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# Pulse pressure amplification, pressure waveform calibration and clinical applications

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ABSTRACT

Obtaining pulse pressure non-invasively from applanation tonometry requires the calibration of pressure waveform with brachial systolic and diastolic blood pressure. In the literature, several calibration methodologies are applied, and clinical studies disagree about the predictive value of central hemodynamic parameters. Our aim was to compare 4 calibration methodologies and assess the usefulness of pulse pressure amplification as an index independent of calibration. We investigated 108 subjects with tonometry in carotid, femoral, brachial, radial and dorsalis-pedis arteries; pulse pressure amplification between arterial waveforms was calculated. Four methods to calibrate the waveforms were compared: the 1/3 rule, the 40% rule, the integral of radial and brachial waveforms. Pulse pressure amplification in 5 arterial territories (carotid-femoral, carotid-brachial, carotid-radial and carotid-pedis amplifications; femoral-pedis amplification) was studied. Pulse pressure was successfully measured non-invasively at the 5 arterial sites. Pulse pressure was markedly dependent on calibration, with differences up to 18 mmHg between methods. Calculation of pulse pressure amplification eliminated effects of calibration method. Furthermore, pulse pressure amplifications in the 5 arterial sites presented a distinct pattern of clinical/biological determinants: heart rate and body height were common determinants of carotid to brachial, radial and femoral amplifications; diabetes was related to carotid to brachial amplification and pulse wave velocity to femoral to pedis amplification. In conclusion, the calibration of pulse pressure will influence results of clinical trials, but calculation of pulse pressure amplification can avoid this. We also suggest that the alteration of amplification in each arterial territory might be considered as a signal of clinical/subclinical damage.



## 1. Introduction

In recent years, many devices enabling non-invasive study of peripheral and central blood pressure (BP) have been developed. The arterial systolic blood pressure (SBP) and pulse pressure (PP) can be non-invasively determined through applanation tonometry and, once the pressure waveform (PW) is obtained, a calibration procedure is used to get absolute values of arterial BP. Generally, PWs are calibrated by mean arterial pressure (MAP) and diastolic blood pressure (DBP), assuming that they remain constant along the arterial tree [1].

One of the main problems of the calibration procedure is MAP estimation, because the only precise way to measure MAP is by using an intra-arterial catheter. However, several arithmetic and integration methodologies can be applied [2–7] in order to non-invasively estimate MAP, calibrate PWs, and measure local arterial BP.

At the same time, the finding that a difference exists in the SBPs and the PPs between central and peripheral arteries led to the concept of pressure amplification (PA). In fact, central BP is physiologically lower than peripheral BP [2,8]. This parameter has been poorly evaluated in clinical studies, but PA is considered to be correlated to cardiovascular risk, and it has shown a predictive prognostic value in some population studies [8–10]. Notably, in literature there exist several formula to calculate PA, like the

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subtraction of central to peripheral BP, or the ratio between brachial over central BP. Furthermore, either sphygmomanometric or tonometric brachial BP can be used in the PA formula. This can lead to a situation in which central BP is obtained by PW calibration, while brachial BP is derived from a sphygmomanometric device, not requiring calibration. When calculating PA as a ratio of brachial over central BP, we will obtain a calibration-dependent value. This may contribute to the different prognostic power of PA as various clinical trials and population studies have shown through different calibration methods.

On the other hand, calculating PA as the ratio between two calibrated tonometric PWs contributes to reduce errors related to the different calibration procedures [9].

In this setting, we examined the tonometric PP in five arteries, for the first time: carotid, femoral, brachial, radial, and dorsalis pedis arteries. Then we compared 4 common calibration methods: the 33% and 40% methods, and the brachial and radial PWs integration method. Finally, we studied the PP amplification and its clinical role in 5 arterial sites (district PA): carotid-femoral, carotid-brachial, carotid-radial, carotid-pedis and femoral-pedis.

We will show that: (1) tonometric BP strictly depends on PW calibration; (2) the PA is correlated to organ damage.

## 2. Methods

### 2.1. Study participants

In the present study, 115 consecutive outpatient subjects, aged from 20 to 84 years, were recruited from the Department of the Diagnosis and Therapeutic Center of Hôtel-Dieu Hospital, Paris, France, for the evaluation of one or more cardio-vascular (CV) risk factors, including high BP, smoking, dyslipidemia, diabetes mellitus, and/or family history of premature CV disease, with or without clinical events previously identified. The inclusion criteria were the presence of an adequate quality of PW recording of at least carotid, radial and brachial arteries. Exclusion criteria involved atrial fibrillation and severe heart failure (NYHA III-IV). Informed consent was obtained from all participants. Seven subjects did not have a good quality tonometric signal (6 for the carotid tonometry and 1 for radial tonometry) and were therefore excluded. The final number of patients was 108.

### 2.2. Anthropometric measurements and clinical information

Clinical characteristics concerning family history diseases, smoking habits and pharmacological treatment were obtained from patients' documents. Smoking was defined as a history of smoking and/or current smoking. Body height (BH) and weight (BW), waist and hip circumferences (WC, HC) were measured. Body mass index (BMI) was calculated by routine formula. Hypertension was defined as systolic BP (SBP) >140 mmHg and/or diastolic BP (DBP) above 90 mmHg, with a minimum of three casual measurements during the previous month, or when antihypertensive therapy was present.

Brachial BP was determined using a validated oscillometric device (SCVL, Paris, France), after at least 5 min rest in supine position. Brachial sphygmomanometer SBP and DBP was then recorded just before each tonometric PW recording; brachial MAP was automatically calculated by the oscillometric device with the formula: $DBP + (0.412 \times (SBP\text{-}DBP))$ [5].

### 2.3. Tonometric analysis and estimation methods

Applanation tonometry provides accurate profile of intra-arterial BP curves through the application of a piezoresistive sensor -the tonometer- over an artery through the skin. PulsePen (DiaTecne s.r.l., Milan, Italy) is a light and compact device for transcutaneous applanation tonometry that provides pulse wave velocity (PWV) and pulse wave analysis (PWA) assessments [11]. A PW registration of at least 12 s is considered acceptable for the subsequent analysis. Therefore, PWs of five artery sites (carotid, brachial, radial, femoral and dorsalis pedis arteries) were obtained with PulsePen by a skilled physician with the following methodology.

Firstly, brachial artery SBP and DBP were achieved using the sphygmomanometer. Secondly, MAP is calculated with four different methods. Methods 1 and 2 are the 33% and the 40% rules: $MAP = PP/3 + DBP$ and $MAP = PP/2.5 + DBP$ respectively. As far as the other two methods are concerned, sphygmomanometric SBP and DBP are used to calibrate radial (Method 3) and brachial (Method 4) tonometric PWs; the area under the curve (AUC) of the tonometric radial and brachial PWs is then automatically calculated and represents MAP. Finally, we utilized MAP obtained from the 4 estimation methods to recalibrate each PW, and calculate PP in mmHg in each of the 5 arteries, assuming MAP as constant along the arterial tree [1].

In order to calculate PWV, simultaneously ECG recordings were achieved and the foot-to-foot method was applied to the waveform as described elsewhere [11]. The distal and proximal distances were measured with a caliper from carotid to suprasternal notch, and then from suprasternal notch to peripheral artery. Carotid-peripheral artery distances were calculated as distal distance subtracted by proximal distance. We calculated carotid-femoral and femoral-pedis PWV.

### 2.4. Definitions of amplification of each particular site

Carotid artery PW was considered as a surrogate of the central BP [12–14], and the tonometric PP amplification between the 2 arterial sites was calculated according to the following formula: peripheral PP/central PP. We obtained PA as a dimensionless number, without any unit in 5 different sites: carotid to femoral, brachial, radial and pedis amplifications, and femoral to pedis amplification.

### 2.5. Statistical analysis

Statistics were performed with NCSS 2000 software (Kaysville, Utah, USA). A $P < 0.05$ was considered as statistically significant. We represent data as mean ± standard deviation. We compared the differences in PP and PP amplification between the 4 methods and between the 5 arteries with ANOVA. We also investigated the possible determinants of PA in different sites with multiple regression analysis. We compared the determinants in a regression model for each arterial district, forcing age, gender and MAP in all the models, and choosing only the 3rd estimation method (Radial AUC), as frequently used in literature.

Furthermore, we studied the factors influencing PA independently of each particular site. For this purpose, we built a single multiple-regression model with PA as the dependent variable and sex, age quartiles, heart rate (HR), BMI, waist to hip ratio (WHR), distance, mean arterial pressure, diabetes, ankle-brachial index (ABI), LDL-cholesterol, proteinuria, hypertension, smoking as the independent variables.

## 3. Results

The final number of patients was 108. Table 1 shows the characteristics of the study participants. Compared to women, we found in men higher BH, BW and DBP, and lower HR (data not shown).