Determinants of Pulse Pressure

Nikos Stergiopulos, Nico Westerhof

Abstract—We have searched to define the major arterial parameters that determine aortic systolic (P_s) and diastolic (P_d) pressure in the dog. Measured aortic flows were used as input to the 2-element windkessel model of the arterial system, with peripheral resistance calculated as mean pressure divided by mean flow and total arterial compliance calculated from the decay time in diastole. The windkessel model yielded an aortic pressure wave from which we obtained the predicted systolic (P_{s,wk}) and diastolic (P_{d,wk}) pressures. These predicted pressures were compared with the measured systolic and diastolic pressures. The measurements and calculations were performed for 7 dogs under control conditions during aortic occlusion at 4 locations (the trifurcation, between the trifurcation and diaphragm, the diaphragm, and the proximal descending thoracic aorta) and during occlusion of both carotid arteries. Under all conditions studied, the predicted systolic and diastolic pressures matched the experimental ones very well: P_{s,wk}=(1.000±0.0055) P_s with r=0.958 and P_{d,wk}=(1.024±0.0035) P_d with r=0.995. Linear regression for pulse pressure (PP) resulted in PP_{wk}=(0.99±0.016) PP with r=0.911. We found the accuracy of prediction equally good under control conditions and in the presence of aortic or carotid artery occlusion. Multiple regression between pulse pressure and arterial resistance and total arterial compliance yielded a poor regression constant (R^2=0.19), suggesting that the 2 arterial parameters alone cannot explain pulse pressure and that flow is an important determinant as well. We conclude that for a given ejection pattern (aortic flow), 2 arterial parameters, total arterial resistance and total arterial compliance, are sufficient to accurately describe systolic and diastolic aortic pressure. (Hypertension. 1998;32:556-559.)

Key Words: arterial compliance ▪ vascular resistance ▪ windkessel ▪ cardiac output

Systolic and diastolic pressure, and thus pulse pressure, are determined by the complex interaction of the heart and the arterial and venous systems. Studies in the isolated cat heart loaded with an artificial arterial system showed that with a decrease in compliance and leaving peripheral resistance and cardiac parameters (diastolic filling, heart rate, and contractility) constant, systolic pressure increased very little but diastolic pressure decreased considerably.1 In the intact dog, when arterial compliance was decreased in such a way that peripheral resistance and heart rate remained the same while other cardiac parameters could vary, the increase in systolic and decrease in diastolic pressures were about the same.2 Comparison of these results shows that cardiac parameters such as diastolic filling and contractility do affect pulse pressure.

In an earlier theoretical model study,3 we studied the contribution of major cardiac and arterial parameters to systolic pressure, diastolic pressure, and stroke volume. We found that the characteristic impedance of the aorta contributes little to systolic and diastolic aortic pressure. Furthermore, using a distribution model of the arterial tree,4 we have also shown that for a given ejection pattern (aortic flow), systolic and diastolic pressures were very accurately predicted by the 2-element windkessel. Therefore, total arterial compliance and peripheral resistance seem to be the only 2 important arterial parameters determining aortic pulse pressure.5,6

We have therefore put forward the hypothesis that for a given ejection pattern, pulse pressure depends solely on total arterial compliance and peripheral resistance. We tested this hypothesis using data from canine experiments.

Methods

Experimental Data

Aortic pressure and flow waveforms were obtained earlier in closed-chest anesthetized dogs.1 Flow was measured with a previously implanted electromagnetic flow probe on the ascending aorta. Pressure was measured with a catheter tip manometer introduced into the femoral artery and moved to the same aortic location as the flow probe at the day of the experiment. A typical set of aortic pressure and flow recordings simultaneously measured under control conditions is shown in Figure 1. Aortic pressure and flow were also measured under several different conditions. Abdominal and thoracic aortas were occluded totally by means of an inflatable balloon at 4 locations: at the aortic trifurcation, between the trifurcation and level of the diaphragm, at the diaphragm, and at the level of the proximal...
descending thoracic aorta. A fifth intervention was the occlusion of both carotid arteries. The location of the occlusions of the aorta and the carotids is shown schematically in Figure 1, and the interventions are designated by the letters A through E. The purpose of the occlusions was to augment wave reflections and change the topology of wave reflections (A through D) and to change aortic pressure (E). Details regarding the experimental procedure have been published previously.7

Determination of Parameters of 2-Element Windkessel
From the measured ascending aortic pressures and flows, peripheral resistance (R) was obtained as the ratio of mean pressure and flow. Total arterial compliance (C) was estimated by the decay time method, ie, fitting the diastolic part of the pressure wave with a single RC time. The time constant divided by peripheral resistance gave total arterial compliance. From the same beats, systolic and diastolic aortic pressures were obtained.

Systolic and Diastolic Pressure Predicted From Windkessel and Flow
Systolic and diastolic pressures were determined as follows. Using measured flow (Q) as input to the 2-element windkessel, the output pressure, \( P_{\text{wk}} \), was calculated by integration of the governing equation: 
\[ \frac{dP_{\text{wk}}}{dt} = \frac{P_{\text{wk}}}{RC} - \frac{Q}{C}. \]

The maximal and minimal values of \( P_{\text{wk}} \) were designated as predicted systolic and diastolic pressures. Systolic and diastolic pressures were determined for a randomly selected cardiac cycle taken from series of steady-state heart beats (approximate duration, 10 seconds) in all 7 dogs. One hundred twelve cycles were analyzed (n=112); 69 were for control conditions (including control measurements before and after interventions) and the rest for occlusion at the aorta and the carotid arteries.

Data Analysis
Linear regression was applied to determine the relation between measured and predicted systolic, diastolic, and pulse pressures. Paired t tests were performed to assess the differences between predicted and measured pressures for control and during interventions. Bland and Altman plots were used to check the agreement between the measured and estimated systolic and diastolic pressures. Multivariate analysis was applied to assess the relation between pulse pressure (dependent variable) and peripheral resistance and total arterial compliance (independent variables).

Results
Predictions of Systolic, Diastolic, and Pulse Pressures
A cumulative graph showing the comparison between the measured and predicted systolic and diastolic pressures for all 7 dogs and all cases (control, aortic and carotid occlusion) is shown in Figure 2A. The dashed lines are the lines of identity. Linear regression (slope±SEM) with intercept forced to zero yielded \( P_{s,wk} = (1.000±0.0055) \) \( P_s \) (r=0.958) for the systolic pressure and \( P_{d,wk} = (1.024±0.0035) \) \( P_d \) (r=0.995) for the diastolic pressure. We conclude that both systolic and diastolic pressures are accurately predicted for all cases studied. Figure 2B shows a plot of the predicted versus the measured pulse pressure (PP). Linear regression resulted in \( PP_{wk} = (0.99±0.016) \) PP (r=0.911). Multiple regression analysis applied to the entire data set, with peripheral resistance and compliance as independent variables and pulse pressure as dependent, yielded \( R^2 = 0.19 \).

Bland and Altman plots for the entire set (control and interventions) of measured and predicted systolic and diastolic pressures.
ic pressures are given in Figure 3. The mean of the difference between measured and predicted pressures was 0.1 mm Hg and 1.4 mm Hg for the systolic and diastolic pressures, respectively; the corresponding standard deviations were 7 mm Hg and 2.7 mm Hg. Apart from a small, consistent positive difference in the diastolic values, the differences are clustered around the zero value, and no specific trends (ie, dependence on pressure) in the distribution are observed.

**Effect of Occlusions**

Measured versus predicted systolic, diastolic, and pulse pressure under control conditions (X); with aortic occlusion at A, B, C, and D; with occlusion of the 2 carotids (E); and after deflation of the balloon occluding the aorta (R) are plotted in Figure 4. Good agreement between measured and predicted systolic, diastolic, and pulse pressures is found for all conditions. We observed an increase in pulse pressure with aortic occlusion, which became progressively more important as the aortic occlusion site moved closer to aorta (A through D). Data for the mean values and standard deviation of hemodynamic parameters under control conditions (groups X and R) and during interventions (groups A through D and G) are given in the Table. Paired t tests showed that for all groups, the difference between measured and predicted pressures was not statistically significant, except for the diastolic pressures under control conditions (X and R), with the mean difference in diastolic pressure for these 2 groups being <2 mm Hg.

**Discussion**

Systolic and diastolic pressure are important markers of cardiovascular function and disease. Diastolic and systolic hypertension are known to be precursors to a wide spectrum of cardiovascular dysfunctions and diseases. Systolic pressure, which relates to maximum wall stress (Laplace’s law) and therefore determines heart muscle load, has been shown to be a factor implicated in cardiac hypertrophy.9 Also, systolic pressure is an important determinant of myocardial oxygen consumption.10 Recent studies have shown that pulse pressure is one of the strongest predictors of coronary heart disease and cardiovascular mortality.11,12 It is therefore important to know the major vascular and cardiac parameters that determine systolic, diastolic, and pulse pressure.

We studied aortic pressures in the dog under control conditions and under obstruction of the aorta and the carotids. Using aortic flow as input, and thus accounting for the changes in the venous system (preload) and in the heart (heart rate, contractility), we could study the contribution of the arterial load on systolic, diastolic, and pulse pressure. We found that peripheral resistance and total compliance are the only 2 arterial parameters that determine systolic and diastolic pressure virtually completely. The data show that systolic and diastolic pressures are well predicted by the 2-element windkessel, irrespective of the large changes in arterial load and the distribution and topology of the reflection sites in the arterial system. In our earlier study describing the pulse pressure method, we attributed the good predictions of the pulse pressure by the 2-element windkessel model to the fact that the 2-element windkessel matches well the true input impedance at low frequencies.3 Because the first few harmonics contain the major part of the information on the wave shape, these harmonics mainly determine the systolic and diastolic pressure.3,5
These findings have an important implication: systolic and diastolic pressure do not depend on the distribution of the wave reflection sites and are simply determined by the combined properties (R and C) of the arterial system. The Table shows that >60% of the total arterial compliance resides in the ascending and descending aorta (compare C values under control and total occlusion at D). Therefore, to further simplify the clinical aspect of the problem, pulse pressure is determined mainly by the periphery (R) and the elastic properties of the aorta (C).

In an earlier article, we derived analytically the dependence of aortic systolic and diastolic pressure on the major arterial and cardiac parameters. We have shown that cardiac parameters such as heart rate, contractility, and venous pressure have a profound effect on aortic pressure. This means that when analyzing the effects of arterial parameters such as compliance and peripheral resistance on pulse pressure, one needs to consider also the modulating effect of cardiac parameters; otherwise, the correlation between pulse pressure and arterial parameters may be poor. To illustrate this point, we performed a multiple regression analysis between the pulse pressure (independent variable) and peripheral resistance and compliance (dependent variables) for the entire dog data set (n=112). Multiple regression analysis yielded a result of $r^2=0.19$, suggesting that the 2 arterial system parameters alone cannot explain all the variability in the data. This also explains the rather poor correlation between pulse pressure and arterial compliance reported from cross-sectional studies in humans.

We conclude that for a given aortic flow, systolic and diastolic aortic pressures are determined by only 2 arterial parameters: peripheral resistance and total arterial compliance. In general, however, cardiac parameters such as heart rate, contractility, and filling pressure also contribute and therefore should always be taken into account.

References


<table>
<thead>
<tr>
<th>Type (n)</th>
<th>R</th>
<th>C</th>
<th>$Q_m$</th>
<th>$P_n$</th>
<th>$P_s$</th>
<th>$P_{swk}$</th>
<th>$t$ Test*</th>
<th>$P_d$</th>
<th>$P_{swk}$</th>
<th>$t$ Test*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (7)</td>
<td>3.7 ± 1.2</td>
<td>0.16 ± 0.07</td>
<td>19.5 ± 3.5</td>
<td>72 ± 22</td>
<td>96 ± 21</td>
<td>101 ± 14</td>
<td>0.24</td>
<td>47 ± 25</td>
<td>48 ± 27</td>
<td>0.30</td>
</tr>
<tr>
<td>B (7)</td>
<td>5.3 ± 1.6</td>
<td>0.16 ± 0.06</td>
<td>19.7 ± 4.5</td>
<td>97 ± 18</td>
<td>130 ± 10</td>
<td>128 ± 10</td>
<td>0.49</td>
<td>67 ± 29</td>
<td>69 ± 30</td>
<td>0.10</td>
</tr>
<tr>
<td>C (11)</td>
<td>6.7 ± 2.7</td>
<td>0.13 ± 0.06</td>
<td>17.2 ± 5.4</td>
<td>105 ± 22</td>
<td>138 ± 20</td>
<td>143 ± 21</td>
<td>0.35</td>
<td>72 ± 26</td>
<td>72 ± 30</td>
<td>0.76</td>
</tr>
<tr>
<td>D (9)</td>
<td>6.0 ± 2.5</td>
<td>0.11 ± 0.04</td>
<td>15.9 ± 6.1</td>
<td>105 ± 21</td>
<td>145 ± 19</td>
<td>145 ± 21</td>
<td>0.98</td>
<td>66 ± 27</td>
<td>68 ± 29</td>
<td>0.14</td>
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<tr>
<td>G (9)</td>
<td>6.0 ± 1.8</td>
<td>0.15 ± 0.10</td>
<td>18.4 ± 5.0</td>
<td>102 ± 9</td>
<td>126 ± 12</td>
<td>126 ± 13</td>
<td>0.67</td>
<td>78 ± 10</td>
<td>80 ± 8</td>
<td>0.12</td>
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<tr>
<td>R (24)</td>
<td>3.9 ± 1.5</td>
<td>0.18 ± 0.06</td>
<td>22.2 ± 5.5</td>
<td>81 ± 20</td>
<td>105 ± 20</td>
<td>105 ± 21</td>
<td>0.90</td>
<td>57 ± 22</td>
<td>58 ± 22</td>
<td>0.02</td>
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<tr>
<td>X (45)</td>
<td>4.2 ± 1.4</td>
<td>0.19 ± 0.07</td>
<td>20.0 ± 3.5</td>
<td>82 ± 22</td>
<td>104 ± 20</td>
<td>103 ± 19</td>
<td>0.42</td>
<td>59 ± 26</td>
<td>61 ± 26</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are given as mean ± SD. $Q_m$ and $P_n$ are mean flow and mean pressure, respectively.

*P value of paired t test for comparison of predicted and measured systolic and diastolic pressures.

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