Controlled Cardiac Output Studies in Dogs (Part I)
Simple Method for Estimation of Coronary Return Blood Flow in Dogs and Its Evaluation under Conditions of Controlled Cardiac Output

By Eric C. Elliot, M.D., B.Sc.

During experiments on dogs, the use of right-heart bypass was found to be satisfactory for the study of coronary venous return, as has been noted by others.\(^1\)\(^2\) It has been established that coronary blood flow is related to blood pressure\(^3\)–\(^8\) and is also well correlated with oxygen consumption.\(^2\)\(^7\)–\(^9\)\(^10\) Our experiments confirmed these relationships. It is the purpose in Part I of this report, by utilizing such relationships: (1) to show the derivation of a regression equation for the prediction of coronary return blood flow; and (2) to present an evaluation of the equation and of its intended application.

Methods

A total of 21 dogs were used in the experiments, 13 of which were included for the actual correlations reported herein. These dogs ranged in weight between 13 and 17 Kg., with a mean weight of 14.6 Kg. and an S.D. of 1 Kg. The animals were anesthetized with sodium pentobarbital, 30 mg./Kg. injected intravenously. The animals were placed in a supine position and secured to an operating table with the right chest slightly uppermost. Sterile technique was not employed, all animals being sacrificed at the termination of the procedure. Dogs were heparinized with 2 mg./Kg. of heparin*/Kg. of body weight. Figure 1 illustrates the complete right-heart bypass procedure employed to study the different parameters.

The experiment was conducted so that, over a period of one to one-and-one-half hours, three bleeding. The respirations were maintained during the open-chest phase by pure \(O_2\) with the aid of a mechanical respirator connected to an endotracheal-cuffed tube. The superior and inferior venae cavae were taped and the azygos vein ligated. A large pericardial incision exposed the aortic-root area and the pulmonary outflow tract.

A 22 or 24 F. catheter, slightly beveled at the tip, with no side holes, was introduced into the pulmonary artery through a stab wound in the pulmonary outflow tract of the right ventricle and secured with a previously placed purse-string suture. After dissection between the anterolateral angle formed by the ascending aorta and the pulmonary artery, a blunt-nosed Mixter forceps was passed around the posterior portion of the pulmonary artery from left to right and a heavy silk suture pulled through. In addition, a 16 F. catheter, with one side hole near the tip, was introduced into the cavity of the right ventricle through a stab incision in its anterior wall and secured with a purse-string suture.

The superior and inferior venae cavae were cannulated by means of a plastic thimble through which two 20 F. catheters (3 to 4 inches in length) were introduced into two holes in the bottom of the thimble. By this means, it was possible to cannulate the cavae, with just one incision in the right atrial appendage.

Method of Bypass and Measurements

As the tapes about the cavae were tightened, the clamps on the caval and pulmonary blood conduit lines were removed and the Sigmamotor pump turned on. In a few moments, the suture around the pulmonary artery was tightened, while simultaneously removing the clamp on the 16 F. catheter to vent the right ventricle. The coronary venous return thus entered the small reservoir, as illustrated in figure 1.

The pump initially was set approximately at the rate of 1 L./min. and the reservoir primed with 300 to 500 ml. of fresh heparinized blood, or at the rate of 700 to 800 ml./min. and the reservoir primed with 150 to 200 ml. of normal saline. All the conduits had been previously filled with normal saline.

The experiment was conducted so that, over a period of one to one-and-one-half hours, three
Table 1

<table>
<thead>
<tr>
<th>Equation no.</th>
<th>Y = a + bx</th>
<th>Number of dogs or experiments</th>
<th>x</th>
<th>y</th>
<th>Sey</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ECR = 8.6381 + 0.06806 CO</td>
<td>174 10</td>
<td>545.0</td>
<td>45.8</td>
<td>10.1</td>
<td>0.86</td>
</tr>
<tr>
<td>2</td>
<td>ECR = 10.45 + 0.468 MABP</td>
<td>167 10</td>
<td>76.5</td>
<td>46.2</td>
<td>10.1</td>
<td>0.87</td>
</tr>
<tr>
<td>3</td>
<td>ECR = 0.6614 + 6.59 qO₂</td>
<td>27 7</td>
<td>5.9</td>
<td>39.1</td>
<td>3.97</td>
<td>0.96</td>
</tr>
<tr>
<td>4</td>
<td>ECR = 4.8354 + 41.055 (MABP X HR)</td>
<td>115 7</td>
<td>0.87</td>
<td>40.7</td>
<td>6.5</td>
<td>0.90</td>
</tr>
<tr>
<td>5</td>
<td>qO₂ = 1.5714 + 0.2163 (MABP X HR)</td>
<td>27 7</td>
<td>0.83</td>
<td>5.91</td>
<td>1.23</td>
<td>0.80</td>
</tr>
<tr>
<td>6</td>
<td>MCR × 100 = 11.7942 -0.0043 CaR</td>
<td>174 10</td>
<td>500.4</td>
<td>9.54</td>
<td>2.42</td>
<td>0.40</td>
</tr>
<tr>
<td>7</td>
<td>qO₂ = 3.2253 + 0.046 MABP</td>
<td>27 7</td>
<td>57.8</td>
<td>5.91</td>
<td>1.85</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*Statistics and regression analysis were performed by standard mathematical procedures.\(^\text{18}\)

List of abbreviations used in tables 1 and 2 as follows:

ECR = Estimated coronary return in ml./min.

CO = Cardiac output in ml./min.; in Part I of this report it is always considered equivalent to the rate of the Sigmanotor pump, pumping blood into the pulmonary artery.

MABP = Mean femoral arterial blood pressure in mm. Hg.

HR = Heart rate in beats/min.

qO₂ = Myocardial oxygen consumption in ml./min.

MCR = Measured coronary return in ml./min. from catheter in right ventricle.

CaR = Caval return in ml./min., which was calculated by subtracting the value for the measured coronary return in ml./min. from the cardiac output in ml./min.

N = Number of observations.

X = Mean value.

Y = Mean value.

Sey = Standard error of estimate.

r = Coefficient of correlation.

S.D. = Standard deviation.

to four different pump rates or levels of cardiac output were studied, as follows: Starting at the upper flow rate, a period of 10 to 20 minutes was allowed for stabilization, and then simultaneous measurements of coronary return flow, mean arterial blood pressure, and heart rate were made. The procedure was repeated at successively lower pump flow rates. The different gauge settings on the Sigmanotor pump were noted, so that it could be calibrated immediately postperfusion (with the reservoir and the open end of the pulmonary artery catheter at the same level above the reservoir as during the perfusion). The individual coronary return flow measurements were carried out by letting the flow of blood from the 16 F. catheter pass into a graduated cylinder for a period of 30 seconds and recording simultaneously the elecrocardiogram and the mean femoral arterial blood pressure on a Gibson Medical Electronics Miniploygraph, utilizing a Statham transducer. Approximately six separate coronary flow estimations were made at each of the three to four levels of cardiac output studied.

Oxygen content of the arterial blood and coronary venous blood was determined by the Van Slyke apparatus and procedure. The myocardial oxygen consumption was calculated by the formula (A-V) O₂ content difference times coronary return flow in ml./min. divided by 100 and expressed as qO₂ ml./min.

Results and Discussion

This work is based upon the assumption that if blood were pumped into the taped
pulmonary artery (fig. 1), thus preventing regurgitation into the right ventricle, equivalent amounts of blood would be ejected into the arterial system by the left ventricle; this is a reasonable assumption. Seely et al.\textsuperscript{11,12} described a complete right-heart bypass procedure in which they considered that the controlled rate of blood flow through the pulmonary artery was equivalent to the cardiac output; they found good correlation between calculated cardiac output, utilizing the Fick principle and the measured cardiac output equivalent to the pulmonary artery controlled flow.

A summary of the regression analysis is presented in table 1. These results indicate good correlation between cardiac output and coronary return flow (see equation 1, table 1); however, it has been pointed out by Braunwald et al.\textsuperscript{7} and Allela et al.\textsuperscript{9} that cardiac output per se is not a direct determinant of coronary flow. For instance, if the blood pressure is held constant and the cardiac output increased, there occurs not nearly as large an increase in the coronary flow as if the cardiac output were held constant and the blood pressure were increased. Cardiac output probably exerts its effect secondarily through the blood pressure.

In these experiments, there was good correlation between the coronary return blood flow and the mean arterial blood pressure (see equation 2, table 1). But the best correlation existed between coronary flow and the oxygen consumption (see fig. 2; equation 3, table 1). It is now well established that oxygen consumption is one of the factors with which coronary blood flow is best correlated.\textsuperscript{2,7,8,10} However, in the manner in which it has been proposed to carry out the "controlled caval return" studies, it is technically not feasible to attempt arteriovenous sampling to obtain values for $q_{O_2}$. One would also have to rely upon the coronary sinus blood for the venous content of oxygen, which is not necessarily representative of coronary circulation.

Sarnoff et al.\textsuperscript{13} reported that there was correlation between the tension-time index and oxygen consumption. Gerola et al.\textsuperscript{14} and Katz and Feinberg.\textsuperscript{15} noting this relationship, reported that the product of mean arterial blood pressure times heart rate was also correlated with the oxygen consumption. Accordingly, since there exists excellent correlation between the coronary blood flow and oxygen consumption, it was reasonable to assume a correlation between the coronary blood flow and product of blood pressure times heart rate. This was found to be the case, and the results are graphically illustrated in figure 3. In fact, this plot was better than the correlation of oxygen consumption versus the product of mean arterial blood pressure times heart rate (see equations 4 and 5, table 1), and much better than the plot of oxygen consumption versus mean arterial blood pressure (see equation 7, table 1).

Since both the mean arterial blood pressure and the heart rate are readily obtainable in the "control caval return preparation," an
Table 2

Summary of Data for the Six Experiments Used to Evaluate Equation 4, Table 1, and Data Comparing CaR and the Sum of CaR + ECR, as Indices of Cardiac Output

<table>
<thead>
<tr>
<th>X</th>
<th>MCR</th>
<th>ECR</th>
<th>ECR—MCR</th>
<th>CaR × 100</th>
<th>CaR + ECR × 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>77</td>
<td>77</td>
<td>77</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>Mean</td>
<td>33.4</td>
<td>42.5</td>
<td>+9.0</td>
<td>+30.4</td>
<td>-6.0</td>
</tr>
<tr>
<td>Range</td>
<td>22-(+70)</td>
<td>22-(+56)</td>
<td>+21-(−14)</td>
<td>+72−(−27)</td>
<td>−3.1−(−9.9)</td>
</tr>
<tr>
<td>S.D.</td>
<td>7.6</td>
<td>8.1</td>
<td>8.0</td>
<td>27.0</td>
<td>1.7</td>
</tr>
</tbody>
</table>

*Abbreviations in the above table are explained in the footnote of table 1.

Experiments were carried out, utilizing the "complete right-heart bypass preparation" to determine the error between estimated coronary return and measured coronary return and thereby ascertain its usefulness in the "control caval return preparation." This is reported below:

Evaluation of the Regression Equation for Coronary Return Equal to the Product of Mean Arterial Pressure × Heart Rate and an Evaluation of Its Intended Application in the "Control Caval Return Preparation"

In the "control caval return preparation," described in Part II, cardiac output is not completely controlled, owing to the fact that there is no way of including the coronary venous return with the caval return as the coronary blood returns intracardially. However, this problem has been circumvented, to a degree, by applying the regression equation described above for coronary return equal to the product of mean arterial blood pressure times heart rate. The purpose is to evaluate this equation and also to show that the resultant sum of estimated coronary return, plus known caval return blood flow, gives a better index of cardiac output than if caval return blood flow is used solely.

Methods

The above-mentioned evaluation was studied in six dogs, ranging in weight between 12.5 and 16 Kg., with a mean weight of 14.4 Kg. The cardiac output of each dog was held constant for a period of two hours by means of the complete right-heart bypass procedure. The only difference between the preparation used in this experiment and that illustrated in figure 1 was the method used for caval blood flow drainage. In the experiment described below, it was found easier to performed caval drainage by placing a catheter in the left external jugular vein to the level of the superior vena cava and a tapered catheter in the femoral vein to the level of the bifurcation of the inferior vena cava. Thus, upon occlusion of the cavae, blood flowed in a retrograde manner into the large venous reservoir.

A different value for the cardiac output was used in each of the six dogs. Several direct measurements of the coronary return blood flow in ml./min. were made during the two-hour perfusion, approximately 10 minutes apart, for purposes of comparison with the predicted or estimated values for coronary return. At each of these particular coronary return measurements, the mean femoral arterial blood pressure and the heart rate were recorded on the Gilson recorder. The value for the caval return was calculated by subtracting the actual measured value for the coronary return in ml./min. from the cardiac output in ml./min., which was considered equivalent to the rate at which the Sigmanator pump was pumping blood into the taped pulmonary artery. The estimated coronary return was then calculated by means of equation 4, recorded in table 1.

Results

The results are summarized in table 2 and figure 4. The latter shows graphically the difference between the values for actual coronary return flows and the estimated coronary return flows during the two-hour period of "controlled cardiac output." It was observed that if the caval return only was used as an index of cardiac output, there resulted an average error of 6 per cent in the true cardiac output, with a standard deviation of 1.7 per cent. However, if the estimated coronary flow...
Illustrates the relationship between coronary return and oxygen consumption of the myocardium. The coronary return measurements and the oxygen consumptions were obtained during three to four series of "steady states" of constant cardiac outputs per experiment, passing successively from high to low cardiac outputs (see text).

were added to the caval flow and this value used as an index of cardiac output, there resulted in the six dogs an average error of only 1.4 per cent in the cardiac output with a standard deviation of 1.5 per cent; this represented a reduction of 60 to 70 per cent in the error.

Discussion

If other methods, which have been described for the determination of coronary flow, were used in this experiment, certain difficulties would arise. For instance, in the "control caval return preparation," if the method of Kety and Schmidt\textsuperscript{10} were used, the coronary return would have to be expressed in terms of so many milliliters of coronary return per gram weight of left ventricle, but this does not give a value for the total coronary return. There is also the technical infeasibility of multiple blood sampling, as mentioned earlier.

Allela et al.\textsuperscript{9} have described a multiple regression equation for the prediction of coronary flow, but the myocardial qO\textsubscript{2} is required for its application.

Comparisons have been made of the pump rate in the "control caval return preparation" with the cardiac output by Huggins et al.\textsuperscript{17} They reported that the cardiac output was on the average 6.7 per cent higher than the pumping rate of the blood into the right atrium; the authors felt that this may have been due to the fact that the coronary venous return was not accounted for in the "control caval return preparation." The coronary return could be predicted by means of the plot of the ratio of coronary return to caval return versus caval return; however, if the equation for this plot (equation 6, table 1) is applied in the above six experiments, a greater error between measured and predicted coronary returns occurs than if equation 4, table 1, is used.

It can be seen from figure 4, that the formula for the coronary return equal to the product of mean arterial blood pressure times heart rate is only semiquantitatively predictive. However, for the purpose of reducing the error in cardiac output in the "control caval return preparation," it would appear to be helpful.

It is noteworthy that the individual variations for each coronary return measurement during the two-hour period were reasonably
Each inset in the above graph refers to one of the six experiments performed to test equation 4, table 1. In each experiment, the cardiac output was held at a constant value for 120 minutes, but in each experiment at a different value, so that the equation would be tested over a range of cardiac outputs. The black dots refer to the measured coronary return (MCR) and each circle directly above each black dot refers to the estimated coronary return (ECR) for that particular MCR. The ECRs were obtained by substitution of the MABP and the HR in equation 4, table 1. See text for discussion.

reflected in the predicted values, as can be seen in figure 4. No explanation was found as to why the predicted or estimated values for coronary return were usually higher than the actual values, unless it was that in the method used to obtain the regression line sufficient length of time did not elapse to reach a steady state before the measurements were made.

Finally, it is pointed out that the use of the regression equation referred to above is only applicable under the experimental conditions which were used to formulate it, namely: (a) that pure oxygen be used as the respiring agent; (b) that the cardiac outputs studied be in the range between 150 and 1,000 ml./min.; and (c) that the dogs undergoing investigation range in weight between 12 and 17 Kg.

One difficulty, to which there was no obvious experimental approach, was the fact that in the "complete right-heart bypass preparation" the right heart was essentially empty, while in the "control caval return preparation" the right heart contained a considerable amount of blood, depending upon the rate of caval return. This variable amount of blood may influence the dynamics in regard to the coronary return.

Also, the chest cavity was open in the "complete right-heart bypass preparation" and closed in the "control caval return preparation." However, it is felt that this would have little consequence on the coronary return, because both the caval return and the method of respiration were essentially the same in both preparations.

Summary

A method has been presented whereby a semiquantitative estimation of the coronary flow in dogs can be made (within certain experimental limits) by means of a regression equation based on the relationship that coronary flow appears to bear to the product of mean arterial blood pressure times heart rate. The data, from which the regression equation was derived, were obtained by means of the utilization of the "complete right-heart bypass preparation" in seven dogs. The equation for the prediction of coronary return was tested in an additional six dogs, using the "complete right-heart bypass preparation" and the results showed that, if the value for the estimated coronary return were added to the value for caval return, the resultant sum would give a significantly better estimate of the cardiac output than if the value for caval flow only were used as the index.

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References


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