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REVIEW ARTICLE

J.R.C. Jansen

The thermodilution method for the clinical assessment of cardiac output

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J.R.C. Jansen (✉)
Department of Pulmonary Diseases,
Erasmus University, Room Ee2251,
P.O. Box 1738, NL-3000 DR Rotterdam,
The Netherlands

Introduction

There is no simple 'push button' method for accurately measuring cardiac output and no method can be used by untrained operators.

The interest in cardiac output for the clinician is illustrated by the number of methods developed (Table 1). These techniques can be classified as in invasive and non-invasive methods, and subdivided in continuous and intermittent measurements.

The non-invasive methods are not yet sufficiently reliable to be recommended for general use. The Fick and thermodilution technique are accurate and reproducible, but they are invasive, and should be used with a standardized approach.

Most often used clinically is the thermodilution method, because it is simple, safe and swift. Therefore, the clinical evaluation of new methods (Table 1) is usually done by comparison with the thermodilution method. Since, 1954, when Fegler [1] introduced the thermodilution technique to measure mean cardiac output, many studies have been devoted to this topic. This is in part due to insufficient knowledge of the theory of the method and the difference between theory and practice.

Theory of the thermodilution method

The thermodilution method is based on the law of conservation of thermal energy. A certain amount of cold is injected upstream and detected, in diluted form, downstream. An accurate estimate of cardiac output is made if, (i) there is no loss of cold between the sites of injection and detection, (ii) mixing of indicator and blood is complete, and (iii) the induced temperature change $T_{b,i}(t)$ (by injecting of cold fluid) can be discriminated accurately from the baseline temperature $T_b(t)$, giving a temperature difference $\Delta T_b(t) = T_{b,i}(t) - T_b(t)$. Then the equation for the thermodilution method can be formulated as:

$$\varrho_i S_i \int_{t_1}^{t_2} \dot{Q}_i(t)[T_b(t) - T_i(t)]\,dt = \varrho_b S_b \int_{t_1}^{t_2} \Delta T_b(t)\,\dot{Q}_b(t)\,dt \quad (1)$$

In this equation the injected amount of cold is on the left side, the detected amount on the right side. $\dot{Q}_b(t)$ is blood flow, $\dot{Q}_i(t)$ is the input flow of indicator, T is the

Table 1 Methods of cardiac output assessment used in clinical practice

Method	Non-invasive	Invasive	Intermittent	Continuous
Echo-Doppler	×	×		×
Echocardiograph	×	×		×
Impedance cardiography	×			×
Single breath (acetylene)	×		×	
Pulse-contour	×	×		×
Model flow	×	×		×
Radionuclide		×	×	
Cineangiography		×	×	
Fick (direct or indirect)		×	×	
Dye dilution		×	×	
Thermodilution		×	×	×
Conductance catheter		×		×
Electromagnetic		×		×

temperature, ϱ is the density and S is the specific heat of the indicator (i) and blood (b) respectively, t is time, t_1 is time of injection and t_2 is the end of integration when all cold has passed the detector site.

If the injection of cold is fast (bolus injection) then $\int \dot{Q}_i(t)\,dt = Q_i$, $T_b(t)$ and $T_i(t)$ are constant, and the left side of the equation can be rewritten as:

$$\varrho_i S_i Q_i (T_b - T_i) = \varrho_b S_b \int_{t_1}^{t_2} \Delta T_b(t)\,\dot{Q}_b(t)\,dt \tag{2}$$

where Q_i is the injected volume of cold fluid.

If blood flow, $\dot{Q}_b(t)$, is constant then the classical Stewart Hamilton equation is found:

$$\dot{Q}_b = \frac{\varrho_i S_i Q_i (T_b - T_i)}{\varrho_b S_b \int_{t_1}^{t_2} \Delta T_b(t)\,dt} \tag{3}$$

The most difficult variables in this formula to assess are $(T_b - T_i)Q_i$, the input of thermal indicator, and the $\int_0^\infty \Delta T_b(t)\,dt$, which is the area under the dilution curve measured in the pulmonary artery.

Input of thermal indicator

The temperature of the injectate is not uniform. Before an injection the intra-corporeal part of the injection channel in the Swan-Ganz catheter has attained blood temperature and the other part room temperature. The sequence of temperatures during injection is; 1) the volume of the intra-corporeal part of the catheter at body temperature; 2) the extra-corporeal part of the catheter and connecting lines at room temperature; 3) the bolus of cold fluid from the syringe, and 4) the cold from the fluid that remains in the intra-corporeal part of the catheter, conducted through the wall of the catheter into the blood. This last "injection" will extend the tail of the dilution curve. To eliminate this effect most cardiac output computers are programmed with an empirical correction factor (C_T) [2].

Temperature response in pulmonary artery

The tail of the dilution curve is mainly due to the slow conduction of cold through the wall of the injection catheter. This post-injection part of the curve can be separated from the curve if the indicator dilution process can be described with a mixing chamber model. The thermodilution curve will closely follow the washout pattern of a single mixing chamber, which is mono exponential, if no disturbances occur as: (i) unstable blood flow, (ii) cyclic baseline fluctuations and (iii) slow drift of the baseline. Most cardiac output computer programs extrapolate the downslope exponential to the baseline temperature.

This leads to the formula:

$$\dot{Q} = \frac{S_i \varrho_i (60)\, C_T Q_i (T_b - T_i)}{S_b \varrho_b \int_0^\tau \Delta T_b(t)\,dt + A} \tag{4}$$

where C_T is a correction factor for the injectate temperature rise as it passes through the catheter; τ is the variable data endpoint of data acquisition which depends on the downslope of the curve, usually taken where the curve is decreased to 30% of its peak value; A is the area under the temperature-time curve between τ and the extrapolated end of the curve, obtained from an exponential fit of the curve between 80% of the peak and τ; 60 is a conversion factor from seconds to minutes.

In practice $\varrho_b, \varrho_i, S_b, S_i, C_T$, 60, and Q_i are grouped together giving a computation constant CC. The correct value for this constant has to be entered into the cardiac output computer. The value of CC depends on the catheter used, the type of fluid injected (saline or glucose), the injection temperature (room or iced), and the injection volume. It can be derived from a table in the operation manual of the cardiac output computer [2] or the documentation sheet of the particular Swan-Ganz catheter model.

Method related problems

Computation constant errors

There is a direct proportional relation between the value of the computation constant and the estimated cardiac output. A too low value entered into the computer results in a too low estimate of cardiac output. Therefore, it is important to check the apparatus on the correct computation constant CC after each change in measurement configuration. Fortunately, there is a simple way to correct for a wrong computation error afterwards. For the more modern cardiac output computers you have to enter the correct computation constant and the machine recalculates the cardiac output [2].

For the older ones apply the formula:

$$CO_{correct} = \frac{CC_{correct}}{CC_{incorrect}} CO_{incorrect} \tag{5}$$

Injection site

Injections of cold fluid are usually performed via the injection lumen of the Swan-Ganz catheter. Occasionally, there is a need to inject via an alternative injection lumen.

Several authors compared the use of alternative lumens with the standard injection port. The cardiac output estimates after injections via (i) the proximal infuse lumen [3], (ii) the right ventricular port [4, 5], (iii) the central venous port [6], or (iv) via a separate injection catheter ending near the atrium [5] were not significantly different from those after injection obtained from the standard injection lumen. These studies suggest that alternative injection ports can be used if the standard injection lumen becomes nonfunctional.

However, injection via the introducer set of the Swan-Ganz catheter into the peripheral vein gives an overestimation of cardiac output [7]. This can be explained by the loss of cold via the wall of the veins [8]. Such loss results in a smaller area under the dilution curve, giving a too high cardiac output value.

Iced versus room temperature

When using multiple measurements with iced injectate, either the first measurement has to be discarded or the system has to be flushed [2], because the first bolus will contain warmed fluid in the catheter and the connecting lines to the injecting syringe. Therefore, the averaged temperature of the first bolus will be higher than that of subsequent injections. This will lead to an overestimation of cardiac output for the first measurement.

It is not necessary to discard the first measurement when using room temperature. In many clinical situations, where the patient condition is fairly stable, injection of injectate at room temperature give reliable results [9–13].

Iced injectate yields a greater signal to noise ratio then an equivalent volume of injectate at room temperature. Nevertheless the mean of consecutive measurements is the same for iced injectate as for injectate at room temperature. However, the variance found was lower for iced injectate. If CO is high (>8 l/min) or low (<3 l/min) a systematic difference was found in the estimate of cardiac output [13]. Therefore, if an accurate reading is needed over a wide range of cardiac output values, the use of iced injectate is recommended, unless a patient does not tolerate iced injectate [14].

Injection volume

There is a proportional relation between the volume injected and the cardiac output value estimated (see formula 3). If the value entered into the computer is higher than the volume injected, cardiac output will be overestimated.

Pearl et al. [11] studied the effect of volume and temperature on cardiac output determinations by combinations of 10, 5 and 3 ml with room temperature or at 0 °C. They recommended the use of 10 ml at room temperature or at 0 °C in adult patients. If the volume administration has to be minimized the use of 5 ml, even at room temperature, is acceptable. However, smaller injection volumes will result in a large increase in variability due to the smaller signal to noise ratio [9, 11, 12].

Manual versus automated

Injectate will heat fast when held in a hand. A volume of 10 ml of iced injectate can easily warm up 10 °C [15], which may lead to an error up to 25%. Using an automatic injector in combination with a closed injectate delivery system will reduce errors by accidental changes in injection temperature, volume and speed. An automatic time sequence, with filling just before injection, minimizes the effect of heating of injectate [16, 17].

Nelson and Houtchens [18] showed indeed that automatic injectors improved injection time, rate and consistency in injected volume compared to manual injection.

Closed versus open injection systems

Closed systems for the delivery of iced injectate or injectate at room temperature are available from various suppliers. These systems provide a sterile conduit of injectate source to the catheter and patient. They are particular convenient for the automatic injection of injectate solutions [16, 17, 19, 20]. In combination with an in-line temperature measurement at the entrance of the Swan-Ganz catheter it minimizes errors related to the injectate temperature.

In addition, these systems can be maintained, and exchanged at intervals of 48 h, without a significant incidence of bacterial growth, whereas in open and in double-bag systems significant incidences of bacterial growth were found [21–23].

Patient related problems

Valve insufficiency

The Stewart-Hamilton equation is based on constant blood flow and the condition that indicator passes the thermistor on the Swan-Ganz only once. In case of tricuspid or pulmonary valve insufficiency a forward and backward flow occurs. Therefore, tricuspid or pulmonary valve insufficiency leads to an underestimation of cardiac output [24].

Flow variability

Variability of blood flow occurs during mechanical ventilation, shivering, variations in heart rate, cardiac arrhythmias, and other causes of hemodynamic instability [15–17, 25]. Usually, the cardiac output estimates are unreliable during these conditions. An exception can be made for the errors related to mechanical ventilation, these will be discussed separately.

Temperature baseline fluctuations

The temperature baseline fluctuations can be subdivided in three groups: (i) random fluctuations; (ii) changes in body temperature as occurs after cardiopulmonary bypass; and (iii) cyclic changes.

In 1954 Fegler described already a large error introduced when respiratory movement was considerably. After that, several authors [25–29] described cyclic changes in temperature of the pulmonary artery blood due to respiration. The amplitude of such cyclic baseline fluctuations is probably dependent on the patients condition. A baseline correction of each dilution curve is advisable to get a curve representing the accurate response to the injection of cold per se. We have previously shown how to correct for this, as is shown in Fig. 1 [27, 28]. The recorded thermodilution curve (Fig. 1 a) has to be corrected for variations in baseline temperature concomitant with the ventilatory cycle (Fig. 1 b), trends in body temperature (Fig. 1 c) and the leakage of cold from the intra-corporeal part of the Swan-Ganz catheter (Fig. 1 d).

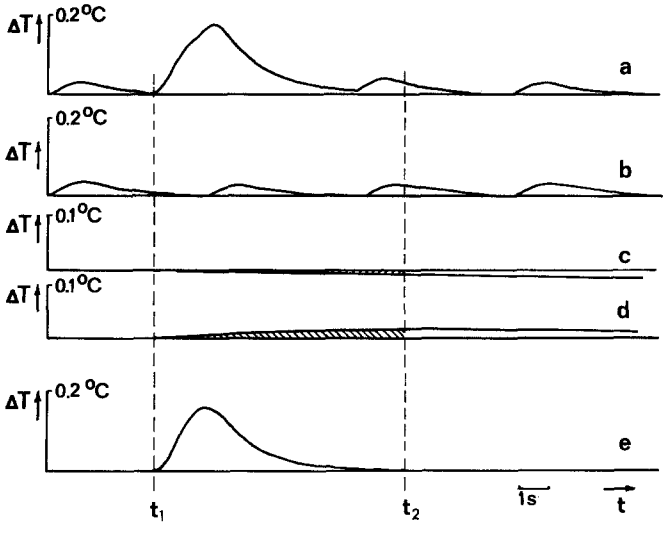

Fig. 1 Corrections to the thermodilution curve. *a* the curve as actually measured; *b* baseline fluctuations during each ventilatory cycle; *c* change in body temperature; *d* loss of cold from catheter dead space and *e* the corrected dilution curve after subtraction of *b*, *c* and *d* from the original curve *a*. From [27]

Unfortunately, most cardiac output computers are not equipped with programs that correct the dilution curve for the various types of baseline fluctuations. Therefore, it is recommended to examine the dilution curves, and to accept only those that begin and end with a stable baseline.

The estimation of cardiac output during mechanical ventilation

Many authors have shown cyclic changes in stroke volume during spontaneous breathing [31] as well as during mechanical ventilation [32], which implies that the condition of constant blood flow over the period of a measurement is not fulfilled. This leads to a misuse of the thermodilution method on theoretical grounds. Especially during mechanical ventilation with intermittent positive pressure, ignorance of this misuse may lead to a considerable scatter in cardiac output values, as is demonstrated in Fig. 2. Twelve thermodilution measurements were performed consecutively at intervals of 1–2 min at the phases 0%, 25%, 50%, 75%, 8%, 33%, 58%, 83%, 16%, 41%, 66%, and 92% in the ventilatory cycle. Phase zero was chosen at the begin of inflation. After sorting the series of 12 measurements with respect to the moments of injection in the ventilatory cycle a cyclic pattern of modulation of the estimates appeared, with the same periodicity as the ventilation.

More detailed analyses of the variation in cardiac output estimates, related to the moment of injection in the ventilatory cycle, were published for animals [27, 28, 33] and humans [16, 19, 34].

Improvement of the method during mechanical ventilation

Several techniques can improve the accuracy of the thermodilution method during conditions of mechanical ventilation.

Injections at a fixed moment in the ventilatory cycle. As illustrated in Fig. 2, the relationship between the thermodilution cardiac output values and the moment of injection in the ventilatory cycle is not the same for each patient. Furthermore, this relationship is changed, if either the ventilatory pattern or the frequency or the end-expiratory pressure or the blood volume is changed [27, 28, 33, 34]. Therefore, we do not recommend to inject the cold bolus at a fixed moment in the ventilatory cycle as suggested by other authors [35, 36], when an estimate of the mean value of cardiac output is desired.

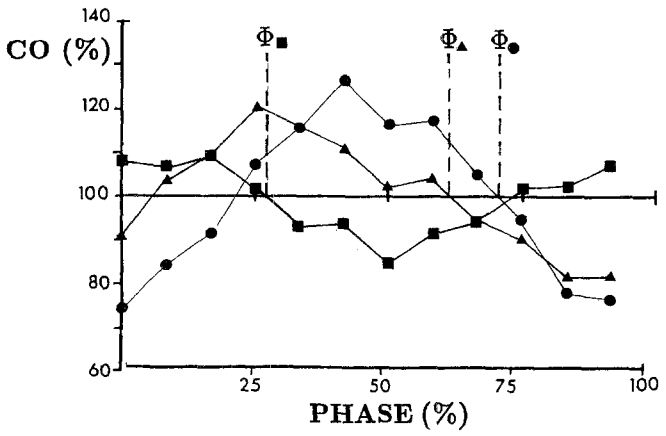

Fig. 2 Three individual series of 12 cardiac output (CO) measurements in three patients, plotted against the moment of injections as a percentage phase of the ventilatory cycle. Phase zero is begin of inflation. The patients were ventilated with an intermittent positive pressure and a rate of 10 per min. 100% CO is mean of each series of 12 estimates. $\Phi_{\blacktriangle}$, $\Phi_{\blacksquare}$ and $\Phi_{\bullet}$ are the phases at which the 100% value is crossed in negative direction. The determinations were done with time intervals of at least 1 min. From [17]

An increase in the ventilatory rate. At a higher respiratory rate the amplitude of the real modulation of blood flow will be smaller due to a lower tidal volume. Also, the higher frequency on itself diminishes the range of cardiac output estimates by thermodilution [28, 37]. But, a change in the ventilatory settings may influence gas transport and the hemodynamic status of a patient. This affects the value of cardiac output to be determined. So, an increase in ventilatory rate for a more accurate estimate of cardiac output must be dissuaded.

Breathhold procedures. During a prolonged expiratory pause as well as during an inspiratory hold maneuver constant hemodynamic conditions were found [38]. However, the cardiac output estimated during prolonged end-expiratory pauses were significantly higher than mean cardiac output during the preceding normal cycles of mechanical ventilation [39, 40]. This overestimation was not constant when hemodynamic circumstances changed. For the calculation of oxygen delivery we need mean cardiac output. Therefore, the estimate of cardiac output during a prolonged pause will lead to erroneous conclusions.

Averaging of estimates. In a patient study [16] we have analyzed the differences between the averages of randomly performed measurements and the averages of measurements performed equally spread over the ventilatory cycle (Table 2). In both situations an improvement of accuracy was found with an increase of the number of estimates to be averaged. The best result was obtained by averaging four estimates equally spread over the ventilatory cycle (phase selected estimates). The accuracy of mean cardiac output estimated by averaging of two measurements performed at ventilatory phase that differ half a ventilatory cycle appeared to be as good as the average of five randomly performed estimates. Approximately 60% of the single estimates were within 10% of the mean. Thus, with a single estimate the probability is 40% to get a value which deviates more than 10% from the real mean value. All phase selected four point averages were within the accuracy level of 10%, whereas 7% of the averages from random estimates were outside this accuracy level. These results were confirmed by other authors [19, 33, 34].

Summarizing

The errors made in the estimation of cardiac output with the thermodilution method are primarily related to:

1. Violations of the condition of constant blood flow. Variability of blood flow occurs during shivering, mechanical ventilation, variations in heart rate, cardiac arrhythmia, valvular insufficiencies, and other causes of hemodynamic instability.
2. Technical errors, such as heating of injectate, incorrect catheter positioning, or injections with irregular injection speed.
3. Changes in blood temperature in the pulmonary artery not related to the injection of cold.
4. Lack of cardiac output computer accuracy.

Table 2 Averaging techniques

	Systematic				Random				
	Mean %	SD %	% of data within ±10%	% of data within ±5%	Mean %	SD %	% of data within ±10%	% of data within ±5%	*n*
1-s-e	100.0	13.0	58	34	101.8	13.9	57	28	108
2-p-a	100.0	6.1	89	69	102.8	9.7	67	44	54
3-p-a	100.0	3.2	100	89	101.4	7.2	83	54	36
4-p-a	100.0	3.2	100	89	100.3	5.7	93	59	27

1-s-e single estimates; *2-p-a* two-point-averages; *3-p-a* three-point-averages; *4-p-a* four-point-averages. ±10%, ±5%, percentage of total number of measurements within 10% and 5% accuracy respectively; *n* number of values; *SD* standard deviation of the mean, from [17]

Considering these errors, the clinician would expect 5–15% data scatter, even in hemodynamically stable patients [2]. There is, however, good evidence that the mean of many thermodilution measurements will lead to the estimation of an accurate mean cardiac output [27, 28, 37, 41, 42].

A high variance suggests the need to increase the number of measurements and to average them. How many consecutive thermodilution determinations have to be taken per estimation of mean cardiac output depends on the nature of variance (normally or not normally distributed). For a normal distribution of errors the standard deviation will decrease with the square root of the number of observations [28].

New developments

Advanced thermodilution methods are under investigation, which attempt to convert an intermittent process into a continuous process, by an automatic frequent repetition of measurements. Such a system is already available for patients.

Continuous cardiac output (Vigilance/Intellicath®)

This method is based on heating of a filament, positioned into the right ventricle, in a programmed mode (heating on/off) and the detection of very small changes in temperature in the pulmonary artery. After cross-correlating of the heating signal and the detection signal, a thermodilution washout curve can be obtained. Then, the computation of cardiac output is performed according to the Stewart-Hamilton equation [43].

This method can be reliable but needs a long averaging time to eliminate the influence of a noisy temperature baseline. Therefore, every update on the display is an average over the last 5–15 min. This makes the claim of being a continuous cardiac output measurement disputable.

Unclear is how this method deals with cyclic flow and cyclic baseline temperature, because the computations of the method are based on constant flow and non periodical baseline fluctuations. A first study in patients, with a second generation of the system called Vigilance/Intellicath, was published by Lichtenthal and Wade [44]. These authors compared the new technique with conventional thermodilution. They showed a bias of 0.11 to 0.90 l/min and a precision of ±1.8 to ±3.0 l/min in the operating room. The results for the intensive care were less disappointing with a bias of −0.14 to 0.31 l/min and a precision of ±0.76 and ±1.32 l/min.

Conclusion

The thermodilution technique has been shown to measure cardiac output accurately if flow is stationary. During mechanical ventilation the technique can be liable to gross errors. However, if certain precautions are followed mean cardiac output can be accurately estimated, even with a theoretical misuse of the Stewart-Hamilton equation. This can be done best by averaging three or four measurements equally spread over the ventilatory cycle. For this approach manufacturers of cardiac output computers have to be persuaded to include a phase selector and an automatic injector.

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