Oxygen Consumption in Infants and Children during Cardiac Catheterization under Different Sedation Regimens

By David E. Fixler, M.D., Ted Carrell, B.S., Richard Browne, Ph.D., Kathryn Willis, M.D., and William W. Miller, M.D.

SUMMARY
We measured oxygen consumption in 426 infants and children during cardiac catheterization using an open circuit, flow-through technique. Since this method does not require the cooperation of the patient, determinations were readily made in 170 infants. The purpose of this study was to determine those factors which significantly influence oxygen consumption and to determine the potential errors incurred in using predictive equations for estimating oxygen consumption. The type of sedation or anesthesia given was found to be one of the most important variables influencing oxygen consumption; therefore patients were classified into five anesthetic groups. Stepwise regression analysis revealed that each group had a distinctive set of hemodynamic or physical factors which significantly affected oxygen consumption; hence each group required a different predictive equation. Body size in terms of surface area or weight was the only significant variable common to all five patient groups. Using the predictive equations the estimated values differed from measured values by more than 20 percent in approximately one-fifth of the cases. These data indicate that frequently oxygen consumption cannot be accurately estimated from predictive equations. Therefore if blood flow is to be accurately determined by the Fick method in infants and children, oxygen consumption should be measured during the catheterization procedure.

Additional Indexing Words:
Open circuit, flow-through technique Paramagnetic oxygen analyzer Ketamine anesthesia

CARDIAC CATHETERIZATION is an invasive procedure which provides information frequently used in determining operability of children with heart defects. Because of its invasive nature and its important role in decision making, every effort should be made to minimize the variability of the laboratory findings. Since the presence of intracardiac shunts reduces the accuracy of measuring pulmonary blood flow by the indicator dilution technique, blood flow is commonly determined by the Fick method. This method requires simultaneous measurement of arterio-venous oxygen content differences and oxygen consumption during a steady state. Ideally then, oxygen consumption should be measured continuously during the catheterization procedure to determine if a steady state is present at the time of blood sampling and to provide a direct measurement for the Fick determination of cardiac output.

Many cardiac catheterization laboratories do not measure oxygen consumption in infants and small children but assume a value based on predictive tables published in the literature.1 2 Unfortunately, some discrepancies appear in the tables of different studies and none have a large number of determinations in children under 2 years of age. The purpose of the present study was threefold: 1) to describe and critically evaluate a relatively simple flow-through technique for continuous measurement of oxygen consumption; 2) to determine those factors which significantly affect oxygen consumption during the cardiac catheterization procedure; and 3) to present new predictive equations for estimating oxygen consumption and the potential error incurred in their use.

Methods
Measurement of Oxygen Consumption
Oxygen consumption was measured by modification of a flow-through technique.3 In infants and small children the patient’s head, shoulders and arms were enclosed within a transparent, hemispherical hood; in older children only the head was inserted (fig. 1). The opening around the neck or shoulders was sealed with a clear polyethylene wrap and the edges of the hood were sealed to the catheterization table with paper tape. Room air was sucked into the hood at a flow rate of approximately 10 times the patient’s expected minute volume to prevent carbon dioxide accumulation. Gas
was drawn continuously from the hood using a constant speed blower (Rotron Blower MRPU type K 10 Serves 329AS Rotron Manufacturing Company, Woodstock, New York). Flow through the hood was measured by a rotameter (Model 10A 3565S, Fischer-Porter Company, Warminster, Pennsylvania) and regulated by an adjustable valve. The effluent from the hood containing expired gases diluted with room air was sampled with a paramagnetic oxygen analyzer (OA 250, Servomex Controls Limited, Scorborough, Sussex, England) through a side arm and drying chamber at a sampling rate of 125 ml/min. The output signal of the oxygen analyzer was fed through an electronic interface unit for fine adjustment of amplification and base line position.* This signal was continuously recorded on a chart recorder (Model 680 Hewlett Packard). By using a manifold, gas could be sampled either from room air, the hood effluent or two standard gas mixtures. Initially the gain of the interface unit was adjusted using two standard gas mixtures of 21.00% oxygen and 20.15% oxygen for calibration with a known oxygen concentration differential. The base line was then adjusted with room air. At the time of oxygen consumption determinations sequential sampling of hood effluent, room air and repeat hood effluent was made over a five minute period (fig. 2). The 95% response time of the entire system was less than 90 seconds. The oxygen consumption (\( V_{\text{O}_2} \), ml/min standard temperature, pressure, and dry [STPD]) was calculated as the product of hood flow (\( Q_h \), ml/min) times the difference between the fractional concentration of oxygen in inspired room air (\( F_{\text{O}_2} \)) and that in the hood effluent (\( F_{\text{no}2} \)) according to the equation:

\[
V_{\text{O}_2} = Q_h (F_{\text{O}_2} - F_{\text{no}2}) \times \text{STPD factor}.
\]

An evaluation of the continuous flow through technique for measuring oxygen consumption was carried out as described by Kappagoda and Linden. This in vitro assessment was performed by infusing nitrogen at specific flow rates into the sealed hood. The nitrogen displaces an equal volume of air from the stream which theoretically yields an oxygen consumption value equal to the amount of oxygen contained in the displaced volume of air. That is, if the nitrogen were infused at a rate of \( Q_n \) ml/min, the amount of oxygen displaced would be equal to \( Q_n \) times 0.2093, where 0.2093 is the fraction of oxygen in room air.

In both in vivo and in vitro studies the seal around the hood was judged to be satisfactory when the polyethylene wrap tended to be sucked inward. In early preliminary studies when less attention was placed on satisfactory sealing of the hood, initial oxygen consumption values were low and rose with more complete sealing. Kappagoda and Linden report using a hood pressure gauge to insure maintenance of a slight negative pressure.

* Schematic of the electronic interface unit is available on request.
Patient Studies

Oxygen consumption data were obtained in 426 patients undergoing cardiac catheterization at Children’s Medical Center from April 1972 through November 1973. Oxygen consumption was measured in all cases except those requiring oxygen administration. The first 341 study patients were used as a data base upon which the subsequent tables and tabular data were derived. These patients were divided into five groups depending on the choice of premedication or anesthetic ordered by the attending pediatric cardiologist: group I, atropine (0.1 mg/kg) and ketamine (13 mg/kg IM); group II, meperidine (1.0 mg/kg, maximum 50 mg), promethazine (0.5 mg/kg, maximum 25 mg) and chlorpromazine (0.5 mg/kg, maximum 25 mg); group III, morphine sulfate (0.1 mg/kg, maximum 10 mg), nembutal (2.0 mg/kg, maximum 100 mg) and chlorpromazine (0.5 mg/kg, maximum 12.5 mg); group IV, morphine sulfate (0.1 mg/kg, maximum 10 mg); and group V no premedication. Body surface area was estimated on the basis of height and weight from published nomograms. Except for small infants who were permitted glucose water, all children were studied after an overnight fast. Heart rates were determined from the electrocardiogram at the time of the Fick determination. Rectal, skin, and hood temperatures were measured with a multichannel telemeterimeter and appropriate thermister probes (Yellow Springs Instrument Company, Yellow Springs, Ohio). At the time of the oxygen consumption measurement the activity of the patient was graded at five arbitrary levels: level 1, patient asleep, no movement; level 2, patient asleep with occasional movement; level 3, patient awake without movement; level 4, patient awake with infrequent occasional movement; level 5, patient awake, disturbed, with frequent movements. Eight patients were excluded who had activity level of 5, and 6 others were excluded whose oxygen consumption varied by more than 10% of the mean during the two minute period preceding the Fick determination. This resulted in an initial study group of 341 children. Patients were classified as cyanotic if their systemic arterial oxygen saturations were less than 98%. Left to right shunts were categorized according to the ratio of pulmonary flow to systemic flow: category 1, Qp:Qs less than 1.2:1; category 2, Qp:Qs 1.2-2.0:1; category 3, Qp:Qs 2.1-3.0:1; and category 4, Qp:Qs greater than 3.0:1. The patients were also classified according to the presence or absence of pulmonary arterial hypertension, hypertension being defined as peak pulmonary arterial pressure greater than 50 mm Hg.

Statistical Methods

A nonparametric method (Mann-Whitney test) was used to compare the effects of the type of premedication on oxygen consumption adjusted for the linear effects of age and weight. This preliminary evaluation showed that the type of sedation or anesthesia used did significantly influence oxygen consumption, suggesting that each regimen required a distinct equation for predicting oxygen consumption. We used a stepwise regression technique to determine the significant predictor variables of oxygen consumption such as: sex, body surface area, weight, heart rate, presence of cyanosis, age, activity level, presence of pulmonary hypertension, rectal temperature, and magnitude of left-right shunting for each sedation regimen. Basically, the stepwise regression approach attempts to find the number of variables which significantly add to the predictive capability of the regression. Only variables having a P value less than 0.05 were included in the models to minimize the number of variables in each predictive equation.

After the regression equations for predicting oxygen consumption were formulated, the estimated oxygen consumption values of the next 85 patients were compared with the actually measured values to determine the average error incurred in the estimation. From this group, 54 patients were selected who received meperidine, promethazine and chlorpromazine sedation. Linear regression analyses of measured versus predicted oxygen consumption values were performed. Predicted values were calculated from the group II equation of the present study as well as frequently referred to tables in the literature with similar sedation regimens.

Results

The result of the in vitro assessment of this flow-through technique is shown in figure 3. The calculated oxygen consumption data used were derived by determining the amount of oxygen displaced by infused nitrogen, whereas the measured oxygen consumption values were those determined using Servomex output. This evaluation incorporates the errors inherent in Servomex analysis of the gas mixture, the error in measuring hood flow by the rotameter, and the error in measuring the flow rate of the infused nitrogen. Figure 3 shows the data points and regression line comparing calculated to measured oxygen consumption and indicates that within these ranges the flow-through technique provides an accurate estimate of oxygen consumption. Since the regression equation was significantly different from that of the line of identity, this equation was used to correct the measured oxygen consumption values in the patient studies.

![Figure 3](https://example.com/figure3.png)

Comparison of oxygen consumption calculated by nitrogen infusion into the hood versus that measured by a Servomex paramagnetic analyzer. In regression equation $V_{O_{2M}}$ is measured oxygen consumption by Servomex determination; $V_{O_{2C}}$ is calculated oxygen consumption.
The patient characteristics of the five sedation groups are listed in Table 1. It can be seen that groups I, II and III have similar ages and represent older children, whereas groups IV and V represent young infants. These age differences are due to the fact that morphine sulphate (group IV) is used typically in infants at risk of developing hypoxic spells and that no sedation (group V) is used in infants during the first weeks of life. The higher average heart rate in group I compared to that of group II or III, is most likely secondary to the administration of atropine. The average oxygen consumption value was also significantly higher in this group compared to that of group II or III, with patients of comparable age and size.

Table 2 gives the results of the stepwise regression analysis used to select the most significant predictive variables for each patient group. Only the variables listed were significant linear predictors of oxygen consumption ($P < 0.05$) adjusted for other variables. The sum of squares value reflects the correlation of a variable to oxygen consumption excluding the interaction of other variables; the larger the sum of squares the greater the correlation. The $P$ value indicates the probability that the correlation with oxygen consumption is due to chance. For example in each group body size has the highest correlation with oxygen consumption as indicated by the sequential sum of squares. Rectal temperature was an important correlate of oxygen consumption only for group I. However, this does not imply that oxygen consumption is unaffected by changes in body temperature, but rather indicates it is not of predictive value in estimating oxygen consumption in other groups. Both the Qp:Qs ratio and pulmonary hypertension are excluded from Table 2 since neither were significant predictive factors.

We found, as did Wessel et al., an increase in a patient's activity invariably resulted in an increase in oxygen consumption. Since the oxygen consumption values were obtained only after achieving a steady state, the majority of patients remained motionless during the measurements. As a result patient activity was not a significant factor in predicting oxygen consumption.

From the results of the stepwise regression analysis the best predictive equation for each patient group was formulated (Table 3). Note that the predictive equations for the patient groups contained different variables. This suggests that in order to obtain a more accurate prediction of oxygen consumption, the individual patient characteristics and type of sedation should be taken into consideration. For example, if the patient received a meperidine, promethazine and chlorpromazine mixture and had the following characteristics: B.S.A., 0.87 m$^2$; female, cyanosis,
Table 3

Predicted Regression Equations for Predicting Oxygen Consumption

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Predictive equation</th>
<th>95% Tolerance limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>$\dot{V}O_2 \text{ ml/min} = -663.3 + 188 B.S.A. - 1.47 \text{ Weight} + 0.397 \text{ H.R.} + 17.0 \text{ Temp}$</td>
<td>$\pm 37 \text{ ml/min}$</td>
</tr>
<tr>
<td></td>
<td>$+ 22.8 \text{ (if cyanotic)} - 11.3 \text{ (if female)}$</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>$\dot{V}O_2 \text{ ml/min} = -10.56 + 132 \text{ B.S.A.} - 8.20 \text{ (if female)} - 20.6 \text{ (if cyanotic)}$</td>
<td>$\pm 35 \text{ ml/min}$</td>
</tr>
<tr>
<td></td>
<td>$+ 0.263 \text{ H.R.}$</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>$\dot{V}O_2 \text{ ml/min} = 58.96 + 3.29 \text{ Weight} - 11.0 \text{ (if female)}$</td>
<td>$\pm 30 \text{ ml/min}$</td>
</tr>
<tr>
<td>IV</td>
<td>$\dot{V}O_2 \text{ ml/min} = -62.22 + 243 \text{ B.S.A.} + 0.41 \text{ H.R.} - 15.5 \text{ (if cyanotic)}$</td>
<td>$\pm 22 \text{ ml/min}$</td>
</tr>
<tr>
<td>V</td>
<td>$\dot{V}O_2 \text{ ml/min} = -65.75 + 9.37 \text{ Weight} + 0.38 \text{ H.R.} + 19.17 \text{ Age}$</td>
<td>$\pm 13 \text{ ml/min}$</td>
</tr>
</tbody>
</table>

Abbreviations: $\dot{V}O_2 = \text{Oxygen consumption; B.S.A. = Body surface area (m²); Temp. = Rectal temperature (centigrade); H.R. = Heart rate (beats/min); Weight = Kilograms; Cyanotic = Systemic arterial oxygen saturation <88%}; \text{Age} = \text{Years}$.

heart rate 120, then oxygen consumption would be predicted by the following calculations: $-10.56 + (132)(0.87) - 8.20 - 20.6 + (0.263)(120);$ which equals 107 ml/min.

To test the true predictive capabilities of the model equations, the oxygen consumption determinations from the next 85 patients undergoing cardiac catheterization were compared to the predicted values. Figure 4 shows the results of the correlation between the predicted oxygen consumption and measured oxygen consumption in these 85 patients. The average percentage differences between the predicted and measured values was 5.7% ± 21% (standard deviation). Approximately one-fifth of the predicted values differed from the measured values by more than 20%.

Figure 5 shows the results of the linear regression analysis comparing the predicted values with the measured values of oxygen consumption in 54 patients from group II, not included in the original data base of patients. The predicted values were calculated from tables or equations of: 1) Cayler et al.; 2) the present study; 3) LaFarge and Miettinen; 4) Krovetz and Goldbloom. The predicted values using the table from Cayler’s study resulted in an overestimation, whereas those using the equation from Krovetz’s study resulted in a large underestimation. Note the two studies most closely approximating the line of identity were those of LaFarge and the present study.

Discussion

In the present study the open circuit high flow technique was a successful and very practical method for measuring oxygen consumption in infants during cardiac catheterization. The method is based on the Fick principle, that is, if one knows the flow through the circuit, the concentration of oxygen entering and
the concentration of oxygen leaving, then the exchange of oxygen \( (\dot{V}_O) \) in the circuit can be calculated. The requirements for applying the Fick principle are: 1) constancy of flow, 2) ability to measure representative samples of inflow and outflow oxygen concentrations, 3) no loss of gas from the circuit. With the present method, constancy of flow is assured by continuous monitoring with a rotameter. Since the differences between inflow and outflow oxygen concentrations are very small (on the order of 0.50%), the oxygen analyzer must be extremely sensitive and stable. For example, to be able to measure the oxygen concentration differential to within an accuracy of \( \pm 10\% \), the analyzer must be capable of measuring oxygen differences as small as 0.05 percent. Kappagoda and Linden\(^4\) have demonstrated that the Servomex paramagnetic oxygen analyzer has suitable stability and sensitivity. To decrease potential loss of expiratory gases this flow-through technique produces a small negative pressure within the hood. However it is still essential to meticulously seal the edges of the hood to the patient and to the table to insure that loss of expiratory gases does not occur. Previous authors\(^5\) have measured the pressure within the hood using a differential air pressure gauge to check that negative pressure is maintained. It is also important to adjust hood flow such that the oxygen concentration differential between inflow and outflow gases is less than 1.0% to prevent carbon dioxide accumulation.

Many pediatric cardiology laboratories do not measure oxygen consumption in infants and small children but assume a value from predictive tables. The validity of making such an assumption is open to serious questions since the individual patient characteristics may differ significantly from those of the population upon which the tables were based. Unfortunately the amount of oxygen consumed by an individual during the catheterization procedure is extremely variable, being influenced by environmental temperature, level of activity, sedation, and catecholamine secretion. Most cardiac catheterization laboratories make an effort to control environmental temperature, especially when dealing with small infants, to minimize this effect upon metabolism and circulation. Similar precautions were taken in this study; however, rectal temperature was a significant variable influencing oxygen consumption in the patient group anesthetized with atropine and ketamine. These data indicate that when using this regimen, temperature should be monitored and taken into account if assuming an oxygen consumption value.

Baum and coworkers\(^8\) studied the effect of a sedation mixture (meperidine, promethazine and chlorpromazine) on oxygen consumption in children undergoing cardiac catheterization. They found that oxygen consumption fell in all patients during the cardiac catheterization procedure, reaching a minimum one-half to two hours after receiving the sedation and returning to control levels near the end of the procedure. They recommended oxygen consumption be measured at the time of blood sampling because of the temporal changes. In the present study the effect of different sedation regimens on oxygen consumption was determined after oxygen consumption had stabilized thereby insuring that a steady state had been achieved. The data were analyzed by a non-parametric technique taking into account the different patient characteristics of the five sedation groups. The fact that each group had a distinctive set of variables which significantly influenced oxygen consumption indicates that for a most accurate prediction the patient should be classified according to the sedation regimen used. Since combinations of drugs were used in most cases it is difficult to ascribe the action of a specific drug as being responsible for the differences between the sedation regimens.

To our knowledge this is the first study which reports oxygen consumption data in a large number of infants (170) continuously recorded during the cardiac catheterization procedure. The study probably most frequently referred to for estimating oxygen consumption in infants is that of Cayler et al.\(^1\) which reports measurements in only 18 patients under the age of 2 years. We felt that by using a larger data base of patients, regression equations could be formulated which would provide a more accurate prediction of oxygen consumption especially in this younger age group. The patients were separated according to the type of sedation or anesthetic used in order to offset this one particular variable. The patients in Cayler’s study\(^1\) received a sedation mixture similar to our group II (they gave approximately 80 percent more meperidine). Figure 5 shows the results of regression analysis of measured versus predicted oxygen consumption values in 54 patients sedated with this mixture. The predicted oxygen consumption values using Cayler’s tables resulted in a large overestimation of oxygen consumption. A major difference between that study and ours is that they collected expired air using a face mask or a mouthpiece, whereas the present study collected expired gases without disturbing the patient. These data suggest that the application of facial apparatus may significantly increase oxygen consumption and raises the question whether oxygen consumption in undisturbed patients can be predicted accurately from data obtained in infants having masks or mouthpieces. Figure 5 also demonstrates that using the predictive equation published by Krovetz and Goldbloom\(^7\) resulted in a large underestimation of oxy-
gen consumption. This difference may be due to the fact that patients in the present study had significant heart disease whereas their patients had no hemodynamically significant heart disease. This again points out the pitfall of assuming an individual patient has similar characteristics to those of the population upon which the predictive tables were based.

Despite our attempts to minimize the many factors which influence oxygen consumption our predictive equations had rather broad 95% tolerance levels (table 3). These findings are similar to the data of LaFarge and Miettinen who reported that the standard deviation of the differences between measured oxygen consumption/m² and the corresponding value calculated from their regression equation was 28.0 ml/min/m². Kappagoda et al. using a similar flow-through technique as in the present report, found the 95% tolerance limit for predicted values was 30 ml/min. Since it is a dictum of statistics that one can usually predict best with the same data used in deriving the regression equations, we checked the true predictive capabilities by using data obtained in the next 85 patients who were not in the original data base (fig. 4). In this latter sample the average percent difference between the measured and the predicted oxygen consumption values was 5.7% ± 21 (SD). In approximately one-fifth of the cases predicted values differed from measured values by more than 20%. In our own study strict requirements were made to achieve a steady state before oxygen consumption was measured and even then, large errors occurred with estimating oxygen consumption.

Many pediatric centers do not measure oxygen consumption because of the false impression that only by using expensive, complicated instruments and prolonging the catheterization procedure can such measurements be accomplished. Previous reports as well as the present study demonstrate that the flow-through method is particularly suitable for measuring oxygen consumption in the pediatric catheterization laboratory. It has several distinct advantages in that it is not disturbing to the patient, does not interfere with the catheterization procedure itself, is learned readily by the technician, and is relatively inexpensive. In contrast, Douglas bag collections of expired gases are time consuming, may increase oxygen consumption, and require the full cooperation of the patient. In the present study the output of the Servomex oxygen analyzer was recorded continuously, readily allowing recognition of a steady state and thereby indicating when oxygen consumption measurements and blood sampling could optimally be performed.

In conclusion although the present study provides more accurate predictive equations for estimating oxygen consumption, the data indicate that relatively large errors may result when oxygen consumption is estimated. A simple method for measuring oxygen consumption is presented which has been critically evaluated by several investigators. The apparatus is relatively inexpensive and particularly suitable for use in the pediatric laboratory. It is therefore recommended that oxygen consumption not be estimated from tables or regression equations but be measured continuously throughout the catheterization procedure.

Acknowledgment

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References

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