Relation of Arterial Blood Pressure to the Transverse Diameter of the Heart in Compensated Hypertensive Heart Disease

By Eli A. Ramirez, M.D., F.A.C.P., and Pedro H. García Pont, M.D.

The current concept regarding the clinical manifestations and complications of hypertensive heart disease is that they are due to a high diastolic pressure rather than to a high systolic pressure. It is well known, however, that hypertensive patients usually exhibit elevation of both the systolic and the diastolic pressures. In fact, the systolic pressure is frequently more elevated than the diastolic pressure and the pulse pressure is increased.

A recent actuarial study has shown that at any level of diastolic pressure mortality increases progressively with increases in systolic pressure. Within the blood pressure range studied it was shown that the adverse effects of a high systolic pressure are greater than those of a high diastolic pressure. These observations indicate that systolic pressure elevation, which has been generally regarded as an innocent bystander of diastolic hypertension, may have adverse clinical significance of its own.

The object of the present study is to determine the association of systolic and diastolic pressures with the size of the heart in a large group of hypertensive patients. This would enable a distinction between the separate effects of both pressures upon a manifestation of hypertensive heart disease which is associated with significant morbidity and mortality.

Materials and Methods

The data were collected in nine Veterans Administration’s hospitals* which are collaborating in a study of antihypertensive drugs. All patients were hospitalized male veterans who satisfied the criteria of the original protocol as published previously. No selection was made except for the exclusion of patients with surgically curable hypertension, malignancy, uremia, or other conditions that would interfere with adequate follow-up observations.

The blood pressures were taken four times daily in the sitting position. Only patients whose diastolic blood pressure averaged 90 mm. Hg or above from the fourth through the sixth hospital day were included in the study. The diastolic pressure was read at the point of disappearance of all sounds.

The transverse diameter of the heart was measured in the conventional teleroentgenogram and corrected according to the Ungerleider table. Cardiac volume was calculated according to the method of Musshoff and Reindell.

The analysis of the data was done with an automatic IBM computing system. The statistical formulas to calculate correlation coefficients, significance of correlation coefficients, significance of differences, and exclusion of partial effects were taken from standard reference sources. Differences of probability greater than \( p = 0.05 \) were not considered significant.

Results

The correlation coefficients ("r") between systolic pressure, diastolic pressure, and corrected transverse diameter in 535 compensated hypertensive patients are shown in table 1. Although, as shown by the \( p \) values, the correlation coefficients between the pressures and the transverse diameter are highly significant, the degree of association they express is relatively small.

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The calculated lines of regression and the standard errors of the estimates for the relation between the transverse diameter and both pressures are shown in figures 1 and 2. The slopes of the lines are small, showing that both pressures are poor predictive indices of transverse diameter. The slightly smaller standard error of the estimate given by the systolic pressure is consistent with relatively less scatter of heart size for the systolic than for the diastolic pressure.

In order to determine if the degree of association between the systolic pressure and the transverse diameter ("r" = +0.310) is significantly greater than that between the diastolic pressure and the transverse diameter ("r" = +0.209), the data were analyzed with use of a formula suggested by McNemar.9 This formula can be applied to correlated data as in the present instance,* Calculation of the data of table 1 gives a “t” value of 3.56, which indicates that the difference between both correlation coefficients is significant at a p < 0.001 level.

The data were also analyzed by comparing the mean transverse diameters of groups segregated according to the medians of systolic and diastolic pressure. The results are shown in table 2. The differences in mean transverse

*The formula is

\[
t = \frac{(r_{12} - r_{13}) \sqrt{(N - 3) (1 + r_{23})}}{\sqrt{2 (1 - r_{12}^2 - r_{13}^2 + r_{23}^2 + 2 r_{12} r_{13} r_{23})}}
\]
Table 2

Differences between Mean Corrected Tranverse Diameters of 535 Hypertensive Patients When Grouped According to the Medians of the Systolic and Diastolic Pressures

<table>
<thead>
<tr>
<th></th>
<th>Diastolic pressure</th>
<th>Systolic pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median ↓</td>
<td>&gt; Median</td>
</tr>
<tr>
<td>Number of patients</td>
<td>280</td>
<td>255</td>
</tr>
<tr>
<td>Mean corrected transverse diameter</td>
<td>106.48%</td>
<td>109.63%</td>
</tr>
<tr>
<td>Difference</td>
<td>3.15%</td>
<td>7.08%</td>
</tr>
<tr>
<td></td>
<td>S.E.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.083</td>
<td>1.036</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.005</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Difference between differences</td>
<td>3.93%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>S.E.</td>
<td>1.499</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

The median diastolic pressure was 107 mm Hg and the median systolic pressure was 164 mm Hg.

diameters are very significant regardless of the pressure used. However, the difference is significantly greater for the systolic than for the diastolic pressure (p < 0.01). This evidence also points to a significantly greater association of the transverse diameter with the systolic than with the diastolic pressure.

Because of the strong correlation between systolic and diastolic pressure ("r" = +0.764), an attempt was made to determine the independent association of each pressure with the transverse diameter. The formula excludes mathematically the partial effect of each pressure.* When the calculation is done with the data of table 1, the correlation coefficient which remains after the exclusion of the partial effect of diastolic pressure is +0.238, which is significant at a p < 0.001 level. However, after the exclusion of the partial effect of systolic pressure, the correlation coefficient which remains for the association between diastolic pressure and transverse diameter is -0.045, which is not significant.

The combined correlation of both the systolic and diastolic pressures with the transverse diameter was also determined by calculating the multiple correlation coefficient "R." The multiple correlation coefficient for our data is +0.313. It will be noted that this coefficient is practically the same as the correlation coefficient of the systolic pressure alone with the transverse diameter.

The results suggest that the diastolic pressure is not truly associated with the transverse diameter. In other words, the correlation between diastolic pressure and transverse diameter may be significant only because most individuals who have diastolic hypertension also have systolic hypertension, and it is the latter pressure that carries the correlation with the transverse diameter.

If systolic pressure correlates better than diastolic pressure with the transverse diameter, pulse pressure should also correlate positively with the transverse diameter. To test this point the correlation coefficient between pulse pressure and transverse diameter was calculated in the 535 patients. The coefficient obtained was +0.269, which is highly significant (p < 0.001).

The correlation coefficient was also calculated between the transverse diameter and a mean pressure estimated according to the formula: mean pressure = diastolic pressure + pulse pressure. The value obtained was 3

+ 0.277, which falls between the values for diastolic pressure and systolic pressure.

The relationship of age to the correlation between systolic pressure and transverse diameter is shown in table 3. As shown by the p values, these correlation factors are highly

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*The formula is

\[ r_{12.3} = \frac{r_{12} - (r_{13} r_{23})}{\sqrt{(1 - r_{13}^2) (1 - r_{23}^2)}} \]
significant although the degree of association they express is relatively small. The results admit the possibility that age might be the underlying reason for the relationship between systolic pressure and transverse diameter.

Correlation coefficients are inaccurate when the distribution of one of the variables is abnormal. The 535 patients exhibit the bimodal age distribution characteristic of the veteran population. There are peaks at 42.0 and 62.26 years corresponding to the major armed conflicts. These peaks introduce a lack of homoscedasticity in the age axis of the scattergram and therefore restrict the significance of the correlation coefficients obtained.

In order to determine if age is the underlying reason for the association between systolic pressure and transverse diameter, the relationship was studied in two different age groups selected arbitrarily (fig. 3). The first group consisted of 99 patients of 30 to 40 years of age and the second of 155 patients of 60 to 70 years of age. In the first group there were 43 patients with a systolic pressure above 160 mm. Hg and 56 patients with a systolic pressure below 160 mm. Hg. In the second group the corresponding figures were 102 and 53 patients. Within each group those patients with the higher systolic pressures had significantly greater transverse diameters than those patients with the lower systolic pressures. The levels of significance were \( p < 0.001 \) in the 30 to 40 year group and \( p < 0.002 \) in the 60 to 70 year group.

**Discussion**

From the point of view of the complications associated with increase in the transverse diameter of the heart, the findings of the present study are inconsistent with the importance customarily given to diastolic pressure in the evaluation of the cardiac status of hypertensive patients. In fact, calculation of the index of forecasting efficiency indicates that in predicting the transverse diameter, the diastolic pressure increases the efficiency by only 2.2 per cent. The systolic pressure is also quite poor for this purpose. The same calculation indicates that the systolic pressure increases the efficiency for predicting the transverse diameter by only 4.37 per cent. Therefore, although the transverse diameter is significantly better associated with the systolic than with the diastolic pressure, the difference is of little practical importance in individual patients. Nevertheless, if one pressure were to be chosen to evaluate this particular aspect of the cardiac status of hypertensive patients, it would have to be the systolic rather than the diastolic pressure.

**Table 3**

Correlation Coefficients ("r") between Systolic Pressure, Corrected Transverse Diameter and Age in 535 Compensated Hypertensive Patients

<p>| | | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Systolic vs. corrected transverse diameter</td>
<td>+0.310 ((p &lt; 0.001))</td>
<td>(r_{12})</td>
</tr>
<tr>
<td>Age vs. corrected transverse diameter</td>
<td>+0.225 ((p &lt; 0.001))</td>
<td>(r_{23})</td>
</tr>
<tr>
<td>Systolic vs. age</td>
<td>+0.1708 ((p &lt; 0.001))</td>
<td>(r_{13})</td>
</tr>
</tbody>
</table>

**Figure 3**

The mean transverse diameter in 99 patients of 30 to 40 years of age and in 155 patients of 60 to 70 years of age when each group is divided into those with a systolic pressure either above or below 160 mm. Hg. Corrected transverse diameter is expressed as percentage of normal.
The accuracy of the methods used in the present investigation needs to be considered. It was already reported⁴ that in patients of the present study treated double blind with placebos, the baseline blood pressure determined as described previously was almost identical to the average blood pressure obtained daily by the patients in their homes. This observation indicates that the baseline pressure here used represents a fair approximation to the usual blood pressure to which the patients are exposed.

It has long been known that arterial blood pressure cannot be measured with precision by a pneumatic cuff manometer. Nevertheless, because of the convenience and simplicity of the auscultatory method, it is generally regarded as an adequate bedside procedure to estimate blood pressure.

There is uniform agreement that the systolic pressure should be read at the start of sounds. In practice there is little difficulty in recognizing this point. In the case of the diastolic pressure, although it is generally accepted that the disappearance of all sounds is the best index,¹⁰ agreement is not universal.¹¹ Under certain hemodynamic circumstances, cessation of sounds does not occur and the muffling of sounds must be used as the end point. In practice there is no question that at times it is difficult to determine where the sounds disappear and then it is necessary to use the muffling point.

It is possible that enough such instances may have occurred in the large number of observations of the present study to increase significantly the scatter of the diastolic pressure determinations over that of the systolic pressure. It has been shown, however, that the mean error of determination of clinical blood pressure measurement is similar for both systolic and diastolic pressures.¹⁰ In our data the standard error of the estimate to predict pressure from heart size is 23.04 mm. Hg for the systolic pressure and 13.56 mm. Hg for the diastolic pressure. This indicates that the variability of the systolic pressure is considerably larger than that of the diastolic pressure. For these reasons it seems unlikely that error of determination can account for the significantly different association of both pressures with the transverse diameter.

The transverse diameter was used as a measure of heart size because it was practical and feasible to standardize its determination in the participating hospitals. Admittedly, the accuracy of the method is less than that attainable with other methods such as biplane angiography. On the other hand, other methods do not lend themselves as well to application in many subjects in different institutions. The large number of observations made possible by the use of the transverse diameter compensates in part for the inaccuracy of the method by diminishing the statistical standard errors.

An estimate of the relative accuracy of the transverse diameter may be obtained from the following comparisons. In a sample of 101 patients of the present study the correlation coefficient between transverse diameter and cardiac volume was +0.802 (fig. 4). This indicates a rather satisfactory agreement between the transverse diameter and a measure of heart size, which is generally considered to be more exact. In a sample of 41 unselected patients not of the present study who died in...
Figure 5
The scattergram of the transverse diameter versus empty heart weight in 41 unselected males showing regression line and standard error of the estimate.

our hospital within 6 months after having a teleroentgenogram, the transverse diameter was correlated with the actual weight of the empty heart at autopsy (fig. 5). The correlation coefficient obtained was +0.882 and the standard error of the calculated line of regression was 61.79 Gm. This compares with a standard error of 23.3 Gm. which Dodge et al. obtained for the prediction of left ventricular mass using biplane angiography. The comparison is not too unfavorable, since the angiographic studies were done postmortem on hearts under controlled conditions. Biplane angiography is regarded as the most accurate available method to determine left ventricular mass in vivo.

In view of these observations it seems unlikely that the poor correlations between pressures and transverse diameter obtained in the present study can be explained on the basis of relative inaccuracy of the measurements. It is worth noting that comparably low levels of correlation which barely suggest a linear relationship have been reported in anatomicopathologic studies of mean pressure and left ventricular weight. The obvious conclusion is that the association between cardiac size and hypertensive disease is in all probability a multifactorial complex in which the level of pressure is but one of the important components.

It is generally believed that, barring the possibility of intrinsic myocardial changes, heart size increase in hypertension is probably the result of increased cardiac work. Cardiac work may be expressed according to the formula:

\[
W = QR + \frac{M(V)^2}{2g} \text{Kg. m./sec.}
\]

Where \( W \) = work in Kg. m./sec.
\( Q \) = cardiac output in liters/sec.
\( R \) = mean pressure in meters.
\( M \) = blood mass expelled in Kg./sec.
\( V \) = blood velocity in meters/sec.
\( g \) = gravity constant (9.81 m./sec.)

The static component is usually considered to be the major factor of cardiac work. The formula shows the reason why an increase in pressure results in an increase in cardiac work. It should be noted, however, that an increase in flow can also result in an increase in cardiac work.

Sarnoff et al. have shown that external cardiac work is directly proportional to myocardial oxygen consumption only when the increase in work is due to increase in mean systolic pressure. When the increase in external work is due to increase in flow, the oxygen consumption is not increased and the ratio of extrinsic work to oxygen consumption indicates a high external myocardial efficiency. In contrast, systolic hypertension causes an increase in oxygen consumption which leads to relative myocardial hypoxia. The ratio of extrinsic work to oxygen consumption is decreased, indicating a low external myocardial efficiency.

After differentiating experiments Sarnoff et al. found that the mean systolic pressure is not the fundamental determinant of myocardial oxygen consumption. Myocardial oxygen consumption actually correlates best with the tension-time index which is defined as the product of the mean systolic pressure and the
duration of the tension state. Nevertheless, these authors observed in their flow experiments that whenever there was an increment in myocardial oxygen consumption, it was consistently a function of the associated increment in aortic systolic pressure; this was true at different ranges of cardiac output, flow, and pressure.

Burch et al.\textsuperscript{16} have shown that the structure and mechanisms of the normal heart are such that it exerts less force per unit cross section at the end of systole than at the isometric phase of contraction. Therefore, at the end of systole the normal heart consumes less oxygen and economizes effort even though the internal tension is higher. This economy is possible because according to the law of Laplace, the shortening of the integrated ventricular radii of curvature during systole permits the development of more internal tension with less force and less oxygen consumption.

In the pathologically dilated heart, the integrated ventricular radii of curvature do not shorten enough at the end of systole to permit an economy of energy. The wall is at a mechanical disadvantage. The total internal systolic tension cannot be developed unless the force per unit of cross section increases and more oxygen is consumed. If systolic hypertension is present, it adds its own increased oxygen consumption to that required by the dilatation.

Linzbach\textsuperscript{17} believes that the ratio of oxygen consumption to heart mass is one of the most important biologic settings of the body. He is of the opinion that for any level of oxygen consumption there is an optimal amount of heart muscle which yields the maximum energy economy. Therefore, when oxygen consumption is increased, the stimulus to hypertrophy may reside in an adjustment mechanism which restores the best energy economy ratio of heart mass to oxygen consumption by increasing the heart mass.

These concepts are in agreement with the findings of the present study. They point to the systolic load rather than the diastolic load as the one principally responsible for the enlargement of the heart in hypertensive disease. Unquestionably, there are other factors involved among which may be mentioned metabolic changes in the myocardium, neurohormonal mechanisms, and those factors leading to cardiac dilatation. It is difficult to quantitate their effects, particularly under the changing circumstanes of daily life. irrespective of other factors, the findings of the present study suggest that systolic pressure rather than diastolic pressure is relatively important in determining clinical cardiac enlargement in hypertension.

In view of these observations, the question why hypertensive patients exhibit more or less systolic hypertension for any given level of diastolic pressure may have considerable importance. A possible explanation is the well-known fact that when the distensibility of the large arteries is reduced, systolic pressure increases. The reduced distensibility could be due to the same process that increases the peripheral resistance or to arteriosclerosis. Another possible explanation is that the level of systolic pressure may depend on cardiac hemodynamic changes that affect pressure and flow in hypertension.\textsuperscript{18} Overfilling of the aorta with blood under increased pressure may lead to a maximal stretching of the aortic wall, which restricts further distention. The findings of the present study do not clarify this question, although the fact that the association of the systolic pressure with the transverse diameter is independent of age might suggest that a degenerative process is not involved.

Cardiac enlargement is accepted as a significant prognostic index in hypertensive disease. In untreated patients, graded degrees of cardiac enlargement have been associated with progressively higher mortality rates irrespective of age and sex.\textsuperscript{19} In our own experience, hypertensive patients in congestive heart failure have larger hearts than those without. In addition, those patients who have significantly larger hearts tend to go more frequently into congestive heart failure than those who do not. In view of these observations the relationship between systolic pressure and cardiac enlargement appears to be of

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clinical importance in the diagnosis, prognosis, and therapy of hypertensive patients. It is considered likely that this relationship may account in part at least for the actuarial data quoted at the beginning of this article, which link progressive increases of systolic hypertension with a higher mortality.

Summary
In 535 male hypertensive patients the correlation coefficient between the corrected transverse diameter of the heart and the systolic pressure was +0.301. With diastolic pressure the correlation coefficient was +0.209. Both coefficients were significant (p < 0.001), but the association between the variables was quite small in both correlations. The correlation between the corrected transverse diameter and the systolic pressure was significantly better than with the diastolic pressure, (p < 0.001). The correlation between the corrected transverse diameter and the systolic pressure was independent of age.

Conclusion
From the point of view of the complications associated with increase in the transverse diameter of the heart, the findings presented are inconsistent with the importance customarily given to diastolic pressure in the evaluation of the cardiac status of hypertensive patients. Both systolic and diastolic pressures correlate poorly with the transverse diameter of the heart. Nevertheless, if one pressure were to be chosen to evaluate this particular aspect of the cardiac status of hypertensive patients, it would have to be the systolic rather than the diastolic pressure.

These findings agree with physiologic concepts that link systolic pressure, oxygen consumption, cardiac mechanics, and the size of the heart. If diminished aortic distensibility or hemodynamic cardiac changes are involved in the pathogenesis of a high systolic pressure, they may represent significant adverse factors in hypertensive disease.

Since cardiac enlargement is a significant prognostic factor in hypertensive disease, the findings of the present study may explain, at least in part, the reported association between progressive increases of systolic hypertension and a higher mortality. By the same token, the relationship between systolic hypertension and cardiac enlargement appears to be a significant clinical observation in the diagnosis, prognosis, and therapy of hypertensive patients.

Acknowledgment
I am indebted to Dr. Edward Freis for his helpful criticism and stimulating support, and acknowledge the help of Mrs. Esther V. Aviles and Mrs. Carmen C. Rivera in the secretarial and statistical work.

References
12. Dodge, H. T., Rackley, C. E., Coble, Y. D.,


Historical Perspective

Some scientists regard an interest in the history of their subject as mere antiquarianism, and it may be that the very remote past consists largely of mistakes to be avoided. But it deserves to be remembered that the history of any scientific discipline intimately determines the current modes of investigation. The frames of reference which appear eligible at any given epoch, the instruments accepted as respectable, and the types of "fact" taken to have evidential value are historically conditioned. To pretend otherwise is to claim for human reason, as manifested in scientific progress, a universality and fixity it has never manifested.—MAX BLACK. The Definition of Scientific Method, Science and Civilization, Edited by ROBERT C. STAUFFER, The University of Wisconsin Press, Madison, 1949.
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