Influence of noninvasive peripheral arterial blood pressure measurements on assessment of dynamic cerebral autoregulation

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A novel method of peripheral noninvasive arterial blood pressure (AP) measurement has been introduced. This method, the Finapres (Ohmeda), records arterial pressure by using the principle of arterial volume clamping to record ABP in the digital artery (26). The purpose of the present work was to compare the Finapres-derived measurements with the corresponding estimates obtained from invasive measurements in the aorta. Dynamic cerebral autoregulation (CA) is the maintenance of cerebral blood flow velocity (CBFV) relatively constant despite large changes in arterial blood pressure (ABP). The introduction of noninvasive devices for monitoring ABP and CBFV has allowed the study of dynamic CA in populations whose invasive ABP measurement would not be appropriate for ethical, logistic, or safety reasons. Most of these noninvasive devices, like the Finapres, Portapres, or Finometer, use the principle of arterial volume clamping to record ABP in the digital artery (26).

Innovative Methodology

Two technological developments have contributed to a growing interest in the noninvasive assessment of CA. First, the excellent temporal resolution of transcranial Doppler ultrasound has allowed the analysis of transient CBF velocity (CBFV) responses to induced or spontaneous changes in ABP (20). Second, the introduction of devices that can measure ABP continuously by noninvasive means has allowed the study of dynamic CA in populations whose invasive ABP measurement would not be appropriate for ethical, logistic, or safety reasons. Most of these noninvasive devices, like the Finapres, Portapres, or Finometer, use the principle of arterial volume clamping to record ABP in the digital artery (26).

As methods for assessing dynamic cerebral autoregulation move from the research laboratory to clinical practice, it becomes increasingly important to establish any differences in results that could be ascribed to the techniques adopted to record continuous ABP. Noninvasive finger ABP (ABPfin) has been the object of many validation studies, mainly compared with intravascular ABP measurements in the brachial or radial arteries (1, 31). Second, the introduction of devices that can measure ABP continuously by noninvasive means has allowed the study of dynamic CA in populations whose invasive ABP measurement would not be appropriate for ethical, logistic, or safety reasons. Most of these noninvasive devices, like the Finapres, Portapres, or Finometer, use the principle of arterial volume clamping to record ABP in the digital artery (26).

METHODS

Subjects and measurements. Recruited subjects were scheduled for routine elective percutaneous coronary interventions. Exclusion criteria included conditions potentially affecting the blood flow to the hands such as Raynaud’s phenomenon. Patients were screened in advance of their elective procedure with the Finapres device, to exclude those who displayed a difference $>$5% between the systolic and diastolic ABP values of their right and left hands. Patients were not excluded on the basis of their individual pathologies or medications, since each would act as his/her own control. The local ethics committee approved the study, and all patients were provided with detailed written information regarding the intent and procedures of the study. All measurements were conducted in the morning after a fasting period of 6 h, during which time patients were asked to refrain from...
alcohol and nicotine. Left heart catheterization was performed by the femoral artery percutaneous Seldinger technique. After the elective procedure, a catheter-tip pressure transducer (Mikro-Tip SPC-454E; Millar Instruments, Houston, TX), balanced to zero atmospheric pressure, was advanced over a 0.028-inch guide wire, under fluoroscopic guidance to the ascending aorta (2–3 cm above the aortic cusps), and measurements were performed with subjects in a supine position. Bilateral middle cerebral artery (MCA) velocity measurements were obtained via acoustic windows using transcranial Doppler ultrasound (TCD; 2 MHz; Scimed QVL 842X, Bristol, UK), probes being immobilized by an adjustable head frame set. Depth of insertion was between 45 and 55 mm.

\( \text{ABP}_{\text{fin}} \) was measured by the Finapres device (Finapres 2300; Ohmeda, Engwood, CO), attached to the middle finger. The arm was rested at the patient’s side at atrial level with the hand kept warm by a blanket. The Finapres cuff was repositioned until a stable waveform was achieved with the servo-adjust on, waveforms being considered stable when the period between servo-adjusts was >30 beats duration (11). Once this had been achieved, the servo-adjust was switched off, to avoid unwanted artifacts, and calibration signals from the Finapres and Millar catheter were recorded before each measurement. Three standard chest leads were used to record the ECG. Transcutaneous \( \text{CO}_2 \) levels were measured (TINA; Radiometer, Copenhagen, Denmark).

Simultaneous and continuous measurements of ECG, TINA, \( \text{ABP}_{\text{fin}} \), TCD, and \( \text{ABP}_{\text{ao}} \), data were recorded on digital audiotape (DAT Sony PC-208AX), for 10 min. The Finapres servo was switched back on, the system was allowed to restabilize, and then the servo was switched off again. This was followed by another calibration of the Finapres and intra-arterial catheter and a second 10-min recording.

**Data analysis.** Signals recorded on DAT tapes were transferred to a computer for offline editing and analysis. The maximum cerebral blood flow velocity was calculated every 5 ms using the fast Fourier transform (FFT) algorithm. All other analog signals were also digitized at 200 samples/s. The editing process first involved calibration of both ABP signals, followed by visual inspection and removal of artifacts. The two Doppler signals were then median filtered with a window width of 5 samples, and all signals were low-pass filtered by a zero-phase Butterworth filter, with a cut-off frequency of 20 Hz, to prevent aliasing, while preserving their most significant harmonics. The beginning and end of each cardiac cycle were automatically marked from the ECG to allow beat-to-beat estimates of mean, systolic, and diastolic CBFV and ABP.

The beat-to-beat mean CBFV and ABP time series were spline interpolated and then resampled at 5 Hz to create a uniform time base. Transfer function analysis of ABP (input) and CBFV (output) was performed with standard techniques (19, 21, 34). In brief, spectral estimates were obtained with an FFT algorithm, and the Welch method was used to estimate the coherence function, gain, and phase of the ABP-CBFV transfer function were calculated for three separate frequency intervals, corresponding to low frequency (LF, 0.0–0.1 Hz), mid-frequency (MF, 0.1–0.25 Hz), and high frequency (HF, 0.25–0.4 Hz).

**Statistical analysis.** Only subjects with good-quality CBFV signal recordings for both MCAs were accepted for analysis. Separate analyses were performed for the right and left MCA to compare the consistency of estimates derived from each side. Agreement between estimates of dynamic CA obtained from the Finapres, with corresponding values derived from \( \text{ABP}_{\text{ao}} \), was assessed with Bland-Altman plots and calculation of correlation coefficients. The bias and precision of parameters were obtained from the mean and SD of differences between the Finapres and aorta-derived parameters. The dynamic relationship between the two ABP sources was also quantified by the coherence function between beat-to-beat values of mean \( \text{ABP}_{\text{ao}} \) and mean \( \text{ABP}_{\text{fin}} \). A paired Student’s \( t \)-test was used to assess the significance of differences, assuming a critical value of \( \bar{P} = 0.05 \). Multiple comparisons were corrected by the Bonferroni procedure. The influence of age on the differences between parameters derived from the Finapres and aortic pressure was tested by linear regression.

**RESULTS**

Forty-five patients were recruited, but good quality Doppler recordings for both MCAs were only obtained in 27 subjects who were used in the analysis. The main reason for rejection was the absence of a suitable acoustic window in one or both sides. The demographic, clinical profile, and baseline characteristics of the population studied are given in Table 1.

### Table 1. Demographics, clinical profile, and baseline characteristics of the study population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>SD or ( n )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female</td>
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<td>25/2</td>
</tr>
<tr>
<td>Ethnicity, Caucasian/Asian</td>
<td>25/2</td>
<td>25/2</td>
</tr>
<tr>
<td>Age, yr</td>
<td>61.4±11.2</td>
<td>27.4±3.5</td>
</tr>
<tr>
<td>Body mass index, kg/m(^2)</td>
<td>27.4±3.5</td>
<td>27.4±3.5</td>
</tr>
<tr>
<td>Cholesterol, mmol/l</td>
<td>4.4±1.1</td>
<td>4.4±1.1</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.74±0.05</td>
<td>1.74±0.05</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>83.0±11.2</td>
<td>83.0±11.2</td>
</tr>
<tr>
<td>Drug therapy</td>
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<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>Lipid-lowering agent</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Nitrates</td>
<td>19</td>
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</tr>
<tr>
<td>Beta adrenoeceptor antagonist</td>
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<td>18</td>
</tr>
<tr>
<td>ACE or angiotensin II receptor antagonist</td>
<td>14</td>
<td>14</td>
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<tr>
<td>Clopidogrel</td>
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<td>14</td>
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<tr>
<td>Calcium channel blocker</td>
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<td>12</td>
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<tr>
<td>Potassium channel inhibitor</td>
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<td>4</td>
</tr>
<tr>
<td>Diuretic</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Percutaneous coronary intervention (PTCA/CoA)</td>
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<td>23/4</td>
</tr>
<tr>
<td>Mean ( \text{ABP}_{\text{fin}} ), mmHg</td>
<td>94.0±16.0</td>
<td>94.0±16.0</td>
</tr>
<tr>
<td>Systolic ( \text{ABP}_{\text{fin}} ), mmHg</td>
<td>138.5±23.7</td>
<td>138.5±23.7</td>
</tr>
<tr>
<td>Diastolic ( \text{ABP}_{\text{fin}} ), mmHg</td>
<td>72.8±13.4</td>
<td>72.8±13.4</td>
</tr>
<tr>
<td>Mean ( \text{ABP}_{\text{ao}} ), mmHg</td>
<td>96.5±14.5</td>
<td>96.5±14.5</td>
</tr>
<tr>
<td>Systolic ( \text{ABP}_{\text{ao}} ), mmHg</td>
<td>134.2±25.8</td>
<td>134.2±25.8</td>
</tr>
<tr>
<td>Diastolic ( \text{ABP}_{\text{ao}} ), mmHg</td>
<td>69.7±10.7</td>
<td>69.7±10.7</td>
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<tr>
<td>( \text{CBFV}_L ), cm/s</td>
<td>42.1±13.0</td>
<td>42.1±13.0</td>
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<tr>
<td>( \text{CBFV}_R ), cm/s</td>
<td>45.7±15.5</td>
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<tr>
<td>Heart rate, beats/min</td>
<td>58.6±8.3</td>
<td>58.6±8.3</td>
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<tr>
<td>( \text{TcCO}_2 ), mmHg</td>
<td>27.4±9.3</td>
<td>27.4±9.3</td>
</tr>
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</table>

Values are means ± SD or \( n \). Study population \( n = 27 \). PTCA, percutaneous transluminal coronary angioplasty; CoA, coronary angioplasty; \( \text{ABP}_{\text{fin}} \), finger arterial blood pressure; \( \text{ABP}_{\text{ao}} \), aortic arterial blood pressure; \( \text{CBFV}_L \), left cerebral blood flow velocity; \( \text{CBFV}_R \), right cerebral blood flow velocity; \( \text{TcCO}_2 \), transcutaneous \( \text{CO}_2 \).
The bias and SD of differences for ABPfin - ABPao for the systolic, diastolic, and mean ABP were 4.3 ± 18.0 (P = 0.22), 3.2 ± 7.0 (P = 0.027), and -2.5 ± 8.4 mmHg (P = 0.14), respectively. The total mean ABP power was not significantly different between ABPfin and ABPao, but the Finapres power was significantly higher for the LF range (11.75 ± 10.40 vs. 9.74 ± 9.50 mmHg^2, P = 0.014) and significantly lower for the MF range (1.48 ± 1.59 vs. 2.63 ± 3.94 mmHg^2, P = 0.020).

As shown in Fig. 1, there was a high coherence between mean ABPao and mean ABPfin, but with a sharp reduction for frequencies <0.05 Hz. The mean ± SD coherences for the low, middle, and high frequency ranges were 0.87 ± 0.08, 0.87 ± 0.12, and 0.84 ± 0.18, respectively.

Figure 2 illustrates the differences in step response pattern and ARI values that can be obtained using either ABPao or ABPfin as the input pressure, for the same CBFV output signal. For the population as a whole, significant differences were obtained for most parameters from transfer function analysis and the ARI index, for both MCAs, as shown in Table 2. The exceptions were LF coherence and LF phase, for both MCAs, and HF phase for the left MCA (Table 2). The correlation coefficients between transfer-function analysis and time-domain estimates of dynamic CA obtained with the Finapres and from ABPao are given in Table 3.

The differences observed for the ARI and ΔSTEP indicate that ABPfin results in higher values for calculated dynamic CA response, and this is confirmed by the plots in Fig. 3, showing a lower LF gain, higher MF phase, but mainly an average step response that drops significantly more than the response obtained with ABPao.

Figure 4 shows the Bland-Altman plots of gain, phase, ARI, and step response recovery for the right MCA. The only plot which showed a significant trend was the LF gain, with differences becoming more negative as the gain increased (P = 0.008), but this trend became nonsignificant when the negative outlier was removed. Similar results were obtained for the left
MCA, but the differences observed were smaller, and no trends were observed in any plots. The two subjects who showed outlier differences in LF phase (Fig. 4B) also displayed outliers in the step response recovery (Fig. 4D), and one of them also contributed to the ARI result outlier (Fig. 4C).

Linear regressions of differences in ARI or ΔSTEP (Finapres-aortic) against age (range 41–81 yr old) were not significant.

DISCUSSION

The accuracy and precision of the Finapres device have been assessed in a variety of physiological and pathological conditions (12), but we are not aware of any previous studies dealing with its influence on estimates of dynamic CA. Other characteristics of our study are also unique, for example regarding the usual method of comparing standard ABP parameters between the Finapres and intra-arterial ABP recordings at rest. Most of these studies recorded intra-arterial pressure in the brachial or radial arteries. Of the few studies that measured ABP in the aorta, two used fluid-filled catheters with an external transducer, which can lead to distortions, mainly in systolic pressure values (9, 26). Hope et al. (11) used high-fidelity solid-state catheter-tip transducers, as in this study, but compared aortic pressure against a radial tonometer, rather than the Finapres.

These methodological differences need to be considered when comparing the values of bias and precision that we obtained with the wide range of corresponding values reported in the literature (12). In our case, significant differences were only observed for diastolic pressure, with a small bias of 3.2 mmHg, thus showing a very good agreement between the two pressure sources.

The coherence function between the two pressure sources showed that mean beat-to-beat values of ABPfin were significantly coupled to corresponding values of mean ABPao for the entire frequency range <0.5 Hz. Notably, the highest population average coherence occurred ~0.05 Hz and decreased quite sharply for lower frequencies (Fig. 1). The drop in coherence in the LF range was probably associated with the significantly higher variability of the mean ABPfin in this frequency range, in relation to mean ABPao, which could have been caused by vasomotion under the finger cuff. Overall, the average coherence function between the ABPao and ABPfin compares well with population curves previously reported (15, 18).

From the reduced bias in ABP parameters and the elevated values of coherence, we should expect a good agreement between estimates of dynamic CA derived from the two different pressure sources. On one hand this expectation was confirmed by the average population values shown in Fig. 3 and the relatively small differences observed in the parameters (Table 2 and Fig. 4). In particular, Fig. 4 shows satisfactory agreement for gain, phase, ARI, and ΔSTEP, except for two subjects who contributed with outlier values. On the other hand, the directional consistency of those differences, and their relatively small scatter, led to statistically significant differences for several parameters that characterize dynamic CA in the frequency and time domain (Table 2). Frequency-domain parameters were averaged for three different spectral bands, but special consideration should be given to the LF range where we can expect dynamic CA to be more active. For frequencies <0.1 Hz, only the gain was significant, for both hemispheres, although the P values for coherence and phase were close to reaching significance (Table 2). Conversely, the two time-domain parameters showed highly significant differences, which could be explained by their reflecting the simul-
taneous contributions of gain and phase for the entire spectrum. Again, these differences in gain, ARI, and ΔSTEP are likely to be the consequence of the greater variability observed in mean ABPfin in the LF range compared with the corresponding power of ABPao in the same frequency band. For frequencies >0.1 Hz, the significantly superior coherences between CBFV and ABPao, in relation to the Finapres (Table 2 and Fig. 3A), confirmed the premise that aortic pressure provides a better approximation to MCA pressure than ABPfin.

Both the ARI and the step response indicate that ABPfin tends to give higher values for the efficiency of dynamic CA in relation to values derived from ABPao (Table 2 and Fig. 3D). This result is important bearing in mind when approaching the large body of literature that has accumulated in recent years on human dynamic CA studies, based on ABP measurements in the finger. The vast majority of those studies dealt with specific groups of subjects, and, given the small differences between group averaged parameters (Table 2), it is less likely that their conclusions would have been different if ABPao had been used instead. On the other hand, results could have been different in studies that analyzed individual patients or very small groups of subjects, mainly when there was reason to suspect of a beta-error. One such example is the failure to detect any effects of ageing on dynamic CA (3, 14, 30). For this reason, we have also tested the possible influence of ageing on our set of data but did not find any significant effects. Nevertheless, our youngest subject was 41 yr old, and different results could have been obtained with younger (and healthier) subjects.

The main limitation of this study is the impossibility of extrapolating its findings to healthy subjects and other patient groups. Similarly to other studies involving continuous recordings of aortic pressure, we performed measurements in patients undergoing catheterization of the coronary arteries (10, 11, 27). The fact that these patients might have an increased probability of having both extracranial and intracranial atherosclerotic disease does not invalidate our results since the same CBFV recording was used for the dynamic CA estimates obtained for both ABP sources. Furthermore, these patients are a representative group of individuals that could have been studied with the Finapres for assessment of dynamic CA for a number of different reasons. Our initial findings in this particular group of subjects should encourage further studies covering a wider spectrum of ages and clinical conditions. Seventy-six percent of the subjects included in the study used β-adrenergic antagonists (β-blockers) to treat their cardiovascular disease. Significantly, the recent CAFE (Conduit Artery Function Evaluation) study by Williams et al. (33), found that β-blockers augment systolic ABPao by slowing the heart rate. This prolongs systolic ejection time and thereby allows time for reflected waves to summate the incident wave during its systolic phase. Therefore, we cannot exclude the possibility of altered hemodynamics in the ascending aorta influencing the discrepancies currently reported. Also, we did not measure aortic compliance, which is a known determinant of the preanacrotic phenomena. However, the study by Philippe et al. (27) found no significant correlation between compliance and factors affecting pulse-wave amplification, as well as the Finapres ABP bias.

Under ideal conditions, simultaneous recordings of invasive peripheral ABP would had been useful to identify the source of
the differences in dynamic CA that were observed in parameters derived from the Finapres. For ethical reasons, it was not possible to insert an additional catheter in the radial artery in this study, and we cannot rule out the possibility that similar differences would have been observed in dynamic CA parameters extracted from invasive peripheral ABP measurements. Previous studies that relied on invasive peripheral ABP recordings to calculate dynamic CA parameters reported similar patterns for coherence function, gain, phase frequency response, and CBFV step response (23), but because the Finapres data showed relatively small differences in relation to the ABPao results in this study (Fig. 3), a dedicated investigation is necessary to determine how much of the differences observed can be apportioned to the measurement site, i.e., propagation and reflection effects, and how much could be due to limitations in the accuracy of the Finapres.

Previous studies of dynamic CA employed different maneuvers to induce changes in ABP, such as sudden thigh cuff deflation (1, 5, 19, 20, 31, 32, 34), to elicit large changes in CBFV and to reduce the duration of physiological recordings. On the other hand, these maneuvers could have accentuated differences between parameters derived from the Finapres, in relation to the aortic estimates. Birch and Morris (2) have shown that ABP measured by applanation tonometry in the wrist leads to a different time course in relation to the Finapres tracing during thigh-cuff maneuvers. On the other hand, the relatively small fluctuations in ABP observed during recordings at rest, as adopted in this study, could be seen as a more stringent test for the agreement between intra-aortic and noninvasive measurements, due to the relatively worse signal-to-noise ratio of this modality (35).

One common limitation of studies based on transcranial Doppler recordings is the assumption that changes in CBFV reflect changes in CBF, which is only valid if the cross-sectional area of the insonated vessel remains constant. The subjects we studied were at rest, without large changes in ABP or PaCO2, and hence less likely to exhibit changes in MCA diameter than other patient groups (29). In this study, the potential influence of MCA diameter changes was even less of a concern since the same CBFV recording was used for the two different estimates obtained from each ABP source.

In summary, we have shown that estimates of dynamic CA derived from intra-aortic ABP measurements show similar frequency-domain patterns for coherence function, gain, and phase frequency response, as well as similar time-domain CBFV step responses to those previously reported based on peripheral recordings of ABP obtained by invasive or noninvasive methods. Nevertheless, dynamic CA parameters obtained with the Finapres show small, but significant, differences from those extracted from intra-aortic recordings. Future research in this area should investigate the validity of our findings for healthy subjects or other patient groups. Whether similar results would be obtained for intra-arterial measurements in the brachial or radial arteries should also be the subject of further investigations.

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GRANTS

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