK}}$) was calculated as the ratio of $V'\text{O}_2$ to the $\text{CaO}_2$ – $\text{CvO}_2$ difference. Each of the $Q_{\text{FICK}}$ values used in the subsequent comparisons corresponded to 10 min measures of $V'\text{O}_2$.

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 ($Q_{\text{THERM}}$) 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

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 | ICU death |
|         |             |     |               | Pulmonary edema | Returned home |
| 4       | 64          | Female| 67          | Cardiogenic shock | ICU death |
| 5       | 66          | Female| 111         | Hemorrhagic shock | ICU death |
| 6       | 74          | Male| 46            | Cardiogenic shock | Discharged from ICU |
|         |             |     |               | Pulmonary edema | Returned home |
| 7       | 69          | Female| 59          | Sepsis syndrome | ICU death |
| 8       | 84          | Male| 41            | Acute respiratory distress syndrome | Discharged from ICU |
|         |             |     |               | Influenza | Hospital death |
| 9       | 39          | Female| 56          | Acute respiratory distress syndrome | ICU death |
|         |             |     |               | Septic shock | ICU death |
| 10      | 51          | Male| 51            | Septic shock | ICU death |
| 11      | 84          | Male| 68            | Cardiogenic shock | ICU death |
|         |             |     |               | 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 | ICU death |
|         |             |     |               | Pneumonia | ICU death |
| 15      | 68          | Male| 65            | Cardiogenic shock | ICU death |
|         |             |     |               | 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.
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 QTTherm 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 QTFick and of QTTherm 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 QTFick and QTTherm 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±SD.

Results
Whole population
The values for QTFick ranged from 2.2 to 11 l/min (mean ± SD = 5.2 ± 2.0 l/min), whereas the values for QTTherm ranged from 2.8 to 11.2 l/min (mean ± 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 QTFick and QTTherm was −0.8 l/min, with a lower limit of agreement (magnitude of underestimation of QTFick by QTTherm) at −2.3 l/min and an upper limit (magnitude of overestimation of QTFick by QTTherm) at 0.8 l/min (Fig. 1a).

The results of the Passing and Bablok regression of QTFick against QTTherm 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].

Comparison of cardiac output determined using the thermodilution method (QTTherm) and cardiac output determined using the metabolic (Fick) method (QTFick) 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 QTTherm values ≤ 5 l/min (n=17, range = 2.8–5 l/min, mean ± 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 QTFick and QTTherm 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 QTTherm versus QTFick 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 QTFick values never exceeded the QTTherm values.
mean difference between QT<sub>FICK</sub> and QT<sub>THERM</sub> was 
-0.8 l/min, with a lower limit of agreement (magnitude of 
derestimation of QT<sub>FICK</sub> by QT<sub>THERM</sub>) at -2.2 l/min and an 
upper limit (magnitude of overestimation of QT<sub>FICK</sub> by 
QT<sub>THERM</sub>) at 0.7 l/min (Fig. 3a). The Passing and Bablok 
regression of QT<sub>FICK</sub> against QT<sub>THERM</sub> (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 QT<sub>THERM</sub> values <5 l/min, the 
mean difference between QT<sub>FICK</sub> and QT<sub>THERM</sub> was 
-0.6 l/min (range, -1.2 to -0.02 l/min). For QT<sub>THERM</sub> values 
>5 l/min, the mean difference between QT<sub>FICK</sub> and QT<sub>THERM</sub> 
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 thermodi-
lution 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 differ-
ent, their limits of agreement ranged from -2.7 to 4.8 l/min. 
From this, the authors insisted on the notion that clinical deci-
sion 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 gen-
erally 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].
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 QTHERM and QT FICK become major only for high cardiac outputs. The agreement between QTHERM and QT FICK 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 QTHERM never underestimated QT FICK. 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, Hoeper 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.
Cardiac output is high. High cardiac output values should 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.

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.

Key messages

• This study confirms that the method chosen to evaluate cardiac output in critically ill patients can influence the results, and that this methodological 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 dysynchrony, 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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