Can a clinically useful aortic pressure wave be derived from a radial pressure wave?†

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Background. The information contained in arterial pressure waveforms is probably under-used by most clinicians who manage critically ill patients. It is not generally known that an aortic pressure wave can be synthesized by applying a generalized transfer function to the radial arterial pressure wave. We validated a commercially available system, SphygmoCor™ (PWV Medical, Sydney).

Methods. Ascending aortic pressure waves were synthesized and comparisons were made between the synthesized aortic waveforms, the measured aortic and radial arterial waveforms. Ascending aortic pressure waves (catheter-tip manometer) and radial artery pressure waves (short fluid-filled catheter) were recorded simultaneously in 12 patients with angina pectoris (age 62–76 years) undergoing cardiac catheterization. Patients were studied at rest, following midazolam, sublingual nitroglycerin and during Valsalva manoeuvres.

Results. Both midazolam and nitroglycerin lowered mean arterial pressure but nitroglycerin caused a more selective decrease in the measured and synthesized aortic systolic pressures than in the radial artery pressure. The synthesized aortic systolic pressure was less, by 6–8 mm Hg (SD 2–3) and the synthesized aortic diastolic pressure greater, by 4 mm Hg (SD 2). Despite these differences in pulse pressure, the synthesized waveform tracked the measured waveform before and during interventions.

Conclusions. By deriving an aortic waveform from the radial pulse, monitoring of left ventricular afterload can improve without more invasive means.

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Some health workers assume that peripherally measured systolic, diastolic and pulse pressures represent these pressure values throughout the arterial tree. However, the aortic systolic and pulse pressures are usually less than those measured peripherally.¹–⁴ These differences in arterial pressures have been explained on the basis of wave reflection at peripheral sites.⁵ The difference is increased with some, but not all, vasodilating agents,⁶ ⁷ in shock and with tachycardia.⁸ Such effects are usually hidden, since we lack simple, practical methods to measure central systolic pressure. Hence, the cardiac consequences of relatively large changes in proximal aortic pressure are often unseen and neglected. Furthermore, the cuff sphygmomanometer sets numbers to the extremes of arterial pressure but carries no information about the dynamics of arterial pressure during the cardiac cycle. To overcome this lack of information, new non-invasive methods have evolved to generate the ascending aortic pressure wave from the radial or brachial pressure wave.⁹ One such system, SphygmoCor™ (PMV Medical, Sydney) synthesizes the ascending aortic pressure wave from the radial pressure wave.

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wave through a generalized transfer function so that cardiac and vascular interactions can be calculated.\textsuperscript{10–14} A transfer function is a mathematical description of the change in pulsatile phenomena between two sites, expressed in the frequency domain in terms of modulus and phase, and is widely used in engineering sciences. A generalized transfer function is a transfer function that can be used in different persons under different circumstances.\textsuperscript{9,15} This is the first formal investigation of the SphygmoCor technique applied to an intra-arterial radial waveform. We chose to study elderly patients scheduled for percutaneous transluminal coronary angioplasty (PTCA) since they have a non-compliant arterial system. This increases wave reflection, induces systolic hypertension and is thus an additional cardiac risk factor during major surgery. Perioperative monitoring of such patients includes a radial arterial cannula. The aim of this study was therefore to compare the synthesized aortic (SA) pressure wave derived from the measured intra-arterial radial (MR) waveform by comparing SA with the directly and simultaneously measured (catheter-tip manometer) ascending aortic pressure wave (MA). Our protocol included control recordings, and recordings during the Valsalva manoeuvre, vasodilatation with midazolam and nitroglycerin, followed by a second Valsalva manoeuvre.

**Methods**

The study was approved by the Sahlgrenska University Hospital ethics committee and informed consent was obtained from each patient. Twelve patients with angina pectoris, 8 men and 4 women, mean age 67 years (range 62–76 years), scheduled for PTCA were included. They all had left ventricular ejection fractions greater than 50% calculated at echocardiography or previous coronary angiography and none had any clinical evidence of heart failure. The measurements were done in the morning, fasting, before the PTCA. Patients treated with β-receptor antagonists (\(n=8\)) received their regular morning dose. No other drugs were administered before the study.

Aortic recordings were obtained with an 8F Cordis catheter-tip manometer with a pressure interface (Sentron, The Netherlands).\textsuperscript{16} The catheter has a flat frequency response up to 180 Hz. Following local anaesthesia, the catheter was introduced from the femoral artery and positioned in the ascending aorta just proximal to the brachiocephalic trunk. The right radial artery was cannulated with a 45 mm Ohmeda (Swindon, UK) arterial cannula (inner diameter 1.0 mm) and connected to an external pressure transducer (Peter van Berg, Kirschseeon, Germany) by high-pressure tubing that was only 10 cm long to minimize signal distortion. When tested in our laboratory according to Gardner\textsuperscript{17} this pressure measurement system had a natural frequency of 25 Hz and a damping coefficient of 0.35–0.5. This implies that the signal has minimal distortion. The Siemens Sirecust 1281 cardiovascular monitoring system (Siemens Medical Electronics Inc., Danvers, MA) that we used had a high-pass filter with a cut-off at 16 Hz.

The Valsalva manoeuvre was accomplished by a prolonged forced exhalation through a facemask with an attached resistance. Airway pressure was measured at the mask and a positive airway pressure of 10–70 mm Hg was generated. In relation to the Valsalva manoeuvres, measurements of systolic and diastolic pressures were made on individual pulse waves because the SphygmoCor software is based on averaging 8 s of stable pulse waves. Pressures were measured immediately before and during the peak effect of the manoeuvre, with arterial pressure at its nadir.

All signals (ECG, radial arterial, aortic and airway pressures) were digitized (MP 100, Biopac, Cal., USA) at 200 Hz and processed in the data acquisition software (Acqknowledge, Biopac, USA). Data were later processed off-line in the SphygmoCor 128 Hz. The generalized transfer function used by SphygmoCor is based on data from Karamanoglu et al.,\textsuperscript{11} who studied patients with coronary artery disease. This is virtually identical to the generalized transfer function described by Chen et al.\textsuperscript{9} During each period of measurement a recording of a stable 8 s wave train was ensemble-averaged by the SphygmoCor into a single waveform for each of MA, SA and MR, and timing and pressure data (systolic, diastolic and end systolic pressures) calculated. End systolic pressure (ESP) was determined by identification of the cardiac inscica through use of differentials. Indices were: time–pressure area during systole (As) and diastole (Ad) and their ratio (Ad/As), systolic pressure augmentation index (AI), which defines the relation between the first (P1) and second (P2) systolic shoulder/peak (i.e. AI=100×(P2–P1)/pulse pressure).\textsuperscript{18,19}

Since the exact sagittal position of the aortic catheter in relation to the zero level of the external pressure transducer was unknown, mean values of both synthesized and measured pressures were set to be the same as in the pressure in the radial artery. All aortic pressure values were then adjusted arithmetically.

**Experimental plan**

Measurements started with a control period after 20 min of rest (\(n=12\)), followed by the first Valsalva manoeuvre (\(n=11\)). We then gave midazolam 1–2 mg i.v. and took recordings after 3–5 min (\(n=12\)). Immediately after this, nitroglycerin 0.25–0.5 mg was administered sublingually. Two sets of recordings were then taken, reflecting both early (after 2 min, \(n=11\)) and maximal nitroglycerin effect (after approximately 5 min, \(n=11\)). Statistics and Bland–Altman plots were calculated using the mean of these two measurements. With nitroglycerin effect still at its peak, a second Valsalva manoeuvre was performed (\(n=15\)).
Statistical analysis
Data are presented as mean (SD). Data were compared using paired Student’s t test. Individual data from all interventions are shown in Bland–Altman plots. ANOVA for repeated measurements was used to test the consistency of the differences between MA and SA, and between MA and MR during the different pharmacological interventions, with Tukey’s post-hoc test.

Results
The Valsalva manoeuvre was studied on 27 occasions, 12 before any drugs were administered and 15 after the administration of midazolam and nitroglycerin (Figs 1 and 2). During the Valsalva manoeuvre systolic pressure decreased by 51 (22) mm Hg in MA. The difference in systolic pressure between MR and MA increased from 9 to 14 mm Hg during the Valsalva manoeuvre, and the difference between systolic pressure in SA and MA disappeared during the peak effect, from 4 to 0 mm Hg. The response to the Valsalva manoeuvre was similar before and after the administration of nitroglycerin.

The decrease in systolic and mean arterial pressure induced by midazolam was accentuated by nitroglycerin (Table 1). However, nitroglycerin caused a more pronounced fall in systolic pressure and pulse pressure in the aorta (MA) than in the radial artery (MR). Ad/As was markedly increased only by nitroglycerin, with a more pronounced decrease in As. The latter was associated with decreases in systolic augmentation in MA, SA and MR, and with a typical pointed appearance of the radial pulse wave (Fig. 3). Heart rate was not significantly affected by midazolam or by the addition of nitroglycerin.

Changes in pulse waves induced by changes in stroke volume and wave reflection are shown as changes in systolic augmentation and pulse wave contour and have been classified by Murgo et al.18 Before administration of any drug, true aortic pulse waves (MA) were monophasic (Fig. 3) and the SphygmoCor software could not detect inflection during systolic upstroke in five out of 12 patients, meaning that these pulse waves were not classified. The remaining seven patients were classified as Murgo type A, which implies an early systolic shoulder followed by an augmented late systolic peak (as seen in the SA waveforms in Fig. 3).

Data from individual patients are displayed in Table 2. When arterial pressure was affected by midazolam and later by nitroglycerin, systolic augmentation in MA decreased (Table 1) and early systolic inflection points could be detected by the software in all but one of 34 MA pulse waves. (All 12 patients received midazolam, all but one received nitroglycerin, and the nitroglycerin effect was measured twice, i.e. 12+11+11=34.) In the SA pulse waves early systolic inflection was detected in 45 out of 46 recordings (including control measurements). Thus the Murgo classification was identical between MA and SA in 92% (36 out of 39 recordings). Accordingly, because of failure of detection of systolic inflection, AI could not be
calculated in 13% of the MA, 4% of the SA and 9% of the MR registrations. ESP decreased, in parallel with the fall in systolic pressures, in MR, MA and SA.

Mean values of the differences between measured and synthesized aortic pulse waves (MA±SA) and between MA and radial pulse waves (MA±MR) are shown in Table 3. Analysis of variance for repeated measurements (not including the Valsalva manoeuvre) showed no changes in the differences between MA and SA for systolic and diastolic pressures, AI or Ad/As. The difference between ESP in MA and SA showed a minor but significant change (Table 3A) in the analysis of variance. When comparing the differences between MA and MR, however (Table 3B), ANOVA indicated changes in the differences concerning systolic pressure and ESP and Ad/As.

The SphygmoCor SA pulse wave consistently underestimated aortic systolic pressure by 6–8 mm Hg (SD 2–3) and overestimated aortic diastolic pressure by 4 mm Hg (SD 2) (Table 3A). SA followed the decrease in aortic systolic pressure when nitroglycerin was added to midazolam, whereas the MR did not. Although the difference between systolic pressure in the radial artery and in the SA pulse wave (MR±SA) was larger than the ‘true’ difference (MR–MA), both gradients increased similarly during nitroglycerin (Table 1).

Systolic AI in SA approximated that in MA. The magnitude of the changes in pulse wave parameters induced by midazolam and the further addition of nitroglycerin were always similar in the measured and synthesized aortic pulse waves (Table 1).

Individual values are shown as Bland–Altman plots in Fig. 4A–D. Figure 4A shows a consistent underestimation of the SA systolic pressure compared with MA and a large scatter in MR compared with MA systolic pressures during nitroglycerin. The resemblance between MA and SA is good with regard to ESP and AI (Fig. 4B–C). SA consistently underestimated systolic and overestimated diastolic pressure areas compared with MA.

**Discussion**

The SA pressure waveform derived by SphygmoCor closely followed the MA waveform beat by beat and also during changes in arterial pressure induced by vasodilators or the...
Valsalva manoeuvre. This was also true for ESP, which is an important but normally difficult value to measure when ventricular/vascular interactions are being studied.\textsuperscript{21}

**Pressure**

The aortic pulse pressure was underestimated using the SphygmoCor software. This was largely the result of a discrepancy in systolic pressure. The underestimation may be explained in several ways. A small but systematic bias was introduced in the study by setting measured and SA mean pressures identical to radial mean pressure. Normally the aortic mean pressure should be 1–3 mm Hg higher than the radial mean pressure.\textsuperscript{4} More importantly, the generalized transfer function used by the SphygmoCor is based on data from a younger population (mean age 54 years)\textsuperscript{11} than investigated in the present study (mean age 67 years). In younger individuals, pulse pressure amplification along the arterial tree results in a higher peripheral systolic pressure. The less compliant arterial system of an elderly individual will equalize peripheral and central systolic pressure. Indeed, similar resting aortic and radial systolic pressures were observed in the present study. Furthermore, the generalized transfer function is based on pooled data including pressure waveforms at rest, as well as during infusion of nitroglycerin.\textsuperscript{11} Individualized transfer functions have been evaluated previously\textsuperscript{9} and were found to be only marginally superior to the generalized transfer function in reconstructing central pressures. Further validation studies should involve young individuals with normal and compli-
Fig 4 Bland–Altman plots displaying the differences between measured aortic waveform (MA) and measured radial waveform (MR) (left panel) and between MA and synthesized aortic waveform (SA) (right panel) for systolic and diastolic pressures (A); end systolic pressures (B); augmentation index (C); and systolic and diastolic areas (D). True aortic systolic pressure was underestimated by SA and diastolic pressure overestimated, but variation in systolic pressure, especially with nitroglycerin, was reduced compared with MR. In A, B and C, circles indicate controls, squares indicate midazolam and triangles indicate nitroglycerin intervention. In D, squares indicate systolic area and circles indicate diastolic area. Dotted lines display mean and 2SD.
ant arterial vasculature. It can be argued that the fluid-filled radial catheter system could introduce damping and thus lower the pulse pressure in the SA wave. This seems unlikely, however, since the extremely short fluid-filled radial system had a natural frequency and damping coefficient well above monitoring standards. Longer extensions have so far not been validated. About 90% of the power in the aortic pressure is within the first three harmonics and these are unlikely to be affected by the length of the tubing. Longer extensions, however, will decrease the natural frequency of a fluid-filled external system, making it susceptible to false amplification during tachycardia. In such a system a high heart rate may introduce errors which were not encountered in the present study.

**Waveform**

A monophasic systolic peak was observed in the aortic pressure waveform. This pattern differs from the original work by Murgo et al., who describe a late systolic peak as a result of the reflected pressure wave (type A waveform), considered typical in elderly or hypertensive individuals. Again, differences in the composition of study populations may explain the different waveforms observed. The study by Murgo et al. was of a population with a mean age of 34 years, compared with 67 years in this investigation. The pressure wave reflection in an elderly group of individuals with a less compliant arterial vascular tree is probably so fast that the incident wave meets and blends with the reflected wave very early in systole.

The waveform can be described as a supply/demand relationship. The area under the diastolic part of the pulse wave, Ad, is hence divided by the systolic area, As (i.e. Ad/As), where Ad represents the potential for coronary perfusion enabling the cardiac workload, As. Interestingly, in our study, this relationship was altered only by nitroglycerin, despite a more pronounced decrease in systolic pressure during midazolam. This shows that nitroglycerin can decrease not only stroke volume but also pulse wave reflection.

The AI indicates vascular stiffness, reflecting both structural vascular changes as in hypertension or diabetes and pharmacologically induced dynamic changes in pulse wave reflection where the second systolic peak represents the reflected pressure wave. Perhaps in patients with intact endothelial function changes in AI could indicate depth of anaesthesia and sympathetic tone.

**Clinical implications**

We found that systolic pressure and AI from a radial cannula should be used with caution even as a rough estimate of aortic data (Fig. 4, left-hand panels). Whereas midazolam did not affect the gradient between radial and aortic pressures, the addition of nitroglycerin did (Fig. 3). With midazolam the radial and aortic pulse wave changes suggested that midazolam elicits an arteriolar vasodilatation without major changes in stroke volume. Midazolam and nitroglycerin in combination affected the pulse waves in the same way as when nitroglycerin was given alone, which suggests dilatation of small arteries and reduced stroke volume. The Valsalva manoeuvre decreased transmural aortic pressure and pulse wave velocity and reduced stroke volume, with increased heart rate and vasoconstriction. The net effect of these changes on pulse wave reflection was a delay of the reflected wave into diastole. In the present study the agreement between measured and synthesized aortic pressure improved during the Valsalva manoeuvre. Speculatively, both reduced stroke volume and increased heart rate during the Valsalva manoeuvre could lower central systolic pressure more than radial pressure, similar to the effects of nitroglycerin. If this difference in pressure reduction equals the underestimation of aortic systolic pressure by the SphygmoCor, measured and SA aortic pressures would coincide. These observations are similar to those made by Chen et al.

The information contained in arterial pressure waveforms is probably underused in anaesthesia and intensive care. The present study shows that if the radial pulse wave is continuously translated into an aortic pulse wave, the level of monitoring can improve without more invasive means. Continuous monitoring of aortic pressure and waveform gives a better estimate of left ventricular afterload than does radial monitoring and is of importance in volume and drug therapy. There is no reason why the detailed information contained in the arterial pressure waveform should be overlooked by the anaesthetists and intensivists who are regularly confronted with arterial pressure waveforms. Further studies should assess pulse wave reflection and late systolic augmentation. The present study illustrates the benefits and possible pitfalls of using a generalized transfer function in elderly patients. The SA pulse wave will be damped, causing a moderate but consistent underestimation of pulse pressure and systolic time-pressure area. The underestimation of systolic pressure is not seen with an increased intrathoracic pressure.

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