Estimation of Stroke Volume in the Dog by a Pulse Contour Method

By Nicholas T. Kouchoukos, M.D., Louis C. Shepard, B.S., and Donald A. McDonald, D.M., D.Sc.

ABSTRACT

A method for estimating the stroke volume (SV) from the systolic area of a single-channel record of the central aortic pressure has been tested in 12 anesthetized open-chest dogs. The formula used was \( SV = K \cdot P_{sa} - (1 + T_s/T_d) \), where \( P_{sa} \) is the area under the systolic part of the curve above end-diastolic pressure, \( T_s \) and \( T_d \) are the durations of systole and diastole, respectively, and \( K \) is an arbitrary constant derived from measurement of an initial SV by electromagnetic flowmeter in each dog and used thereafter without change, in that dog. In the 12 dogs, 541 simultaneous determinations of SV by the pressure contour and electromagnetic flowmeter methods were compared under normal and altered circulatory conditions employing 12 different interventions. The total range of SV was 2.4 to 28.1 ml, of heart rate 35 to 207/min, and of mean arterial pressure 24 to 166 mm Hg. The overall correlation coefficient \( r \) was 0.928 with a regression line \( y = 1.04x + 0.21 \) ml (SE) of estimate, ±17.4%. Except for three sympathomimetic drugs, the \( r \) values for all other interventions ranged from 0.93 to 0.99. These observations compare favorably with those of previously reported pulse contour methods. The windkessel origin of the formula is noted, and a new derivation from a modification of the "water-hammer" equation is given.

ADDITIONAL KEY WORDS: wave-equation derivation of "contour method" catecholamine effects on pulse wave-velocity windkessel theory Otto Frank waterhammer equation time-derivative of aortic pressure statistical analysis of derived flow measurement

It has been said that "the discovery of a technically simple and non-traumatic way of estimating the output of the heart per beat is something of an El Dorado" (1). Ignoring the mythological implications of this remark, we have been exploring the validity, accuracy and feasibility of various methods that have been proposed and used to make this estimation. The method described in this paper is the simplest of the ones tested in any detail. It requires only one central pressure recording and in essence derives the summed systolic outflow in each beat from the area under the systolic portion of the aortic pressure curve.

The hemodynamic assumptions that this implies are explored in the Discussion. From these, conclusions are drawn as to how this method might be improved, although, as some of the major assumptions are not susceptible to estimation from a single pressure recording, such hope of improvement must be regarded as optimistic. Nevertheless, the results have correlated far better with the flow recorded with an electromagnetic flowmeter than expected.

The main purposes of this paper are the study of the reliability of the method under controlled variations of cardiac and peripheral vascular conditions in the dog and a discussion of its rationale. Comparable studies in humans have been reported elsewhere (2). As the formula used is recognizable as one of the large family of related formulas of the windkessel family, it was taken as being, by nature, essentially empirical. Therefore, the
The traditional order of presentation is somewhat inverted, and Methods and Results are presented first, and a derivation in the light of currently accepted hemodynamic concepts is given in the Discussion in an attempt to see why the method succeeds as well as it does. This derivation was done, since it was made some time before becoming aware of Frank's treatment in 1930 (3). It, in fact, goes further than his analysis in that paper because he was assuming that the volume elasticity of the aorta was known.

**Methods**

Twelve adult mongrel dogs weighing 15 to 26 kg were anesthetized with sodium pentobarbital, 30 mg/kg iv. A cuffed endotracheal tube was inserted in each animal and connected to a Harvard respirator. The ascending aorta was exposed through a median sternotomy and an appropriately sized Statham Q series electromagnetic flow transducer was placed around the ascending aorta just above the coronary arteries. The right femoral or the right common carotid artery was exposed, and in eight experiments a no. 7 French cardiac catheter (U.S.C.I.) was inserted and the tip manually positioned directly beneath the electromagnetic flow transducer. The catheter was connected to a Statham P23Gb, P23Db, or SF-1 pressure transducer. In the other four experiments a Statham SF-1 catheter-tipped pressure transducer was used and the tip also positioned beneath the flow transducer. This caused no discernible alteration in the flow signal. The resonant frequencies for the various catheter-manometer systems were determined by the step or "pop" technique and always exceeded 70 Hz and, more usually, 100 Hz. The resonant frequency of the SF-1 is approximately 2,000 Hz and has been shown to be accurate within 1% up to 90 Hz (4).

The electromagnetic flow transducer was connected to a Statham-Medicon model M4000 flowmeter for recording pulsatile flow. The various transducers were dynamically calibrated in vitro using a sine wave generating pump (4). The responses of the transducers were linear over a wide range of flows using both saline and whole blood with various hematocrits in the physiologic range. Calibration factors were determined for each transducer and were used to convert observed deflections on the flowmeter and recorder to ml/sec. Comparisons of the flowmeter in vivo with the flow measured by the dye dilution technique were also made (see below). The pressure and flow signals and the electrocardiogram (RCC) were recorded on a Honeywell Visicorder using a paper speed of 200 mm/sec. The frequency response of the pressure and flow signals was limited by the output characteristics of the recording system. The amplitude frequency response of the Visicorder galvanometers used to record pressure and flow was ±58 to 35 Hz.

**Calculations**

Stroke volume in ml was determined from the pulsatile flow tracings by planimetric integration of the forward flow component during systole, assuming zero flow in late diastole. The equation used to derive stroke volume from the aortic pressure contour was

\[
SV = K \cdot \frac{P_{sa}}{1 + \frac{T_s}{T_d}},
\]

where \(SV\) is stroke volume in ml, \(K\) is an arbitrary constant, \(P_{sa}\) is the area under the systolic portion of the pressure curve above a horizontal line drawn from the diastolic pressure and bounded by a vertical line through the lowest point in the incisura (the units are therefore mm Hg-sec), \(Ts\) is the duration of systole in msec and \(Td\) is the duration of diastole in msec (Fig. 1) (5). The \(P_{sa}\) term for each pressure contour analyzed was determined by planimetric integration of this area of the pressure tracing. The constant, \(K\), was determined from simultaneous pressure and flow tracings by substituting the flowmeter value for stroke volume and solving the equation for \(K\). One pair of simultaneous pressure and flow tracings was used to determine \(K\) for each of the 12 dogs studied. This measurement was obtained at the beginning of each experiment and represented baseline conditions. This \(K\) value was used to determine stroke volume under all subsequent experimental conditions in each dog by the pulse contour method. The values for stroke volume determined from the pressure tracings and the constants were compared to

![Figure 1](http://circres.ahajournals.org/)

**FIGURE 1**

Pressure tracing from the ascending aorta showing the variables measured and used in equation 1.
those simultaneously determined with the electromagnetic flowmeter.

Mean arterial pressure was determined by electronic integration of the pulsatile pressure signals at each baseline and experimental level where measurements of pulsatile flow and pressure were made. Heart rate was determined from the ECG. Regression analyses of the data were performed using standard digital computer programs.

**EXPERIMENTAL PROCEDURES**

Numerous interventions were introduced to produce changes in stroke volume, heart rate, arterial pressure, and the configuration of the aortic pressure pulses; they are summarized in Table 1. They were applied sequentially in the 12 dogs, and baseline conditions were generally established between them. The number of interventions varied in each dog. Comparisons of stroke volume by the pressure and flowmeter methods were made both during the baseline conditions and at intervals during the interventions. An average of three pressure and flow determinations were made both during the baseline and experimental levels, and the average heart rate fell from 141 to 63 beats/min. The mean arterial pressure fell an average of 171 mm Hg.

**Hemorrhage.**—Blood samples of 50 or 100 ml were withdrawn rapidly at intervals from four dogs and flow and pressure measurements were obtained between the periods of hemorrhage. This produced a maximal average decrease of 38% in stroke volume. Heart rate did not vary appreciably during these periods in individual dogs. Mean arterial pressure fell an average of 47 mm Hg.

**Inferior Vena Cava Occlusion.**—The inferior vena cava of five dogs was rapidly occluded with a tourniquet to produce a rapid reduction in stroke volume to a maximal average decrease of 73%. Heart rate did not change appreciably. Mean arterial pressure fell an average of 67 mm Hg.

**Arrhythmias.**—Spontaneous arrhythmias occurred in three dogs (supraventricular tachycardia in one and ventricular premature contractions in two). These produced a maximal average decrease of 69% in stroke volume. The heart rate increased an average of 41 beats/min. The mean arterial pressure did not change appreciably in the individual dogs.

**Pacing.**—Ventricular pacing with a Grass S4 stimulator was performed in one dog. Stroke volume fell from 10.5 to 4.9 ml (47%), and heart rate rose from 65 to 147 beats/min. The mean arterial pressure fell an average of 67 mm Hg.

**Vagal Stimulation.**—The distal end of the severed right vagus nerve in one dog was...
A stimulated from 3 to 7 Hz using 4 or 5 V. This produced an increase in stroke volume from 7.3 to 14.1 ml (93%) with a concomitant fall in heart rate from 126 to 43 beats/min. The mean arterial pressure fell from 114 to 87 mm Hg.

Epinephrine.—Constant infusions of an epinephrine solution (1.2 to 2 \( \mu \)g/min) were administered for several minutes to five dogs. The maximal average increase in stroke volume was 87%. The average heart rate increased from 122 to 171 beats/min, and the mean arterial pressure increased an average of 34 mm Hg.

Isoproterenol.—Isoproterenol, 1 \( \mu \)g/min, was infused over 3 to 5 minutes in five dogs. This produced a maximal average increase of 76% in stroke volume. The average heart rate increased from 130 to 153 beats/min. The mean arterial pressure increased an average of 7 mm Hg.

Metaraminol.—A constant infusion of metaraminol, 120 to 200 \( \mu \)g/min, was administered over 3 to 5 minutes in three dogs. This produced a maximum average increase of 50% in stroke volume. The average heart rate increased from 123 to 143 beats/min. The mean arterial pressure increased an average of 53 mm Hg.

TABLE 2
Correlation Coefficients and Regression Analyses for Comparisons of Stroke Volume by the Pulse Contour and Flowmeter Methods in the 18 Dogs

<table>
<thead>
<tr>
<th>Dog</th>
<th>No. of points</th>
<th>r</th>
<th>Slope</th>
<th>Intercept</th>
<th>Mean SV (ml)</th>
<th>S</th>
<th>/mean SV (Pass)</th>
<th>RR (mm)</th>
<th>MAP (mm Hg)</th>
<th>SV/EMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>0.846</td>
<td>0.844</td>
<td>1.37</td>
<td>10.36</td>
<td>10.17</td>
<td>1.62</td>
<td>16.42</td>
<td>27-174</td>
<td>23-43</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>0.891</td>
<td>0.971</td>
<td>1.63</td>
<td>10.03</td>
<td>9.75</td>
<td>1.11</td>
<td>11.51</td>
<td>49-173</td>
<td>33-114</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>0.841</td>
<td>1.087</td>
<td>-0.10</td>
<td>14.10</td>
<td>15.11</td>
<td>2.17</td>
<td>14.84</td>
<td>35-165</td>
<td>26-142</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>0.853</td>
<td>1.154</td>
<td>0.22</td>
<td>7.25</td>
<td>9.70</td>
<td>2.24</td>
<td>21.96</td>
<td>65-203</td>
<td>28-165</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>0.828</td>
<td>1.015</td>
<td>0.16</td>
<td>5.81</td>
<td>0.06</td>
<td>1.97</td>
<td>17.96</td>
<td>63-207</td>
<td>59-115</td>
</tr>
<tr>
<td>6</td>
<td>101</td>
<td>0.855</td>
<td>1.144</td>
<td>-1.48</td>
<td>8.47</td>
<td>8.50</td>
<td>0.82</td>
<td>10.00</td>
<td>65-151</td>
<td>53-136</td>
</tr>
<tr>
<td>7</td>
<td>101</td>
<td>0.855</td>
<td>1.242</td>
<td>-0.36</td>
<td>8.73</td>
<td>10.00</td>
<td>0.90</td>
<td>9.00</td>
<td>65-151</td>
<td>53-125</td>
</tr>
<tr>
<td>8</td>
<td>101</td>
<td>0.894</td>
<td>0.573</td>
<td>3.76</td>
<td>8.30</td>
<td>8.35</td>
<td>0.17</td>
<td>6.02</td>
<td>164-166</td>
<td>70-75</td>
</tr>
<tr>
<td>9</td>
<td>12</td>
<td>0.812</td>
<td>14.21</td>
<td>-9.79</td>
<td>7.16</td>
<td>9.28</td>
<td>0.99</td>
<td>11.95</td>
<td>98-103</td>
<td>60-88</td>
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<tr>
<td>10</td>
<td>12</td>
<td>0.878</td>
<td>0.630</td>
<td>2.77</td>
<td>7.54</td>
<td>7.54</td>
<td>0.94</td>
<td>12.35</td>
<td>127-161</td>
<td>62-114</td>
</tr>
<tr>
<td>11</td>
<td>12</td>
<td>0.907</td>
<td>0.851</td>
<td>1.15</td>
<td>15.48</td>
<td>14.32</td>
<td>0.48</td>
<td>3.31</td>
<td>118-135</td>
<td>92-119</td>
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<tr>
<td>12</td>
<td>12</td>
<td>0.970</td>
<td>1.248</td>
<td>-0.26</td>
<td>16.53</td>
<td>16.09</td>
<td>1.05</td>
<td>6.92</td>
<td>218-147</td>
<td>69-111</td>
</tr>
<tr>
<td>Total</td>
<td>561</td>
<td>0.928</td>
<td>1.954</td>
<td>0.21</td>
<td>9.46</td>
<td>10.09</td>
<td>1.23</td>
<td>17.40</td>
<td>33-207</td>
<td>28-100</td>
</tr>
</tbody>
</table>

r = correlation coefficient; EMF = electromagnetic flowmeter; Pass = pulse contour method; sv = standard error of estimate; SV/mean SV (Pass) = standard deviation of estimate expressed as a percent of the mean stroke volume by the pressure contour method; HR = heart rate; MAP = mean arterial pressure; SV = stroke volume.

*The results in this row were obtained by performing a regression analysis on all observations as a single group.
Levarterenol—An infusion of levarterenol, 1 \(\mu\)g/min, was given over 3 to 5 minutes to two dogs. No appreciable change in stroke volume or heart rate occurred, although the mean arterial pressure rose an average of 84 mm Hg.

**Results**

The comparisons of stroke volume by the flowmeter and aortic pressure contour methods in the individual dogs are shown in Table 2. As noted previously, the number of interventions varied in each dog, and in the early experiments, a number of interventions were applied sequentially. The points used for determination of the constants are not included in the comparisons. Considerable variation in stroke volume as measured by electromagnetic flowmeter was produced in all but one of the dogs studied (dog 9) and was associated with changes in heart rate and arterial pressure. Figure 2 shows a comparison of stroke volumes by the two methods in dog 6. With a number of interventions introduced to vary stroke volume, the agreement between the methods was good \(r = 0.953\) over a wide range of values for stroke volume, heart rate, and mean arterial pressure (Table 2). Figure 3 shows the comparison of the methods in dog 5. Although the correlation coefficient was 0.838 and the standard error of estimate high (\(\pm 18\)), the directional changes in stroke volume were consistently detected by the pressure contour method. With few exceptions, this was true in all 12 experiments. The correlation coefficient for the straight line

| TABLE 2
<table>
<thead>
<tr>
<th>Correlation Coefficients and Regression Analyses for the Pulse Contour and Flowmeter Methods with the Twelve Interferences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
</tr>
<tr>
<td>Dextran</td>
</tr>
<tr>
<td>Positive pressure respiration</td>
</tr>
<tr>
<td>Hemorrhage</td>
</tr>
<tr>
<td>Occlusion, inferior vena cava</td>
</tr>
<tr>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Pacing</td>
</tr>
<tr>
<td>Crush of sinoatrial node</td>
</tr>
<tr>
<td>Vagal stimulation</td>
</tr>
<tr>
<td>Epinephrine</td>
</tr>
<tr>
<td>Isoproterenol</td>
</tr>
<tr>
<td>Metaraminol</td>
</tr>
<tr>
<td>Levarterenol</td>
</tr>
</tbody>
</table>

See footnote to Table 2.

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equation describing the relationship for 541 determinations in all 12 dogs was 0.928 \( (y = 1.04x + 0.21 \text{ ml}) \) and the standard error of estimate = ±17.4\% (Table 2, Fig. 4). The broken lines in Figure 4 represent the 95\% confidence limits relative to the mean \( y \). They were obtained by drawing lines parallel to the regression line at 1.96 times the standard error of estimate above and below the mean \( y \). When the various interventions were considered separately, certain differences became apparent (Table 3). Excellent correlations \( (r = 0.928 \text{ to } 0.990) \) were observed with all interventions except the infusion of isoproterenol, metaraminol and levarterenol (Fig. 5). With these three agents, the stroke volumes using the pressure contour method consistently overestimated those determined with the electromagnetic flowmeter. The possible reasons for this major deviation from all other types of intervention are considered in the Discussion.

Discussion

It is widely accepted that a method for measurement may use very coarse approximations and yet be of considerable value. It is in this spirit that the results given above are regarded as sufficiently good to merit a theoretical exploration. The potential usefulness of the method gives this, as it were, a pragmatic sanction. Nevertheless, the collapse of reliability when sympathomimetic agents were used suggests that some theoretical analysis is necessary to pinpoint the source of the error with a view to future improvement.

The Original Windkessel Derivation—Equation 1 was taken from Warner et al. (5), where it was listed as one of the methods used for comparison with a newly derived formula for calculation of stroke volume. No reference to its original author was made. Its inspiration, if not its exact formulation, was undoubtedly in the writings of Otto Frank, particularly the paper referred to previously (3). This work has been reviewed, together with a detailed development, in the recent monograph of Wetterer and Kenner (6). It was enlarged by the valuable concept of "serial windkessels" in series by Remington (7), and the \((1 + Ts/Td)\) term to the equation finds its first expression, to our knowledge, in this
Tracings of an experimental record in which the flow curve is scaled so that the peak height is comparable to the peak systolic pressure. The dashed and dotted lines illustrate some points in the Discussion. The dotted line following the flow curve indicates the nature of a pressure resulting from this flow injection if there were no reflections, i.e., in a tube of infinite extension, or one terminating in a matched impedance. The shaded triangle below the systolic area is the addition to the measured Psa which the term \((1 + T_d/T_s)\) is intended to estimate. The sloping dashed line is an approximation of the last portion of the diastolic decline in pressure due to continuous drainage out of the arterial tree through the capillary beds. It is drawn as a straight line rather than an exponential for simplicity to show proportional areas in systole and diastole. The continuous drainage is assumed, in windkessel at least, to be solely due to the capillary "leak," i.e., mean flow or cardiac output, but in early diastole at least, a considerable part of this fall is due to the elastic recoil of the distended aorta redistributing blood throughout the arterial tree—a witness the development of diastolic forward flow in the more peripheral arteries. It is by no means certain that this process is complete in the latter part of cardiac diastole.

A simplistic attempt to describe this derivation which makes an allowance for the peripheral drainage during systole is presented in Figure 6. Although this would be more correctly represented by an exponential, a straight-line extrapolation is drawn in an attempt to explain the term \((1 + T_d/T_s)\) by triangulation. An exact derivation could not be achieved.

The windkessel theory, however, could not adequately explain the peripheral pulse waveform, e.g., the dicrotic wave. Important factors such as elasticity (or reciprocally, the distensibility) of the elastic chamber led to a number of additional but often incompatible concepts (8). It is these concepts that have been the target for criticism (9) rather than the central idea of the windkessel theory. Attempts to quantify theoretical formulations for the windkessel chamber in cadavers (10) or in patients against measured cardiac outputs (11) have been uniformly unsuccessful.

The work of Warner et al. (5) showed that these dubious theoretical predictions could be avoided by an initial calibration against methods for determination of cardiac output, which by 1953 had become standard (Fick and indicator-dilution) and that the method could be made reasonably successful. The concept was reintroduced by Jones et al. (12) to apply the time-derivative method used by McDonald (1, 13) as proposed by Womersley (14, 15). With the introduction of a reliable electromagnetic flowmeter, the pulsatile flow can be recorded and the interpretation of diastolic drainage and reflected components of the pressure wave is made much easier (below and Fig. 6).

The windkessel theory assumes that the arterial pressure pulse is a transient phenomenon imposed on a system essentially at rest. A more tractable approach in the sense of using the well-established hydrodynamic wave equations is to take the pulse as a periodic phenomenon or steady-state oscillation (9). It
has been argued that the approximations involved in both are not dissimilar (1).

Steady-State Oscillation Derivation.—For an elastic tube (radius \( R \)) which is longitudinally restrained (16) and filled with a viscous liquid, the modulus, or amplitude, of the characteristic impedance, \( Z_0 \), (in the absence of reflections) is

\[
Z_0 = \frac{\rho c}{\pi R^2 (1 - \sigma^2)^{1/2}} \left(M'_{10}\right)^1.
\]

where \( c \) is the wave velocity when the fluid is inviscid (i.e., a measure of distensibility), \( \rho \) is the density of the liquid, and the term \( M'_{10} \) (1, 15, 16) is a Bessel function term which is dependent on a parameter \( \sigma \), which varies directly with the radius and the square root of the frequency. With large arteries \( M'_{10} \) approximates to 1.0. \( Z_0 \) is here defined as \( P/V \) where \( P \) is pressure and \( V \), the average velocity across the tube, is the volume flux, \( Q \), divided by the cross-sectional area, \( \pi R^2 \); \( \sigma \) is Poisson’s ratio and for an incompressible wall is 0.5 (16).

This equation can thus be rewritten

\[
\dot{Q} = \frac{P \cdot \pi R^2}{c} \cdot \frac{(1 - \sigma^2)^{1/2}}{\rho}.
\]

As \( \rho \) and \( \sigma \) are known, it can be seen that the last term of equation 3 is a constant and is a small modification of the elastic water-hammer equation (rewritten) for a very thin-walled tube,

\[
\dot{Q} = \frac{P \cdot \pi R^2}{c} \cdot \frac{1}{\rho},
\]

which was the starting point for Frank’s derivation (3).

Doing a geometric integration for stroke volume, we know that the form of the flow curve approximates to a triangle (Fig. 6) whose height is the peak flow, \( \dot{Q} \), and whose base is the systolic duration (\( T_s \)). Then we obtain

\[
SV = \frac{1}{2} T_s \cdot \dot{Q}.
\]

and since, if the pressure were not modified by reflections, it would be a similar form to flow (Fig. 6) we can, letting \( P \) represent pulse pressure, write the following from equations 3 and 5:

\[
SV = \left(\frac{1}{2} T_s \cdot \dot{Q}\right) \cdot \frac{\pi R^2}{c} \cdot \frac{(1 - \sigma^2)^{1/2}}{\rho}.
\]

(6)

However, the integrated pressure area (\( P_{sa} \)) is not triangular and indeed varies in shape. By introducing an arbitrary constant, \( k \), to reduce it to its triangular, or flow integral, equivalent, equation 6 can be rewritten

\[
SV = kP_{sa} \cdot \frac{\pi R^2}{c} \cdot \frac{(1 - \sigma^2)^{1/2}}{\rho}.
\]

(7)

While \( k \) is still arbitrary, it has well-defined limits between 1.0 when the pressure curve is triangular, and 0.5 when the curve is rectangular. In the present series it ranged between 0.56 and 0.74 and is, therefore, a minor variable.

It can thus be seen that the “calibration” factor \( K \) (equation 1) is now defined by the collection of terms modifying \( P_{sa} \) in equation (7). Taking mean radius values for the proximal large arteries and their wave velocities (17) it can be shown that (after converting to cgs units) the \( K \) values predicted from equation 7 are comparable to those measured (predicted range \( K = 0.92 \) to 3.69, measured range \( K = 0.89 \) to 3.37). The main component in the variation is arterial diameter, and we have found that the \( K \) values measured in patients are larger by amounts that could be predicted from arterial size. We thus feel that the analysis does relate reasonably to reality.

It will be noted that, as \( P \) is a notation for the pulse pressure when the flow pulse is injected at the diastolic pressure, a combination of equations 5 and 6 shows a fairly simple relation between pulse pressure and stroke volume. Following the extensive series of papers by Remington, Hamilton and associates on various aspects of measuring stroke volume, Hamilton stated that he thought the pulse pressure was the term that correlated best with stroke volume (18). Remington (19) has published a table predicting the cardiac index from the pulse pressure (assuming zero blood flow at 20 mm Hg). Provided that the assumptions set out above hold fairly
constant, and the length of systole, the mean pressure (which largely determines both the cross-sectional area and the wave velocity in any individual aorta), and peripheral resistance remain fairly constant, the correlation between pulse pressure and stroke volume should be, and is, quite good. In the present series, however, heart rates as well as mean pressure and resistance were deliberately altered. Statistical correlations of pulse pressure and stroke volume were determined in several of the present experiments but were significantly lower than with the area method. Warner et al. showed similar results (5).

It would thus appear from equation 7 that errors must arise from the variable factor \( \pi R^2/c \) as a component of the calibration constant (K) determined at the start of the experiment. That the wave velocity varies with the mean distending pressure has been widely known since the paper of Bramwell and Hill in 1922 (20). More recently, Anliker et al. (21) have measured the wave velocity in the thoracic aorta with imposed waves in the frequency range 40 to 200 Hz. With an increase in distending pressure, however, the cross-sectional area of the aorta will also increase so that the ratio of area to wave velocity will not change as much as either of the two individual parameters. From the Bramwell and Hill finding that the wave velocity increases linearly with the mean, or diastolic, pressure, it can be shown that an increase in mean pressure from 100 to 150 mm Hg will actually decrease the ratio \( \pi R^2/c \) by some 14%. With the more physiological data of Anliker et al., the change over this range is negligible. A mere change in mean arterial pressure, with the large arteries regarded as passive nonlinear elastic tubes will not, therefore, account for the large discrepancy in results found with sympathomimetic agents.

If, however, the considerable amounts of smooth muscle in the walls of the large arteries play an active role, this could well alter the effective elastic modulus based on a passive nonlinear model and in a way that the crucial ratio is radically changed. Evidence that the distensibility of major arteries is changed by catecholamines has been published by Wiggers and Wegria (22), Alexander (23), Pieper and Paul (24), and Dobrin and Rovick (25). No precise data are available as to the quantitative change in the ratio \( \pi R^2/c \) produced by catecholamines. The action of catecholamines will be dual in that, apart from the postulated effect on the smooth muscle in the large arteries, they will also alter the small vessel size and, by affecting the peripheral resistance and impedance, will alter the distributed reflection component of the central aortic pressure—i.e., the value of \( k \). This latter effect is, based on our calculations, much too small to account solely for the measured discrepancies. The precise solution of this is a matter of physiological importance that arises from the present study.

Consideration of Experimental Results.—Evaluation of the reliability and accuracy of the estimates of stroke volume in this study has been based on the statistical analyses, and the data will be compared here only with the other published data on experiments in the dog. The paper of Warner et al. (5) is thus excluded because it was done on humans. It is of interest to note that their results with the present method did not differ significantly from the more complex formula which that paper examined in detail. As an ancillary limitation, we emphasize that at the present time, with alternative reliable methods of measuring cardiac output available, we cannot consider in detail methods of predicting flow which predate the time when such check values were available.

Initially, the comparative methods for measurement of stroke volume and cardiac output were checked in our own laboratory. In experiments in five dogs that have not been separately reported, Kerr and Kouchoukos found a correlation between duplicate simultaneous dye-dilution (Cardiogreen) measurements, i.e., calculated from samples withdrawn from different sites following a single injection, that gave \( r = 0.990, y = 0.937 + 88.0 \) ml/min, with \( \alpha = 5\% \) \( (n = 60) \). They then found that dye-dilution cardiac output compared with the electromagnetic flowmeter in
five dogs gave $r = 0.98$, $y = 0.922x + 182$ ml/min, with $se = \pm 10\%$ (n = 31). In these experiments the cardiac output by dye dilution ranged from 0.5 to 5.0 liters/min. The overall series comparing the pressure contour method with the electromagnetic flowmeter has a variability ($\pm 17.4\%$) higher than this (Table 2). However, Table 3 shows that the individual series with many of the interventions were considerably better than the overall correlation. The analysis of all points except those during infusions of the four sympathomimetic drugs gave $r = 0.946$, $y = 1.06x + 0.016$ ml with $se = \pm 16.8\%$ (n = 338).

The best comparison for practical purposes, of course, is with other methods based on deriving stroke volume from aortic pressure. It is unfortunate that no studies on contour methods have been found showing an analysis to which these statistical criteria can be applied, except those reported in the cadaver by Starr and Schid (10), which all give far worse values for the correlation coefficients (0.64 to 0.74) but report no other factors. However, in all their methods, the parameters involving arterial elasticity and cross-sectional area were derived from previously published formulas and did not invoke a direct match on the first measurement as we have done.

The criterion of basing comparisons of results on statistics makes it difficult to discuss the series of papers by Remington and his associates (7, 19, 26-28). At a time when there were no agreed values for cardiac output and hence no firm criterion of comparison, they discarded the whole array of increasingly complex formulas coming from the German school of Frank's pupils and reinvestigated more precisely the distribution of elastic properties of the windkessel. From the published diagrams of their data it would seem that their results were comparable to ours, but statistical judgments by eye are difficult to defend.

A method for estimation of stroke volume which has been reported by Warner (29) changes the original formulation (5) by replacing the term for mean distending pressure ($P_{md}$) with $\sqrt{P_{md}}$. A full theoretical justifica-

The measurement of beat-by-beat heart output, most workers have used the Fry simplification of the pressure gradient equation of Womersley (32, 33) or, more commonly, the substitution of his formulation for the pressure gradient using the time derivative of the pressure. The first paper to introduce the latter method and to avoid the use of a second pressure channel by using a calibration constant determined by comparison with another method (in this case dye-dilution) was that of Jones et al. (12). In eight dogs the cardiac output was varied by changing the left atrial pressure with a reservoir of adjustable height. Also, in six dogs the "cardiovascular status was further varied by infusions of first epinephrine and then methoxamine." The range of output varied up to three or four times the minimum in individual dogs; ranges of mean arterial pressure and heart rate were not reported, although they were stated to
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vary widely. The overall correlation coefficient was 0.97 (n = 67) with a regression line of 
\[ y = 1.1x - 45 \text{ ml/min} \]; the range of correlation coefficients in the individual dogs was 0.85 to 0.99. The standard error of estimate was not reported. These details of this paper are repeated because they are the best values yet reported for a pressure-based method for measurement of cardiac output or stroke volume. In view of their methods for altering cardiac output, we can compare their results with the correlation coefficients for similar interventions in the present study, e.g., dextran infusion (0.97), occlusion of inferior vena cava (0.968), epinephrine infusion (0.937), and, possibly, the predominant rate changes induced by pacing (0.978) and vagal stimulation (0.99) (Table 3).

A later paper by Jones and Griffin (34) compared stroke volume measured by the same technique with the flow measured by an electromagnetic flowmeter. They altered the cardiovascular system by hemorrhage, transfusion, and administration of methoxamine and nitroglycerine. The statistical results were: \( r = 0.93, y = 0.90x + 9.2 \text{ ml}; \sigma = \sigma = 13.2 \) (n = 300, 5 dogs). The correlation coefficient is the same as our entire series, but the slope of regression line is considerably less than one. The number of interventions with the various drugs and doses used was not recorded. Thus it might be misleading to compare the results solely with our transfusion (dextran) or hemorrhage series.

Another more recent comparison of this method against dye dilution is that of Boyett et al. (35). Changes in output were produced by hemorrhage and amyl nitrite. In five dogs the overall correlation coefficient for cardiac output was 0.92 (range 0.735 to 0.972) and the regression line was \( y = 1.029x - 56 \text{ ml/min} \). The 95% confidence limits were shown, but not enumerated, and appear similar to our own (Fig. 4). Again, our statistical data for hemorrhage, \( r = 0.988, y = 1.034x + 0.83 \text{ ml} \), easily bear comparison with the more complex method.

The several papers of Fry and his colleagues on this topic are not discussed here because the statistical comparisons are confined to the estimated peak flow in the cycle, a more critical test. Note should be made, however, of the critique of the method by Greenfield and Fry which appeared as the last of a series of measurements in dogs (36).

The data of Kerr and Kouchoukos, quoted above, emphasize a point often overlooked, i.e., that the comparison method never has any claim to absolute accuracy. No exact estimate can be given of the precision of the electromagnetic flowmeter, which can vary according to the care taken with application of the transducer and (in gated sine-wave or square-wave forms) the precise setting of the gate. The data from this laboratory in dogs indicate that the flowmeter is about as accurate in measuring cardiac output and stroke volume as a careful indicator-dilution measurement.

In conclusion, the results of this study show that estimation of stroke volume by a simple pressure contour method using a wide range of interventions to alter cardiovascular dynamics was as good or better statistically as all other methods using derivations from pressure. The "contour" methods have been criticized in the past as being rather empirical in nature, although some attempt had been made to examine the underlying assumptions (1). Now a derivation is presented, with clearly stated assumptions, which shows that the basis for the method appears less crude on close inspection than at first sight. Furthermore, the method has proved reliable under a variety of conditions. It tends to become unreliable with the administration of catecholamines and other sympathomimetic drugs. No way of circumventing this has been conceived at the present time, nor does the development of the equation show clearly any way this might be done. It is, however, of some help if the method is used clinically to be able to predict when it is unreliable, and use of an indicator-dilution measurement or other method for measurement of stroke volume or cardiac output is then recommended.

References


Estimation of Stroke Volume in the Dog by a Pulse Contour Method
NICHOLAS T. KOUCHOUKOS, LOUIS C. SHEPPARD and DONALD A. McDONALD

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