Wave Reflection in Systolic Hypertension: Smaller Stature, Shorter Aorta: Higher Pulse Pressure?

Tom Richart, Tatiana Kouznetsova, Harry Struijker-Boudier and Jan A. Staessen

Hypertension 2008;51:e37-; originally published online Apr 7, 2008; DOI: 10.1161/HYPERTENSIONAHA.108.110254

Hypertension is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 75231

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Wave Reflection in Systolic Hypertension: Smaller Stature, Shorter Aorta: Higher Pulse Pressure?

To the Editor:

In a recent issue of Hypertension, Mitchell et al\(^1\) suggested that, among patients with systolic hypertension, reduced aortic diameter and increased wall stiffness, rather than premature wave reflection, are primarily responsible for increasing pulse pressure (PP). We share the concerns gently expressed in the accompanying editorial\(^2\) that conceptual and methodologic issues do not substantiate the conclusions put forward by Mitchell et al.\(^1\)

First, the authors subdivided their patients according to median PP. This arbitrary dichotomization of the study population led to an overrepresentation of women with small stature in the high PP group (56% versus 28%). Body height averaged 166 cm as opposed to 172 cm in the high and low PP groups, respectively. This imbalance might flaw the interpretation of the results as proposed by Mitchell et al.\(^1\) Indeed, at similar heart rates, early wave reflection and, hence, systolic augmentation occur more readily in shorter individuals because of the shorter length of the aorta. Small stature is associated with increased peak systolic pressure and shorter travel time of reflected waves.\(^3\) In a recent longitudinal study by Regidor et al,\(^4\) short stature was independently associated with increased PP in women. In the same study, height was inversely associated with systolic blood pressure but positively with diastolic blood pressure, although an independent association between height and diastolic blood pressure was found only in women.\(^4\)

Second, in Figure 3, Mitchell et al\(^1\) pooled women and men without providing any statistical evidence that the regression lines in the sexes were coincident, with no differences in intercepts or slopes.

Third, cyclic overstretching of the proximal aorta by elevated peak systolic blood pressure and subsequent elastin fracture contribute to the stiffening of the central arteries. We calculated the wall tension at the level of the aortic root as described by Laplace's law (Table) from the diameter and systolic and diastolic blood pressures, while assuming a 0.125 wall:radius thickness ratio, because no direct measurement of wall thickness was available in the article by Mitchell et al.\(^1\) The wall tension in the high PP group appears to be higher (Table). The impedance mismatch in individuals with both a small outflow tract and smaller stature might predispose the proximal aorta to earlier mechanical wear.

We conclude that the 2 hypotheses on the pathogenesis of increased PP (small aortic outflow diameter versus increased wave reflection through arterial stiffening) might not be mutually exclusive. Only properly conducted longitudinal studies, not the analysis of an arbitrarily subdivided cross-sectional study, can inform a definite conclusion. Future studies should also include a proper quantification of “pump-and-tubing” geometry through state-of-the-art imaging techniques to avoid the use of the Moens-Korteweg equation for more objective results.

Disclosures

None.

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<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aortic Root Diameter, Mean±SD, cm</th>
<th>Systolic Blood Pressure, Mean±SD, mm Hg</th>
<th>Estimated Wall Thickness, mm</th>
<th>Tension at Aortic Root, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PP</td>
<td>2.99±0.36</td>
<td>173.5±12.0</td>
<td>0.184</td>
<td>2.86115</td>
</tr>
<tr>
<td>Low PP</td>
<td>3.13±0.28</td>
<td>155.7±9.5</td>
<td>0.195</td>
<td>2.59345</td>
</tr>
</tbody>
</table>

Values are point estimates for tension at the wall of the aortic roots.

(Hypertension. 2008;51:c37.)
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DOI: 10.1161/HYPERTENSIONAHA.108.110254
Letter to the Editor

Questions Regarding the Aortic Measurements of Mitchell et al

To the Editor:

Mitchell et al1 conclude that reduced proximal aortic diameters, in addition to wall stiffness, account for the increase in pulse pressure associated with systolic hypertension. This observation is surprising in view of the strong relations of aging to both systolic hypertension and progressive aortic dilatation. In their study, aortic diameter represented the "proximal aortic root" measured from 2D long-axis images. The average aortic root diameters reported in their Table 2 (3.13 ±0.28 cm in individuals with pulse pressure ≤75 mm Hg and 2.94 ±0.36 cm in individuals with pulse pressure >75 mm Hg) are surprisingly small given an average age of >60 years for the entire population and average body mass indices in the high-overweight to obese range. This may reflect measurement of aortic diameters just distal to the anulus but not at the maximum diameter of the sinuses of Valsalva, as specified in standard nomograms widely used to identify normal aortic diameters in relation to body surface.2 Thus, the authors should more precisely describe the location of their measurements. Of even greater pathophysiologic importance, hypertension-associated increases in aortic diameters measured from 2D echocardiographic images occur at the level of the supra-aortic ridge and in the proximal ascending aorta.3 Because reported dimensions appear to have been measured in the portion of the aorta that does not dilate in response to hypertension, the study conclusions should perhaps be tempered by the understanding that measurement at a slightly higher level in the proximal aorta might have altered the study findings by identifying an area where volume capacitance was greater, not less, in patients with higher pulse pressures.

Disclosures

None.

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2. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, St John Sutton M, Stewart WJ. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18:1440–1463.

(Hypertension. 2008;51:e38.)

Hypertension is available at http://hyper.ahajournals.org

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DOI: 10.1161/HYPERTENSIONAHA.108.112102

We thank Richart et al1 and Roman and Devereux2 for their careful reading of our article3 and thoughtful feedback. Richart et al1 raise 3 points, described below.

First, dichotomization of the sample at the overall median pulse pressure led to overrepresentation of women, who are shorter, in the high pulse pressure group. Wave reflection may have contributed substantially to higher pulse pressure in these shorter individuals. Second, in our Figure 3, women and men are pooled without any evidence that the slopes of the regression lines are the same in men and women. Third, peak wall tension seems to be higher in the proximal aorta in the high pulse pressure group and may have contributed to premature mechanical wear and consequent wall stiffening.

They conclude that contributions of smaller diameter and increased wave reflection to increased pulse pressure may not be mutually exclusive and add that only properly conducted, longitudinal studies, not the analysis of an arbitrarily subdivided cross-sectional study, can inform a definite conclusion.

Regarding dichotomization of the sample at the median pulse pressure, we wish to point out that the primary pulse pressure model, presented in our Table 3 and Figure 3, considered pulse pressure as a continuous variable. Furthermore, as noted in the article, the models in Table 3 were also run separately for men and women to test for effect modification. Those results are summarized on page 106,3 top of the left column. In essence, pulse pressure was related inversely to diameter and directly to wall stiffness in men and women; however, wave reflection and mean pressure did not enter the model in men. In response to this letter, we tested an interaction term between aortic diameter and sex in the pulse pressure model (Table 3, model 3), and it was not significant ($P=0.37$). Furthermore, we compared the slopes of the relations between pulse pressure residual and diameter (Figure 3A) for men versus women, and they did not differ ($P=0.27$). Therefore, smaller aortic diameter is associated with higher pulse pressure in men and women in our sample.

Regarding peak wall tension, we would first like to note that wall thickness is not needed to compute wall tension. We agree that improper matching between aortic diameter and sex in the pulse pressure model (Table 3, model 3), and it was not significant ($P=0.37$). Furthermore, we compared the slopes of the relations between pulse pressure residual and diameter (Figure 3A) for men versus women, and they did not differ ($P=0.27$). Therefore, smaller aortic diameter is associated with higher pulse pressure in men and women in our sample.

Regarding separate contributions of reduced diameter and increased wave reflection to elevated pulse pressure, we refer the authors to epidemiological observations first made in the Framingham Offspring Study and confirmed in several large studies.4 Augmentation index, a measure of wave reflection, increases dramatically before 50 years of age, at a time when brachial pulse pressure changes little or actually falls. Augmentation index then plateaus or falls after 60 years of age, at a time when pulse pressure increases dramatically. These simple observations suggest that the contributions of early wave reflection to elevated pulse pressure are likely to be modest, consistent with the model that we have presented in our Table 3. We strongly agree with the authors and with Vasan,5 who, in his editorial commentary, underscored the urgent need for a more detailed assessment of the contribution of regional aortic properties (wall thickness and stiffness and lumen diameter) to systemic hemodynamics.

Roman and Devereux2 raise 3 points, described below.

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and flow with the hope that new treatments directed at the primary problem (excessive forward pressure wave amplitude) may be discovered.

Disclosures

None.

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