Heart Rate, Arterial Stiffness, and Wave Reflections in Paced Patients

Pierre Albaladejo, Xavier Copie, Pierre Boutouyrie, Brigitte Laloux, André Descorps Déclère, Harry Smulyan, Athanase Bénétos

Abstract—Elevated heart rate (HR) and pulse pressure (PP) have a cumulative effect on cardiovascular risk, with the exception of HR ≥100 bpm. How an increase in HR may influence the PP level has never been investigated. In 11 patients with pacemaker monitoring, aortic (pulse-wave analysis) and digital (photoplethysmographic device) blood pressure were measured at 3 different levels of HR, together with determinations of carotid dimensions (echo tracking technique), wave reflections (pulse-wave analysis), and aortic pulse-wave velocity. Increased HR is associated with the following: (1) a significant increase of digital systolic, diastolic, and mean blood pressure; (2) a significant reduction of digital and carotid PP, with a more pronounced reduction of the carotid than of the digital PP, resulting in a significant PP amplification; and (3) a reduction in the time required for the backward pressure wave to return toward the heart, without any change of arterial stiffness. Increased HR significantly enhances PP amplification, leading to an increase of peripheral blood pressure without comparable change in central blood pressure. These results are important to consider for a better understanding of cardiovascular risk and the mechanism of white-coat hypertension. (Hypertension. 2001;38:949-952.)

Key Words: pacemaker ■ arteries, stiffness ■ heart rate ■ hypertension, white coat

Epidemiological studies have shown that heart rate (HR) is a significant risk factor for cardiovascular (CV) and non-CV death (see review1). Nevertheless, the predictive role of HR on CV risk has been observed in the overall population but primarily in subjects with hypertension.1,2 This observation suggests that HR and brachial arterial blood pressure act synergistically in the development of CV complications, a finding widely accepted for systolic blood pressure (SBP) and diastolic blood pressure (DBP).2,3 Regarding the synergistic effect of brachial pulse pressure (PP) and HR on CV risk, Thomas at al3 have observed that a cumulative effect is indeed observed, but only within certain limits. The synergistic effect was lost in men when the PP was >63 mm Hg and the HR was >100 bpm.3 This finding is not unexpected, because for a given cardiac output, increased HR results in a parallel decrease in stroke volume, which is one of the main hemodynamic factors influencing PP.

In terms of hemodynamic mechanisms, PP is a very complex parameter. PP is determined not only by the ejection pattern of the left ventricle but also by aortic stiffness and the amplitude and timing of wave reflections. The PP propagates along the arterial tree, with higher PP values in peripheral (brachial, radial, and digital) arteries than in central (aortic and carotid) arteries. The relationship between central and peripheral PP is determined by transfer functions, which are known to be highly frequency dependent.4 O'Rourke5 has shown that left ventricular ejection time (LVET) is negatively related to aortic to brachial amplification, a finding implying that PP amplification is likely to increase with HR and, thus, to be responsible for significant differences between aortic and brachial SBP and DBP levels.

The aim of the present study was to evaluate, in subjects with pacemaker monitoring, the influence of acute changes in HR on PP amplification and, hence, on SBP and DBP measured at different arterial (digital and carotid) locations. It will be shown that these changes in amplification may have a significant influence on both the diagnosis and the epidemiologic aspects of hypertension.

Methods

Six men and 5 women (age 69±14 [mean±1 SD] years) who were undergoing regular evaluation of pacemaker monitoring were included in the study; the diagnoses had been as follows: atrioventricular block (n=6), sick sinus syndrome (n=5), dilated cardiomyopathy (n=3), and miscellaneous (n=5). Body weight and height were 66±13 kg and 166±10 cm, respectively. Supine SBP and DBP after 15 minutes of rest were 128±26 and 74±13 mm Hg, respectively; HR was 77±11 bpm. Eight patients had antihypertensive therapy involving diuretics (n=7), β-blockers (n=5), calcium antagonists (n=5), and miscellaneous (n=4), alone or in combination.
The present study was performed in patients between 9:00 and 11:00 AM after 15 minutes of rest. Supine mean blood pressure (MBP), SBP, and DBP were measured automatically on the left arm with a Dinamap apparatus and on the opposite arm with the use of a finger photoplethysmographic device (Finapres, Ohmeda). Subjects rested 10 minutes between each set of measurements. The average time to perform all measurements for the 3 different HRs was 90 minutes. No discomfort, syncope, or chest pain occurred in any patient. From the carotid artery waveform measured with a Dinamap apparatus and on the opposite arm with the use of a finger photoplethysmography (45.2±10.1 mm Hg) and by radial tonometry (46.4±9.8) were compared, resulting in a difference of −1.9±5.2 mm Hg.

In each individual, 3 different levels of HR were chosen. All beats were paced from the atrium. The upper and lower limits of HR were constantly between 40 and 130 bpm. The lower HR (>40 bpm) was that below which there was a spontaneous rhythm, and the upper HR limit (<130 bpm) was chosen to avoid any clinical discomfort. The middle HR value was determined as the average value between the lower and upper HRs. Hemodynamic measurements at each HR level were randomized according to the Latin square method. Informed consent was obtained from all subjects after a detailed description of the procedure.

After the setting of each HR level, the subjects rested for 10 minutes. Then digital blood pressure, carotid arterial diameter and PP, and carotid-femoral pulse-wave velocity (PWV) were measured successively for the corresponding HR, with the use of validated methods. Subjects rested 10 minutes between each set of measurements. The average time to perform all measurements for the 3 different HRs was 90 minutes. No discomfort, syncope, or chest pain occurred in any patient. From the carotid arterial waveform measured by aplanatic tonometry, the calculated parameters were as follows: PP; the difference in pressure from the early (Pk) to the late (Pi) systolic peaks (Pk–Pi); the augmentation index, (Pk–Pi)/PP; the travel time from the foot of the pressure wave to the inflection point (Dtp); and LVET. Diastolic decay and carotid compliance and distensibility were calculated as previously described.

Statistical analysis was performed with StatView 5 software (SAS Institute Inc). ANOVA for repeated measures was used. Post hoc analysis was performed by use of paired t tests with P<0.05.

### Results

Low and high HR measurements were 32% (20% to 50%) below and above the middle HR measurements. The RR-interval difference between middle and low HR (357±191 milliseconds) was significantly higher than the interval between high and middle HR (164±55 milliseconds). When the totality of measurements was analyzed in the overall population, there was a positive relationship between mean carotid PP and RR intervals (data not shown).

The Figure shows carotid and digital SBP and DBP at low, middle, and high HR. There was a significant increase in digital (and carotid) DBP between the low, middle, and high HR groups (P<0.01). For digital blood pressure measurements, there was a significant increase in SBP in the middle and high HR group (149±25 and 150±27 mm Hg, respectively) compared with the low HR group (134±31 mm Hg) (P<0.05). For carotid pressure measurements, there was no significant increase in SBP from low to middle and high HR (133±34, 135±22, and 137±28 mm Hg, respectively).

The Table shows that (1) MBP was significantly higher at middle and high HR compared with low HR (P<0.01); (2) digital PP decreased significantly, but only between middle and high and not low HR (P<0.01); and (3) carotid PP was significantly lower for middle and high HR compared with low HR (P<0.01). The decrease in carotid PP was mainly due to a significant increase in DBP (Figure). Compared with digital PP, carotid PP decreased markedly. As a result, amplification between carotid and digital PP was significantly (P<0.01) higher at middle and high HR (19% and 23.6%, respectively) than at low HR (−6.4%). Although not significant, higher carotid to femoral PWV was noted in the high HR group, in parallel with the increase in MBP (Table).

The Table shows carotid artery changes in diameter between the 3 different HR groups. There was a significant decrease in percent change in diameter between high and low HR (P<0.01), which was mainly due to an increase in diastolic diameter (P<0.01) without a significant change in systolic diameter. The observed changes in carotid diameters paralleled those of blood pressure. Cross-sectional carotid compliance at MBP was not significantly different for the 3 levels of HR. The distensibility index at MBP was higher for the low HR than for the middle and high HRs (P<0.05), in relation to the significant changes in diastolic diameter.

Regarding carotid pressure waveform (Table), both LVET and diastolic time significantly decreased at high HR (P<0.01). Dtp decreased significantly (P<0.01) for high HR compared with low HR (P<0.01). A significant increase in the diastolic decay was observed at high HR (P<0.01). No significant change in the Pk–Pi difference was observed, whether measured in absolute or percent value.

### Discussion

In the present study, which was performed in subjects who regularly underwent pacemaker follow-up, high HR during pacing was associated with an increase in MBP and a decrease in central (carotid) and peripheral (digital) PP. The
Digital and Carotid Arterial and Pressure Waveform Changes and PWV Measurements

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Low HR</th>
<th>Middle HR</th>
<th>High HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, bpm</td>
<td>60.4±14.6</td>
<td>87.7±11.9*</td>
<td>114.2±12.7‡†‡</td>
</tr>
<tr>
<td>MBP, mm Hg</td>
<td>93±24</td>
<td>105±24*</td>
<td>111±26*§§</td>
</tr>
<tr>
<td>Digital PP, mm Hg</td>
<td>54±22</td>
<td>56±21</td>
<td>48±21‡</td>
</tr>
<tr>
<td>Carotid PP, mm Hg</td>
<td>54±17</td>
<td>42±10*</td>
<td>35±10‡</td>
</tr>
<tr>
<td>Amplification of Car to digital PP, %</td>
<td>−6.4±25.4</td>
<td>19±21*</td>
<td>23.6±13.4*</td>
</tr>
<tr>
<td>Car-femoral PWV, m · s⁻¹</td>
<td>17.9±6.7</td>
<td>20.2±8.3</td>
<td>21.5±9.1</td>
</tr>
<tr>
<td>Car Dd, mm</td>
<td>6.73±0.96</td>
<td>6.93±0.96</td>
<td>7.10±0.81*</td>
</tr>
<tr>
<td>Car De, mm</td>
<td>7.10±0.98</td>
<td>7.18±1.0</td>
<td>7.34±0.86</td>
</tr>
<tr>
<td>Car De−Dd, μm</td>
<td>369±109</td>
<td>250±82*</td>
<td>239±81*</td>
</tr>
<tr>
<td>Car (Ds−Dd/Dd, %)</td>
<td>5.55±1.59</td>
<td>3.58±1.0*</td>
<td>3.33±1.01*</td>
</tr>
<tr>
<td>Car compliance, 10⁻⁵ · mm² · Pa⁻¹</td>
<td>421±139</td>
<td>404±112</td>
<td>447±171</td>
</tr>
<tr>
<td>Car distensibility, AU</td>
<td>741±227</td>
<td>469±127†</td>
<td>409±63†</td>
</tr>
<tr>
<td>Car Pk−Pi, mm Hg</td>
<td>10.3±7.5</td>
<td>6.5±6.3</td>
<td>4.8±3.0</td>
</tr>
<tr>
<td>Car (Pk−Pi)/PP, %</td>
<td>12.8±7.4</td>
<td>13.2±12</td>
<td>10.4±5.7</td>
</tr>
<tr>
<td>Car Dtp, ms</td>
<td>140±34</td>
<td>112±34</td>
<td>104±23*</td>
</tr>
<tr>
<td>Fmin</td>
<td>3.89±1.22</td>
<td>4.88±1.51</td>
<td>5.08±1.05*</td>
</tr>
<tr>
<td>LVET, ms</td>
<td>311±35</td>
<td>262±18</td>
<td>230±12‡</td>
</tr>
<tr>
<td>Diastolic time, ms</td>
<td>759±277</td>
<td>457±113</td>
<td>353±74‡‡</td>
</tr>
<tr>
<td>Diastolic decay, mm Hg/s</td>
<td>45.2±26.8</td>
<td>54.7±22.4</td>
<td>59.7±28.5*</td>
</tr>
</tbody>
</table>

Car indicates carotid; Dd, diastolic diameter; Ds, systolic diameter; AU, arbitrary units; Pk−Pi, maximal peak of blood pressure curve minus inflection point (absolute pressure amplification); (Pk−Pi)/PP, relative pressure amplification; Dtp, travel time of reflected wave from the foot of pressure wave to Pi; and Fmin, first minimum frequency of impedance modulus. Values are mean±SD.

*P<0.01 and †P<0.05 vs low HR; ‡P<0.01 and §P<0.05 vs middle HR.

Because MBP was increased in parallel with the increase of HR and because the association of high HR and low stroke volume results in normal or low cardiac output, the weight of evidence suggests that during the investigation, peripheral vascular resistance was increased markedly, in parallel with the increase of HR and MBP.

In the past, several investigations involving young and middle-aged patients have shown that PP tends to be lower in the central than in the peripheral arteries. Because MBP was increased in parallel with the increase of HR and because the association of high HR and low stroke volume results in normal or low cardiac output, the weight of evidence suggests that during the investigation, peripheral vascular resistance was increased markedly, in parallel with the increase of HR and MBP.

In the past, several investigations involving young and middle-aged patients have shown that PP tends to be lower in the central than in the peripheral arteries. This physiological difference in PP tends to disappear with aging. In the present study, this hemodynamic pattern was readily observed when subjects were investigated under baseline conditions and particularly in the presence of low HR (Figure). However, it has been previously shown that at any age, an increased HR (and, thus, a shortened ventricular ejection) will decrease PP but increase pulse amplification. The decreased PP is due in part to an increase of DBP, which in turn is due to a combination of the pacing-induced increase in diastolic decay and reduced diastolic time. Stroke volume was also probably reduced as a consequence of pacing, but carotid SBP did not change, probably because of a shortened LVET and the elevated baseline PWV. Finally, the major point to emphasize in the present study is that the PP decreased less with tachycardia in peripheral (digital) than in central (carotid) arterial territories, resulting in PP amplification. In the present study, the decrease in carotid PP at high HR was associated with a decrease in Dtp. Because the travel time of reflected waves was not associated with a significant change in central PP was significantly larger in magnitude than was the decrease in digital PP, resulting in a significant increase in central to peripheral PP amplification. These results were not associated with a significant change in carotid compliance or aortic stiffness but with a reduction in Dtp, thus suggesting a modification in the sites of pressure wave reflections and/or reflection coefficient levels.

These results were obtained for a specific population involving older paced patients with various CV diseases, mainly hypertension. Baseline aortic stiffness, as measured by PWV, was markedly increased in these subjects, with wide variations in PP, which is considered to be a typical finding in the aged (mean age of the population was 69 years). Hemodynamic consequences of pacing have been widely described in the literature. Increasing HR results in a decrease in left ventricular end-diastolic and stroke volume in subjects with normal hearts as well as in those with coronary and hypertensive heart disease or with dilated cardiomyopathy. In normal subjects, an increase in paced HR induces a rise in the cardiac index, but in patients with hypertension or cardiomyopathy, the cardiac index falls. Hence, it may be assumed that in our population of patients, increasing the HR resulted in a decrease in stroke volume and in cardiac index. These changes are in association with 2 properties of conduit arteries: (1) a marked increase in baseline aortic stiffness, which remained unmodified after pacing, and (2) a pacing-induced change in Dtp, which represents the change in the travel time of wave reflections during the investigation.
in arterial stiffness, the changed timing of reflected waves must have been due to a modification in the location of reflection sites. In the present study, the finding of increased MBP and probable increased peripheral vascular resistance favors this latter interpretation. Indeed, the sites of the resistance arterioles are the most effective reflectors of the primary pulse.5,15

Because the present study has shown that an increased HR results in an increased PP amplification between central and peripheral arteries, it appears that peripheral SBP and PP measurements may overestimate aortic SBP and PP in subjects with spontaneous tachycardia. Aortic blood pressure might be normal if aortic blood pressure could be measured. This observation may have important clinical implications for the understanding of white-coat hypertension.16 On the other hand, epidemiological studies by Thomas et al3 have shown that the association of HR and brachial PP has cumulative effects on all-cause and CV mortality except in the group of subjects with HR $\geq$100 bpm and PP $\geq$63 mm Hg. Outside these limits, it is likely that brachial PP is largely higher than aortic PP, because of this methodological error in the PP measurement that is due to the overestimation of brachial PP compared with aortic PP.

In conclusion, the present study has shown that increased HR has specific consequences on the peripheral PP level, resulting mainly in an increase in PP amplification. This amplification does not imply a change of arterial stiffness but only an altered interaction between stroke volume and the HR-altered wave reflections. This particular pattern may have important consequences for the clinical diagnosis of subjects with white-coat hypertension.

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References


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