DETERMINATION OF LEFT TO RIGHT SHUNT BY THERMODILUTION IN PATIENTS WITH VENTRICULAR SEPTAL DEFECT

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A modified thermodilution technique was used to determine the quantity of shunt in patients suffering from congenital heart disease with a left to right shunt. In our modification, the thermistor was placed within the pulmonary artery and an indicator was injected into both sides of the heart. In a series of 33 cardiac catheterizations in children (1-17 years) with ventricular septal defect (VSD), pulmonary blood flow (Qp), systemic blood flow (Qs) and the ratio of Qp to Qs (Qp/Qs) were determined by this and ordinary oximetry (Fick) methods. Correlation coefficients between indexes obtained by these methods were 0.54 (Qp), 0.78 (Qs), and 0.75 (Qp/Qs). The estimates of Qp and Qp/Qs obtained by thermodilution were smaller than those obtained by the Fick method. This modification of thermodilution is simple, rapid, and useful in clinical practice.

It is necessary to determine the quantity of shunt in order to decide whether or not surgical treatment is indicated in patients with congenital heart disease. At present, oximetry (Fick method), indicator dilution (dyes, hydrogen, etc.), or radionuclide angiography are available to determine the absolute or relative size of the shunt, but each of these methods has drawbacks that limit their usefulness in obtaining an accurate and valid value. We used a modified thermodilution method to evaluate the shunt in children with ventricular septal defect (VSD).

MATERIALS AND METHOD

Principle

Figure 1 shows the model of the method. Three basic conditions should be for its use: 1.

Key words:
Shunt
Thermodilution
Ventricular septal defect
Cardiac catheterization

There should be no shunt other than interventricular communication. 2. There should be a unidirectional left-to-right shunt, i.e., the blood flows only from left to right through the defect of interventricular septum, and 3. There should be no regurgitation of atrioventricular valves, i.e., no reverse flow from ventricles to atria.

When these conditions are satisfied, pulmonary blood flow (Qp) consists of systemic blood flow (Qs) plus left to right shunt (Qsh); that is

\[ Qp = Qs + Qsh \]  

(1)

The theory of thermodilution states that the blood flow (Vb) at the thermistor (for measuring blood temperature) is

\[ Vb = \frac{\text{Si} \times \text{Ci} \times (Tb - Ti) \times Vl \times CT}{\text{Sb} \times \text{Cb} \times \int_0^\infty (Tb - Tt) dt} \]  

(2)

where, \( \text{Si} \): specific gravity of indicator, \( \text{Ci} \): specific heart of indicator, \( Tb \): temperature of whole body blood (i.e., body temperature), \( Ti \): temperature of indicator, \( Vl \): volume of indicator, \( Sb \): specific gravity of blood, \( Cb \): specific heat of

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Japanese Circulation Journal Vol. 53, October 1989 1205
blood, t: time after injection of indicator, Tb(t): temperature of the blood around the thermistor at the time of t, and CT: correction term for the loss of heat from indicator during injection.\textsuperscript{1,2} The integral within the equation (2) means that of temperature change of time after indicator is injected and corresponds to the area under the temperature-time curve (Figure 2).

If conditions are unchanged during an examination, Si, Sb, Ci, Cb, Ti and Tb are constant and are in all expressed as a single constant K. That is

\[ K = \frac{Si \times Ci \times (Tb - Ti)}{Sb \times Cb}. \]

In addition, the integral is rewritten as I:

\[ I = \int_{0}^{\infty} (Tb - Tb(t))dt. \]

Rearranged in terms of K and I, equation (2) is

\[ Vb = \frac{Vi}{I} \times K \times CT \quad \ldots \ldots \ldots \ldots \quad (3) \]

---

Figure 1. A model of the flow system. A thermistor is placed within the pulmonary artery, and an indicator is injected into the right heart or the left ventricle. The output from the pulmonary artery and the return to the left ventricle is pulmonary flow (Qp). The output from the aorta and the return to the right heart is systemic flow (Qs). Since the shunt is unidirectional, left to right shunt (Qsh) is subtracted from Qp. Qsh then added to Qs makes Qp. The formula (1) [Qp = Qs + Qsh] is thus obtained.

Figure 2. Diagrams (left) and actual recordings (right) of the temperature-time curve after indicator is injected into the left ventricle (upper) and into the right heart (lower). We name the integral of temperature depression IL and IR respectively. The recorded curve temporarily fell to the baseline in the midst of the downward slope. At this moment, depression of temperature corresponds to 30% of its peak amplitude, and the computer terminates integration. The integral is compensated for the remaining portion and is used for further computation.\textsuperscript{3}

\textit{Japanese Circulation Journal} Vol. 33, October 1989
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(Abbreviations) VSD = ventricular septal defect; PH = pulmonary hypertension; PS = pulmonary stenosis; DORV = double-outlet right ventricle; sup = supracristal type; postop = postoperative state

When a certain volume (V) of indicator is injected into the right side of the heart and if the integral of temperature change of time after that is IR, pulmonary blood flow (Qp) is calculated using the equation (3).

\[
Q_p = \frac{V}{IR} \times K \times CTR \quad \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots (4)
\]

where CTR is the correction term for the right heart catheter. On the other hand, if the same volume of indicator is injected into the left ventricle in the presence of an interventricular left to right shunt, a fraction of indicator

\[
\frac{Q_{sh}}{Q_p} \times V
\]

flows into the right heart. In this situation, if the integral of temperature change of time is IL, pulmonary blood flow (Qp) expressed using formula (3) is

\[
Q_p = \frac{V}{IL} \times \frac{Q_{sh}}{Q_p} \times K \times CTL \quad \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots \ldots (5)
\]

*Japanese Circulation Journal Vol. 53, October 1989*
where CTL is the correction term for left heart catheter. Since the right sides of equations (4) and (5) are equal (to \( Q_p \)),

\[
\frac{V}{IR} \times K \times CTR = \frac{V}{IL} \times \frac{Qsh}{Q_p} \times K \times CTL.
\]

\( V \) and \( K \) are cancelled as common terms. Consequently,

\[
\frac{Qsh}{Q_p} = \frac{IL}{IR} \times \frac{CTR}{CTL} \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots (6)
\]

The left side of equation (6) is the ratio of the shunt to pulmonary blood flow. Equation (6) implies that \( \frac{Qsh}{Q_p} \) is expressed as the ratio of the integral of temperature multiplied by \( CT \) after the indicator is injected into the left ventricle to that after the indicator is injected into the right heart. As has been already stated, the integral of temperature change of time is obtained by measuring the area under the temperature-time curve, i.e., by planimetry (Fig. 2).

It is possible to avoid planimetry, a time-consuming and tedious technique. A thermodilution computer can automatically process the data; i.e., receive the temperature as an electrical signal, perform integration, substitute actual values for the variables of formula (2), and display the result as blood flow in liters per minute. We have only to feed the computer a coefficient derived from \( V, T, C, T \) etc. After a certain volume (\( V \)) of indicator is injected into the right heart, the computer display reads

\[
DR = \frac{V}{IR} \times K \times CTR \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots (7)
\]

where \( DR \) is the reading of the display. \( DR \) is equal to pulmonary flow (\( Q_p \)). That is

\[
DR = Q_p \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots \cdots (8)
\]

Just afterwards, if the same volume of indicator is injected into the left heart, the computer display (\( DL \)) will read

\[
DL = \frac{V}{IL} \times K \times CTR \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots (9)
\]

Note that the correction term of equation (9) is not CTL but CTR, since it is set for the right heart catheter. Equation (7) divided by equation (9) yields

\[
\frac{DR}{DL} = \frac{\frac{V}{IR} \times K \times CTR}{\frac{V}{IL} \times K \times CTR} = \frac{IL}{IR} \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots (10)
\]

Because the ratio \( CTR/CTL \) is a constant almost equal to 1 (See below), the right side of equation (10) is almost equal to that of equation (6). Hence,

\[
\frac{Qsh}{Q_p} \approx \frac{DR}{DL} \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots (11)
\]

As \( Q_p \) and \( Qsh/Q_p \) are obtained using formulas (4), (6), (8) and (11), systemic blood flow (\( Q_s \)) and the ratio of pulmonary flow to systemic flow (\( Q_p/Q_s \)) are also obtained with the following formulas based on equation (1):

\[
Q_s = Q_p - Qsh = Q_p \times \left(1 - \frac{Qsh}{Q_p}\right) \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots (12)
\]

\[
\frac{Qp/Qs}{Q_p} = \frac{Q_p}{Q_p \times \left(1 - \frac{Qsh}{Q_p}\right)} = \frac{1}{1 - \frac{Qsh}{Q_p}} \quad \cdots \cdots \cdots \cdots \cdots \cdots \cdots (13)
\]

**Patients**

Thirty-two children with congenital heart defects including ventricular septal defect underwent 33 cardiac catheterizations. Age, sex and diagnoses are listed in Table I. Age at the time of catheterization ranged from one year and seven months to 19 years. Seventeen were boys and 15 were girls. Every patient had a ventricular septal defect. The majority were examined before cardiac surgery but others were examined to confirm that surgical correction was unnecessary. One of the patients underwent examination twice, immediately before and approximately three years after surgery (Nos. 7 and 22), reflecting the efficacy of treatment at the latter examination. Another patient was examined because she continued to suffer from congestive heart failure three months after correction of a double-outlet right ventricle with subaortic ventricular septal defect (No. 27). In both cases a residual defect of the ventricular septum was suspected.

In no patient included in the study, did angiocardiography and oximetry during cardiac catheterization reveal a shunt except interventricular communication. There was also no significant regurgitation of atrioventricular valves and no right-to-left (or bidirectional) shunt through the defect. Four of the patients (Nos. 5, 6, 16 and 33) had mild pulmonary stenosis with a small pressure gradient between the right ventricle and the pulmonary artery, but this complication appeared to have little or no influence on the patient’s cardiovascular function.
Determination of Shunt by Thermodilution

TABLE II ANOVA TABLE (DR)
(Number of patients = 33; repetition = 3 times each patient)

<table>
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<th>Source of Variation</th>
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<th>MS</th>
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<td>4.44</td>
<td>1.07</td>
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</table>

\[ MS \text{ patients} / MS \text{ repetition} = 83.94 \; (p < 0.01) \]

Estimated Variance Component = 1.86

(Abbreviations) df = degrees of freedom; SS = sum of squares; MS = mean squares; %v = percent variation

TABLE III ANOVA TABLE (DL)
(Number of patients = 33; repetition = 3 times each patient)

<table>
<thead>
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<th>Source of Variation</th>
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\[ MS \text{ patients} / MS \text{ repetition} = 95.07 \; (p < 0.01) \]

Estimated Variance Component = 107.95

(Abbreviations) See TABLE II.

Since this study was undertaken as one of the diagnostic procedures performed during cardiac catheterization, informed consent for the study was obtained from guardians of the patients, together with consent to carry out cardiac catheterization itself. Consent was also obtained from the patients if possible.

Procedures
Cardiac catheterization was performed in each patient according to a routine program. After measurement of intracardiac pressure and collection of blood samples for oximetry, a Swan-Ganz type catheter for thermodilution Edwards 93-32-5F) was introduced intravenously into the pulmonary artery. The thermistor at the tip of the catheter was placed within the main pulmonary artery or one of its major branches, and the injection orifice approximately 15 centimeters behind the thermistor was positioned within the right ventricle or the right atrium. Next, a left ventricular catheter was introduced through the artery and was used to inject two types of fluid into the left ventricle; a contrast medium for left ventriculography and an indicator for thermodilution. The Swan-Ganz type catheter was connected to a thermodilution computer (Edwards 9420A) and the temperature-time curve was recorded on a polygraph (Electronics for Medicine VR-12).

As an indicator, 5 ml of dextrose solution at 0°C was injected into the right heart through the venous catheter. The computer display then showed the DR of formula (7). Thereafter, the same volume of indicator was injected into the left ventricle through the arterial catheter. This time, the computer display showed the DL of formula (9).

The correction terms, CTR and CTL, which correct heat loss from indicator, are functions of length and volume of a catheter and of the speed of injection. They are, however, obtained empirically. In our settings, CTR was 0.833 and CTL was in the range from 0.726 to 0.818. Since these values are similar, we regarded them as equal.

\[ CTL \equiv CTR = 0.833 \]

and, therefore,

\[ \frac{CTR}{CTL} \equiv 1. \]

While the procedures were performed, the temperature-time curve was monitored. If the shape of the curve was irregular or interrupted, measurement and computation were considered to be inadequate and the data abandoned. The indicator was injected at least three times into each side of the heart. Three adequate results
were adopted, and the mean value was reserved for further computation.

Analysis of data

Body surface area was calculated from body height and weight using the formula of Dubois and Dubois. Oxygen consumption was estimated according to sex, age, heart rate, and body surface area by the formula of LaFarge and Miettinen. The oxygen content of blood samples was calculated from hemoglobin concentration and oxygen saturation measured by a photometer (Radiometer OSM2). Cardiac output (Qs), pulmonary blood flow (Qp) and the ratio of pulmonary flow to systemic flow (Qp/Qs) were calculated by the Fick method from oxygen content of blood samples and estimated oxygen consumption. Since oxygen saturation of arterial blood exceeded 95% in every patient studied, right to left shunt, i.e., arterial desaturation was thought to be absent or, if present, to be negligible.

Supplementing readings of the thermodilution computer (DR and DL) into formulas (11), (12) and (13), we obtained Qp, Qs and Qp/Qs. The area under the temperature-time curve could be measured by a digitizer system (Tektronix 4956 graph tablet and 4051 graph analyzer with our own programming), so that Qp and Qs could also be obtained by formulas (4), (6), (12) and (13). The accuracy of computation of the thermodilution computer was thus warranted.

In order to evaluate the reproducibility, single classification analysis of variance (ANOVA) was used, and correlations of the data from different procedures were tested using the correlation coefficient test.

RESULTS

Tables II and III are ANOVA (model 2) tables showing the source of variation of DR and DL which are measured 99 times (three times in 33 patients totally). In each of DR and DL, the fraction of variation within patients (= percent variation of repetition) is quite small in comparison with that among patients (= percent variation of patients). Since variance of DR and DL mainly stems from patient-to-patient difference, we think the procedure is satisfactorily reproducible.

Pulmonary blood flow (Qp) determined by thermodilution is plotted against Qp determined by the Fick method in Fig. 3, and systemic blood flow or cardiac output (Qs) is plotted in the same manner in Fig. 4. There appears to be a proportional relation, but correlation is less good.

Figure 5 shows the relation of the ratio (Qp/Qs) determined by these two methods. Though in some cases Qp/Qs widely deviated from predicted values, a positive correlation was observed. In one case, Qp/Qs determined by Fick method was twice the value obtained by thermodilution. In another three cases, Qp/Qs determined by the Fick method was much lower than that determined by thermodilution. In these cases, exa-
Thermo Qp/Qs

![Graph showing Thermo Qp/Qs relationship](image)

Fig. 5. The ratio of pulmonary flow to systemic flow (Qp/Qs) determined by thermodilution is plotted against Qp/Qs determined by the Fick method. The plot marked by an asterisk is a duplicated one.

minations may not have been properly conducted. Thermodilution produces Qp/Qs values that are much lower than those provided by the Fick method, and accordingly, the identity of Qp/Qs is not so good as its correlation.

Equation (13) substituted by formula (11) yields

\[
\frac{Qp}{Qs} = \frac{1}{1 - \frac{DR}{DL}} 
\]

(14)

In our patients, Dr (= Qp) was within the range of approximately two to nine liters per minute. On the other hand, the reading of the thermodilution computer after left ventricular injection (DL) was in the range of four to approximately 50 liters per minute. Equation (14) implies that the larger DL, the smaller will be Qp/Qs where the range of DL is much broader than that of DR.

Figure 6 shows the relation of Qp/Qs determined by the Fick method (ordinate) against DL (abscissa). There appears to be an inverse proportion. In addition, in no patient whose DL is larger than 15 L/min, does the Qp/Qs determined by Fick method exceed 1.5. It is widely accepted that in most patients with an uncomplicated ventricular septal defect whose Qp/Qs is less than 1.5, surgical correction is not required. It may therefore be said that, based solely on the quantity of shunt, closure of the defect was not required in our patients whose DL is more than 15 L/min. DL may be used in addition to Qp/Qs, which is a useful index of the severity of disease.

**DISCUSSION**

*Methods to determine shunt*

Several methods are available to determine shunt; the Fick method (oximetry), indicator dilution methods (dye dilution, hydrogen dilution, thermodilution, etc.), radionuclide angiography, etc. Nevertheless, it is well-known that none of these methods is free of faults or limitations in clinical practice. Problems associated with the Fick method include the lack of assurance that the mixing of oxygen (especially red blood cells) within the cardiac chambers is sufficient, and the considerable amount of time required to collect blood samples and to measure oxygen content. It is usually difficult to measure oxygen consumption. Dye dilution not only requires cumbersome settings and calibration but also cannot be performed repeatedly. As for hydrogen dilution, it is difficult to make the patient inhale the gas. Radionuclide angiography requires a costly and large-scale device, and the effects of irradiation, even though small in amount, should not be overlooked. In short, an ideal method for determining shunt has yet to be
found. Therefore, the search for an alternative method should be continued.

**Determination of shunt by thermodilution**

Thermodilution is useful in the measurement of blood flow in children. In the past, the method had been used only in cases without a shunt. Recently, it has been shown to be useful also in the presence of a shunt, and determination of the shunt itself has also been found possible.

There are two different approaches to the determination of shunt by thermodilution. The first is to analyze the waveform of the temperature-time curve after a single injection, and the second is to inject or detect at more than two different sites. In the former, additional depression of temperature due to recirculation of the shunting indicator is detected and the size of the shunt is estimated from either height of the "second peak" or from the area under the curve after reappearance of the indicator. For the sake of convenience, this type of analysis is called the "recirculation method". The recirculation method is a standard technique in indicator dilution (especially dye dilution) or radionuclide angiography. A significant difficulty with analysis of data from the recirculation method is that it often requires tedious calculations involving a large quantity of numerical data. However, the method has become more practical with the advent of the digital computer. Among studies on thermodilution with the recirculation method, a system for radionuclide angiocardiography was actually used.

Another approach to the shunt is similar to that used in this study and is referred to as the "separate injection method" or "separate detection method". In our study, right atrium or right ventricle and left ventricle were the sites of injection. The idea of injecting indicator into two portions was originally adopted as a modification of dye dilution and it was later applied to thermodilution. Studies have been carried out on double injection sites and double thermistors (thermodilution performed in the right and left heart independently) with a single injection site and double thermistors or with double injection sites and a single thermistor. The main drawback of the separate injection (or detection) method is its technical complexity in clinical practice. We designed a modification which makes the method easier to be performed during cardiac catheterization.

**Conditions and limitations**

Three conditions should be met: absence of regurgitation of atrioventricular valves, presence of a unidirectional left to right shunt and absence of any shunt other than an interventricular communication. These conditions are mandatory when indicator dilution is used (no matter which indicator or what type of modification used). Therefore, the usefulness of indicator dilution methods would be severely limited if few patients satisfied these conditions. Fortunately, in children with ventricular septal defect, pulmonary blood pressure rarely exceeds systemic pressure, and a majority of these children satisfy such conditions. It should be stressed, however, that unless it is clear that the conditions are met, the accuracy of this method is in doubt and should be confirmed by other methods (e.g., angiography, oximetry, etc.).

The results obtained by thermodilution were compared with those obtained using the Fick method, now widely accepted as the best reference (though not entirely accurate). In our study, correlation of Qp was poor, and values Qp and Qp/Qs determined by thermodilution were considerably lower than those obtained by the Fick method. We should point out three potential causes of these discrepancies; recirculation of the indicator, conduction of heat across the septal wall, and incomplete mixing of the indicator.

Recirculation of the indicator always causes error in dilution methods. Indicator injected into any site of the heart will ultimately flow into the pulmonary artery. It then cools the thermistor again, and excessive cooling of the thermistor leads to increase in the integral of temperature change of time, and to underestimation of Qp (= DR) [Refer to formula (4) and (7)]. The integral of temperature change of time (= IR) appears in the denominator. Following injection into the left ventricle, recirculation of the indicator, together with deprivation of heat across the septal wall, also cools the blood within the pulmonary artery. Then, DL will be smaller [Refer to formula (9)]. The integral (= IL) will be greater.

Mixing of the indicator is a major premise. Though adequate mixing of heat within cardiac chambers is admitted there are disadvantages in our study, which may make the mixing of an indicator insufficient. In the right heart, the indicator mixed with a systemic venous return should again be mixed with the shunting blood.
Incomplete mixing of a systemic return with the shunt is sometimes observed by angiocardiography (though the mode of mixing of a contrast medium is different from that of heat), and it might have been the cause of poor correlation of Qp. As for the left heart, an injection orifice in the left ventricle might have been too close to or too far from the septal defect due to the position of the catheter that the volume of shunting indicator would be accordingly larger or smaller. In consequence, IL (and DL) of formula (9) and, therefore, Qs and Qp/Qs would contain some error.

Correction for heat loss during injection of indicator is another problem.23 As stated above, the correction terms of the catheter (CTR and CTL) were not equal, but were arbitrarily considered as equal in order to facilitate the procedure and calculation. This might have brought about a deviation of the result. (Since CTR was slightly larger than CTL, Qs would be overestimated and Qp/Qs would be underestimated by thermodilution).

Advantages of the method

Finally, we would like to suggest the benefits of our method. The principle and procedures of the method are simple. It requires no more than catheters and a thermodilution computer. These are now readily available in most catheterization laboratories. It takes only a short time to work out the size of the shunt, because one needs only to divide DR by DL to obtain the ratio of left to right shunt to Qp (Qsh/Qp). Furthermore, DL itself may be an index of the quantity of shunt. Since every other method requires more time, this saving of time may be the major advantage of our method.

In order to determine blood flow by thermodilution, some values (ie., Si, Sh, Ci, Cb, Ti, Tb, and CT of the formula (2)) should be known previously.2,12,24 This is one of the drawbacks of thermodilution. The separate injection method, which yields the estimate of Qp/Qs without such constants, is free of this problem, because these values are cancelled during the calculation (refer to equations (6), (9) and (10)). It should be noted, however, that this is only the case in calculating the ratio of Qp/Qs. If one wishes to obtain the absolute value of Qp and/or Qs, they are still necessary.

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