Noninvasive characterization of the effect of aortic impedance on left ventricular structure: a question of utility

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The concept of vascular impedance is based on a number of fundamental assumptions that originate from the analogy of blood pressure (BP) and flow in arteries with voltage and current in electrical circuits [1]. A stationary system in steady-state oscillation can be characterized by the relationship of the input and output signals in the frequency domain; in arteries, blood flow (input signal) is transformed to BP (output signal) by the impedance of the whole arterial tree downstream of the site of measurement. Impedance has been used to characterize the hemodynamic load of vascular beds [2,3] and to model the underlying parameters of vascular structure [4]. Impedance is a complex quantity, thus being described as modulus and phase as a function of frequency. The impedance spectrum is such that it has a high value at zero frequency (i.e., the peripheral resistance) and falls rapidly to settle at a stable value at high frequencies. This value at higher frequencies is the characteristic impedance.

The notion of characteristic impedance also comes from transmission systems, such as electrical transmission lines. Whereas total impedance is determined by the sum of the impedances of the system components, characteristic impedance is determined by the physical properties of the proximal segments of the system. Any mismatch between the characteristic impedance and the terminal impedance of a segment will result in reflection of the propagating waves. For the aorta, the total impedance spectrum describes the dynamic load on the ejecting ventricle [2–4]. This includes the effect of both proximal and distal vascular segments, and so the effect of wave reflection. In transmission lines and elastic tubes, this is seen as the fluctuation of impedance values around the characteristic impedance. Thus, the geometric and wall stiffness properties of the proximal segments constituting the characteristic impedance determine the forward pressure wave not affected by wave reflection, and so characteristic impedance might be considered as an intrinsic parameter of left ventricular load that depends on the vascular structure.

An important consideration regarding characteristic impedance is that, although it is a theoretically valid concept, it is quite difficult to measure with a certain degree of accuracy. When obtained from the measurements of pressure and flow, it is estimated in the frequency domain by averaging values at high frequencies (4–10 Hz in humans). However, as the power of pressure and flow signals at high frequencies is low, small changes in power will give rise to great variability in the ratio of pressure and flow magnitude. Thus, the variability of impedance values at high frequencies is generally high. Estimation of characteristic impedance using physical measurements of arterial segments is also challenging, requiring accurate measurements of vessel caliber, wall thickness, and mechanical stiffness of the wall material.

The study by Pucci et al. [5] addresses the concept of aortic characteristic impedance as a parameter of ventricular load by assessing its relationship with left ventricular mass and geometry in a large cohort (n = 438) of untreated hypertensive individuals. Aortic impedance is determined from the derived pressure and flow signals. Aortic pressure is estimated from a validated mathematical model of the brachial transfer function applied to the radial pulse using the SphygmoCor device [6,7]. Aortic flow is estimated by a second mathematical model (ArcSolver) applied to the derived central aortic pressure and using parameters optimized based on the predefined criteria [8,9]. For all individuals, the estimated flow signal is scaled from 0 to 100 arbitrary units. Aortic characteristic impedance is then determined from the aortic pressure signal and the estimated flow signal. The overall finding of the study is that aortic characteristic impedance is associated with left ventricular mass in both men and women, but with left ventricular geometry only in women. The study is significant in that it highlights the potential of noninvasive technology for the assessment of cardiovascular function, and that can readily be applied both to mass screening and also to patient assessment at the bedside. However, the study also has a number of significant limitations that need to be placed in context for proper interpretation of results.

The method of computing aortic characteristic impedance has an inherent redundancy. Aortic flow is determined from the aortic pressure wave using a model. This, by definition, is a model of aortic input impedance. The derived flow wave is then used with the same pressure...
wave to determine aortic impedance, from which is determined characteristic impedance. This suggests that the computed characteristic impedance is therefore, necessarily, partly dependent on the model. This may explain the fact that the association between aortic characteristic impedance and left ventricular structural parameters is relatively weak, notwithstanding the cohort being hypertensive. A direct association of aortic characteristic impedance was found with left ventricular mass index ($r = 0.19$, $P < 0.001$) and relative wall thickness ($r = 0.14$, $P < 0.01$). This suggests that in this large sample of hypertensive individuals ($n = 438$), characteristic impedance is directly associated with $3.6\%$ variation in left ventricular mass index and $2\%$ variation in relative wall thickness. In contrast, a much higher association was found in a normotensive group of much smaller sample size ($n = 70$, $r = 0.3$ association with left ventricular remodeling, $P < 0.01$), in whom measurements of aortic pressure and flow were not interdependent [10].

The differences in characteristic impedance values (in arbitrary units) for normal and abnormal left ventricular mass were $12.2\%$ in men and $8.4\%$ in women, respectively. For left ventricular geometry, it was $10.8\%$ for women only. These relative differences in the calculated characteristic impedance are also within the range of the interoperator agreement for left ventricular measurements of $90\%$ [5], implying an uncertainty of left ventricular measurements of some $10\%$. Undoubtedly, uncertainties in the left ventricular parameter measurements would be randomly distributed, and in such a large cohort would most likely represent a much smaller effective uncertainty. However, this would be a relevant consideration when interpreting the relatively low level of association between computed characteristic impedance values and measured left ventricular functional parameters.

Notwithstanding the above limitations, the study does show that aortic characteristic impedance may be a significant contributor to left ventricular adaptation to increased proximal hemodynamic load by undergoing remodeling in terms of both muscle mass and geometry. A potentially significant finding is also that the association is independent of arterial pressure. In addition, the study shows a marked difference between men and women in the left ventricular parameters. Geometric remodeling is only significant in women and not in men. This is consistent with a number of observations regarding the difference in the prevalence of cardiovascular disease in women [11,12], as well as women showing a consistently higher late-systolic augmentation of the central aortic pressure compared with men [13]. Indeed, higher augmentation in women is seen from early childhood [14].

A significant feature of the noninvasive methodology used in the study by Pucci et al. [5] is the estimation of flow. The algorithm used is model based and optimized so as to obtain zero flow during diastole [8,9]. The result is an ejection wave with a form which resembles the usual flow wave seen in the ascending aorta, that is, a rapid increase to a peak around a third of the ejection time, and then a decrease to zero at end systole. The morphology of the derived flow wave closely resembles a triangular shape (as illustrated in Fig. 1 of the study by Pucci et al. [5]). Indeed, this may be a feature that is responsible for the robustness of the procedure. The use of triangulation for the estimation of flow was extensively examined in previous studies [15], with respect to the effect of waveform deviation from the triangular shape on estimation of amplitude of forward and backward waves and indices of wave reflection. It was found that concavity and convexity of the waveform in the flow deceleration phase had minimal effect, as did the variation of the time of peak flow over a range of some $30\%$. The analysis suggested that triangulation of the flow waveform using the features of the central aortic pressure wave was a robust method with which to analyze central aortic hemodynamics [15,16]. These techniques have shown significant predictive power for cardiovascular risk in large cohorts [17].

Scaling the derived flow in the study by Pucci et al. [5] to an identical arbitrary range (0–100 arbitrary units) for all individuals suggests that the computed value of aortic characteristic impedance is highly dependent on the amplitude of aortic pressure, or more precisely, on the magnitude of the pressure between beginning of systole and the first inflection corresponding to the time of peak flow (often referred to as P1, Fig. 1). This is because the value of characteristic impedance determined from the impedance spectrum is generally similar to that determined from the slope of pressure and flow in early systole [18]. Hence, if the flow axis is invariant in a pressure–flow phase plot, because of the similar scaling in all individuals, the value of characteristic impedance must necessarily be determined predominantly by the height of P1 (Fig. 1). In the study by Pucci et al. [5], the claim that the association of aortic characteristic impedance and left ventricular structure is pressure independent came from the multiregression analysis using central and peripheral SBP and DBP. It would be of interest to know whether the effect is independent of P1.

A positive aspect of the flow normalization to a similar range (0–100 arbitrary units) is that it is analogous to having the flow described in units of velocity. As peak velocity is of the same order in large arteries (of the order of 100 cm/s in the ascending aorta), it allows comparison of impedance spectra in conduit vessels of different caliber, as would be the case between men and women and across different ages [1]. This aspect often attracts controversy in the studies comparing individuals of different sizes and which take into account the anatomical dimensions in the analyses [11,19].

Numerous studies have shown that the mechanical properties of the large aortic conduits, including the ascending aorta and the aortic trunk, are significant in determining the pulsatile load on the ejecting ventricle [20–23]. Imaging modalities such as MRI can offer possibilities to measure accurate changes in the vessel caliber associated with noninvasive pressure to assess the regional and global mechanical stiffness [24]. However, such techniques are necessarily limited to small cohorts and are not entirely suitable for screening. The techniques proposed in the study by Pucci et al. [5] suggest the potential use of noninvasive measurement of central aortic pressure from the peripheral pulse and the estimation of aortic flow to obtain aortic hemodynamic parameters to determine aortic characteristic impedance. The study indicates a significant association between the characteristic impedance so determined and the parameters of left ventricular structure. This would have the potential of risk stratification based on the aortic properties related to characteristic impedance.
Aortic impedance and left ventricular structure in hypertension