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An adequate strategy for the thermodilution technique in patients during mechanical ventilation

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Abstract. The application of the thermodilution method in conditions associated with variations in blood flow implies a misuse of the Stewart Hamilton equation. Therefore, we studied the reliability of the thermodilution method for the estimation of mean cardiac output (CO) during mechanical ventilation in patients ($n = 9$). Variation of the injection moment in the ventilatory cycle elicited a cyclic variation of CO estimates. This variation was not the same for all patients neither in phase nor in amplitude. Therefore, no specific phase in the ventilatory cycle could be selected for an accurate estimation of mean CO. Averaging CO estimates randomly distributed in the ventilatory cycle led to an improvement of accuracy with the square root of the number of observations. The averaging of CO estimates spread equally over the ventilatory cycle led to a much better result, e.g., the variation in the average of two estimates equally spread in the ventilatory cycle was similar to the variation in the average of four random estimates. We conclude that averaging of 3 or 4 estimates spread equally over the ventilatory cycle is an adequate strategy to estimate mean cardiac output in patients reliably.

Key words: Cardiac output – Mechanical ventilation – Multiple injections – Thermodilution

For an accurate estimation of mean cardiac output using the thermodilution method several conditions have to be fulfilled: (i) no loss of indicator, (ii) complete mixing of indicator and blood, (iii) a constant bloodflow, and (iv) a constant baseline temperature. Under these conditions the Stewart-Hamilton equation, as incorporated in many commercial cardiac output computers, can be used. During mechanical ventilation, when bloodflow is modulated by cyclic changes in intra-thoracic pressure [1, 2], the Stewart-Hamilton equation is misused. In practice this may lead to a considerable scatter in random estimates of cardiac output even when the measurements are performed during otherwise haemodynamically stable conditions. These cardiac output values are dependent on the moment of injection of indicator in the ventilatory cycle, in pigs [3–5], dogs [6, 7], and men [8, 9].

Recommendations for an accurate estimation of mean cardiac output during mechanical ventilation are contradictory. Stevens et al. [9] recommended multiple injections at the end of expiration, whereas Okamoto et al. [8] recommended paired measurements at mid-inspiration and mid-expiration. From our animal studies [3–5] we concluded that mean cardiac output could be estimated accurately by calculating the averaged value of four measurements equally spread over the ventilatory cycle. Schneider and Powner [7] confirmed this conclusion in dogs and in one patient.

The objective of the present clinical study was to evaluate the errors in the thermodilution cardiac output estimates during mechanical ventilation in patients in order to find an adequate strategy for a reliable estimation of mean cardiac output.

Methods

Nine male patients aged 55 to 67 years were studied after coronary artery bypass surgery. All suffered from multiple vessel disease, without previous myocardial infarctions, and all had stable angina pectoris with normal ventricular function. None had acute or chronic pulmonary disease. As premedication, the patients received 5 mg of lorazepam p.o.. Anaesthesia was induced with fentanyl (100 µg/kg IV), administered over 5 minutes and pancuronium bromide (0.1 mg/kg) was given to assure complete muscle relaxation. Additional small doses of fentanyl and pancuronium were used as needed. To control blood pressure after sternotomy and to facilitate rewarming after the extracorporeal circulation, sodium nitroprusside was administered (2–4 µg/kg/min). In none of the cases were cardiac stimulants needed. The patients were ventilated with an oxygen/air mixture at a rate of 8–10 breaths per min and an insufflation/inspiratory pause/expiratory ratio of 25%/20%/55%. The ventilatory volume was adjusted to maintain a P_aCO_2 between 32 and 42 mmHg. No positive and expiratory pressure was applied.

The instrumentation of the patients was not different from the normal clinical routine. A radial artery cannula and a 7.5 F Swan Ganz catheter were inserted. The Swan Ganz catheter (Edwards 93A–131–7) was inserted via the internal jugular vein and special attention was given to the position of the thermistor in the pulmonary artery to avoid an

extreme distal location. The thermistor was connected to a cardiac output computer (Edwards COM 1).

Measurements and estimation of cardiac output

Electrocardiogram, radial arterial pressure, pulmonary arterial pressure, central venous pressure, tracheal pressure, ventilatory flow, and body temperature were monitored on a chart recorder (Gould ES 1000) to check the stability of the patients during a series of 12 measurements. Patients with a change in one of the pressures of more than 5% over the period of a series were excluded from the study.

Injection of 5 ml glucose solution (5%) at room temperature was automatically performed by a phase controller and a pneumatically driven syringe, after a manual start of the cardiac output computer. The injectate was delivered through the Swan Ganz catheter, within 1 s. After 12 seconds the syringe was automatically refilled. The moment of injection was dependent on a start signal given by the operator and the moment in the ventilatory cycle set on the phase controller. The moment in the ventilatory cycle was derived from the Siemens servo ventilator (900 B). This ventilator delivers 100 impulses during each ventilatory cycle giving a subdivision in percentages. These impulses were used to feed a counter in the phase control unit. The counter was reset at the start of each insufflation.

Experimental protocol

A series of twelve thermodilution measurements was carried out during haemodynamically stable conditions. A cardiac output measurement was repeated if the COM 1 computer showed an alert signal and the tracing of the dilution signal showed an abnormal curve. At least five ventilatory cycles were inserted in between two measurements, so each series was performed in approximately 9–10 minutes. The injections were done successively at the phases 0%, 25%, 50%, 75%, 8%, 33%, 58%, 83%, 17%, 42%, 67%, and 92% of the ventilatory cycle, where phase zero was chosen at the start of insufflation. The mean of all twelve cardiac output estimates was accepted to be the real mean cardiac output. Each measurement was expressed as a percentage of this mean value.

Averaging of estimates

Two types of selection procedures were used: a *systematic* selection and a *random* selection of single estimates (Fig. 1), as described in detail before [4] and briefly summarized here.

Systematic selection

A two-point-average was obtained by the average of two points half a ventilatory cycle apart. There were 6 such two-point-averages available from a series of 12 single estimates, i.e., 0%+50%, 8%+58%, etc. up to 42%+92%. Four three-point-averages were calculated similarly, i.e., 0%+33%+67%, 8%+42%+75%, 17%+50%+83%, and 25%+58%+92%. The three four-point-averages per series were obtained from the phases 0%+25%+50%+75%, 8%+33%+58%+83%, and 17%+42%+67%+92%, respectively.

Random selection

As in the systematic procedures again two- to four-point-averages were calculated. For example a four-point-average was obtained by taking four random single estimates, each from the full series of twelve. Thus, it was possible to select, by chance, the same value four times. This random selection was not completely analogous to four injections at the same phase in the ventilatory cycle, because the estimates would then have been mutually different due to instability of the patients and measurement errors.

Statistical analysis

p-levels for differences between measurements within the same patient were calculated according to a paired Student's t-test for small samples. Significance was determined at $p<0.05$.

Results

In all nine patients the haemodynamic variables (Table 1) were stable for the series of 12 observations. Mean values ±SD were for radial artery pressure 89±5 mmHg, pulmonary arterial pressure 19±4 mmHg, and central venous pressure 9±1 mmHg.

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. Figure 2 shows the results of three selected series of 12 CO estimates for 3 patients. All these patterns of modulation have the same periodicity as the ventilation, but are shifted in phase (Φ) and have different amplitudes of variation. In this figure we have indicated the point where the curves crossed the 100% line in the negative direction. This point has been expressed as a percentage of the whole cycle, starting with insufflation. In agreement with this figure for three patients we observed marked differences in the amplitude and the phase of the pattern of modulation for all patients.

The variance in the phase (Φ) for the nine patients is given in Table 2, together with the mimimum CO_{min} and maximum (CO_{max}) values of the single estimates in percentages of the mean cardiac output. The maximum dif-

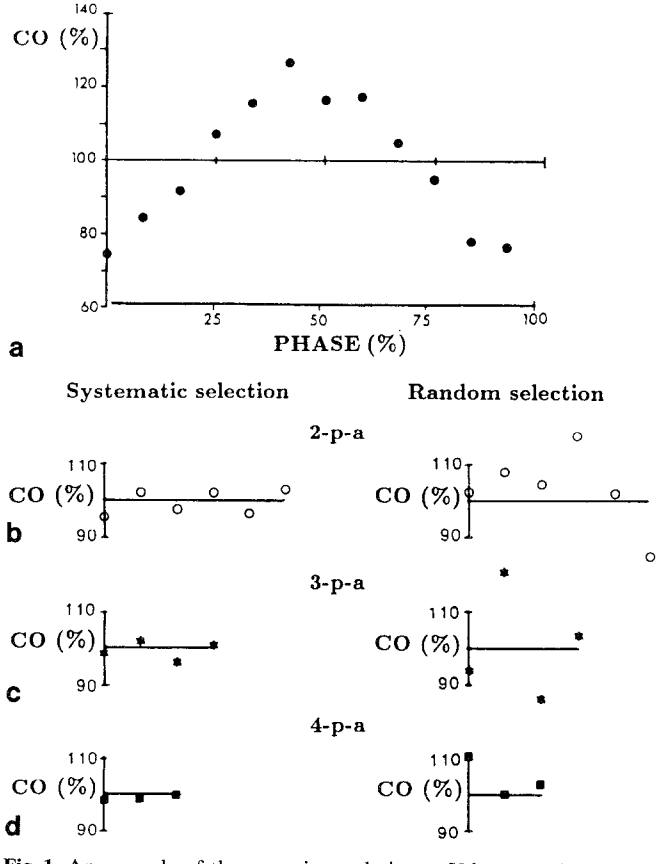

Fig. 1. An example of the averaging techniques. Values are given in % of the mean of a series of all 12 single estimates. **a** 12 single estimates of a patient plotted against the moment of injection in the ventilatory cycle. Phase 100% is the same as phase 0% which coincide with the start of insuffation. **b** 6 two-point-averaged (2-p-a) values consecutively plotted on the horizontal axis, **c** 4 three-point-averaged (3-p-a) values. **d** again, 3 four-point-averaged (4-p-a) values. For further explanation see text

Table 1. Data of the nine patients in the study. CO, mean to twelve cardiac output estimates; P_{ra}, arterial pressure measured in the radial artery; P_{pa}, pulmonary artery pressure; P_{cv}, central venous pressure; SD, standard deviation of the mean

Patient	CO l/min	P_{ra} mmHg	P_{pa} mmHg	P_{cv} mmHg	Weight kg	Age years
1	3.35	90	28	12	78	55
2	5.27	97	20	11	90	61
3	5.78	94	19	10	82	67
4	4.42	93	20	9	75	56
5	6.15	79	16	8	74	59
6	3.83	90	19	10	83	62
7	3.54	87	22	8	68	64
8	3.97	84	15	9	94	55
9	4.14	88	15	8	78	57
Mean	4.49	89	19	9	80	60
SD	1.00	5	4	1	8	4

Table 2. Phase and amplitude of the modulation in the nine patients. Φ, phase at which the CO variation in the ventilatory cycle crossed the 100% in negative direction, see also Fig. 2. $CO_{min,max}$, minimal and maximal values for a series of 12 estimates; SD, standard deviation of the mean

Patient	Φ (%)	CO_{min} (%)	CO_{max} (%)
1	33	83	113
2	33	82	130
3	27	75	128
4	27	83	114
5	50	85	114
6	62	82	121
7	71	80	112
8	70	71	129
9	71	76	127
Mean	49	80	121
SD	20	5	8

ference between the largest and the smallest values of the estimates in a series of 12 measurements in a patient was 58%. The mimimum difference was 29%.

The results of the averaging procedures for all series are presented in Table 3. In the systematic procedures all mean values were, by definition, 100%, because all measurements are always involved. In the randomly selected population the mean was slightly different from 100%, because some data points were selected more than once and others not at all.

Taking a random set of cardiac output estimates gave approximately the same mean and variance as the total original set of estimates with an SD of approximately 13%. The standard deviation decreased close to a factor $\sqrt{2}$ for the randomly selected two-point averages and with a factor 2 for the systematically selected two-point averages. The largest improvement in accuracy of the estimation of cardiac output can be seen in the systematically selected estimates for the two- and three-point averages. The further improvement in accuracy when using 4 estimates was smaller. Averaging three or four estimates equally spread in the ventilatory cycle gave almost 100% of all values within the 10% confidence limits and approximately 90% within the 5% confidence limits.

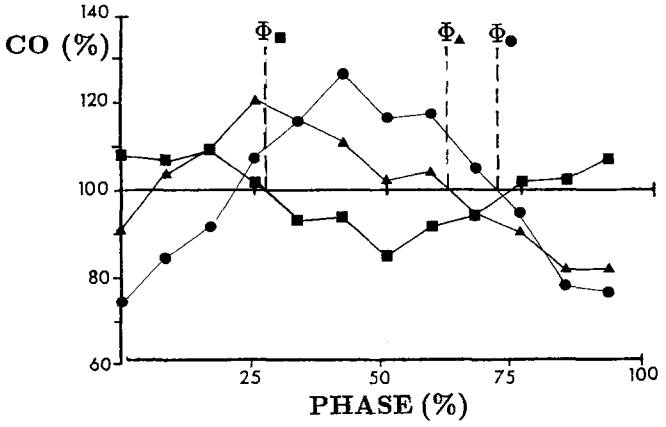

Fig. 2. Three individual series of 12 cardiac output (CO) measurements in three patients, plotted against the moment of injection as a percentage phase of the ventilatory cycle. 100% is the mean of each series of 12 estimates. $\Phi_{\blacktriangle}$, $\Phi_{\blacksquare}$ and $\Phi_{\bullet}$ are the phases at which the 100% value is crossed in negative direction

Discussion

Although, under the circumstances of mechanical ventilation, the Stewart-Hamilton equation is not valid, cardiac output computers based on this formula are applied clinically. We studied the errors from this type of application to find a solution for this theoretical misuse.

Cyclic variation in cardiac output

Our study in patients showed the presence of a cyclic modulation in cardiac output estimates related to ventilation (Figs. 1 and 2). This result is in agreement with the data found in animals [3, 4, 6, 7] and humans [8, 9]. On the cyclic modulation a random variation was present. This random variation may be caused by (i) haemodynamic instability of the patients [11], (ii) slow and rapid baseline temperature fluctuations during the measurement, and (iii) errors in the cardiac output device. Repeated measurements at a chosen moment in the ventilatory cycle will decrease the random errors for a specific patient. But the choice of one moment for cardiac output estimation will give different values for different pa-

Table 3. Averaging techiques. 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 the total number of measurements within 10% and 5% accuracy respectively; n, number of values; SD, standard deviation of the mean

	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	53	36
4-p-a	100.0	3.1	100	89	100.3	5.7	93	59	27

tients, because of the inter-individual differences in modulation pattern of the cardiac output estimates (Fig. 2 and Table 2).

Monitoring of changes in cardiac output

It is believed that relative changes in CO can be followed if injections are made at a fixed moment in the ventilatory cycle [9, 10]. This approach needs a constant phase relationship in CO variations versus ventilatory cycle. It was demonstrated that the phase relationship between the CO estimates and the ventilatory cycle is changed, when either ventilatory pattern, frequency, end expiratory pressure or blood volume conditions are changed [3, 4]. In this study we observed different patterns and phase relationships of the CO estimates in the ventilatory cycle for different patients, which were presumably due to differences in haemodynamic conditions.

Averaging of estimates

To determine cardiac output clinically a general accepted method is the averaging of multiple random measurements. From animal studies [3, 4, 7], where we compared the thermodilution method and the Fick method, we know that the mean of 12 estimates equally spread over the ventilatory cycle represents an accurate estimate of the mean cardiac output. We assumed that the mean of twelve such measurements in our patients represented mean cardiac output.

Averaging CO estimates of randomly distributed injections led to an improvement in accuracy with the square root of the increase in number of oberservations. Thus, the average of two random estimates improves accuracy with a factor 1.4 compared with the single average of random estimates. Actually, the random selection was restricted to measurements at twelve different, but equally spread, moments in the ventilatory cycle. We have good evidence to regard these twelve estimates as a representative substitute for estimates at all moments in the ventilatory cycle. Firstly, the improvement in the accuracy with a factor $\sqrt{2}$ when doubling the number of estimates for averaging indicates a normal distribution of all twelve estimates. Secondly, the improvement in the estimation of cardiac output by an increasing number of single estimates randomly selected from the 12 estimates is similar to that found in the same procedures selected from 50 estimates in animal studies [4].

A better result was obtained from the averaging of systematically selected CO estimates. The average of two estimates with a phase difference of half a ventilatory cycle proved as accurate as the average of four random estimates. Because of the superior properties of the systematic averaging technique as shown in Table 3 we rejected the recommendation of Stetz et al. [10] to average three randomly performed observations. Okamoto et al. [8] confirmed our rejection [3, 4] of cardiac output measurements only made at the end of expiration, and recommended the estimation of mean cardiac output by calculating the average of two measurements, one performed half way during insufflation and one half way during expiration. These points in the ventilatory cycle could be synchronized "by hand" for injections by listening to noise of the ventilator and by monitoring either intratracheal pressure or chest wall movements. We would only follow the recommendation of Okamoto et al. when these points in the ventilatory cycle have a difference of half a cycle.

It has been argued that measurements equally spread over the ventilatory cycle are a technically demanding exercise [9]. However, our instrumentation was relatively simple, and can be easily incorporated in new cardiac output computers.

Based on the presented clinical study and on our results from animal experiments [3–5] we concluded that mean cardiac output can be best estimated by averaging 3 or 4 measurements initiated at 3 or 4 equally spaced intervals over the ventilatory cycle. This will reduce both random noise and systematic deviations to an acceptable level of accuracy for follow-up in one patient and mutual comparison of results between different patients.

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