Determination of Cardiac Output by Rebreathing Method; with Special Reference to Its Reliability and Merit in Clinical Use

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The $P\bar{V}CO_2$ was determined graphically by the rate of rise in CO_2 concentration while rebreathing pure oxygen. The reproducibility of consecutively determined $P\bar{V}CO_2$ was fairly well and it correlated significantly with the $PaCO_2$ directly measured from arterial blood.

To make the procedure determining the cardiac output strictly non-bloody, $PaCO_2$ was also determined indirectly by the end-tidal gas analysis. The CO_2 output was measured conventionally. The $P\bar{V}CO_2$ and $PaCO_2$ were converted to their content with CO_2 dissociation curve for fully oxygenated blood, then the cardiac output was calculated applying these values to the Fick's formula.

The range of the cardiac output determined consecutively during an hour was considered small enough to be included within the physiological fluctuation, and the cardiac output thus determined correlated significantly with that by direct Fick method. The cardiac output was significantly different between one another in three groups (healthy, ischemic heart disease and ischemic heart failure). The result agreed with that made by the dye dilution method and apexcardiogram.

Having fairly good reproducibility and showing good accordance with the results by the other techniques, it was proved that this indirect Fick method is of great clinical use. Besides, the procedure does not give almost any mental or physical load to subjects.

THE DIRECT FICK and the indicator dilution technique are considered to be the standard methods to determine the cardiac output.¹ These methods, however, are not always easy to carry out. On not a few occasions, more handy and physiological procedures are wanted. Completely non-bloody procedure, if satisfactorily reliable, would be of great clinical use.

Trials to assess the cardiac output by the indirect Fick method using the intrinsic CO_2 as an indicator, which can be determined by the expiratory gas analysis, have been made.
4, 6, 8, 9, 10

Present investigations were made to check the reliability of the "rebreathing method" described by DEFARES⁸ and KLAUSEN,⁴ which

is one of these non-bloody procedures assessing the cardiac output. Then some clinical applications of this method were also carried out.

SUBJECT AND METHOD

(1) Measurement of $P\bar{V}CO_2$

Determination of the $P\bar{V}CO_2$ in 25 subjects, either healthy or having various heart disease, were made by the rebreathing method as is described below. Indirectly to prove the accuracy of the $P\bar{V}CO_2$ determinations by this technique, the dependency of the $P\bar{V}CO_2$ thus measured upon the $PaCO_2$ determined directly from the arterial blood sample was seen.

The oxygen in an anaesthetic bag was rebreathed through a mouth-piece connected to the bag with three way stop-cock. The capacity of the bag was about 3.0 L, and the oxygen within the bag was about

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(Received for publication, June 21, 1968)

1.5 L. The frequency of the breath was adjusted with a metronom to become 30 times per minute. The three way stop-cock was turned to let the bag oxygen be breathed at the end of expiration, while the subject was at the resting condition (Fig. 1).

CO₂ concentration within the bag was continuously recorded with the Medical Gas Analyzer (Beckman LB-I) during the rebreathing (Fig. 2). The recorded CO₂ concentration was converted into the partial pressure (P_{CO₂}), and was plotted to form time-P_{CO₂} curve during the first 12 to 15 seconds, just until the second rapid rise in the P_{CO₂} by the recirculation was observed. As was described by DEFARES,⁸ the theoretical equilibrium point between the alveolar P_{CO₂} and the P_{CO₂} within the bag can

be determined as follows (Fig. 3). The time axis of the curve was divided into 6 equal intervals. Cor-

Fig. 1. Block diagram for measuring CO₂ in lung-bag system during rebreathing.

Fig. 2. Actual record of CO₂ concentration rise with gas analyzer.

Fig. 3. Graphical analysis to obtain the theoretical equilibrium point in lung-bag system. Left; Time-P_{CO₂} curve. Right; P_{CO₂} values from a to g on the curve corresponding to values of time axis which was divided into 6 equal intervals were plotted against one another. The intersection of the line extrapolating these points with the 45° line gives the equilibrium point.

responding values on the curve give 7 points, named alphabetically from a to g here. These 7 values were put into the graphical analysis, then the theoretical equilibrium point was obtained.

The measurement of the partial pressure of CO_2 in the arterial blood sample was made with Severinghaus electrode, calibrated by the same gas that was used for the calibration of the Medical Gas Analyzer.

(2) Calculation of cardiac output

The Fick's formula for the cardiac output can be transformed as follows to use CO_2 as an indicator instead of O_2 .

$Q = \dot{V}_{\text{CO}_2} / (\bar{C}_{\text{VCO}_2} - C_{\text{ACO}_2})$ Here, Q is cardiac output, $\bar{C}_{\text{VCO}_2}$ is CO_2 content in mixed venous blood and C_{ACO_2} is arterial CO_2 content respectively.

$\dot{V}_{\text{CO}_2}$ was measured by analyzing the expiratory gas accumulated for 7 minutes into the Tissot gasometer. Determination of the alveolar PCO_2 (PACO_2) was made by the alveolar gas analysis with the end-tidal sampling technique. This PACO_2 was substituted for PCO_2 in the arterial blood as PaCO_2 , to make the procedure strictly non-bloody. Our preliminary investigation had proved the PACO_2 thus determined was the satisfactory substitute for PaCO_2 . The $\text{P}\bar{\text{VCO}}_2$ was determined by the rebreathing method as was already described. In all occasions, measurement of the CO_2 concentration was made with the Medical Gas Analyzer and the CO_2 concentration was converted into partial pressure. Then with the CO_2 dissociation curve of fully oxygenated blood, $\text{P}\bar{\text{VCO}}_2$ and PaCO_2 were converted into the CO_2 content of the respective blood. Thus, values needed for the Fick's formula modified for CO_2 were determined by the strictly non-bloody and physiological procedure.

To check the reliability of the cardiac output thus determined, correlation between the cardiac output measured by the rebreathing method and that by the direct Fick method was studied in 10 subjects in whom the rebreathing method was carried out during the right heart catheterization.

(3) Clinical application

The cardiac index was compared among the following three groups with one another; 8 healthy subjects, 14 ischemic heart disease without manifest heart failure and 9 ischemic heart disease with congestive heart failure. Relationships between the cardiac index and the peak concentration time (PCT) in the dye dilution curve, and between the DFW/T in the apexcardiogram were studied also, to make further analysis of our previous investigations on the cardiac function of the ischemic heart disease.³

RESULTS

(1) $\text{P}\bar{\text{VCO}}_2$

Seven measurements were repeated during an hour on 2 subjects respectively to see the reproducibility of this procedure. Ranges of these determinations were considerably small, standard deviations being $\pm 1.2 \text{ mmHg}$, and $\pm 0.9 \text{ mmHg}$ respectively (Fig. 4).

Besides, $\text{P}\bar{\text{VCO}}_2$ determined by the rebreathing method correlated with arterial blood sample

Fig. 4. Reproducibility of the $\text{P}\bar{\text{VCO}}_2$ obtained from 7 consecutive measurements during an hour in 2 subjects.

Fig. 5. Correlation diagram of $\text{P}\bar{\text{VCO}}_2$ and PaCO_2 .

very well, correlation coefficient being 0.860, $p < 0.01$ (Fig. 5). Reliability of the Pv_{CO_2} determination by the rebreathing method was thus shown satisfactorily.

(2) Cardiac output

Seven consecutive determinations of the cardiac output were made on a normal subject and on a patient with mitral stenosis during an hour. The ranges of these determinations were small enough to support the accuracy of this procedure,

Fig. 6. Reproducibility of cardiac index obtained from 7 consecutive measurements during an hour in 2 subjects.

standard deviations being $\pm 0.4 \text{ L/min/m}^2$, and $\pm 0.6 \text{ L/min/m}^2$ respectively (Fig. 6).

The correlativity of the determination by the

Fig. 8. Cardiac index of three groups; healthy subjects, ischemic heart disease and ischemic heart failure.

Fig. 7. Correlation diagram of direct and indirect Fick method.

rebreathing method with that by the direct Fick method was significant, correlation coefficient being 0.908, $p < 0.01$ (Fig. 7).

(3) Clinical application

The cardiac index determined by the rebreathing method showed statistically significant difference when compared between each of the three groups mentioned before, being the smallest in the ischemic heart failure and showing the inclination of approaching the value in the non-failing ischemic heart disease (Fig. 8).

The cardiac index thus determined showed significant correlations with either PCT in the

dye-curve or DFW/T in the apexcardiogram, each of which is a fairly good indicator of the cardiac function, as was previously reported (Fig. 9, 10).

DISCUSSION

As procedures to determine $P\bar{V}CO_2$ indirectly, breath-holding method,⁵ single-breath method⁶ and rebreathing method^{7,8,10} have been reported. In each method, the principle is to obtain the alveolar P_{CO_2} which is equal to the $P\bar{V}CO_2$ resulting from the equilibrium by the expiratory gas analysis.

Fig. 9. Correlation diagram of cardiac index and PCT.

Fig. 10. Correlation diagram of cardiac index and DFW/T.

The shortcoming of these methods becomes apparent when the uneven distribution of the inspired gas exists, especially the unevenness in reference to pulmonary perfusion or uneven distribution of V/Q ratio comes into question,² even though very rapid diffusion of CO₂ within the lung is taken into consideration. It is, therefore, debatable to apply these techniques to the patients with cardio-pulmonary dysfunction. In fact, ventilatory dysfunction of varying degree especially expiratory disorder, though of moderate degree, has been demonstrated in various heart diseases.¹³ Rebreathing method, however, has some advantage compared with other two methods with regard to getting even distribution of the intrapulmonary gas.² So this technique might be almost ideal in such study as the analysis of the cardiac function in the ischemic heart disease in whom no considerable unevenness of the intrapulmonary gas distribution was observed in our previous study using N₂ as an indicator.¹²

The next difficult problem in this procedure is that $\overline{Pvco_2}$ has to be measured with such accuracy that the error is at most 1.0 mmHg to determine the cardiac output with error within 25 per cent.² Standard deviation of 7 serial determinations of $\overline{Pvco_2}$ was about ± 1.0 mmHg, and standard deviation of the cardiac output calculated was about ± 0.5 L/min/m². The range of this 7 consecutive determinations of the cardiac output during an hour can well be considered within the range of normal spontaneous fluctuations.

KLAUSEN⁴ reported that the behavior of the cardiac output determined by the rebreathing method during exercise agreed fairly well with that determined by other techniques (ASMUSSEN and NIELSEN, HOLMGREN et al.). In our present study, the cardiac output by this method correlated significantly with that by the direct Fick method. These results made it clear that the rebreathing method is of satisfactory reliance in clinical investigation. The range of normal value of the cardiac output by the rebreathing method is shifted lower compared with that determined by other methods. This is most probably due to the fact that this procedure requires subjects much less mental and physical burden, as was mentioned by

PODLESCH and ULMER.¹¹

Lastly, results of clinical application of the rebreathing method was not conflicting with our previous report that not a few of the ischemic heart disease had "latent heart failure".³ The range of the cardiac output shifted lower in the following order; healthy subjects, ischemic heart disease without manifest heart failure and ischemic heart failure. The difference between one another was statistically significant. As we reported previously, PCT in the dye dilution curve was significantly different between one another in these three groups, being longest in the failed ischemic heart disease. The same was found about the ratio of the diastolic filling wave to the total amplitude of the apex-cardiogram, DFW/T. So the PCT and the DFW/T were considered to be good indicators of the cardiac function at least as far as its tortuosity to lead to the manifest heart failure concerns.³ And the fact that the cardiac output correlated significantly with either of them suggested the decrease of cardiac output as one of the underlying causes of prolongation of the PCT and enlarging of the DFW/T.

SUMMARY

(1) The reproducibility of the $\overline{Pvco_2}$ determined by the rebreathing method was seen by consecutive measurements. The standard deviations of the consecutive determinations were small enough to prove the reliability of this procedure.

(2) The range of the cardiac output calculated applying this $\overline{Pvco_2}$ to the Fick's formula was small enough to be included within the normal physiological fluctuation.

(3) The cardiac index by this method was in good accordance with that by the direct Fick method.

(4) The results of applying this technique on the study of the hemodynamics in the ischemic heart disease were agreed well with the results made previously by the dye dilution method and so on.

(5) This method is excellent, not giving the subjects almost any load, to assess the cardiac output of the subjects whose ventilatory dysfunction is not extensive as long as the $\overline{Pvco_2}$ determination is accurate enough.

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