Empirical estimates of mean aortic pressure: advantages, drawbacks and implications for pressure redundancy

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ABSTRACT

Mean arterial pressure (MAP) is estimated at the brachial artery level by adding a fraction of pulse pressure (form factor; $= 0.33$) to diastolic pressure. We tested the hypothesis that a fixed form factor can also be used at the aortic root level. We recorded systolic aortic pressure (SAP) and diastolic aortic pressure (DAP), and we calculated aortic pulse pressure (PP) and the time-averaged MAP in the aorta of resting adults ($n = 73$; age $43 \pm 14$ years). Wave reflection was quantified using the augmentation index. The aortic form factor (range $0.35–0.53$) decreased with age, MAP, PP and augmentation index (each $P < 0.001$). The mean form factor value (0.45) gave a reasonable estimation of MAP ($\text{MAP} = \text{DAP} + 0.45 \times \text{PP}$; bias $= 0 \pm 2 \text{ mmHg}$), and the bias increased with MAP ($P < 0.001$). An alternative formula ($\text{MAP} = \text{DAP} + \text{PP}/3 + 5 \text{ mmHg}$) gave a more precise estimation (bias $= 0 \pm 1 \text{ mmHg}$), and the bias was not related to MAP. This latter formula was consistent with the previously reported mean pulse wave amplification of $15 \text{ mmHg}$, and with unchanged MAP and diastolic pressure from aorta to periphery. Multiple linear regression showed that $99\%$ of the variability of MAP was explained by the combined influence of DAP and SAP, thus confirming major pressure redundancy. Results were obtained irrespective of whether the marked differences in heart period and extent of wave reflection between subjects were taken into account. In conclusion, the aortic form factor was strongly influenced by age, aortic pressure and wave reflection. An empirical formula ($\text{MAP} = \text{DAP} + \text{PP}/3 + 5 \text{ mmHg}$) that is consistent with mechanical principles in the arterial system gave a more precise estimate of MAP in the aorta of resting humans. Only two distinct pressure-powered functions were carried out in the (SAP, DAP, MAP, PP) four-pressure set.

INTRODUCTION

Mean arterial pressure (MAP) is estimated at the brachial artery level by adding a fraction of pulse pressure (form factor; $= 0.33$) to diastolic pressure. Although true MAP is the area under the blood pressure curve divided by cardiac cycle length, clinical and epidemiological studies currently approximate brachial MAP by using an empirical formula where a fraction of pulse pressure (form factor; $= 0.33$) is applied.
is added to the diastolic pressure [3,4]. This empirical formula implies that MAP is twice as sensitive to diastolic as it is to systolic pressure (MAP = 2/3 \times diastolic pressure + 1/3 \times systolic pressure). Increased MAP is an important component of vascular overload and cardiovascular risk, and the redundant relationship between systolic, diastolic and mean pressure may have implications for cardiovascular risk stratification [5–7]. The main drawbacks of this formula arise from unpredictable changes in form factor related to age and vasomotor tone [5,8,9].

According to this empirical formula, it is generally assumed that, at a given MAP, increased pulse pressure reflects an increased systolic pressure (and thus left ventricular systolic load) and a decreased diastolic pressure, which may compromise coronary perfusion [10,11]. However, central and not brachial blood pressure reflects the true workload placed on the left ventricle and determines myocardial oxygen consumption and coronary perfusion pressure. The MAP and diastolic arterial pressure show little difference between central and peripheral arteries, whereas systolic pressure increases from aorta to periphery. This pulse wave amplification depends on the characteristics of pressure wave transmission and reflection, and is mainly influenced by arterial compliance, body length, heart rate, MAP, age and sex [10–14]. The form factor value, which relates to pulse contour characteristics, is approx. 0.50 in central arteries (sine-wave pattern), thus implying that MAP is roughly as sensitive to diastolic aortic pressure (DAP) as it is to systolic aortic pressure (SAP) [4]. However, the precise relationship between the steady and pulsatile components of blood pressure remains to be documented at the aortic root level.

In this preliminary prospective study, we tested the hypothesis that a single form factor value can be used to reliably estimate MAP at the aortic root level. We also present the advantages and drawbacks of MAP empirical formulas, together with their pathophysiological implications in terms of left ventricular load, coronary perfusion pressure, peripheral arterial haemodynamics and pressure redundancy.

METHODS

Patients

This prospective study included patients (n = 73; 65 males) with symptoms of chest pain or other cardiovascular symptoms who were referred to the catheterization laboratory for diagnostic or routine right and left heart catheterization. Patients with end-stage heart failure, rhythm disturbances or aortic or mitral valve insufficiency were excluded from the study. The final diagnosis was as follows: subjects with normal cardiac function and coronary angiograms, n = 11; subjects with miscellaneous cardiac diseases (mainly idiopathic dilated cardiomyopathy, coronary artery disease, right ventricular disease, grafted heart and hypertrophic cardiomyopathy), n = 62. In patients receiving vasoactive drugs, treatment was discontinued 24 h before the investigation. At the time of the study, 18 patients (25%) had a SAP > 140 mmHg at baseline. Four patients (5%) suffered from diabetes mellitus. All patients gave informed consent, and the ethical committee of our institution approved the protocol.

Catheterization technique and recordings

Patients were studied according to our routine protocol [15]. All patients were in the fasting state for at least 12 h before the investigation. No premedication was administered. Lidocaine (1%) was used for local anaesthesia, and 5000 units of heparin was administered intravenously. The percutaneous femoral approach was used. The left heart pigtail catheter was an 8F single lumen catheter with a lateral high-fidelity transducer (Cordis/Sentron, Roden, The Netherlands) [16]. The catheter was advanced from the femoral artery to the aortic root. After a 5-min equilibrium period, pressure data were recorded at base over a 15 s period. The data were computed on a Toshiba 3200 SX with customized software (sampling rate 500 Hz). Cardiac output was determined by the thermodilution technique (Cardiac Output Computer model 9520A; Edwards Laboratories).

SAP and DAP were measured automatically, and aortic pulse pressure (PP) was calculated as PP = SAP − DAP. Pressure wave reflection was evaluated by calculating the pressure augmentation index [14]. In 65 out of 73 patients (89%), a well-defined systolic pressure inflection point (P) divided the aortic pressure wave form into early and late systolic phases, and we calculated the augmentation index as follows:

\[
\frac{\Delta P}{PP} = \frac{(SAP - P)}{PP}
\]

Subjects were divided into three groups according to the classification proposed previously by Murgo et al. [14]: type A (n = 51), \(\Delta P/PP > 0.12\); type B (n = 11), 0 < \(\Delta P/PP \leq 0.12\); type C (n = 3), \(\Delta P/PP \leq 0\). Thus, according to this classification, 78% subjects were type A, 17% were type B and 5% were type C. Given that 81% of patients were older than 30 years, this finding is consistent with earlier studies [2,14]. The systolic inflection point could not be clearly defined in eight subjects.

Reference MAP value

The time-averaged MAP in the aorta was taken as the reference value. The MAP was calculated as the total area under the pressure curve divided by the heart period.
Estimates of MAP

\[ \text{MAP} = \text{DAP} + (\text{form factor} \times \text{PP}) \]
In each patient, the form factor was calculated as follows:

\[ \text{MAP} = \text{DAP} + (\text{form factor} \times \text{PP}) \]
\[ \text{Form factor} = (\text{MAP} - \text{DAP}) / \text{PP} \]

The mean form factor value was calculated in the overall population, so as to propose an improved, new empirical estimation of MAP.

\[ \text{MAP} = \text{DAP} + \frac{\text{PP}}{3} + 5 \text{ mmHg} \]
This formula has been proposed more recently at the aortic root level [17].

Statistical analysis

Results are expressed as means ± S.D. Pressures and time parameters were averaged over 10 consecutive cardiac cycles. We tested the predictive performance of the empirical formulae against the reference MAP value, using single linear regression. In addition to the \( r^2 \) statistics, the predictive performances of all regression analyses were assessed by the bias, calculated as the mean difference (± S.D.) between predicted and reference MAP values. We tested the hypothesis that MAP was redundant when SAP and DAP values were given. To this end, a multiple linear regression of SAP and DAP was applied to the whole data set. Comparisons between groups were performed by using ANOVA. Linear regression was studied using the least-squares method. A \( P \) value of \( < 0.05 \) was considered statistically significant.

RESULTS

The characteristics of the study population are given in Table 1. Significant linear relationships were found between the four aortic pressures under study (SAP, DAP, PP, MAP), and the correlation coefficients are summarized in Table 2. The augmentation index was positively related to age (\( r = 0.52 \)), MAP (\( r = 0.56 \)) and PP (\( r = 0.72 \)) (each \( P < 0.001 \)) and was negatively related to height (\( r = -0.39, P < 0.01 \)), similar to previous findings [8, 18, 19]. Age and PP were also positively related (\( r = 0.39, P < 0.01 \)), but there was no relationship between age and MAP (\( r = 0.18 \)).

\[ \text{MAP} = \text{DAP} + (\text{form factor} \times \text{PP}) \]
On average, the fraction of PP that must be added to DAP so as to obtain the time-averaged MAP (i.e. the form factor) was 0.45. The form factor (range 0.35–0.53) decreased linearly with age (\( r = -0.69 \)), MAP (\( r = -0.41 \)), PP (\( r = -0.73 \)) and \( \Delta PP/PP \) (\( r = -0.83 \)) (each \( P < 0.001 \)) (Figure 1). The form factor increased with height (\( r = 0.37, P < 0.01 \)), and was unrelated to body weight, surface area, heart rate and cardiac index. The form factor was higher in patients with SAP > 140 mmHg (0.46 ± 0.04) than in the remaining subjects (0.42 ± 0.04; \( P < 0.001 \)). The form factor was similar in controls (0.46 ± 0.03) and in patients with miscellaneous cardiac diseases (0.45 ± 0.04; \( P = 0.28 \)). By applying this single form factor value of 0.45 to the overall population, we obtain:

\[ \text{MAP} = \text{DAP} + 0.45 \text{PP} \]

This formula gave a precise estimation of MAP (100 ± 16 mmHg; mean bias = 0 ± 2 mmHg). The bias ranged from -3 to +8 mmHg and increased with MAP (\( r = 0.40, P < 0.001 \)) (Figure 2, upper panel), age (\( r = 0.67, P < 0.001 \)) and \( \Delta PP/PP \) (\( r = 0.76, P < 0.001 \)). The bias was not influenced by heart rate (\( r = -0.24 \)).

\[ \text{MAP} = \text{DAP} + \frac{\text{PP}}{3} + 5 \text{ mmHg} \]
This formula gave a precise estimation of MAP (100 ± 15 mmHg; bias = 0 ± 1 mmHg). The bias ranged from -3 to +3 mmHg. The bias was not influenced by MAP (\( r = -0.19 \); Figure 2, lower panel) or heart rate (\( r = -0.14 \)). The bias increased with age (\( r = 0.61, P < 0.001 \)) and \( \Delta PP/PP \) (\( r = 0.30, P < 0.01 \)). This formula can be rewritten as follows:

\[ \text{MAP} = 0.67 \text{DAP} + 0.33 \text{SAP} + 5 \text{ mmHg} \]

Pressure redundancy

Multiple linear regression indicated that 99% of the variability of MAP was explained by the combined

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Correlation matrix (n = 73)</th>
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<tr>
<td></td>
<td>SAP</td>
</tr>
<tr>
<td>SAP</td>
<td>0.794</td>
</tr>
<tr>
<td>DAP</td>
<td>0.945</td>
</tr>
<tr>
<td>MAP</td>
<td>0.668</td>
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All relationships are \( P < 0.0001 \) except * \( P = 0.0003 \).
influence of DAP and SAP (multiple $r^2 = 0.9914$). The equation was as follows:

$$\text{MAP} = 0.70 \text{DAP} + 0.32 \text{SAP} + 4 \text{ mmHg}$$

This equation is very close to the formula given above and gave a precise estimation of MAP ($100 \pm 15 \text{ mmHg}$; bias $= 0 \pm 1 \text{ mmHg}$). The bias ranged from $-3$ to $+3 \text{ mmHg}$ and was not influenced by MAP ($r = -0.13$, $P = 0.27$). Assuming that the pressure bias is small enough to be negligible, this implies that two subjects with the same DAP and SAP had the same MAP, irrespective of their pressure waveform and heart rate (Figure 3). The addition of age, $\Delta P/\text{PP}$ or both to the multiple regression increased the multiple $r^2$ value slightly (0.9949, 0.9928 and 0.9950 respectively). The SAP value was predicted accurately when MAP and DAP values were given [bias $= 0.7 \pm 4.2 \text{ mmHg}$ (i.e. $0 \pm 3\%$); range $-9$ to $10 \text{ mmHg}$].

**DISCUSSION**

The fraction of PP that must be added to DAP so as to obtain the time-averaged MAP was 0.45 at the aortic root level. Although this gave a reasonably good estimation of MAP, the form factor was influenced by age and aortic pressure, and a better estimate was obtained by using an alternative formula ($\text{MAP} = \text{DAP} + \text{PP}/3 + 5 \text{ mmHg}$). The unusual accuracy of this empirical formula suggested that two pressures were enough to describe the (SAP, DAP, PP, MAP) four-pressure set. Pressure redundancy was confirmed by multiple linear regression, showing that 99% of the variability of MAP was explained by the combined influence of DAP and SAP.

In the peripheral arteries of adults, MAP is estimated by adding $0.33 \times$ (pulse pressure) to diastolic pressure [3, 4]. The form factor may depend on arterial pressure, age and arterial location. In newborns, it has been recommended that form factors of 0.40 and 0.50 are used for the tibial artery and the radial artery respectively [20]. In adults, the assumed weakness of the empirical estimate of MAP is illustrated throughout aging, where the form factor of 0.33 becomes closer to 0.50. This could be responsible for the levelling off of estimated MAP after age 50–60 years, thus also explaining why MAP is no longer a surrogate measurement of vascular resistance [5]. Validation of the form factor value is hampered by the small calibre of the brachial artery and by the need for miniaturized high-fidelity pressure recording systems. Overall, these limitations could explain the difficulty in
Estimation of mean aortic pressure

Figure 2 Empirical estimates of MAP

Upper panel: correlation between the true time-averaged MAP and the pressure bias obtained using a single form factor of 0.45 \[\text{bias} = (\text{DAP} - 0.45 \times \text{PP}) - \text{MAP}\] \((n = 73)\). Mean bias and 95% confidence interval are indicated. The bias increased with MAP. Lower panel: correlation between the true time-averaged MAP and the pressure bias obtained using the alternative empirical formula \[\text{bias} = (\text{DAP} + 0.33 \times \text{PP} + 5 \text{mmHg}) - \text{MAP}\] \((n = 73)\). Mean bias and 95% confidence interval are indicated. The bias was not influenced by MAP.

Precisely documenting the role of MAP in cardiovascular risk. Such a role is, however, intuitive, as MAP accounts for more than 80% of the total hydraulic load put on the left ventricle and is considered as the perfusion pressure through each tissue bed [1,2].

Central aortic pressure reflects the workload put on the left ventricle, and determines myocardial oxygen consumption, coronary perfusion pressure and the prevailing pressure for aortic baroreflexes. Furthermore, arterial pressure at any point of the vascular tree depends on both central aortic pressure and the characteristics of pressure wave transmission and reflection. Both the large aorta diameter and the possibility of using high-fidelity pressure catheters make it possible to reliably compare the true MAP and empirical estimates.

Although reasonably accurate \((\text{bias} = 0 \pm 2 \text{mmHg})\), this formula has several drawbacks. First, there is no theoretical/physiological background upon which to predict such a formula. Secondly, the formula gives the false impression that the form factor value is constant. Conversely, we observed that MAP was as sensitive to DAP as it was to SAP in young patients, and in patients with a low PP value and a small extent of wave reflection (form factor approx. 0.50). The relative contribution of DAP increased in older patients, and in those with a high PP value and enhanced wave reflections, in whom MAP tended to be twice as sensitive to DAP as it was to SAP (form factor approx. 0.33). The pathophysiological implications may be important. The left ventricular systolic wall stress and coronary perfusion pressure depend

Figure 3 Pressure redundancy

A typical example is presented, where two subjects with the same DAP (67 mmHg) and SAP (105 mmHg) have the same time-averaged MAP (85 mmHg), despite marked differences in pressure waveform, dicrotic notch pressure and cycle length. Subject #1, beat no. 1 (dotted line) and subject #20, beat no. 6 (solid line) are presented. In the overall population, MAP could be estimated from DAP and SAP only, assuming that the pressure bias \((0 \pm 1 \text{mmHg})\) was small enough to be negligible.

Aortic form factor

At the aortic root level, the form factor value we report here \((0.45)\) lies between the classical empirical value \((0.50)\) [4] and experimental values obtained from carotid pulse tracings \((0.43)\) [3] and ascending aorta recordings \((0.41)\) [21]. Meaney et al. [21] recently documented the aortic form factor in cardiac patients (mainly with coronary artery diseases; 67% male). These authors used fluid-filled catheters and electronic damping of the signal for MAP calculation. When compared with their study [21], our slightly higher form factor value could be explained by differences in the catheters (we used high-fidelity pressure catheters), our method for calculating the reference MAP (time-averaging) and the characteristics of the study population. We suggest that aortic MAP could be estimated using the following formula:

\[
\text{MAP} = \text{DAP} + 0.45 \times \text{PP}
\]

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strongly on SAP and DAP respectively [1,2,22]. Our results may reflect the coupling between arterial load and the myocardial oxygen supply/demand ratio. For a given MAP, the form factor decreased from ~0.50 to ~0.33 in cases where PP was increased, and this may reflect beneficial protection of the coronary circulation, with preserved (instead of decreased) DAP values when pulsatile stress is increased.

\[
\text{MAP} = \text{DAP} + \frac{\text{PP}}{3} + 5 \text{ mmHg}
\]

This formula has three advantages. First, the accuracy of this formula was excellent (bias = 0±1 mmHg), and this confirmed previous results [17]. Secondly, there is a strong theoretical/physiological background upon which to predict such a formula. This formula is consistent with mechanical principles in the arterial system, if one assumes a form factor of 0.33 in peripheral arteries. Indeed, MAP and diastolic arterial pressure show little difference between central and peripheral arteries, while systolic pressure increases from aorta to periphery [10–14]. Two studies have shown that radial artery pulse pressure is 15 mmHg higher than aortic PP in the overall population (mean value) [12,13]. The +5 mmHg extra factor is in fact foreseeable, as it encompassed one-third of the pulse wave amplification:

\[
\text{MAP} = \text{DAP} + \frac{\text{peripheral PP}}{3}
\]

\[
= \text{DAP} + \frac{\text{aortic PP} + 15}{3}
\]

\[
= \text{DAP} + \frac{\text{aortic PP}}{3} + 5 \text{ mmHg}
\]

Thirdly, this formula was very similar to the equation obtained by multiple linear regression (see the Results section), and thus can be viewed as a simplified formalization of pressure redundancy, as discussed below.

Implications

The novelty of our result is not that aortic MAP could be approximated by using DAP and SAP only, but rather that an empirical formula gave an unusually accurate estimation of MAP. Pressure redundancy was confirmed by multiple linear regression, showing that 99% of the variability of MAP was explained by the combined influence of SAP and DAP. For a given DAP, MAP contains virtually no additional information independent of SAP, assuming that the pressure bias (0±1 mmHg) is small enough to be negligible. Results were obtained irrespective of whether the marked differences in wave reflection and heart period were taken into account.

Because all clinical and epidemiological studies use a fixed form factor of 0.33 to estimate MAP at rest, pressure redundancy is commonly admitted (although not yet demonstrated) for peripheral arteries, and it is likely that this has clinical implications in terms of risk stratification [5–7]. Pressure redundancy may appear as an unifying concept [23,24] for central and peripheral haemodynamics, and may relate to the general physiology of the human circulation at rest. One explanation could be that redundancy reflects the overlap of the main haemodynamic variables regulating SAP, DAP, MAP and PP [22,25]. Efforts must be directed towards the confirmation of pressure redundancy at the peripheral arterial level. If confirmed, this could indicate that two pressures [i.e. either (SAP, DAP) or (PP, MAP)] are enough to characterize the four-pressure set.

The practical implications of our results must be discussed. Our study improved estimation of central MAP, and thus may help carotid artery pressure calibration using applanation tonometry. Further studies are needed to confirm this point. Finally, in a population similar to ours, we suggest that central SAP could be reasonably estimated from peripheral MAP and diastolic pressure values (mean bias = 0±3%) if one assumes unchanged MAP and diastolic pressure from aorta to periphery. However, further studies are needed to confirm this point, given that peripheral arterial pressure was not measured in our study.

Strengths and limitations of the study

To the best of our knowledge, this is the first study to document form factor values using high-fidelity pressure catheters. For an invasive study, the number of subjects was large (n = 73) and likely to be sufficient to justify the conclusions we have drawn from the data. The results pertain strictly to the population under study. The design of our study (i.e. prospective and invasive) explains why we have included control subjects and patients with various forms of cardiac diseases, ranging in age from 19 to 77 years. Our results are thus strengthened by the fact that data were obtained from a heterogeneous population and over a wide range of cardiac function (stroke index ranging from 15 to 87 ml/m²), heart period (from 506 to 1267 ms) and extent of wave reflection (pressure augmentation index ranging from 0 to 0.53). Since only 5% of patients were Murgo’s type C [14], our results need to be confirmed in patients with small or diffuse reflections.

Results were also obtained over a wide range of SAP (from 83 to 181 mmHg), MAP (from 66 to 134 mmHg) and PP (from 27 to 89 mmHg) values. Although 25% of patients had a SAP >140 mmHg at baseline, further studies are needed to confirm our results in patients with hypertension. For ethical reasons, we did not test the acute effects of vasodilators, and the lowest DAP was 50 mmHg. Thus further studies are needed to document the form factor value in patients with very low pressures (e.g. patients in intensive care units). Finally, our results apply strictly to aortic pressure at rest. They do not apply to other arterial sites (e.g. brachial artery), nor to dynamic conditions.
Conclusions
In conclusion, in the aortic root of resting humans, the form factor was strongly influenced by age, aortic pressure and wave reflection. The high accuracy of the empirical formula (MAP = DAP + PP/3 + 5 mmHg) was consistent with the previously reported mean pulse wave amplification of 15 mmHg, and with unchanged MAP and diastolic pressure from aorta to periphery. Aortic pressure redundancy was demonstrated by multiple linear regression, showing that 99% of the variability of MAP was explained by the combined influence of DAP and PP pressure set redundancy, and only two pressure-powered functions were carried out in the (MAP, PP) pressure set and the (MAP, PP) pressure set were redundant, and only two pressure-powered functions were carried out in the (SAP, DAP, MAP, PP) four-pressure set.

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