Pulse Wave Velocity: Relevance of Age in Normotensive, Essential Hypertensive and Borderline Hypertensive Patients

Velocidad de la onda de pulso: relevancia de la edad en normotensión, hipertensión esencial e hipertensión límite

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ABSTRACT

Background: Among the various parameters used to describe arterial function, pulse wave velocity (PWV) is the only one allowing direct measurement of arterial stiffness. Loss of arterial elastic capacity with increasing age, a process known as vascular aging, is enhanced in hypertensive patients.

Objectives: The aim of this study was to normalize PWV in normotensive (NT), essential hypertensive (HT) and borderline hypertensive (BL) patients and differentiate the effects of aging on PWV from those associated to hypertension.

Methods: A total of 221 consecutive male and female patients were included in the study. They were classified into three groups according to their blood pressure (BP) values: NT (n=120, 46±13 years): BP<135/85 mm Hg; HT (n=60, 50±13 years): BP>140/90 mm Hg; and BL (n=41, 47±12 years): BP=135-139/85-89 mm Hg. They were then stratified into four groups according to age: G1<40 years, GII=40-50 years, GIII=50-60 years and GIV>60 years. Mechanographic transducers and computerized calculation were used to measure PWV. Data analysis was performed using ANOVA, Newman-Keuls, and multivariate linear regression tests.

Results: Pulse wave velocity increased with age in all age groups (p<0.05). Mean PWV (m/s) in G1 was: NT (n=42): 8.6±1.1, HT (n=16): 9.5±1.3, BL (n=10): 9.0±0.5; in GII: NT (n=24): 9.5±1.2, HT (n=16): 10.7±1.2, BL (n=14): 9.8±0.8; in GIII: NT (n=30): 10.3±1.5, HT (n=12): 12.1±1.5, BL (n=11): 11.0±1.3; and in GIV: NT (n=24): 11.4±1.8, HT (n=16): 14.1±2.4, BL (n=6): 13.3±1.1. Regression equations were: for NT, PWV=0.08 × age + 0.04 × systolic blood pressure (SBP) + 1.07 (r=0.71); for HT, PWV=0.12 × age + 0.06 × SBP - 2.51 (r=0.81); and for BL, PWV=0.10 × age + 0.02 × SBP + 2.90 (r=0.73) (p<0.05).

Conclusions: Pulse wave velocity increased with age, and was higher in HT patients for each age group. Borderline hypertensive patients presented intermediate values between the other two groups. These results suggest additional vascular impairment induced by hypertension over that of aging. This surplus effect could be estimated from the regression equation obtained for each group.

Key words: Blood Pressure - Pulse Wave Analyses - Hypertension - Arteries, Pathophysiology

RESUMEN

Introducción: Se han descrito varios parámetros de medición del estado de la función arterial y, de ellos, la velocidad de la onda de pulso (VOP) es el único que permite una medición directa de la rígidez arterial. A medida que aumenta la edad del individuo se va produciendo una pérdida de la capacidad elástica, conocida como envejecimiento vascular, proceso este que estaría acelerado en los pacientes con hipertensión arterial.

Objetivos: Normalizar por décadas los valores de la VOP en pacientes normotensos (NT), hipertensos esenciales (HT) e hipertensos límite (LT) y diferenciar los efectos del envejecimiento sobre la VOP de los vinculados a la hipertensión arterial.

Material y métodos: Se estudiaron 221 pacientes consecutivos, de ambos sexos, que fueron clasificados, por sus valores de presión arterial (PA), en tres grupos: NT (n=120, 46±13 años): PA < 135/85 mm Hg; HT (n=60, 50±13 años): PA > 140/90 mm Hg; y LT (n=41, 47±12 años): PA = 135-139/85-89 mm Hg. Posteriormente fueron divididos en cuatro grupos por edades: GI < 40 años, GII = 40-50 años, GIII = 50-60 años y GIV > 60 años. La VOP se midió con transductores mecanográficos y cálculo computarizado. Se utilizaron las pruebas de ANOVA, de Newman-Keuls y de regresión lineal multivariada.

Resultados: La VOP aumentó significativamente (p < 0,05) con la edad en todos los grupos etarios (m/seg): GI: NT (n = 42): 8,6 ± 1,1, HT (n = 16): 9,5 ± 1,3, LT (n = 10): 9,0 ± 0,5; GII: NT (n = 24): 9,5 ± 1,2, HT (n = 16): 10,7 ± 1,2, LT (n = 14): 9,8 ± 0,8; GIII: NT (n = 30): 10,3 ± 1,5, HT (n = 12): 12,1 ± 1,5, LT (n = 11): 11,0 ± 1,3; y GIV: NT (n = 24): 11,4 ± 1,8, HT (n = 16): 14,1 ± 2,4, LT (n = 6): 13,3 ± 1,1.

Las ecuaciones de regresión halladas fueron: en NT, VOP = 0,08 × edad + 0,04 × presión arterial sistólica (PAS) + 1,07 (r = 0,71); en HT, VOP = 0,12 × edad + 0,06 × PAS - 2,51 (r = 0,81); y en LT, VOP = 0,10 × edad + 0,02 × PAS + 2,90 (r = 0,73) (p < 0,05).

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INTRODUCTION

Arteries have an active participation in blood flow with two hemodynamically distinct, but related, functions: delivery of an adequate blood supply from the heart to the peripheral tissues, or conductive function, and attenuation of blood pressure (BP) oscillations produced by pulsatile or intermittent left ventricular ejection, or damping function. (1)

Various parameters measuring arterial function have been described, such as pulse wave velocity (PWV), arterial compliance (measure of arterial wall distensibility), central pulse pressure and the augmentation index, expressing the arrival of the reflected pulse wave during cardiac systole. (2-4) Among them, PWV, described for the first time almost a century ago, is the only one enabling a direct measure of arterial stiffness, whereas the others are measurements derived from blood pressure through mathematical derivation. (5-7)

It is known that with increasing age, arteries lose their elastic capacity, (8) a process known as vascular aging. This process would be accelerated in hypertensive patients, appearing even at early ages in accordance to the number of associated cardiovascular risk factors. (1, 9)

From a pathological point of view, there are conditions which modify the structure of the arterial wall (fibrosis, atheromatosis, hypertrophic increase of the muscular layer, and functional changes of the smooth muscle) with the ensuing alterations in distensibility. (10)

Previously described methods quantifying PWV have demonstrated the relationship between PWV, BP, pulse pressure and arterial wall stiffness, and the association with increased cardiovascular and renal risk. (10, 11-14) This, in addition to the detection of altered arterial contractility, has allowed patient follow-up and start, if necessary, early treatment to reduce the acceleration of arterial stiffness. (9, 15, 16)

We postulate that although Hypertension Guidelines and Consensuses provide a normal mean PWV value (17-19) as preclinical injury marker, they do not consider the phenomenon of arterial aging according to the subject’s age clinical condition (hypertensive or non-hypertensive). Therefore, the aims of the present study are:

- To determine PWV behavior according to age in normotensive, essential hypertensive and borderline hypertensive patients.
- To differentiate the effects of vascular aging typical of age in normotensive subjects from those associated with essential or borderline hypertension.
- To build a formula to estimate PWV as a function of patient age and blood pressure.

METHODS

Population

The study included 300 subjects who consecutively attended the outpatient clinic for a hypertension etiologic study. All patients underwent weight and height measurements, clinical anamnesis and physical examination. Among them, 221 individuals from both sexes, without target organ injury, secondary hypertension or cardiometabolic disease with clinical expression were included in the study. These patients were classified according to mean daytime BP measured during 24 hours with an ambulatory blood pressure monitoring (ABPM) equipment (90207 ABP, SpaceLabs HealthCare, Snoqualmie, Washington, USA), in:

- Normotensive Group (NT): defined by daytime BP<135/85 mm Hg.
- Hypertension Group (HT): defined by daytime BP≥140/90 mm Hg. These patients had been recently diagnosed and were not receiving antihypertensive or hypolipidemic drugs.
- Borderline Hypertensive Group (BL): defined as daytime BP between 135/85 and 139/89 mm Hg. Similar to the HT Group, these patients were not receiving drugs.

These three populations were divided, according to age, into four different groups by age decades:
- Group I: ≤39 years.
- Group II: between 40 and 49 years.
- Group III: between 50 and 59 years.
- Group IV: ≥60 years.

The criteria for excluding 79 patients were: secondary hypertension, non-representative AMBP, intolerance to the equipment, bad recording signal, target organ injury (24-hour microalbuminuria, echocardiographic diagnosis of vascular plaque or ventricular hypertrophy), cardiometabolic disease (dyslipidemia, dysglycemia or diabetes mellitus), or previous antihypertensive or hypolipidemic treatment. Any other type of respiratory, renal, cardiac, brain or systemic disease was also reason for exclusion.

Assessment of pulse wave velocity

Baseline BP was measured in the non-dominant arm using
an automatic sphygmomanometer (Dinamap 8100T NIBP Monitor, Critikon, Tampa, Florida, USA), as previously described. (20)

Subsequently, with the corresponding previous preparation, the same operator performed simultaneous assessments of instantaneous left carotid and femoral artery pressure waves, with mechanographic transducers attached to a polygraph recorder (RS 3800, Gould Electronics, Cleveland, Ohio, USA) in adequate baseline conditions, and always between 10 am and 12 am, as previously described. (11) These measurements were digitally stored using an S/D converter and a computer program specially prepared by our work team (PWV Analysis, V2.0). Then, PWV was automatically calculated taking the distance between both transducers (carotid and femoral) as a function of time. (11) The average of five PWV measurements with acceptable tracings for correct calculation was taken for each patient.

**Statistical analysis**

Values are presented as mean± standard error of the mean. Statistical analysis was performed with SigmaStat (Versión 3.0, 2003, Systat Software Inc., San Jose, California, USA) software package. Comparison among groups was performed using ANOVA, with the Newman-Keuls test for post hoc analysis. A multivariate lineal regression test was used to analyze the relationship between PWV and the rest of the variables in the three groups of patients. A p value < 0.05 was considered as statistically significant.

**Ethical considerations**

This study was reviewed and approved by the Hospital Universitario Fundación Favaloro Board.

**RESULTS**

Table 1 shows the characteristics of the 221 study patients, divided into three groups (NT, BL and HT). There were no differences in age or percent distribution by gender (% M/F) in: NT (56.7/43.3) and in BL (58.5/41.5). In HT, the distribution was 85/15 (p<0.05).

Table 2 exhibits BP and PWV values in NT, BL and HT patients of age groups I and II. In both groups, the difference was statistically significant (P<0.05) only between NT and HT groups.

Table 3 displays BP and PWV values in NT, BL and HT patients of age groups III and IV. Same as in the above groups, the difference was statistically significant only between NT and HT groups for BP and PWV (p<0.05).

Figure 1 shows the relationship of PWV with the four age groups. Each group evidenced increased PWV, which was only significant (p<0.05) for HT compared with NT (§) patients. Regarding the four age groups there was a significant increase in NT, HT and BL (p<0.05) as a function of age (*, †, ‡), with significant correlation coefficients for each group (NT: 0.998; BL: 0.972; and HT: 0.993).

Figure 2 shows the linear correlation of PWV with age. The velocity of PWV increase in HT patients was significantly higher than in NT ones (p<0.01), while it was not significantly different in BL patients.

Results of multiple linear regression analysis between PWV, age, sex, weight, height, systolic blood pressure (SBP), and diastolic blood pressure (DBP) in NT, HT and BL patients, show that age and SBP are determinants of PWV. Therefore, the following formulas are postulated to estimate PWV for each of the subpopulations studied:

NT: \( PWV = 0.08 \times \text{age} + 0.04 \times \text{SBP} + 1.07 \) (r = 0.71; p < 0.05).
BL: \( PWV = 0.10 \times \text{age} + 0.02 \times \text{SBP} + 2.91 \) (r = 0.73; p < 0.05).
HT: \( PWV = 0.12 \times \text{age} + 0.06 \times \text{SBP} - 2.51 \) (r = 0.81; p < 0.05).

**DISCUSSION**

The significance of the results obtained in this study lies on PWV stratification with age and in different stages of daytime BP determined by 24-hour ABPM.

Use of 24-hour ABPM to stratify BP is recommended by the European Society of Hypertension Working Group on Blood Pressure Monitoring. (20)

The study of PWV is a short, safe, non-invasive procedure, easy to perform in clinical practice, with proven reliability and reproducibility. (21-25) Carotid-femoral PWV is not only considered a direct measure of arterial stiffness but also as its gold standard. (7) Therefore, in the last two decades, prospective studies have used PWV to stratify cardiovascular and renal risk in hypertensive patients. (8, 25-27) In this regard, PWV has been established as a predictor of silent ischemia, single and recurrent cardiovascular events, and cardiovascular and all-cause mortality, especially in patients with chronic renal failure, with even better definition than traditional stratification. (7, 25-31) Consequently, as suggested, PWV is included as a biological marker of subclinical organ injury in cardiovascular risk stratification. (9, 19, 29, 32) This predictive power is even greater than that of other arterial function parameters such as pulse pressure and endothelial function. (30, 33, 34)

However, despite it is well known that PWV increases with age due to loss of arterial compliance, (8) to date there are no normal values for our population according to age. Also, the presence of hypertension conditions an additional process to that of aging which may alter normal arterial function.

The cut-off point for normal PWV as predictor of

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics</th>
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<tbody>
<tr>
<td>Group</td>
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<tr>
<td>-------</td>
</tr>
<tr>
<td>NT</td>
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<tr>
<td>BL</td>
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<tr>
<td>HT</td>
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cardiovascular events and mortality has been suggested to be 13 m/s, (25) 12 m/s according to the European Society and the Argentine Society of Hypertension (17- 18) and 10 m/sec in the most recent European guidelines. (19) These values have been successively postulated as potential risk predictors of hypertension, their decrease being considered beneficial, or else to sub-stratify patients within the population or to improve treatment adherence. (4)

However, our results, in agreement with other studies conducted in different European countries, (36) suggest that a single cut-off value should not be considered as normal, since as demonstrated in this study, normal PWV in normotensive subjects changes with age. This implies that the normal PWV values for subjects less than 39 years, in their forties, fifties, or over 60 years, are not the same, consistent with international and national reports. (35-37)

On the other hand, we must also consider that increasing age is associated with reduced arterial compliance, also present in diseases such as hypertension, diabetes mellitus or end-stage renal failure. (25-28, 38-40) Consistent with these results, this study demonstrated that the increase in PWV was higher in

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### Table 2. Blood pressure and pulse wave velocity in age groups I and II

<table>
<thead>
<tr>
<th>Variable</th>
<th>NT (n=42)</th>
<th>Group I (n=16)</th>
<th>NT (n=24)</th>
<th>Group I (n=14)</th>
<th>NT (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31±6</td>
<td>34±6</td>
<td>32±5</td>
<td>44±2</td>
<td>44±3</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>124±7</td>
<td>128±7</td>
<td>146±10*</td>
<td>120±6</td>
<td>129±10</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>76±6</td>
<td>85±5</td>
<td>100±10*</td>
<td>79±5</td>
<td>87±6</td>
</tr>
<tr>
<td>PWV (m/s)</td>
<td>8.6±1.1</td>
<td>9.0±0.5</td>
<td>9.5±1.3*</td>
<td>9.5±1.2</td>
<td>9.8±0.8</td>
</tr>
</tbody>
</table>

SBP: Daytime systolic blood pressure; DBP: Daytime diastolic blood pressure; PWV: Pulse wave velocity. Group I: Patients ≤ 39 years. Group II: Patients aged 40-49 years. NT: Normotensive subjects; BL: Borderline hypertensive patients; HT: Hypertensive patients. Values are expressed as mean ± standard deviation. * p<0.05 NT vs. HT.

### Table 3. Blood pressure and pulse wave velocity in age groups III and IV

<table>
<thead>
<tr>
<th>Variable</th>
<th>NT (n=30)</th>
<th>Group III (n=12)</th>
<th>NT (n=24)</th>
<th>Group IV (n=8)</th>
<th>NT (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54±3</td>
<td>54±2</td>
<td>55±3</td>
<td>64±3</td>
<td>67±5</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>118±10</td>
<td>120±7</td>
<td>142±8*</td>
<td>126±6</td>
<td>135±13</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>74±6</td>
<td>81±6</td>
<td>84±10*</td>
<td>75±6</td>
<td>86±6</td>
</tr>
<tr>
<td>PWV (m/s)</td>
<td>10.3±1.5</td>
<td>11.0±1.3</td>
<td>12.1±1.5*</td>
<td>11.4±1.8</td>
<td>13.3±1.1</td>
</tr>
</tbody>
</table>

SBP: Daytime systolic blood pressure; DBP: Daytime diastolic blood pressure; PWV: Pulse wave velocity. Group III: Patients aged 50-59 years. Group IV: Patients ≥ 60 years. NT: Normotensive subjects; BL: Borderline hypertensive patients; HT: Hypertensive patients. Values are expressed as mean ± standard deviation. * p<0.05 NT vs. HT.

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### Figure 1. Relationship of pulse wave velocity (PWV) with the four age groups. NT: Normotensive subjects; BL: Borderline hypertensive patients; HT: Essential hypertensive patients. Group I: Patients ≤ 39 years; Group II: Patients aged 40-49 years; Group III: patients aged 50-59 years; Group IV: patients ≥ 60 years. * p<0.05 in NT: GI vs. GII; GII vs. GIII; GIII vs. GIV. † p<.05 in BL: GI vs. GII; GII vs. GIII; GIII vs. GIV. t p<0.05 in HT: GI vs. GII; GII vs. GIII; GIII vs. GIV. § p<0.05 NT vs. HT.
hypertensive than in normotensive patients for each age group. This shows the additional deterioration that the disease incorporates to that of aging. If we add that patients with borderline hypertension had intermediate values, between those of the other two groups, we can confirm that a factor inherent to the hypertensive disease is associated to a reduction of arterial wall distensibility.

Accordingly, the definition of the vascular status should be estimated relative to the patient’s age, same as classical cardiovascular risk stratification is based on traditional risk factors. (4)

Finally, considering that the changes observed on the elasticity of the arterial wall are not solely dependent on age, but also on blood pressure, a formula is suggested to calculate PWV as a function of age and SBP, relevant variables from the multiple correlation analysis in the three populations studied. Thus, a more accurate and easily applicable estimation can be performed in everyday medical practice.

A limitation of the study is the need of a greater number of subjects, especially an extension of the analysis to other age decades to establish a comprehensive normogram. Future studies, with a larger number of subjects, should consider assessing a possible difference in PWV by gender (men vs. women). However, we believe that these results are an interesting approach to standardize PWV according to our study population and not to other population data, whose characteristics may differ from those of Argentina.

**CONCLUSIONS**

In the present study, with the methodology used and in the population analyzed, it can be concluded that, in agreement with previous data, PWV increases with age in normotensive, borderline hypertensive and essential hypertensive patients. Therefore, we propose that the definition of vascular status should be estimated individually and in relation to the patient’s age. Finally, given that the increase of PWV was greater in hypertensive than in normotensive patients for each age group, we recommend the use of the regression equation which allows obtaining the patient’s PWV as a function of his/her age and SBP.

**Conflicts of interest**

Sanchez R. has received consulting fees from Merck and Co, and Boehringer Ingelheim in relation to this manuscript. (See author’s conflicts of interest forms in the web / Supplementary Material).

**REFERENCES**


