

Non-invasive assessment of local arterial pulse pressure: comparison of applanation tonometry and echo-tracking

Luc M. Van Bortel^{a,b}, Elisabeth J. Balkestein^a,
Janneke J. van der Heijden-Spek^a, Floris H. Vanmolkot^a, Jan A. Staessen^c,
Johannes A. Kragten^d, Jan W. Vredeveld^d, Michel E. Safar^e,
Harry A. Struijker Boudier^a and Arnold P. Hoeks^a

Objectives Pulse pressure is not constant throughout the arterial tree. Use of pulse pressure at one arterial site as surrogate for pulse pressure at another arterial site may be erroneous. The present study compares three non-invasive techniques to measure local pulse pressure: (i) internally calibrated readings from applanation tonometry, (ii) alternative calibration of pressure waves obtained with applanation tonometry and (iii) alternative calibration of arterial distension waves obtained with echo-tracking. Alternative calibration assumes mean and diastolic blood pressure constant throughout the large artery tree.

Design and methods Study 1 used invasive measurements in the ascending aorta as a reference method and internally calibrated tonometer readings and alternatively calibrated pressure waves at the common carotid artery as test methods. Study 2 used alternatively calibrated pressure waves as a reference method and alternatively calibrated distension waves and internally calibrated applanation tonometer readings as test methods.

Results In study 1, pulse pressure from internally calibrated tonometer readings was 10.2 ± 14.3 mmHg lower and pulse pressure from alternatively calibrated pressure waves was 1.8 ± 5.2 mmHg higher than invasive pulse pressure. Pulse pressure from calibrated distension waves was 3.4 ± 6.9 mmHg lower than pulse pressure from alternatively calibrated pressure waves. According to British Hypertension Society criteria, pulse pressure from the internally calibrated tonometer achieved grade D and

pulse pressure from alternatively calibrated pressure waves achieved grade A. Pulse pressure from calibrated distension waves achieved grade B when alternatively calibrated pressure waves were used as a reference method.

Conclusions Pulse pressure obtained from alternatively calibrated tonometer-derived pressure waves and echo-tracking-derived distension waves demonstrates good accuracy. Accuracy of pulse pressure from internally calibrated applanation tonometer readings at the carotid artery is poor. *J Hypertens* 19:1037–1044 © 2001 Lippincott Williams & Wilkins.

Journal of Hypertension 2001, 19:1037–1044

Keywords: pulse pressure, accuracy, non-invasive assessment, applanation tonometry, echo-tracking

^aDepartments of Pharmacology and Biophysics, Cardiovascular Research Institute Maastricht, Maastricht University, The Netherlands, ^bHeymans Institute of Pharmacology, Ghent University, Belgium, ^cHypertension and Cardiovascular Rehabilitation Unit, University of Leuven, Belgium, ^dDepartments of Cardiology and Vascular Investigation, Atrium Medical Centre, Heerlen, The Netherlands and ^eDepartment of Internal Medicine, Broussais Hospital, Paris, France.

Sponsorship: This study was supported by the Cardiovascular Research Institute, Maastricht.

Correspondence and requests for reprints to Luc M. Van Bortel, Clinical Pharmacology and Pharmacotherapy, Heymans Institute of Pharmacology, Ghent University, De Pintelaan 185, B-9000 Ghent, Belgium.
Tel: +32 9 240 3374; fax: +32 9 240 4988;
e-mail: luc.vanbortel@rug.ac.be.

Received 21 August 2000 **Revised** 7 February 2001
Accepted 8 February 2001

Introduction

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) are determined by mean arterial pressure (MAP) and the pulse pressure oscillating around the MAP [1]. In contrast to MAP [2], pulse pressure is not constant throughout the large artery tree, but increases centrifugally [1,3]. However, this pulse pressure amplification might be attenuated and even lost by early reflected pulse waves due to stiffening of arteries and/or by more proximal reflection sites [1,3]. As a consequence, use of the pulse pressure obtained at one

arterial site as surrogate of the pulse pressure at another arterial site might be erroneous. In recent years, interest in pulse pressure has increased [4] since a high brachial artery pulse pressure has been recognized as an independent risk factor for cardiovascular morbidity and mortality [5–14]. It is likely that pulse pressure at other arterial sites than the brachial artery (i.e. the ascending aorta) may show a stronger association with cardiovascular events.

Applanation tonometry has been proposed to assess

local arterial pulse pressure. It allows non-invasive recording of the arterial pressure waveform and magnitude in both central and peripheral arteries [15,16]. This technique provides pressure waves, being almost identical to those obtained intra-arterially [17]. However, several authors have indicated that the magnitude of the pulse pressure obtained by this internally calibrated applanation tonometry is unreliable [18]. Kelly and Fitchett have proposed an alternative calibration of the tonometer pressure waves [19]: at the reference artery (i.e. brachial artery), peak and nadir of the pressure wave are assigned systolic and diastolic pressures determined by a conventional method (i.e. sphygmomanometry). The mean pressure is calculated from numeric integral of the calibrated pressure wave. With assignment of the same mean and diastolic pressures to the target artery (i.e. carotid artery), the pressure wave at the target artery is calibrated throughout the cardiac cycle. This calibration procedure is based on the observation that mean blood pressure is constant throughout the large artery tree and that diastolic pressure does not change substantially [20,21] and might improve assessment of local pulse pressure. Pauca *et al.* [2] showed that the difference between MAP and DBP (MAP-DBP) was only 0.2 mmHg larger in the radial artery than in the ascending aorta.

Applanation tonometry cannot be applied to all subjects and at all arterial sites [21]. It requires a stiff or bony structure to flatten the artery wall and a lean skin to avoid cushioning of the pressure pulse. In obese subjects, applanation tonometry often is inaccurate at a majority of arterial sites. In lean subjects, good waveforms can be easily obtained at the radial artery, but in a substantial number of subjects applanation tonometry is not reliable at the femoral artery. To overcome this problem, use of a transfer function has been proposed. Since the use of a universal transfer function appears limited to the upper limb, only carotid artery and ascending aorta pulse pressure can be assessed by this latter technique [21].

In contrast to the pressure waves obtained by applanation tonometry, arterial distension waves from echo-tracking devices [22] can be obtained accurately at more arterial sites and also in a majority of obese subjects. Assessment of blood pressure based on calibrated arterial distension waves has been attempted in the past [23,24] but failed because of lack of accurate arterial distension registration. Echo-tracking devices, which have been recently developed, show high accuracy and can measure arterial distension with an error less than 5 μm [22]. If assessment of local pulse pressure by calibrated distension waves is accurate, this method might provide an alternative that can be applied to a larger part of the population and to more arterial sites than applanation tonometry.

To investigate the accuracy of pulse pressure directly obtained from the internally calibrated tonometer signal and the pulse pressure obtained by alternatively calibrated tonometer pressure waveforms (PWF) as proposed by Kelly and Fitchett [19], study 1 compares the internally calibrated tonometer-derived (PP_{tono}) and PWF-calibrated pulse pressure (PP_{pwf}) at the right common carotid artery (CCA) with the pulse pressure obtained intra-arterially in the ascending aorta (PP_{aorta}) at the branch of the right CCA.

Invasive blood pressure recordings can only be obtained in a limited number of subjects and are not suitable for daily practice. Therefore, to investigate the accuracy of the pulse pressure obtained by alternatively calibrated arterial distension waves (DWF), study 2 compares DWF-calibrated pulse pressure (PP_{dwf}) with internally calibrated tonometer (PP_{tono}) and PWF-calibrated pulse pressures (PP_{pwf}) at the CCA in a large population sample.

Methods

The two studies were approved by the local ethics committees and written informed consent was obtained from all subjects.

Study 1

Patients, who underwent a coronary artery catheterization, entered the study. Using radioscopy a 6-Fr pig tail catheter (Bard, Galway, Ireland) was placed in the ascending aorta at the presumed branching off of the right CCA. The catheter was connected to a disposable pressure monitor kit with high pressure line (Becton and Dickinson, Singapore). The pressure signals were amplified (Mingograph 7; Siemens-Elema, Stockholm, Sweden) and digitized at a sample frequency of 200 Hz with resolution less than 0.15 mmHg. Digitized intra-arterial blood pressure recordings were stored on hard disk for offline analysis. PP_{aorta} was calculated beat-to-beat as the difference between the systolic and diastolic blood pressure, being the difference between the peak and the nadir of each pressure wave. Simultaneously, pulse pressure was measured by applanation tonometry at the right CCA. The output of the tonometer (Micro-Tip pressure transducer Model SPT-301; Millar Instruments, Houston, Texas, USA) was connected to the transducer control unit (Model TC-510; Millar Instruments) for online internal calibration. Tonometer tracings were further amplified, digitized and stored on hard disk for offline analysis using the same equipment and methods as for the intra-arterial pressure tracings. PP_{tono} was calculated beat-to-beat as the difference between the pressures registered by the internally calibrated tonometer at peak and the nadir of each pressure wave, respectively. PP_{pwf} was obtained by alternative calibration of the tonometer pressure wave

on the pressure wave of the ascending aorta. PP_{pwf} data are the mean of at least six heartbeats.

Study 2

In 100 subjects from a random population sample [25], brachial artery and CCA pressure and distension waves were obtained using applanation tonometry and echo-tracking (Ultramark V, ATL; Bothell, Washington, USA; combined with Wall Track System, Pie Medical, Maastricht, The Netherlands), respectively. Tonometer readings were obtained with the same equipment as in study 1 except for the signal amplifier (BAP 001; Simonsen & Weel, Albertslund, Denmark). Tonometry and echo-tracking were carried out consecutively at the same CCA and brachial artery. Simultaneously with tonometer and echo-tracking measurements at the CCA, blood pressure was measured at the brachial artery with a semi-automated device (Dinamap; Critikon, Tampa, Florida, USA). Brachial artery pulse pressure was calculated as Dinamap systolic minus diastolic blood pressure. PP_{tono} was calculated as in study 1. PP_{pwf} and PP_{dwf} at the CCA were obtained from alternative calibration of the PWF and DWF on the respective brachial artery waveforms. Data are means of at least eight heartbeats.

The alternative calibration procedure, according to Kelly and Fitchett [19], assumes MAP minus DBP constant throughout the large artery tree. The pulse pressure at the target artery (PP_{tar}) is calculated from the pulse pressure at the reference artery (PP_{ref}) and the K factor at target and reference arteries (K_{tar} and K_{ref} , respectively) by the formula:

$$PP_{\text{tar}} = PP_{\text{ref}} \times K_{\text{ref}}/K_{\text{tar}}$$

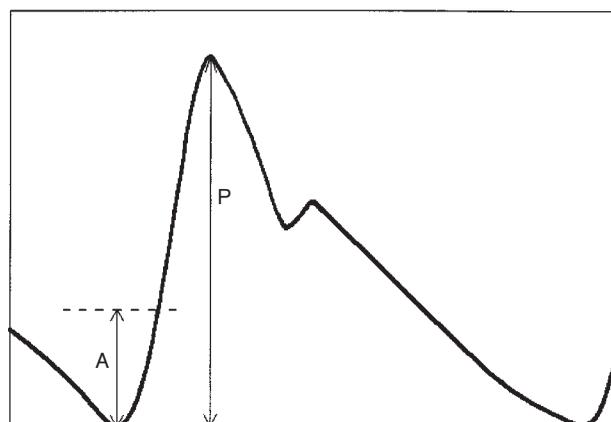
The calculation of the K factor is shown in Figure 1: $K = A/P$ [26].

This alternative calibration procedure can be employed to obtain the pulse pressure using the pressure waveform (PP_{pwf}) as well as the arterial distension waveform (PP_{dwf}).

Statistical analysis

Demographic data are shown as number or as mean \pm SD. Methods were compared according to the American Association for the Advancement of Medical Instrumentation (AAMI) [27] and British Hypertension Society (BHS) [28] criteria for the evaluation of blood pressure measuring devices. Bland and Altman plots [29] and Pearson correlation were used. The influence of age, body mass index (BMI), gender, mean arterial pressure and pulse pressure on the difference in pulse pressure between methods was calculated using stepwise linear regression analysis. If a factor was not

Fig. 1



Pressure wave: y -axis, pressure; x -axis, time. P , pulse pressure; A , MAP – DBP, respectively. A is calculated by dividing the area under the pressure wave by time.

significant, the factor was dropped from the model. $P < 0.05$ was considered statistically significant.

Results

Subjects' characteristics are shown in Table 1. Pulse pressures and differences in pulse pressure between test and reference methods are shown in Table 2 and in Bland and Altman scatterplots (Figs 2 and 3). The effect of age, gender, BMI, MAP and pulse pressure on the differences in pulse pressure between methods are shown in Table 3. Only statistically significant associations are tabulated.

Study 1 compares pulse pressure measured invasively at the ascending aorta (reference method) with pulse pressure at the CCA measured with applanation tonometry (test method). Evaluable readings of both techniques were obtained in 19 patients aged 40–79 years. Measurements were carried out before administration of nitroglycerin in 13 patients and after in six. None of the patients had a haemodynamically significant carotid artery stenosis as measured with Duplex echo/Doppler. According to AAMI criteria for invasive and beat-to-beat measurements, comparison was carried out on 133

Table 1 Subjects' characteristics

| | Study 1 | Study 2 |
|--------------------------|--------------|--------------|
| Number (male/female) | 19 (17/2) | 100 (53/47) |
| Age (years) | 57 \pm 10 | 37 \pm 16 |
| BMI (kg/m ²) | 26 \pm 3 | 24 \pm 4 |
| SBP (mmHg) | 123 \pm 19 | 125 \pm 15 |
| DBP (mmHg) | 69 \pm 11 | 73 \pm 9 |

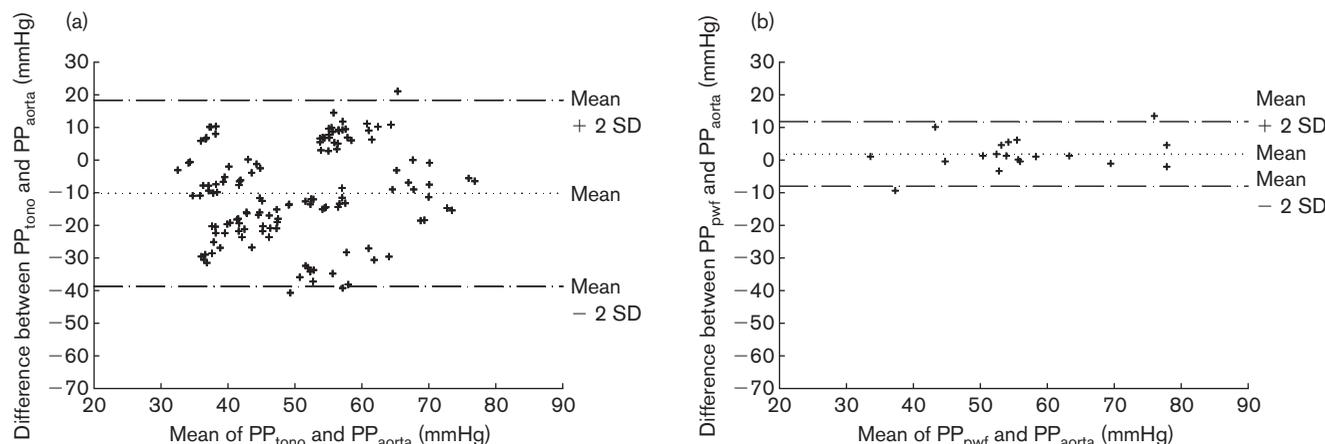
Data are mean \pm SD or number. BMI, body mass index; Systolic blood pressure (SBP) and diastolic (DBP) blood pressure are measured invasively in the ascending aorta in study 1 and non-invasively at the brachial artery in study 2.

Table 2 Pulse pressure (PP) and difference in pulse pressure between methods

| | PP (mmHg) | Method | Difference from method ΔPP (mmHg) | r |
|---------------------|-------------|-----------------------|--------------------------------------|--------|
| Study 1 | | | | |
| PP _{aorta} | 55.2 ± 11.9 | | | |
| PP _{tono} | 45.0 ± 13.8 | PP _{aorta} | -10.2 ± 14.3 | + 0.39 |
| | | PP _{pwf} | -12.0 ± 16.0 | + 0.30 |
| PP _{pwf} | 57.0 ± 13.1 | PP _{aorta} | + 1.8 ± 5.2 | + 0.92 |
| Study 2 | | | | |
| PP _{pwf} | 50.3 ± 12.9 | | | |
| PP _{tono} | 36.6 ± 9.4 | PP _{pwf} | -13.7 ± 16.6 | - 0.09 |
| PP _{dwf} | 46.9 ± 10.8 | PP _{pwf} | -3.4 ± 6.9 | + 0.85 |
| | | PP _{aorta} * | -1.6 ± 6.9 | + 0.85 |

ΔPP, difference in pulse pressure from method; r, correlation coefficient. PP_{aorta}, pulse pressure measured intra-arterially in the ascending aorta at the branching off of the right common carotid artery. PP_{tono}, pulse pressure at the common carotid artery directly obtained from applanation tonometry. PP_{pwf}, pulse pressure at the common carotid artery from calibrated tonometer pressure waveforms. PP_{dwf}, pulse pressure at the common carotid artery from calibrated echo-tracking distension waveforms. *PP_{aorta} in study 2 is estimated by correcting each PP_{pwf} for the systematic difference of 1.8 mmHg from PP_{aorta} in study 1. Data of PP and ΔPP are mean ± SD.

Fig. 2



(a) Agreement between PP_{tono} and PP_{aorta}. Bland and Altman scatterplot ($n = 133$; 19 subjects with seven beats each); PP_{tono}, pulse pressure read from the applanation tonometer at the carotid artery; PP_{aorta}, pulse pressure obtained invasively in the ascending aorta. Lines are drawn for the mean difference and 2 SD around the mean difference. (b) Agreement between PP_{pwf} and PP_{aorta}. Bland and Altman scatterplot ($n = 19$; 19 subjects with one value, mean of six heartbeats); PP_{pwf}, pulse pressure at the common carotid artery from calibrated tonometer-derived pressure waveforms; PP_{aorta}, pulse pressure obtained invasively in the ascending aorta. Lines are drawn for the mean difference and 2 SD around the mean difference.

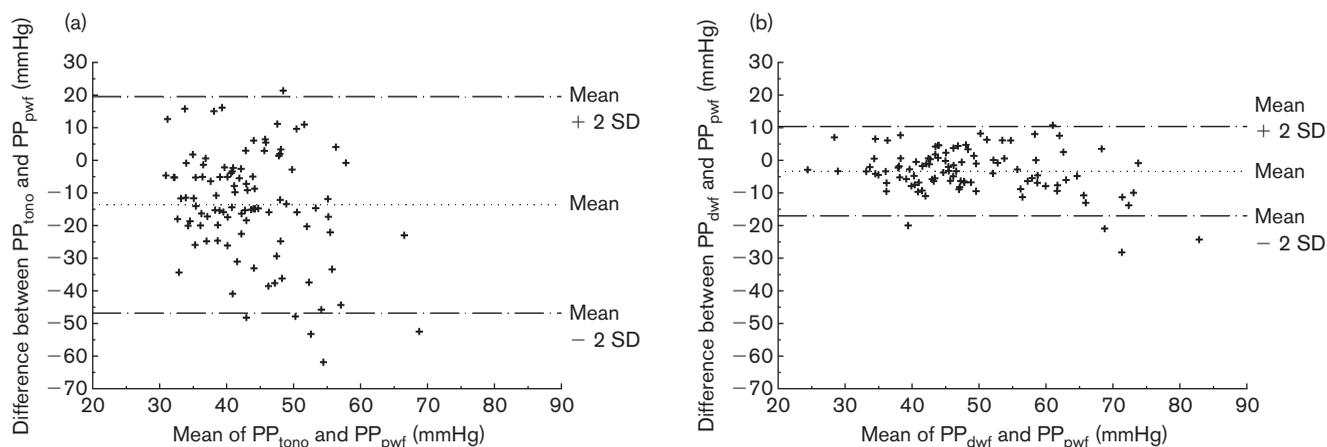
measurements (19 subjects with seven heartbeats each) for PP_{aorta} and PP_{tono}.

PP_{tono} was on average 18.5% lower than PP_{aorta} and did not correlate well with the reference method. PP_{pwf} was on average 3.3% higher and correlated very well with PP_{aorta}. The SD of the difference with PP_{aorta} was 2.75 times smaller for PP_{pwf} than for PP_{tono} (Table 2; Figs 2a,b). The difference between PP_{tono} and PP_{aorta} was negatively related with age, MAP, BMI and pulse pressure (Table 3). The difference between PP_{pwf} and PP_{aorta} was positively related with age, MAP and PP_{pwf}, but not with PP_{aorta}. Because only two subjects were

female in study 1, the influence of gender was not tested.

Study 2 compares pulse pressure from calibrated distension waveforms (PP_{dwf}) with that from calibrated pressure waveforms (PP_{pwf}). Evaluable readings of both techniques were obtained in 100 subjects aged 12–77 years (Table 1). Since in study 1 PP_{pwf} was the most accurate non-invasive method, PP_{pwf} was used as reference method in study 2. PP_{tono} was 37.4% lower than PP_{pwf} and did not correlate with reference PP_{pwf}. PP_{dwf} was on average 9.3% lower than PP_{pwf} and correlated well with PP_{pwf} (Table 2). The SD of the

Fig. 3



(a) Agreement between PP_{tono} and PP_{pwf} . Bland and Altman scatterplot ($n = 100$; 100 subjects with one value, mean of eight heartbeats); PP_{tono} and PP_{pwf} , pulse pressures at the carotid artery read from the applanation tonometer and from calibrated tonometer-derived pressure waveform, respectively. Lines are drawn for the mean difference and 2 SD around the mean difference. (b) Agreement between PP_{dwf} and PP_{pwf} . Bland and Altman scatterplot ($n = 100$; 100 subjects with one value, mean of eight heartbeats). PP_{dwf} and PP_{pwf} , pulse pressures at the common carotid artery from calibrated echo-tracking-derived distension waveforms and from calibrated tonometer-derived pressure waveforms, respectively. Lines are drawn for the mean difference and 2 SD around the mean difference.

Table 3 Influence of age, body mass index (BMI), mean arterial pressure (MAP) and pulse pressure on the difference in pulse pressure between test and reference method

| ΔPP (mmHg) | Confounder | Slope | Intercept | Significance |
|---|-------------------------------------|------------------|-------------------|--------------|
| Study 1 $PP_{\text{tono}} - PP_{\text{aorta}}$ | Age (years) | -0.70 ± 0.10 | $+78.81 \pm 9.07$ | $P < 0.001$ |
| | MAP (mmHg) | -0.21 ± 0.04 | | $P < 0.001$ |
| | BMI (kg/m^2) | -0.89 ± 0.26 | | $P = 0.001$ |
| | PP_{aorta} (mmHg) | -0.20 ± 0.07 | | $P = 0.007$ |
| | PP_{pwf} (mmHg) | $+0.12 \pm 0.03$ | -16.68 ± 3.55 | $P = 0.002$ |
| $PP_{\text{pwf}} - PP_{\text{aorta}}$ | Age (years) | $+0.15 \pm 0.05$ | | $P = 0.004$ |
| | MAP (mmHg) | $+0.04 \pm 0.02$ | | $P = 0.047$ |
| | | | | |
| Study 2 $PP_{\text{tono}} - PP_{\text{pwf}}$ | PP_{pwf} (mmHg) | -1.07 ± 0.07 | $+39.91 \pm 3.80$ | $P < 0.001$ |
| | $PP_{\text{dwf}} - PP_{\text{pwf}}$ | -0.29 ± 0.05 | $+11.25 \pm 2.34$ | $P < 0.001$ |

ΔPP , difference in pulse pressure between methods. PP_{aorta} , pulse pressure measured intra-arterially in the ascending aorta at the branching off of the right common carotid artery; PP_{tono} , pulse pressure at the common carotid artery directly obtained from applanation tonometry; PP_{pwf} , pulse pressure at the common carotid artery from calibrated tonometer pressure waveforms; PP_{dwf} , pulse pressure at the common carotid artery from calibrated echo-tracking distension waveforms. Intercept and slope are regression coefficients \pm SE.

difference with PP_{pwf} was 2.4 times smaller for PP_{dwf} than for PP_{tono} (Table 2; Figs 3a,b). By correcting each PP_{pwf} for the systematic difference of 1.8 mmHg from invasive pulse pressure in study 1, the difference of PP_{dwf} from invasive pulse pressure ($PP_{\text{dwf}} - PP_{\text{aorta}}$) was estimated approximately. Gender, age, BMI and MAP did not influence the difference in pulse pressure between methods (Table 3). The differences of both PP_{tono} and PP_{dwf} from reference method were negatively related with PP_{pwf} .

Table 4 shows the accuracy of the test methods versus the standard method according to the BHS grading criteria. In studies 1 and 2, PP_{tono} achieved the lowest

grade of accuracy (D). In study 1, PP_{pwf} achieved the best grade of accuracy (A). In study 2, with PP_{pwf} as reference method, PP_{dwf} achieved grade B for good accuracy. After correction of each PP_{pwf} value in study 2 for the systematic error (1.8 mmHg) of PP_{pwf} versus PP_{aorta} in study 1, PP_{dwf} achieved grade A for accuracy.

Discussion

No standard criteria for the evaluation of local pulse pressure assessment exist. Although developed for the evaluation of SBP and DBP, the AAMI and BHS criteria for the evaluation of pressure measuring devices can also be applied to pulse pressure.

Table 4 British Hypertension Society grading criteria

| | Absolute difference between standard and test method | | | Grade |
|---|--|-----------|-----------|-------|
| | ≤ 5 mmHg | ≤ 10 mmHg | ≤ 15 mmHg | |
| Study 1 | | | | |
| PP _{tono} - PP _{aorta} | 17 | 51 | 68 | D |
| PP _{pwf} - PP _{aorta} | 75 | 93 | 100 | A |
| Study 2 | | | | |
| PP _{tono} - PP _{pwf} | 26 | 36 | 57 | D |
| PP _{dwf} - PP _{pwf} | 51 | 89 | 96 | B |
| PP _{dwf} - PP _{aorta} * | 60 | 93 | 96 | A |

Grades are derived from percentages of readings within 5, 10 and 15 mmHg. To achieve a grade, all three percentages must be equal to or greater than the threshold values for the grade. PP_{aorta}, pulse pressure measured intra-arterially in the ascending aorta at the branching off of the right common carotid artery; PP_{tono}, pulse pressure at the common carotid artery directly obtained from applanation tonometry; PP_{pwf}, pulse pressure at the common carotid artery from calibrated tonometer pressure waveforms; PP_{dwf}, pulse pressure at the common carotid artery from calibrated echo-tracking distension waveforms. *PP_{aorta} in study 2 is estimated by correcting each PP_{pwf} for the systematic difference of 1.8 mmHg from PP_{aorta} in study 1.

Because it has been shown that pulse pressure in the common carotid artery is identical to the ascending aorta at the branching off of the CCA [18], PP_{aorta} can be used as surrogate for real pulse pressure in the CCA.

In both of the present studies, PP_{tono} was not related to reference pulse pressure. On average, PP_{tono} largely underestimated the invasive reference pulse pressure. In addition, Bland and Altman analysis showed that PP_{tono} could also overestimate the pulse pressure in a substantial number of assessments. Both the systematic error and the large variation indicate a poor agreement and precision of the pulse pressure obtained directly from the internally calibrated tonometer in our hands. Although there is no direct guide to indicate optimal applanation, it is suggested that this condition occurs when the operator adjusts the hold-down force so that the waveform has a stable baseline, maximum amplitude and a 'reasonable' configuration [18]. Since there is substantial soft tissue between the external probe tip and the carotid artery *in situ*, it is more difficult to ascertain when this optimal state is achieved [18]. Therefore, it has been proposed that applanation tonometry needs a well-skilled investigator. All measurements in each study were carried out by one investigator, but the investigator differed between the two studies. The two investigators obtained independently similar poor results for PP_{tono}: the mean difference and standard deviation of the difference between PP_{tono} and PP_{pwf} were comparable in study 1 and study 2. As presumed by other investigators [18], we conclude that also in our hands pulse pressures at the CCA obtained from internally calibrated applanation tonometry are inaccurate.

In contrast to PP_{tono}, pulse pressures at the CCA assessed by the alternatively calibrated tonometer pressure waveforms (PP_{pwf}) did correlate very well with

PP_{aorta}. There was on average a slight (1.8 mmHg) but acceptable overestimation of the pulse pressure (with a small SD) in the Bland and Altman analysis. This deviation from the reference method was largely within the acceptability limits of the AAMI criteria (5 ± 8 mmHg). In addition, according to the BHS criteria, PP_{pwf} obtained the best grade of accuracy. The difference between PP_{pwf} and PP_{aorta} was influenced by age, MAP and the level of the pulse pressure, where all are conditions for which the applanation pressure has to be high to flatten the artery wall and to obtain a good pressure wave. Whether in these conditions inertia of the hand may influence the results is not clear. To investigate this, pencil applanation tonometry held by hand (as used in the present study) should be compared with applanation tonometry using a micromanipulator or a wristband. Alternatively, it cannot be excluded that aortic pulse pressure measured invasively with a fluid-filled catheter may slightly underestimate real pulse pressure. Data from the present study 1 show that assessment of the pulse pressure by alternatively calibrated tonometer pressure waveforms is accurate in the population studied. It also demonstrates that accurate PP_{pwf} can be obtained despite an inaccurate PP_{tono} by scaling the tonometer pressure waveform.

As a consequence of the results from study 1, PP_{pwf} was used in study 2 as non-invasive reference method. Data from study 2 confirm the inaccuracy of PP_{tono} in our hands. In contrast, and despite presumed confounding factors such as viscoelasticity and non-linearity of the pressure–distension relationship of the arterial wall, PP_{dwf} at the CCA correlated well with PP_{pwf} and was on average 3.4 mmHg lower than PP_{pwf}. Assuming a generalized overestimation of the invasive pulse pressure by 1.8 mmHg with PP_{pwf} in study 1, PP_{dwf} may on average underestimate invasive pulse pressure by 1.6 mmHg, which is a systematic error from invasive

pulse pressure in magnitude comparable to the error of PP_{pwf} in study 1. Bland and Altman analysis also showed a standard deviation of difference from PP_{pwf} for PP_{dwf} less than half that for PP_{tono} , but slightly higher than the standard deviation of the difference between PP_{aorta} and PP_{pwf} in study 1.

In contrast to the simultaneous measurement of PP_{aorta} and PP_{pwf} in study 1, for technical reasons it was not possible to assess PP_{dwf} and PP_{pwf} simultaneously in study 2. The consecutive measurement of PP_{dwf} and PP_{pwf} is expected to increase the variation in difference between PP_{dwf} and PP_{pwf} due to short-term spontaneous change in pulse pressure. In study 1, the short-term variation in pulse pressure was 2.8 ± 4.8 mmHg (data not shown in results). In addition, correlation coefficient of PP_{dwf} with invasive pulse pressure is likely to be higher than the +0.85 correlation coefficient between PP_{dwf} and PP_{pwf} .

The difference in pulse pressure between PP_{dwf} and PP_{pwf} was not influenced by age, gender, BMI and MAP, but was influenced by PP_{pwf} . The slope was -0.29 mmHg per year. Because the effect of pulse pressure on the difference between PP_{pwf} and PP_{aorta} is $+0.12$ mmHg per year in study 1, it can be assumed that approximately 40% (0.12/0.29) of the influence of PP_{pwf} on the difference between PP_{dwf} and PP_{pwf} in study 2 is caused by an error in the estimate of PP_{pwf} and approximately 60% can be attributed to an error in the estimate of PP_{dwf} .

Except for PP_{tono} , the above-mentioned data with respect to mean and SE of difference between test and reference methods are largely within the AAMI criteria of acceptability. In addition, according to the BHS criteria, PP_{dwf} achieved a grade B for good accuracy. This grading can be influenced by a systematic difference between methods [27]. After correction of each PP_{pwf} for the systematic difference of 1.8 mmHg from invasive pulse pressure in study 1, PP_{dwf} met the grade A criteria for excellent accuracy. These data show that assessment of pulse pressure by calibrated distension waves is acceptable for the assessment of local pulse pressure at the CCA in a random population. It is expected that this calibration procedure is also applicable to other arterial sites. Because distension waves can be obtained in subjects and at arterial sites where applanation tonometry and transfer function are not reliable, or not possible for technical reasons, assessment of PP_{dwf} is a valuable asset in the assessment of local pulse pressure and a good alternative to PP_{pwf} .

In conclusion, the present study shows that (i) pulse pressures from the alternatively calibrated tonometer pressure waves and from the alternatively calibrated echo-tracking arterial distension waves show good to

excellent agreement and precision in the population studied. (ii) The accuracy of the two calibration methods is dependent on the pulse pressure. Accuracy in patients with high pulse pressure (> 80 mmHg) has still to be established. (iii) In our hands, agreement and precision of pulse pressures obtained directly from internally calibrated applanation tonometry at the CCA is poor and unacceptable.

Acknowledgements

The expert technical assistance of J. Willigers, I. de Ploeg, G. Wijnands, J. Dacier and M. Knippenberg is gratefully acknowledged. The expert assistance of B. Van Baelen is also acknowledged for statistical analysis.

References

- Safar ME, London GM. The arterial system in human hypertension. In: Swales JD (editor): *Textbook of hypertension*. London: Blackwell Scientific Publications; 1994. pp. 85–102.
- Pauca AL, Wallenhaupt SL, Kon ND, Tucker WY. Does radial artery pressure accurately reflect aortic pressure? *Chest* 1992; **102**: 1193–1198.
- Nichols WW, O'Rourke M. *McDonald's blood flow in arteries. Theoretical, experimental and clinical principles*, 4th edn. London: Arnold; 1998. pp. 170–222; 347–376.
- Black HR, Kuller LH, O'Rourke MF, Weber MA, Alderman MH, Benetos A, et al. The first report of the Systolic and Pulse Pressure (SYPP) Working Group. *J Hypertens* 1999; **17** (suppl 5):S3–S14.
- Darne B, Girerd X, Safar M, Cambien F, Guize L. Pulsatile versus steady component of blood pressure: a cross-sectional analysis and a prospective analysis on cardiovascular mortality. *Hypertension* 1989; **13**: 392–400.
- Madhavan S, Ooi WL, Cohen H, Alderman MH. Relation of pulse pressure and blood pressure reduction to the incidence of myocardial infarction. *Hypertension* 1994; **23**:395–401.
- Fang J, Madhavan S, Cohen H, Alderman MH. Measures of blood pressure and myocardial infarction in treated hypertensive patients. *J Hypertens* 1995; **13**:413–419.
- Benetos A, Safar M, Rudnichi A, Smulyan H, Richard JL, Ducimetiere P, et al. Pulse pressure: a predictor of long-term cardiovascular mortality in a French male population. *Hypertension* 1997; **30**:1410–1415.
- Mitchell GF, Moye LM, Braunwald E, Rouleau J-L, Bernstein V, Geltman EM, et al. Sphygmomanometrically determined pulse pressure is a powerful independent predictor of recurrent events after myocardial infarction in patients with impaired left ventricular function. *Circulation* 1997; **96**:4254–4260.
- Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Pede S, Porcellati C. Ambulatory pulse pressure. A potent predictor of total cardiovascular risk in hypertension. *Hypertension* 1998; **32**:983–988.
- Chae CU, Pfeffer MA, Glynn RJ, Mitchell GF, Taylor JO, Hennekens CH. Increased pulse pressure and risk of heart failure in the elderly. *JAMA* 1999; **281**:634–639.
- Franklin SS, Khan SA, Wong ND, Larson MG, Levy D. Is pulse pressure useful in predicting risk for coronary heart disease? The Framingham Heart Study. *Circulation* 1999; **100**:354–360.
- Millar JA, Lever AF, Burke V. Pulse pressure as a risk factor for cardiovascular events in the MRC mild hypertension trial. *J Hypertens* 1999; **17**:1065–1072.
- Staessen JA, Gasowski J, Wang JG, Thijs L, Den Hond E, Boissel JP, et al. Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials. *Lancet* 2000; **355**:865–872.
- London G, Guerin A, Pannier B, Marchais S, Benetos A, Safar M. Increased systolic pressure in chronic uremia: role of arterial wave reflections. *Hypertension* 1992; **20**:10–19.
- Benetos A, Laurent S, Hoeks AP, Boutouyrie PH, Safar ME. Arterial alterations with aging and high blood pressure. A noninvasive study of carotid and femoral arteries. *Arterioscler Thromb* 1993; **13**:90–97.
- Kelly R, Hayward C, Ganis J, Daley J, Avolio A, O'Rourke M. Non-invasive registration of the arterial pressure pulse waveform using high-fidelity applanation tonometry. *J Vasc Med Biol* 1989; **3**:142–149.
- Chen C-H, Ting C-T, Nussbacher A, Nevo E, Kass DA, Pak P, et al. Validation of carotid artery tonometry as a means of estimating augmenta-

- tion index of ascending aortic pressure. *Hypertension* 1996; **27**: 168–175.
- 19 Kelly R, Fitchett D. Noninvasive determination of aortic input impedance and external left ventricular power output: a validation and repeatability study of a new technique. *J Am Coll Cardiol* 1992; **20**:952–963.
- 20 Milnor WR. The normal hemodynamic state. In: Milnor WR (editor): *Hemodynamics*. Baltimore, Maryland: Williams and Wilkins; 1982. pp. 132–156.
- 21 Nichols WW, O'Rourke M. *McDonald's blood flow in arteries. Theoretical, experimental and clinical principles*, 4th edn. London: Arnold; 1998. pp. 453–476.
- 22 Hoeks APG, Brands PJ, Smeets FAM, Reneman RS. Assessment of the distensibility of superficial arteries. *Ultrasound Med Biol* 1990; **16**: 121–128.
- 23 Correll RW. *Theoretical analysis and preliminary development of an indirect blood pressure recording system*, MS thesis. Cambridge, Massachusetts: MIT; 1978.
- 24 Ghista DN, Jayaraman G, Sandler H. Analysis for the noninvasive determination of arterial properties and for the transcutaneous continuous monitoring of arterial blood pressure. *Med Biol Eng Comput* 1978; **16**:715–726.
- 25 Van der Heijden-Spek JJ, Staessen JA, Fagard RH, Hoeks AP, Struijker Boudier HA, Van Bortel LM. The effect of age on brachial artery properties differs from the aorta and is gender dependent: a population study. *Hypertension* 2000; **35**:637–642.
- 26 Hansen KW, Orskov H. A plea for consistent reliability in ambulatory blood pressure monitors: a reminder. *J Hypertens* 1992; **10**:1313–1315.
- 27 White WB, Berson AS, Robbins C, Jamieson MJ, Prisant M, Roccella E, Sheps SG. National standard for measurement of resting and ambulatory blood pressures with automated sphygmomanometers. *Hypertension* 1993; **21**:504–509.
- 28 O'Brien E, Petrie J, Littler W, de Swiet M, Padfield PL, Altman DG, *et al*. The British Hypertension Society protocol for the evaluation of blood pressure devices. *J Hypertens* 1993; **11** (suppl 2):S43–S62.
- 29 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307–310.