Evaluation of Systolic, Diastolic, and Pulse Pressure as Risk Factors for Severe Coronary Arteriosclerotic Disease in Women with Unstable Angina Non-ST-Elevation Acute Myocardial Infarction

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Objective
To evaluate pressures assessed at the aortic root as risk factors for severe atherosclerotic coronary heart disease in women with unstable angina/compatible clinical history associated with increase in cardiac enzymes (total CPK and CK-MB) 2 times greater than the standard value used in the hospital, with the absence of new Q waves on the electrocardiogram (UA/NSTEMI).

Methods
Five hundred and ninety-three female patients with clinical diagnosis of UA/NSTEMI underwent cinecoronarography from March 1993 to August 2001, and the risk factors for CHD were studied. During examination the pressures, at the aortic root, and coronary obstructions were visually assessed by 2 interventional cardiologists, and those stenosis over 70% were considered severe.

Results
Eight-one per cent of the population was white and 18.3% was black. Mean age was 59.2±11.2 years, and it was significantly higher in patients with severe coronary lesions: 61.9 ± 10.8 years versus 56.4 ± 10.8 years; smoking, diabetes mellitus and climacteric were more frequent in patients with CHD. The average mean arterial pressure and mean systolic blood pressure was the same in both groups, however, average aortic diastolic pressure (17.6 ± 8.7 x 15.1 ± 8.1, p=0.001), and aortic pulse pressure were significantly greater in patients with CHD (7.5 ± 22 x 70 ± 19, p<0.002), while average right ventricle systolic blood pressure and pulse pressure were significantly greater in patients without CHD (79.8 ± 16 x 75.3 ± 17.5, p<0.003). In the multivariable analysis, pulse pressure ≥ 80 mmHg and systolic blood pressure ≥ 165 were independently associated with severe CHD with odds ratio of 2.12 and 2.09, p<0.05, respectively.

Conclusion
CHD is associated with increased pulse pressure and lower diastolic blood pressure in women with UA/NSTEMI. Although average systolic blood pressure has not been associated with CHD in this population, dichotomized values of pulse pressure ≥ 80 mmHg and systolic blood pressure ≥ 165 mmHg determined risk two times greater of severe coronary disease.

Key words
coronary arteriosclerotic disease, unstable angina, acute myocardial infarction, hypertension

Systolic blood pressure, diastolic blood pressure, and pulse pressure are well established as risk factors for cardiovascular disease 1. Pulse pressure is the result of cardiac contraction and the properties of arterial circulation, representing the pulsatile component of blood pressure 2. It is influenced by ejection fraction, large artery stiffness, early reduction of pulse wave, and also by heart rate 2. Mean blood pressure represents the steady component of blood pressure and is a function of left ventricular contractility, heart rate, and systemic vascular resistance 3.

Data from the Framingham study 4 show that systolic blood pressure increases continuously with age in all groups, whereas diastolic blood pressure increases until the age of 60 and then decreases. Epidemiological studies have shown that the increase in systolic blood pressure and pulse pressure is more often related to coronary events, while diastolic hypertension is more often related to stroke 5,6. These pressures may be assessed noninvasively with a sphygmomanometer and, invasively, in a peripheral artery or at the aortic root. It is still not clear what kind of pressure, isolated or combined, has a better correlation with cardiovascular events. A recent study 7 showed that the average of systolic, diastolic, and mean blood pressure was a strong predictor of cardiovascular disease in young men (<60 years), whereas average systolic blood pressure or pulse pressure was a more important predictor in older men (>60 years).

The objective of this study was to evaluate pressures assessed at the aortic root as risk factors for severe atherosclerotic coronary heart disease in women with unstable angina/compatible clinical history associated with increase in cardiac enzymes (total CPK and CK-MB) 2 times greater than the standard value used in the hospital, with the absence of new Q waves on the electrocardiogram (UA/NSTEMI).

Methods
From March 1993 to August 2001, 6,135 cardiac catheterizations were performed in an acute care hospital in São Paulo State, of which 645 were performed in women with a diagnosis of UA/NSTEMI.

Before the procedure, patients underwent a standard clinical history that included data concerning previous cardiovascular risk factors. We included in these factors: systemic arterial hyper-
tension, diabetes mellitus type 1 or 2, smoking status, use of oral contraceptive, lack of exercise, family history of cardiovascular disease, climacteric, and dyslipidemia (information provided by the patient).

Diabetes mellitus – We considered diabetic patients to be those with a history of diabetes mellitus, treated with diet or oral hypoglycemic drugs, insulin, or both.

Family history of cardiovascular disease (CVD) – We included in the family history of CVD, systemic blood hypertension and stroke. The age of occurrence was not investigated.

NSTEMI – Compatible clinical history associated with an increase in cardiac enzymes (total CPK and CK-MB) 2 times greater than the standard value used in the hospital, with the absence of new Q waves on the electrocardiogram.

At the end of cardiac catheterization, left ventricle (LV) and aortic pressures were recorded on millimetric paper.

Left ventricle systolic and diastolic blood pressures, as well as aortic systolic and diastolic blood pressures were studied. Aortic pulse pressure was also assessed, defined as the difference between aortic systolic pressure and aortic diastolic pressure, similar to mean blood pressure calculated by the formula: 2xDP/3+SP/3, in that, DP = diastolic pressure and SP = systolic pressure.

Coronariography was performed using Sones or Judkins techniques, and the coronaries were recorded in several orthogonal projections. All main coronary vessels and their branches, bypass, and mammary grafts were visually analyzed by 2 experienced interventional cardiologists, without knowledge of the patient’s data, including the diagnosis of unstable angina (UA) or NSTEMI. Vascular stenosis visually ≥ 70% was considered severe 8,9.

Ejection fraction was assessed through left ventriculography in the right anterior oblique projection at the hemodynamic laboratory of the Universidade Federal de São Paulo (University of São Paulo), using the Stanford method. It was always performed by the same technician, with specific training for this procedure. This method used angiographic contours during systole and diastole with a millimetric plate or a sphere of known diameter. When these 2 markers are not used, the catheter’s diameter used in the procedure becomes the reference. A caliper factor that varies according to the reference used has to have previously set limits to avoid distortions. In cases where ventriculography was not performed, ejection fraction was determined with echocardiography.

Non categorical variables were compared using the chi-square test; continuous variables with normal distribution were compared through the average, using the Student t test; and continuous variables without normal distribution were compared by averages and analyzed using the Mann-Whitney test. In the analysis of risk factors, a model of logistic regression was made involving all risk factors analyzed using the Mann-Whitney test. In the analysis of risk factors, variables without normal distribution were compared by averages and

Results

We analyzed 593 women; 52 patients were excluded due to lack of data in the chart before the examination or due to incomplete manometry records. Of the 593 patients, almost half (48%) came from the hospital ward, a third came from their houses, and only 16.5% came from the ICU. Unstable angina was present in 512 (86.3%) patients, and NSTEMI was present in 81 (13.7%). No difference existed in the diagnosis in either group (with or without severe CHD). Non-ST segment elevation myocardial infarction and unstable angina was the diagnosis in 47 patients (16.1%) and 245 patients (83.9%) with severe CHD versus 34 patients (11.3%) and 267 patients (88.7%) without severe CHD, respectively.

The mean age of this cohort was 59.2±11.2 years, ranging from 29 to 90 years. Patients with CHD were significantly older: 61.9 ± 10.8 years versus 56.4 ± 10.8 years. Of the risk factors for CHD, smoking, diabetes mellitus, and climacteric were more frequent in patients with CHD. No significant difference existed in relation to other risk factors. A previous history of AMI and myocardial revascularization surgery were more frequent in patients with CHD; however, no significant difference occurred between the groups in relation to the presence of previous angioplasty (tab. I).

In admitted patients, a hemodynamic study was performed, on average, 6 days after admittance. The average mean systolic blood pressure and mean arterial pressure were the same in both groups; however, the average left ventricle diastolic blood pressure and aortic pulse pressure were significantly greater in patients with CHD, while the average aortic diastolic pressure was significantly greater in patients without CHD (tab. II).

### Table I – Risk factors and previous clinical history in the 2 groups of patients (with or without severe CHD)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Patients with CHD N=292 (%)</th>
<th>Patients without CHD N=301(%)</th>
</tr>
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<tbody>
<tr>
<td>Hypertension</td>
<td>237 (81.2)</td>
<td>250 (83.3)</td>
</tr>
<tr>
<td>Diabetes mellitus *</td>
<td>136 (46.6)</td>
<td>79 (26.2)</td>
</tr>
<tr>
<td>Smoking *</td>
<td>108 (37.0)</td>
<td>65 (21.7)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>118 (42.0)</td>
<td>102 (45.3)</td>
</tr>
<tr>
<td>Climacteric *</td>
<td>198 (73.1)</td>
<td>158 (56.6)</td>
</tr>
<tr>
<td>Contraceptive use</td>
<td>21 (7.2)</td>
<td>22 (7.4)</td>
</tr>
<tr>
<td>Lack of exercise</td>
<td>104 (35.7)</td>
<td>111 (47.1)</td>
</tr>
<tr>
<td>Cardiovascular history</td>
<td>116 (39.7)</td>
<td>142 (47.7)</td>
</tr>
<tr>
<td>Previous AMI *</td>
<td>103 (35.3)</td>
<td>33 (11)</td>
</tr>
<tr>
<td>Previous angioplasty</td>
<td>13 (4.5)</td>
<td>7 (2.3)</td>
</tr>
<tr>
<td>Previous surgery</td>
<td>15 (5.1)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

* P<0.001

### Table II – Left ventricle and aortic pressure in mm Hg in the 2 groups of patients (with or without CHD)

<table>
<thead>
<tr>
<th>Pressure in mm Hg</th>
<th>Patients with CHD N=292 (Mean ± SD)</th>
<th>Patients without CHD N=301 (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVSP</td>
<td>150.8 ± 31.7</td>
<td>150.0 ± 27.3</td>
</tr>
<tr>
<td>LVD2P *</td>
<td>15.6 ± 8.7</td>
<td>15.1 ± 8.1</td>
</tr>
<tr>
<td>AOSP</td>
<td>150.8 ± 31.7</td>
<td>150.0 ± 27.3</td>
</tr>
<tr>
<td>AODP †</td>
<td>75.3 ± 17.5</td>
<td>79.8 ± 16.0</td>
</tr>
<tr>
<td>AOPPP ‡</td>
<td>75.5 ± 22.0</td>
<td>70.9 ± 19.0</td>
</tr>
<tr>
<td>MAP</td>
<td>100.5 ± 20.0</td>
<td>103.2 ± 18.0</td>
</tr>
</tbody>
</table>

* P = 0.001; † P = 0.002; ‡ P = 0.003; LVSP - left ventricle systolic blood pressure; LVD2P - left ventricle end diastolic pressure; AOSP - aortic systolic pressure; AODP - aortic diastolic pressure; AOPPP - aortic pulse pressure; MAP - mean arterial pressure
In the univariate analysis of dichotomized pressure in crescent values of 5 mmHg, we observed that no difference existed between the 2 groups in the diastolic aortic pressure spectrum ≥ 95 mmHg up to 120 mmHg. Diastolic aortic pressure spectrum ≤ 90 mmHg down to 65 mmHg, was significantly more frequent in patients without CHD (tab. III).

Regarding systolic blood pressure, no value in the univariate analysis correlated with atherosclerotic disease; however, pulse pressure for any value >75 mmHg was predominant in patients with CHD (55.8% x 44.0%), P = 0.004. Mean arterial pressure had an irregular behavior.

In multivariate analysis (taking into account interaction between systolic blood pressure and age), with all risk factors, and in systolic blood pressure, diastolic blood pressure, mean arterial pressure, and pulse pressure, CHD was not correlated with any of these pressures. When we used only 1 pressure in the regression model, pulse pressure ≥ 80 mmHg and systolic blood pressure ≥ 165 mmHg, a significant association was noted with CHD. Regardless of the association of pressures assessed, pulse pressure and systolic blood pressure above these values were significantly associated with CHD. Additionally, in the regression model, where associated pulse and systolic pressure were used, these pressures acted as independent predictors of CHD, with odds ratios of 1.9 and 2.1, respectively. (tab. IV).

**Discussion**

The main finding of this study is the association of pulse pressure, in univariate analysis, above 75 mmHg, and in the multivariate analysis above 80 mmHg, with severe CHD in women with UA/NSTEMI. Additionally, systolic blood pressure >165 mmHg was also associated with severe CHD, and above these values, were independent predictors of severe CHD.

The prognostic value of pulse pressure has already been assessed in the population of hypertensive patients, and in patients with ventricular function impairment with or without previous acute myocardial infarction. Pulse pressure assessed at the level of the brachial artery proved to be an independent predictor of left ventricular mass, vascular hypertrophy, coronary events, and heart failure.

Our study shows that pulse pressure ≥ 80 mmHg is an independent predictor of severe CHD in women with UA/NSTEMI. The majority of studies reported in the literature that assessed several pressures as risk factors for cardiovascular diseases were cohort studies. Sesso et al. analyzed systolic, diastolic, mean arterial pressures, and pulse pressure as predictors of risk for cardiovascular events, including myocardial infarction, angina, myocardial revascularization, percutaneous coronary angioplasty, stroke, and cardiac death. In this study, 11,150 men were followed-up for 10.8 years on average. In patients under age 60, systolic, diastolic, and mean arterial pressure were important predictors of cardiovascular risk, while in men over 60, only systolic blood pressure and pulse pressure were associated with this risk. The difference between our study and the latter is that regardless of age, systolic blood pressure, and pulse pressure were independent risk factors for severe CHD. Another factor is an exclusively female population, which may explain this result, because in women systolic blood pressure increases up to about age 80, thus systolic hypertension is more frequent in women than it is in men.

In another study, Pope et al. assessed 10,689 patients with a clinical picture of precordial pain, verifying an association between higher PP and those patients who had a final diagnosis of ischemia (P < 0.001). In the Framingham study, pulse pressure was a stronger predictor of cardiovascular events than was diastolic or systolic blood pressure alone. Recently, Millar and Lever, studying hypertensive men, developed an empirical and complex model of logistic regression that took into account the interaction between systolic and diastolic blood pressure as well as pulse pressure to determine risk of coronary events. These authors showed that pulse pressure was the strongest predictive factor to determine cardiovascular risk; however, it was difficult to distinguish it from systolic blood pressure. In all these studies, pulse pressure was assessed noninvasively, distinguishing our study in which this evaluation was central, assessed at the aortic root, and in this case it can be lower than the peripheral measure, since peripheral systolic pressure is slightly higher than central systolic pressure.

Regarding diastolic blood pressure as a risk factor in the 2 groups, our sample corroborates some epidemiological studies that showed an inverse association between diastolic blood pressure and CHD. According to the Framingham study, systolic blood pressure increases with age in all population groups, but diastolic blood pressure increases up to age 60 and then decreases.

Pulse pressure is an index of arterial wall stiffness, which...
changes with age; thus, besides systolic blood pressure, pulse pressure can represent a more important risk factor associated with CHD in women with UA/NSTEMI. Additionally, systolic hypertension is more important in women, which may have also influenced this result. It is important to stress that all previously mentioned studies assessed each and all pressures as risk factors for coronary events of any nature, which is different from our study where pressures were assessed as risks for severe CHD.

Our study has some limitations: it was a retrospective study, we did not eliminate those who were taking antihypertensive medications; diagnosis of hypertension was not done according to the criteria established by AHA/ACC, and the population was heterogeneous regarding this diagnosis. However, this is the first study in a specific population to demonstrate the importance of pulse pressure not for diagnosis of cardiovascular events, but for the presence of severe coronary disease.

In conclusion, we demonstrated that pulse pressure seems to be the most important component of pressure associated with severe CHD in women with UA/NSTEMI. The implications for a therapeutic approach are clear.

References