Pulse Wave Velocity Assessment by External Noninvasive Devices and Phase-Contrast Magnetic Resonance Imaging in the Obese

Laure Joly, Christine Perret-Guillaume, Anna Kearney-Schwartz, Paolo Salvi, Damien Mandry, Pierre-Yves Marie, Gilles Karcher, Patrick Rossignol, Faiez Zannad, Athanase Benetos

Abstract—Carotid-femoral pulse wave velocity (PWV) is considered the gold-standard measurement of arterial stiffness. Obesity, however, can render inaccurate the measurement of PWV by external noninvasive devices. Phase-contrast MRI allows the determination of aortic PWV in multiple aortic locations with intra-arterial distance measurements, as well as the assessment of aortic mechanical properties. The purpose of this study was to assess the reliability of external carotid-femoral PWV values measured by well-validated external devices in comparison with MRI acquisitions of PWV and aortic mechanical properties in a population of obese subjects. PWV was measured with PulsePen and Complior II devices in 32 volunteers (18 men and 14 women), aged 46 to 65 years (mean: 55.7±5.1 years), presenting with isolated abdominal obesity, with a waist circumference >102 cm for men and >88 cm for women, and a body mass index between 27 and 35. These results were then compared with MRI PWV values and cross-sectional MRI thoracic aorta distensibility values. MRI PWV values were positively correlated with PWV measured by both PulsePen (r=0.47; P<0.005) and Complior (r=0.43; P=0.01). Aortic cross-sectional stiffness was positively correlated with PulsePen PWV (r=0.42; P=0.02). The same trend was also observed with Complior PWV (r=0.33; P=0.06). This is the first study comparing transcutaneous PWV measurements with MRI aortic elastic properties in obese subjects. Our results indicate that, for body mass index values ≥35 kg m⁻², PWV measured externally with Complior or PulsePen validly reflect values obtained directly in the thoracic aorta through MRI. (Hypertension. 2009;54:00-00.)

Key Words: arterial stiffness ■ pulse wave velocity ■ obesity ■ MRI ■ aortic distensibility

Arterial stiffness assessed by pulse wave velocity (PWV) measurement is now well accepted as an independent predictor of cardiovascular mortality and morbidity.¹ Rapid and reproducible external noninvasive methods are the gold standard for measuring PWV by recording the pressure waves at respective carotid and femoral sites.² Several recent studies have indicated an effect of obesity on arterial stiffness, especially when associated with metabolic disorders.³⁻⁵ Therefore, measurements of PWV in overweight and obese subjects may be of major interest in assessing cardiovascular risk. However, obesity is a well known factor of technical operator bias when assessing PWV.²⁻⁶ This concerns both difficulties in obtaining pressure curves of good quality and technical difficulties in measuring distance. In this context, PWV assessment is questionable in overweight and obese subjects²⁻⁴⁻⁶⁻⁷; therefore, a comparison between external PWV-recording transcutaneous devices and internal noninvasive methods, eg, phase-contrast MRI, could prove valuable, while also providing morphological information.⁸⁻¹⁰ In fact, the acquisition of cross-sectional MRI aortic vascular structural indices, provided by combined high spatial and temporal resolutions, should not be affected by either body composition or imaging plane.

The current study was designed to assess the relationship between PWV values obtained with 2 well-validated transcutaneous devices (Complior II and PulsePen) and MRI acquisition of PWV along with aortic cross-sectional mechanical properties estimated by aortic distensibility and compliance, aortic elastic modulus, and stiffness index in a population presenting isolated abdominal obesity considered to reflect a high disease risk and defined by a waist circumference >102 cm for men and >88 cm for women in overweight and obese patients (body mass index from 27 to 35 kg m⁻²).

Methods

Subject Selection

Eighteen male and 14 female subjects presenting with isolated abdominal obesity were prospectively recruited by local press
advertisements or referral by general practitioners from an investigator network of the Clinical Investigation Centre. The study protocol was approved by the local ethics committee. Inclusion criteria were as follows: abdominal obesity considered to reflect a high disease risk and defined by a waist circumference >102 cm for men and >88 cm for women; history of diabetes mellitus, previous history of cardiovascular disease, acute or chronic inflammatory disease, renal and pulmonary insufficiency, and, of course, contraindication to MRI. All of the subjects arrived in a fasting state at the Magnetic Resonance Centre for cardiovascular imaging studies, after which hemodynamic and transcutaneous studies were completed. All fasting subjects mentioned above were included in the study, but those with contraindications to MRI were excluded.

Excclusion criteria were as follows: severe obesity defined by body mass index >35 kg m⁻², hypertension defined by a blood pressure >160/90 mm Hg, history of dyslipidemia, the presence of diabetes mellitus, previous history of cardiovascular disease, acute or chronic inflammatory disease, renal and pulmonary insufficiency, and, of course, contraindication to MRI. All of the subjects arrived in a fasting state at the Magnetic Resonance Centre for cardiovascular imaging studies, after which hemodynamic and transcutaneous measurements were performed at rest.

MRI Method
Images were acquired with subjects in the supine position in a 1.5-T magnet (Signa Excite, GE Medical Systems), with a maximum gradient amplitude of 83 mT/m, equipped with an 8-element phased-array surface coil. The acquisition protocol was initiated by the recording of localizing scans in movie mode with an ungated steady-state free precession pulse sequence (the FIESTA sequence from GE Medical Systems) for providing 3 carefully orientated planes encompassing the ascending aorta, aortic arch, and descending thoracic aorta. ECG-gated MRI with in-plane phase encoding technique was used for determining the PWV during free breathing. Scan time was 2 minutes, on average, and temporal resolution was enhanced by the recording of only 1-K space line per segment and 200 phases per cardiac cycle with view sharing. A single section was positioned on the aortic arch pilot scan, passing through the lumen of the right pulmonary artery and perpendicular to the ascending aorta. Acquisition parameters were as follows: 8-mm section thickness, 15° flip angle, 3- to 4-ms echo time, 6- to 7-ms repetition time, 31-kHz bandwidth, 6-K space lines per segment, 32 phases per cardiac cycle with view sharing, unidirectional velocity encoding with a maximal velocity set to 150 cm s⁻¹, field of view as small as possible between 300 and 380 mm with a phase field of view of 0.85, and a 256×128 matrix extended to 512×512 after voxel interpolation. The fast PC Cine sections were computed with the dedicated CV Flow software (GE Medical Systems), where aortic contours are detected automatically.

Analysis of MRI Data
Two sections separated by a distance (dist) of 15 cm were positioned perpendicularly to the descending aorta, with the upper section crossing the median portion of the ascending aorta, to define 3 regions of interest (ROIs). These 3 ROIs enabled PWV measurement between the median portion of the ascending aorta and, at a distal aortic level, under the diaphragm.

A simple equation was used to calculate PWV²,¹²:

\[
PWV = \frac{\Delta \text{dist}}{\Delta t}
\]

The calculation of PWV was also determined by the measurement of arterial length between the different ROIs. The distance between ROI 1 and ROI 2 (dist₁) included the aortic root, arch, and proximal descending aorta and enabled the measurement of a proximal aortic PWV (MRIProx PWV). The section between ROI 2 and ROI 3 (dist₂), including the proximal and mid-descending aorta, enabled the measurement of a distal aortic PWV (MRI Dist PWV). Finally, the section between ROI 1 and ROI 3 (dist₁ + dist₂) enabled the measurement of total aortic PWV (MRI Tot PWV; Figure 1). Time-velocity curves were generated for each ROI.

To calculate aortic vascular parameters (aortic distensibility, aortic compliance, aortic elastic modulus, and aortic stiffness index), cross-sectional areas of the ascending aorta were measured by tracing and were subsequently computerized by the CV Flow software at a transverse plane incorporating the proximal right pulmonary artery and, perpendicular to the ascending aorta, at 2 times the cardiac cycle: peak systolic and end diastolic phases of the cardiac cycle from a PC cine-MRI series.

Aortic distensibility and compliance were calculated according to the following formula²,¹¹:

\[
\text{Aortic Distensibility} = \left[ \frac{\text{compliance}}{(\text{AoArea})_{\text{max}}} \right] = \frac{(\text{AoArea})_{\text{max}} - (\text{AoArea})_{\text{min}}}{(\text{AoArea})_{\text{min}} \times \Delta P}
\]

Figure 1. Left, Sagittal scout MRI showing the aortic arch and the descending aorta. Two sections separated by a fixed distance of 15 cm are positioned perpendicularly to the thoracic aorta determining the 3 ROIs. MRI Prox PWV was determined with distance d₁, and the MRI Dist PWV was determined with distance d₂; MRI Tot PWV was determined by using arterial length (d₁+d₂). Right, Example of 2 normalized (or amplitude) velocity-time curves generated from 2 intra-aortic ROIs (ROI 1 and 3). The curves are scaled to represent the same peak velocity value. Time-delay calculation is based on superimposition and minimization of the square deviation between waveforms.
where $A_{0,Area_{max}}$ and $A_{0,Area_{min}}$ represent the maximal and minimal calculated areas obtained during a cardiac cycle, and $\Delta P$ is the central pulse pressure measured by arterial tonometer.

Because PWV is inversely proportional to the square root of arterial distensibility, the $1/\sqrt{\text{distensibility}}$ variable was used to assess the relationship between PWV and distensibility.

Aortic elastic modulus was determined by the following formula:

$$Ep = \frac{\Delta P (\text{mm Hg})}{S_{AD}}$$

where $S_{AD}$ is the strain of the aortic area defined as:

$$S_{AD} = \frac{(A_{0,Area_{max}} - A_{0,Area_{min}})}{A_{0,Area_{min}}}$$

Both were derived from the aortic area measurements assuming circular geometry of the aorta.

Stiffness index was calculated according to the following formula:

$$\beta = \frac{\ln(SBP/DBP)}{(A_{0,Area_{max}} - A_{0,Area_{min}})A_{0,Area_{min}}}$$

where SBP indicates systolic blood pressure and DBP indicates diastolic brachial blood pressure.

**External Devices for PWV Measurement**

Supine systolic blood pressure and diastolic blood pressure were measured after $\geq 10$ minutes of rest, on the left arm, using a validated electronic device (Omron 705IT). Blood pressure was measured 3 times, with the average of these 3 measurements used for statistical analyses.

Peripheral pulse pressure (pPP) was calculated as the difference between systolic and diastolic pressures ($pPP = \text{SBP} - \text{DBP}$). Central systolic, central diastolic, central pulse pressure, and mean arterial pressure were estimated by recording the carotid pulse wave with the PulsePen tonometry device. The detailed procedures of measurement of the central pressure with the PulsePen device were developed in a previous publication.

Aortic PWV was measured with 2 well-validated external devices: a Complior II (Artec-Medical) and a PulsePen (DiaTecne). Both determined aortic PWV as the delay between carotid and femoral pulse wave. Tests were initiated immediately after MRI time acquisition.

The Complior device, characterized by the simultaneous measurement of pressure pulses, uses dedicated mechanotransducers directly applied to the skin. A first probe was positioned at the common carotid artery, the central detection site, whereas a second probe was placed at the femoral artery site. The sensor, used to detect the pulse, produced a signal that was related to the derivative of the pressure pulse.

With the PulsePen device, the delay between pulse waves was determined by a single high-fidelity applanation tonometer to obtain the carotid and femoral pulse recorded sequentially in highly rapid succession, using the ECG trace as reference. PWV was calculated as the distance divided by the time delay measured between pressure upstroke at each site. For both the Complior and PulsePen device, distance was determined using a sliding caliper subtracting the distance from the carotid location to the sternal notch from the distance between the sternal notch and the femoral site of measurement.

The time delay was measured between the feet of the femoral and carotid waveforms. The foot of the wave was defined at the end of diastole, at the onset of the steep rise of the wavefront for the PulsePen.

**Statistical Analysis**

All of the statistical analyses were performed using the NCSS Statistical Software. Discrete variables were expressed as percentages, and quantitative variables were expressed as mean±SD. Mean PWV values measured with the different methods were compared with parametric ($t$-paired) and nonparametric (Wilcoxon) tests. Univariate analyses of the relationship between PWV and elastic properties of the aorta were tested with Spearman’s correlation coefficient. Comparisons between the various methods of PWV measurements were first analyzed with univariate analysis (Spearman’s correlation coefficient), after which the results were analyzed in 2 steps according the recommendations of Bland and Altman. A $P<0.05$ was considered to be indicative of a significant difference.

**Results**

**Population Characteristics and Hemodynamic Parameters**

The study population included 32 patients, 18 men and 14 women, with a mean age of $55.70\pm5.14$ years, presenting an abdominal obesity considered to reflect a high disease risk and defined by a waist circumference $>102$ cm for men and $>88$ cm for women. Mean values of their demographic and clinical characteristics, hemodynamic parameters, internal and external distance measurements, aortic structural cross-sectional data, and PWV values are given in Table 1. This table also shows mean values of PWV obtained with MRI and with the 2 transcutaneous devices. Total thoracic aorta PWV with

**Table 1. Main Clinical and Hemodynamic Parameters, Distance Measurements, Cross-Sectional Aortic Parameters, and PWV Values in the Studied Population**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients (female/male)</td>
<td>32 (14/18)</td>
</tr>
<tr>
<td>Age, y</td>
<td>55.7±5.1</td>
</tr>
<tr>
<td>Body mass index, kg m$^{-2}$</td>
<td>31.4±2.0</td>
</tr>
<tr>
<td>Hemodynamic parameters</td>
<td></td>
</tr>
<tr>
<td>Peripheral systolic blood pressure, mm Hg</td>
<td>121.4±14.7</td>
</tr>
<tr>
<td>Peripheral diastolic blood pressure, mm Hg</td>
<td>71.5±8.7</td>
</tr>
<tr>
<td>Peripheral pulse pressure, mm Hg</td>
<td>49.9±10.3</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>96.6±10.4</td>
</tr>
<tr>
<td>Central pressure, mm Hg</td>
<td>39.3±9.3</td>
</tr>
<tr>
<td>Central systolic blood pressure, mm Hg</td>
<td>118.5±13.0</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>73.0±10.0</td>
</tr>
<tr>
<td>Internal distance measurements, MRI</td>
<td></td>
</tr>
<tr>
<td>Distance between ROI 1 and ROI 2, cm</td>
<td>12.67±2.23</td>
</tr>
<tr>
<td>Distance between ROI 2 and ROI 3, cm</td>
<td>16.12±0.24</td>
</tr>
<tr>
<td>External distance measurements, external devices</td>
<td></td>
</tr>
<tr>
<td>Suprasternal notch and femoral artery distance, cm</td>
<td>57.15±3.60</td>
</tr>
<tr>
<td>Carotid artery and suprasternal notch distance, cm</td>
<td>9.65±1.10</td>
</tr>
<tr>
<td>Cross-sectional aortic data, MRI</td>
<td></td>
</tr>
<tr>
<td>Aortic compliance, cm mm Hg$^{-1}$</td>
<td>1.69±0.73</td>
</tr>
<tr>
<td>Aortic distensibility, mm Hg$^{-1}$</td>
<td>$2.07\times10^{-3}$±$0.93\times10^{-3}$</td>
</tr>
<tr>
<td>Stiffness index</td>
<td>6.45±4.54</td>
</tr>
<tr>
<td>Elastic modulus, mm Hg</td>
<td>627±439</td>
</tr>
<tr>
<td>PWV</td>
<td></td>
</tr>
<tr>
<td>PulsePen PWV, m s$^{-1}$</td>
<td>9.01±1.64</td>
</tr>
<tr>
<td>Complior PWV, m s$^{-1}$</td>
<td>7.88±1.38</td>
</tr>
<tr>
<td>MRI Prox PWV, m s$^{-1}$</td>
<td>6.80±2.24</td>
</tr>
<tr>
<td>MRI Dist PWV, m s$^{-1}$</td>
<td>9.51±5.50</td>
</tr>
<tr>
<td>MRI Tot PWV, m s$^{-1}$</td>
<td>8.00±2.66</td>
</tr>
</tbody>
</table>

Data are mean±SD unless otherwise described.
Magnetic Resonance Imaging (MRI) was 8.00±2.66 m s⁻¹. As expected, lower PWV values were recorded at the proximal than at the distal aortic PWV (6.80±2.24 m s⁻¹ versus 9.51±5.50 m s⁻¹, respectively; P<0.0005). PWV values obtained with Complior were lower than those observed with the PulsePen, respectively (7.88±1.38 m s⁻¹ versus 9.91±1.64 m s⁻¹; P<0.0001).

Bivariate analyses (Table 2) revealed that both transcutaneous PWVs (Complior and PulsePen) were correlated with age, mean arterial pressure, pPP, and central pulse pressure. Aortic PWV assessed with MRI was significantly correlated with mean arterial pressure, as well as a trend toward correlation with peripheral and central pulse pressure. No statistical association was observed between MRI PWV and age.

On linear regression analysis (Figure 2), a relationship was observed between PulsePen PWV measurements and MRI Tot PWV measurements (P=0.005; r=0.47; Figure 2C), as well as between Complior PWV measurements and MRI Tot PWV measurements (P=0.01; r=0.43; Figure 2E), with good correlation between the different methods in these obese subjects, as confirmed by Bland-Altman analysis (Figure 2D and 2F, respectively).

The same analyses also showed a very significant relationship between PulsePen and Complior PWV measurements (P<0.0001; r=0.75). The Bland-Altman analysis revealed a mean difference of values ±2 SD between the 2 methods of 1.1±1.9 m s⁻¹ (Figure 2A and 2B, respectively).

Figure 3 depicts the relationship between 1/sqrt (distensibility) measured with MRI at the level of the ascending aorta and all 3 of the PWVs (PulsePen PWV, Complior PWV, and MRI Tot PWV; see the Methods section). 1/sqrt (distensibility) was correlated with PulsePen PWV (P=0.02; r=0.42) and MRI Tot PWV (P=0.01; r=0.45), and there was a trend toward correlation with Complior PWV (P=0.06; r=0.33). Aortic cross-sectional compliance assessed with MRI was inversely correlated with PulsePen PWV (P=0.01; r=−0.44) and MRI Tot PWV (P=0.02; r=−0.40), with the same trend.
Obesity is known to be related to metabolic disorders, as well as increases in cardio-cerebrovascular diseases, cardiovascular mortality, and all causes of mortality among middle-aged and elderly subjects. Although some studies have sought to find a link among obesity, fat mass, PWV, and elastic properties of thoracic aorta, pathophysiological mechanisms linking abdominal adiposity with arterial stiffening remain unclear, however, and, thus, the relationship between obesity, per se, and arterial stiffness evaluated by PWV needs to be elucidated. For these reasons, methodological aspects relative to PWV measurements are of major importance in overweight and obese subjects.

Different methods are available for measuring PWV, with the gold standard being the recording of PWV between the common carotid and the femoral artery with transcutaneous devices. The distance between these 2 sites must be divided by the time delay between the pulse pressure wave at the 2 different sites of signal acquisition. In fact, this measured distance is an estimation of the true distance traveled by the front wave and largely depends on body habitus. Moreover, assessment of the quality of the pressure waveform shape is very important because of its implication in the calculation of the time delay by the “foot to foot.”

MRI is the most appropriate technique to measure, both directly and noninvasively, intra-aortic path length from 2D or 3D images and can be considered to be free from operator bias. A previous study composed of a population of normotensive subjects aged 21 to 72 years found that PWV measured by MRI for the entire length of the thoracic aorta was not different from that obtained by applanation tonometry PWV measurements. In the present study, a good correlation was established not only between PWV obtained with both external transcutaneous devices but also with MRI PWV assessments for the entire thoracic aorta (MRI Tot PWV), as well as the proximal and distal segments of the thoracic aorta (MRI Prox PWV and MRI Dist PWV), in a population composed of overweight and obese subjects. The use of a sliding caliper and the method of length calculation between carotid and femoral sites may be the explanation for these good correlations.

For both PulsePen and Complior measurements, the distances between the arterial points were assessed by a straight line, obtained with a sliding caliper, as the distance between the recording site at the femoral artery to the suprasternal notch minus the distance from the recording site at the carotid artery to the suprasternal notch. From a physiological standpoint, such length measurement can be considered as approaching the “true length” assessed by computing MRI between the 2 ROIs on the total thoracic aorta. Although statistically highly significant, the observed correlations between mean MRI PWV values and transcutaneous PWV values are somewhat different; this point is rather expected, because, in the case of transcutaneous measurements, PWV values reflect not only thoracic aorta stiffness, as with MRI, but also abdominal aorta and iliac artery stiffness. The fact that mean MRI proximal PWV values are lower than mean MRI distal PWV values is in concordance with biophysiological knowledge because of the rise in PWV values as the distance from the heart increases.

In MRI, local arterial wall properties are defined as cross-sectional area wall properties and are derived from pulse pressure measurement and vessel dimensions with good spatial and temporal resolutions. As expected, aortic distensibility and compliance assessed by MRI were inversely correlated to MRI Tot PWV, MRI Dist PWV, and PulsePen PWV and positively correlated to the elastic modulus and
aortic stiffness index. Of note, the best relationships between PWV and cross-sectional aortic distensibility were found when we compared PWV with the inverse of the square root of distensibility (see Figure 3), which is theoretically expected from the formula relating PWV and distensibility.13

Perspectives
Assessment of arterial stiffness in overweight and obese subjects may be of major interest in the evaluation of cardiovascular risk. So far, obesity has been considered a technical and practical limitation of transcutaneous measurements of PWV, which is a major indicator of arterial stiffness. The major interest of the results of the present study is the reliability of transcutaneous PWV measurement in subjects with overweight and moderate obesity. A limitation of this study is that we did not include subjects with morbid obesity, and, therefore, we cannot make conclusions regarding the reliability of PWV measurements for body mass index over 35 kg m⁻².

Conclusions
In summary, this is the first study to indicate that, for body mass index values ≤35 kg m⁻², PWV measured externally with a Complior or PulsePen validly reflects values obtained directly in the thoracic aorta through MRI.

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Disclosures
P.S. is a consultant for PulsePen (Dia Tecne, Milan, Italy). The remaining authors report no conflicts.

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