Estimation of central aortic pressure: shedding new light or clouding the issue?

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The adverse cardiovascular consequences of age-related arterial stiffening are now well established, but were appreciated by physicians in the nineteenth century. At that time, life expectancy in many developed populations was relatively low, and few individuals lived long enough to suffer the detrimental effects of arterial stiffening; however, life expectancy is now considerably longer, blurring the boundaries between arterial disease and normal vascular ageing.

Techniques such as pulse wave analysis, which allow for the rapid non-invasive assessment of arterial stiffness and the impact that stiffening has on ventriculo-vascular interaction, are, therefore, likely to be of increasing importance in the effective management of cardiovascular disease in ageing populations. This has already been acknowledged in the recent ESH-ESC (European Society of Hypertension-European Society of Cardiology) Guidelines on the treatment of hypertension [1], which also highlighted the importance of central arterial and pulse pressure as important risk factors for cardiovascular disease. In their recent paper, Cloud et al. [2] measured central arterial pressure non-invasively using the SphygmoCor® system and compared the results with invasive measurements in a small cohort of 30 subjects (age range, 27–84 years), half of whom were > 65 years. They conclude that estimation of central aortic pressure by the SphygmoCor® system is inaccurate and requires calibration with intra-arterial peripheral pressure measurements. If true, their findings would limit the utility of such a system in the clinical arena, but their conclusions are at marked variance with the extensive body of published literature and we believe only serve to cloud the issue.

Previously published data confirm the validity of the transfer function itself in a similar, if larger, sample population [3]. When calibrated with invasive radial pressure, the mean difference between estimated central pulse pressure and actual aortic pulse pressure was only 0.7 ± 4.21 mmHg, considerably more impressive than the errors reported for most commercial oscillometric sphygmomanometers. Indeed, in this setting, the transfer function used in the SphygmoCor® system more than meets the AAMI (Association for the Advancement of Medical Instrumentation) criterion, and the device has recently received FDA approval in the U.S.A. What, therefore, could account for the discrepant findings of Cloud et al. [2]?

The two most important differences in study of Cloud et al. [2] were the use of cuff calibration for the radial waveform and the use of fluid-filled catheters for measuring central pressure. The SphygmoCor® system requires calibration of the pressure wave, most commonly with brachial cuff blood pressure. It is well established that oscillometric sphygmomanometers do not always provide reliable estimates of intra-arterial pressure, and even devices that meet the AAMI criterion are allowed to vary from the gold standard by 8 mmHg. Despite this, many studies have clearly demonstrated that cuff blood pressure predicts outcome. Therefore it is perhaps not surprising that calibration with cuff blood pressure, rather than radial intra-arterial pressure, increases the difference between estimated and actual aortic pressure. Nevertheless, we believe that estimation of central blood pressure still provides important additional clinical information beyond that supplied by simply measuring brachial blood pressure. Indeed, nitrates significantly reduce central blood pressure, measured both directly and indirectly with the SphygmoCor® system, without altering brachial blood pressure [4].

Perhaps more worryingly, a closer examination of the data by Cloud et al. [2] reveals a marked and unexplained discrepancy with the established view of cardiovascular physiology. Many previous studies, using invasive and non-invasive measurement of central blood pressure, have demonstrated repeatedly that, in all but the very oldest individuals, there is amplification of pulse pressure from the aorta to the brachial artery, i.e. pulse pressure increases moving away from the heart [5,6]. This has been
attributed to wave reflection and a change in the viscoelastic properties of the arteries themselves. Yet, Cloud et al. [2] report exactly the reverse, a fall in pulse pressure of more than 12 mmHg moving from the aorta to the brachial artery. Unless the patients they studied had completely different physiology to the large numbers studied in other centres worldwide, it seems that the most likely explanation for their findings is either a calibration error due to the use of a fluid-filled aortic catheter or an error in brachial blood pressure measurement with the oscillometric sphygmomanometer employed in the study. Nevertheless, we believe that this important discrepancy seriously undermines the usefulness of the data reported and the conclusions made by the authors [2]. Perhaps what it does exemplify is that such studies can be heavy weather and, in addition, highlights the problems with measurement of cuff blood pressure.

We would agree that, despite its inherent inaccuracies, the conventional sphygmomanometer has been of clinical value over the last century. However, it is limited to measurement of systolic and diastolic pressures, which provide little, if any, information about central arterial pressure and ventricle–vascular interaction. Such parameters are already increasingly important in older subjects in terms of both prediction of cardiovascular risk and outcome and also of therapeutic intervention. The SphygmoCor® system has already been demonstrated to be of clinical use in the assessment of cardiovascular risk [7] and, as advocated in the ESH-ESC guidelines, is already included in a large number of outcome studies involving patients with hypertension, diabetes and hypercholesterolaemia. When such data is available it is to be hoped that the dark cloud which some researchers have placed over the SphygmoCor® system will lift, allowing a clearer vision for the improved assessment and treatment of cardiovascular disease in future generations.

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contents of 'Pandora’s Box' must be confronted.

The key finding in the study by Cloud et al. [2] was not the issue of Sphygmocor®, the new technique, but that the known and acknowledged amplification of the pressure pulse [3] was actually reversed. Pulse pressure was greater, not lower, in the central aorta than in the brachial artery. Furthermore, the difference in pulse pressure was greater in older compared with younger patients: 91 compared with 75 mmHg in persons over 65 years and 67 compared with 58 mmHg in those below 65 years. Previous studies had shown greater differences in the young and less in the elderly. How could all of this come about?

The authors [2] stated that their “Omron (HEM-705CP) had been validated against the mercury sphygmomanometer”, so assumed that there was some problem with use of a generalized transfer function. They failed to appreciate the huge tolerance accepted for similarity in official U.S. AAMI (Association for the Advancement of Medical Instrumentation) SP10 criteria [4], where a cuff blood pressure instrument showing a mean difference ≤5 mmHg and an S.D. ≤8 mmHg is deemed to be “substantially equivalent” to the K Sound technique, and the K Sound technique is in turn deemed to be “substantially equivalent” to intra-arterial pressure if in comparative studies the mean difference is ≤5 mmHg and S.D. is ≤8 mmHg. Errors compound into the huge scatter published by Cloud et al. [2] for both systolic and diastolic pressure.

The Sphygmocor® process corrects for distortion of the waveform between the aorta and brachial artery and has proved most useful when pressure waveform changes with interventions, such as Valsalva [5], with change in heart rate and rhythm, and with drugs [6]. It cannot be expected to correct for errors inherent in any indirect cuff method for measuring arterial pressure.

There are problems in the methods used by Cloud et al. [2] for comparison of pressure recordings, but I will not haggle about the need for simultaneous recordings, for determination of invasive manometer frequency response and the problems which may arise from reactive hyperaemia in the arm if tonometric recordings are taken immediately after release of the brachial cuff. Such do not detract from the clear-cut results of the study by Cloud et al. [2] and their acknowledgment that Sphygmocor® works well when pressure waves are recorded invasively.

The opening of ‘Pandora’s Box’ by Cloud et al. [2] and others exposes the gross inaccuracies of the cuff sphygmomanometer process for accurate measurement of arterial pressure. Queries on the use of a technique such as Sphygmocor® apply to any technique where non-invasive measurement of blood pressure is applied, i.e. for gauging left ventricular load, vascular risk or arterial properties. When large data sets are analysed, the scatter is reduced [1], but it remains high in assessment of individual patients [7].

How then does one respond to the findings of Cloud et al. [2] or Takazawa et al. [8] and others who reported these problems before? The Sphygmocor® device provides incremental information which is independent of cuff calibration, such as aortic and radial augmentation index, both of which are known to carry independent prognostic information [9,10]. Certainly, we need to be far more circumspect in our interpretation of blood pressure values as measured clinically, and we need to seek other indices of arterial degeneration, such as pressure augmentation and pulse wave velocity, in order to stratify risk and to use drug therapy more intelligently.

Sphygmocor® is a useful new device to complement existing techniques for determining arterial properties and cardiac load. Its ‘Achilles heel’ is its calibration to the inaccurate cuff sphygmomanometer.

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Estimation of central aortic pressure by SphygmoCor® requires intra-arterial peripheral pressures: authors’ reply

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The above letter by Dr Wilkinson and Professor Cockcroft raises two major issues relating to our article [1]. Firstly, they agree with us when they state that they are not surprised that “calibration with cuff blood pressure, rather than radial intra-arterial pressure, increases the difference between estimated and actual aortic pressure”. We reported an average discrepancy of 13 mmHg of systolic pressure between the SphygmoCor® estimates for central systolic pressure and the actual measurements, and we employed cuff measurements to ‘calibrate’ the pulse wave as intended by the manufacturers. We agree that, if we had employed radial intra-arterial pressures, we may have had a better match. The point is that we employed the machine as intended and obtained our discrepant results. We do not agree that the estimation of central blood pressure with cuff calibration provides “important additional clinical information”. The limitations of the fluid-filled catheters have already been addressed in our paper [1].

Their second point is also raised by Professor O’Rourke and is that central blood pressure in our study was higher than the brachial pressure. Table 1 shows the readings of the various pressures derived in the central and brachial artery. It is well known that peripheral pulse pressure is higher than central pulse pressure in adults; however, it is important to know that this only applies when pressure recordings are done invasively. In our study [1], the central recordings were measured using an invasive catheter, and the peripheral recordings were derived from the blood pressure cuff. This accounts for the difference.

A similar study by Davies et al. [2] showed a central pulse pressure of 66 mmHg and peripheral cuff pulse pressure of 57 mmHg. They had a ‘fall’ of 9 mmHg from central aorta to the peripheral, very similar to our finding (Table 1). This study [2] had the same findings, i.e. higher pulse pressures centrally derived from the catheter and lower pulse pressures at the brachial cuff derived non-invasively. The important point to note is that indirect measurements of blood pressure underestimate intra-arterial systolic pressure and overestimate intra-arterial diastolic pressure to give artificially low pulse pressures. In our study [1], we referenced six articles to this effect [3–8] and now are happy to add two more [9,10]. We concluded that the central pressures calculated by SphygmoCor® did not match intra-cardiac measures, as they require intra-arterial pressures and not indirect measurements.

Professor O’Rourke claims that there may not be a problem in using a generalized transfer function, but a problem in assuming that the Omron (HEM-705CP) had been validated against intra-arterial measurements. We did not assume validation against intra-arterial measures. Nevertheless, we would partially agree with Professor O’Rourke’s bottom line that the SphygmoCor® has an ‘Achilles heel’; that is “its calibration to the inaccurate cuff

Table 1 Central and cuff blood pressure readings from [1] and [2]

<table>
<thead>
<tr>
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<th>Cloud et al. [1]</th>
<th>Davies et al. [2]</th>
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<tr>
<td><strong>Mean cuff brachial pressures</strong></td>
<td></td>
<td></td>
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<tr>
<td>Systolic BP (mmHg)</td>
<td>154.9 (27.1)</td>
<td>137 (26)</td>
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<tr>
<td>Diastolic BP (mmHg)</td>
<td>88.4 (15.5)</td>
<td>80 (12)</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>66.5 (18.6)</td>
<td>57</td>
</tr>
<tr>
<td><strong>Mean catheter pressures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>154.8 (32.1)</td>
<td>134 (28)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>77.9 (12.9)</td>
<td>68 (12)</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>78.9 (26.7)</td>
<td>66</td>
</tr>
<tr>
<td><strong>Difference between central catheter</strong></td>
<td></td>
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<tr>
<td>pulse pressure and brachial cuff pulse pressure (mmHg)</td>
<td>12.4</td>
<td>9</td>
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sphygmomanometer”. We would replace the word ‘inaccurate’ by ‘inappropriate’ and have to insist that the transfer function both corrects for distortion of the waveform between the aorta and radial artery (not brachial as stated), but also for the measurement of pressure over the brachial artery by an indirect method.

Rather than trying to confuse the issue further, we should accept the fact that a central blood pressure derived using a transfer function calibrated by cuff blood pressure has major limitations. In our hands, other measurements reported by the SphymoCor® system, such as augmentation index and pulse wave velocity, have greater validity.

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