Central blood pressure and its amplification: a final breakthrough or do we need more?

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Blood pressure is one of the cardinal risk factors for atherosclerosis and cardiovascular diseases. Systolic and diastolic blood pressures are measured at the level of the brachial artery, positioned at a mid-thoracic level with an adequately sized cuff and bladder. Treatment of arterial hypertension with lifestyle and drugs has become one of the cornerstones of contemporary cardiology. Subjects and patients should all have office blood pressures <140/90 mmHg. Office blood pressure measurements have to be complemented by out-of-office measurements in order to rely on frequent rather than punctual measurements. These non-invasive cuff brachial pressures underestimate invasively measured blood pressures, but nevertheless are the firm ground of evidence-based medicine, while invasive pressures are not.

During the last decades, we have witnessed important research on properties of the arterial tree and on distortion of the pressure waveform from the central aorta to the brachial and radial artery. This distortion was attributed to wave travel and wave reflection. This explains why the radial pressure wave is much more peaked than the central aortic or carotid pressure wave, and has a higher systolic pressure. Overall, the minimum (diastolic) and mean blood pressure values change little from one location to the other. On this physiological basis, researchers compute central-to-peripheral pressure amplification and central systolic pressure.

Emerging evidence suggests that central pressure is better related to future cardiovascular events than is brachial pressure, and responds differently to certain drugs. The idea is that central pressure more directly represents pulsatile load imposed on coronary, cerebral, or renal arteries, and hence cardiovascular risk. The evidence for this superiority is, however, not universally accepted and is mainly based on intermediary endpoints in specific patient populations. The 2013 European Society of Cardiology (ESC) Guidelines for the management of arterial hypertension therefore still consider that, although the measurement of central blood pressure and augmentation index is of great interest for mechanistic analyses in pathophysiology, pharmacology, and therapeutics, more investigation is needed before recommending their routine clinical use.

UK investigators (Anglo-Cardiff Collaborative Trial, n = 11,340) previously observed decreased pressure amplification with age, in women or smaller subjects, and with increasing heart rate. They documented less pressure amplification in the presence of hypertension, hypercholesterolaemia, smoking, diabetes, and cardiovascular diseases. In another European population (Asklepios population, n = 1,873), similar effects of age, sex, and heart rate were observed (Figure 1). Pressure amplification was associated with pulsatile load (carotid augmentation index). Of note, pressure amplifications described by the Anglo-Cardiff Collaborative Trialists are much higher than those reported by the Asklepios Investigators, indicating methodological and calibration issues. Data obtained with different devices or techniques are not comparable and may not be used interchangeably.

What is the vascular parameter, related to pulsatile load, which is optimally suited for complementing cardiovascular risk assessment? Is it central systolic blood pressure, central-to-brachial pressure amplification, or is it the analysis of wave reflection? This question was recently addressed in the MESA database. The relative magnitude of wave reflection outperformed pressure amplification and even the augmentation index in the long-term prediction of all cardiovascular events, hard cardiovascular events, and incident heart failure. This information could have been mentioned when referring to this particular study for validating the use of pressure amplification in the investigation under scrutiny.

Several methodologies have been used for estimating central systolic blood pressure and central-to-brachial pressure amplification. The most widely used methodology (SphygmoCor) starts from radial waveforms (tonometry). It reconstructs a central pressure waveform from adjustment of modulus and phase angle of Fourier components, using a generalized transfer function. The radial waveform is calibrated with cuff brachial blood pressures. Of note, the original patent reveals that computation of central systolic pressure is

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but apparently is a linear function, combines several data sets worldwide, totalling 45,000 observations. The methods are mainly based on nondiscriminate and carotid tonometry. Data obtained with non-invasive tonometry, Asklepios population, n = 1,873. Modified from Segers et al. with permission.

Unfortunately, the system is not open-source.

The study by Herbert et al. combines several data sets worldwide, totalling > 45,000 observations. The methods are mainly based on radial tonometry, but include some data sets obtained with carotid distensibility and carotid tonometry. The methods are all considered validated. Validation means that pressures were calibrated with invasive pressure measurements or with head-to-head comparison with another ‘validated’ method. In order to compare data sets, data of the present study were aligned on the basis of differences between the results of each individual technique with the method used for validation. This fairly complex venture results in a huge database allowing data to be presented on computed and re-calibrated central aortic pressures and on central-to-brachial pressure amplification. The study provides normal values in a healthy subpopulation and in the total (reference) population. The authors confirm more pressure amplification in men, and less with age. Cardiovascular risk factors marginally but significantly influenced pressure amplification, with smoking and dyslipidaemia decreasing and levels of blood glucose increasing it. Age-, sex-, and blood pressure-stratified data are now available with a wide geographical representation using several methodological approaches. This is important information and could possibly contribute to better integrating the concept of central blood pressure into cardiological practice.

Such an approach combining retrospective data sets from multiple centres and using several devices is not devoid of methodological limitations.

A first limitation is the variability in the standardization of pressure measurements, and in the reporting of parameters and co-morbidities. With regard to this, it is particularly disappointing that there is no information about racial differences in pressure amplification and central pressure, because there are increasingly known racial differences in left ventricular mass and hypertrophy. Race was not reported and the authors were careful enough not to assume ethnicity based on a centre’s location. The authors were concerned as well about the co-segregation of centres, techniques, and procedures with ethnicity.

Several measuring devices were used. Disparate calibration procedures and re-alignment of data from different methodologies multiply possible errors and increase noise in the data set. Let us for instance ask if the different techniques produced similar values in the end. The answer undoubtedly is no! After comparison, adjusted for covariates, pressure amplification was significantly lower with carotid tonometry and Omron devices than for SphygmoCor devices (the authors’ Supplementary material online, table S8). The differences were considered by the authors to be negligible, as they were smaller than those dependent on age and sex, and as the authors could not exclude a centre effect because centres co-segregate with devices. In each consortium-based investigation, authors should primarily evaluate the balance between an increased number of observations and an increased inhomogeneity of data. In this particular study the balance might have been unfavourable.

Invasive pressure measurements are still considered by some to be the gold standard. These are forcefully performed in a few selected patients, under conditions that are quite distinct from routine blood pressure measurements. They were not always performed with high-fidelity manometers. This limited number of observations will never be representative for the population at large. In addition, it is notoriously difficult to record waveforms in smaller arteries without altering arterial tone and without altering forward and backward travelling waves. A validation procedure that adds noise to the data with no convincing added value should be questioned in depth.

What is the information needed for the cardiological community to endorse central blood pressure in its diagnostic and prognostic armamentarium? First of all, the vascular community should reach a consensus on one single methodology instead of pursuing efforts to compare each other’s techniques. The Asklepios Investigators deliberately chose to walk away from commercially available tools and to use direct carotid tonometry, scaled with brachial tonometry and processed with self-developed software. With this approach, no assumptions are made, and no corrections and no transfer functions are needed. The approach only neglects the small amplification between the central and carotid site, which does exist but has a limited physiological relevance. It might be considered as a non-invasive standard. It admittedly is a demanding technique requiring the development of a skill. This could lead to limited reproducibility and prevent its widespread use. There is therefore room and need for an easier (radial) technology. The technique should be transparent and with open-source software, so that the clinical investigator knows how the numbers that he provides were generated. The technique might be validated with small numbers of high-fidelity invasive pressures, but should mainly be validated with carotid tonometry in a population across wide ranges of age, sex, race, and cardiovascular risk factors. In larger populations we have to produce consistent non-invasive data in their own right, rather than referring to invasive measurements, similarly as in other fields of contemporary cardiology. It then should lead to a cardiovascular risk stratification, which
improves with a significant amount of net reclassification of subjects. Only this (or a similar) approach could lead to a reliable evaluation of the added value of central blood pressure, pressure amplification, reflected waves, and other vascular properties for the risk stratification and management of cardiovascular diseases.

Conflict of interest: the author belongs to the Asklepios Investigators, of whom some data are included in the manuscript under scrutiny. The author has no relationship with waveform device-producing companies.

References


