Quantitative Description of Ventricular Output Curves in Conscious Dogs

By Vernon S. Bishop, Ph.D., and Hubert L. Stone, Ph.D.

ABSTRACT

Ventricular output curves obtained from normal dogs, chronic cardiac-denervated dogs, and dogs with beta-adrenergic blockade were analyzed in terms of a compartmental mathematical model. The model states that the change in ventricular output per change in mean atrial pressure is proportional to the estimated cardiac output reserve. The solution of the differential equation is an exponential build-up curve which agrees in all cases within the statistical fluctuation of the experimental curves. Using this approach, one can analyze each ventricular output curve in terms of its initial slope, estimated reserve and a proportionality constant. Factors affecting the estimated reserve and proportionality constant would thus affect the slope of the ventricular output curve. By using this model, a quantitation of ventricular function from ventricular output curves can be better approached.

ADDITIONAL KEY WORDS

cardiac output reserve mean atrial pressure ventricular function proportionality constant

The performance of the myocardium in pumping blood can be assessed by measuring the ventricular output or ventricular work as a function of increasing atrial pressures (1-5). Samoff, using this technique, popularized the use of ventricular stroke output and ventricular stroke work curves as the parameters most suitable for assessing the ability of the myocardium to pump blood (3). However, in the intact, conscious dog, we have found the ventricular minute output curve to be the most reproducible index and less easily influenced by systemic arterial pressure (5). The use of these curves to study ventricular function has been reported previously (6).

Although ventricular work curves and ventricular output curves have been used to routinely study the ability of the myocardium to pump blood and the factors influencing the pumping ability, little quantitation has resulted from these curves. Only the shift of the curves along the atrial pressure axis or the plateau values have been considered important (1-3, 6). The quantitation of this response in terms of a mathematical description would possibly provide more usable information as to the function of the myocardium and would aid in the control system analysis of the circulatory system. In most mathematical analyses of the circulation, ventricular output curves have been simulated by either a parabolic fit or by a linear approximation (7, 8).
In these cases little physiological basis was
used for the analyses.

The analysis of the ventricular output
curves presented in this report describes the
ventricular output in terms of the estimated
cardiac output reserve, the rate of change of
the cardiac output with respect to the change
in mean atrial pressure, and a proportionality
constant ($K$).

**Method**

**ANIMAL PREPARATION**

Several weeks prior to experimentation on
dogs, sodium pentobarbital was used to anes-
thesize them and catheters were placed in the
right and left atria and an electromagnetic flow
probe was placed about the root of the aorta or
main pulmonary artery. A third, larger catheter
was placed in the left jugular vein. After the
recovery period, ventricular output curves were
obtained by rapidly infusing the animal with
Tyrode's solution through the large jugular vein
catheter until the ventricular output reached a
plateau ($5$). During the infusion, mean ven-
tricular output and mean right and left atrial
pressures were recorded. A plot of ventricular
output as a function of either mean right or
mean left atrial pressure is a typical way of rep-
resenting ventricular output curves.

**MATHEMATICAL ANALYSIS**

A one-compartment model appears to describe
the average ventricular minute output curves as
function of changes in mean atrial pressure.

The differential equation is

$$\frac{dc}{dp} = K(c - C)$$  \hspace{1cm} (1)

where $C$ (ml/min per kg) is the ventricular
output at any mean right or mean left atrial
pressure and $Cm$ (ml/min per kg) is the plateau
level of the ventricular output, $p$ is the change
in mean right or mean left atrial pressure from rest-
ing and $K$ is a proportionality constant with units
of mm Hg$^{-1}$. Equation 1 states that the change
in ventricular output per change in mean right
or mean left atrial pressure is proportional to the
difference between the plateau level and the
ventricular output at that pressure. Following is
the solution of this equation which satisfies the
conditions when $p = 0, C$ is equal to $Co$ (the
resting ventricular output), and when $p = \infty,
C$ is equal to $Cm$:

$$C = Cm - (Cm - Co)e^{-kp}.$$ \hspace{1cm} (2)

The term $(Cm - Co)$ of equation 2 is an esti-
mate of the cardiac output reserve. Thus the
ventricular output at any pressure is equal to the
plateau level minus the product of the estimated
reserve and the exponential term $e^{-kp}$. As the
change in atrial pressure increases, this product
decreases and thus the ventricular output ($C$)
approaches the plateau level ($Cm$).

Equation 2 can be put in the form:

$$\frac{C - c}{Cm - Co} = e^{-kp}.$$ \hspace{1cm} (3)

If the average data for the ventricular output
curves can be described by the model, a semi-
logarithmic plot of $Cm - c / Cm - Co$ against
change in mean atrial pressure would be linear.
In all circumstances studied this has been found to be the case. $K$ is calculated by solving equation 3 for the special case when the left-hand term is equal to 0.5 and by using the corresponding change in mean atrial pressure "FYM." 

**Results**

Shown in Figure 1 is the average ventricular output plotted against change in mean right and mean left atrial pressures. The experimentally obtained data (represented by the dots) are the average of 21 ventricular output curves obtained from 7 conscious dogs. The mathematically derived curve is the solid line. The mathematically derived curve agrees within the standard error of the mean of the experimentally derived curve. The $K$ value for the right ventricular output is .21 mm Hg$^{-1}$ and the $K$ value for the left is .173 mm Hg$^{-1}$.

The average ventricular output curves obtained from 4 chronically cardiac-denervated animals are shown in Figure 2 (10). The experimental points (which are an average of 12 determinations) are again represented by the dot and the mathematically derived curve by the solid curve. The $K$ value for the right ventricular output is .182 and for the left is .128. Both of these values are much less than the control group.

Illustrated in Figure 3 are the average experimentally determined ventricular function curves of a group of 6 animals before and after beta-adrenergic blockade. The beta-adrenergic blockade was accomplished by...
TABLE 1

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mean right atrial pressure</th>
<th>Mean left atrial pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average normal ventricular output curve</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>43.3</td>
<td>31.6</td>
</tr>
<tr>
<td>Average ventricular output curve obtained from</td>
<td></td>
<td></td>
</tr>
<tr>
<td>denervated dogs</td>
<td>15.8</td>
<td>7.7</td>
</tr>
<tr>
<td>Average curve obtained from beta-adrenergic blockade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>36.4</td>
<td>23.1</td>
</tr>
<tr>
<td>Propranolol</td>
<td>17.8</td>
<td>12.2</td>
</tr>
</tbody>
</table>

\[ \frac{dc}{dp} = K(Cm - Co) \]

The effects of the previously discussed experimental conditions on the initial slopes \((dc/dp_u)\) with respect to changes in mean right and mean left atrial pressures are shown in Table 1. The initial slope \((dc/dp_u)\) is equal to the product of \(K(\text{mm Hg}^{-1})\) and the estimated ventricular reserve \((Cm - Co)\). A decrease in \(K\) value or in the estimated reserve, or both, could cause a reduction in the initial slope.

**Discussion**

A mathematical model describing the ventricular output curves obtained from normal, cardiac-denervated, and beta-adrenergic blocked animals has been presented. In all cases, the mathematical analyses resulted in curves which agreed within the standard error of the mean of the experimentally derived points.

The analysis is a one-compartment model whose solution results in an exponential build-up curve. Thus the differential equation states that the change in cardiac output per change in mean atrial pressure is proportional to the estimated cardiac output reserve. This is a first-order system and may appear as an oversimplification of the response of the heart to elevated venous pressure. However, the complete solution of the problem is not solved by a simple first-order differential equation, for we are describing only the course of the ventricular output curves in terms of the estimated cardiac output reserve. The mathematical functions for \(Cm\) and \(Co\) are not considered in this formulation.

Equation 1 does in fact enforce the value of the ventricular output curves. Cardiovascular physiologists have used the ventricular function curve to depict the ability of the heart to pump blood, and have expected the cardiac output to increase as a result of an increase in filling pressure. The equation simply states that the output does increase proportionally to the estimated reserve. Factors reducing this reserve will thus decrease the ventricular output curves.

In analyzing the physiological meaning of this differential equation, one should be aware of the initial slope \((dc/dp_u)\) which yields information as to the dynamic state of the heart, and which is proportional to the
estimated cardiac output reserve which may decrease as the myocardium becomes depressed. The greater the slope \( \frac{dc}{dp} \), the steeper the ventricular output curve will be, indicating that the ventricle is better able to pump blood. The slope can change for a given reserve depending on \( K \) value. The proportionality constant \( K \) can be analyzed in terms of \( \frac{dc}{dp} \) and \( (Cm - Co) \). \( K \) is equal to \( \frac{dc}{dp} \) divided by \( (Cm-Co) \). Important in this analysis is the absolute change in mean atrial pressures and not the actual atrial pressure. This eliminates the small fluctuations in resting mean atrial pressure which often occur in normal and abnormal animals.

The proportionality constant \( K \) was found to be less for the left ventricular output curve than for the right ventricular output curve. This means that change in output per change in mean left atrial pressure is less. Thus the response of the left ventricle to increases in mean left atrial pressure is less than the right ventricle for corresponding increases in mean right atrial pressure. This is also evident from the initial slopes \( \frac{dc}{dp_0} \). The initial slopes of the left ventricular output curves are less than those of the right ventricular output curves (Table 1). This may be related to the compliance of the systemic venous circulation as compared with the pulmonary venous system. If the compliance is less in the pulmonary venous system (pulmonary veins and left atrium) than in the systemic venous system, the mean left atrial pressure would increase more than the mean right atrial pressure following equal increases in volumes in both circuits. The compliance of the pulmonary venous system is, in fact, smaller than that of the systemic venous system (4).

In comparing the acutely cardiac-denervated and beta-adrenergic blocked animals, we see that the \( K \) values for the right and left ventricular output curves obey the same relationship to each other as was described for the normal. The \( K \) values are less following either chronic cardiac denervation or beta-adrenergic blockade. From Table 1 we can also note that the initial slopes \( \frac{dc}{dp_0} \) are less in both of these cases, since both \( K \) value and the estimated cardiac output reserve \( (Cm - Co) \) are depressed. Many factors may influence the estimated reserve, such as nervous innervation and the physiological state of the myocardium, as shown in this study and by others previously (6, 10). Just how the many other physiological conditions affect the proportionality constant \( K \) and the estimated cardiac output reserve \( (Cm - Co) \) has not been defined. By using this mathematical approach, better quantitation of the ventricular function curves may be obtained and factors affecting these curves may be defined.

References
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