Arterial stiffness and pulse contour analysis: an age old concept revisited

“In extreme old age, the arteries themselves, the grand instrument of the circulation, by the continual apposition of earth, become hard, and as it were bony, till, having lost the power of contracting themselves they can no longer propel the blood, even through the largest channels, in consequence of which death naturally ensues.” (John Wesley, 1703–1791)

Hardening of the arteries, and its relation to aging, is far from a new phenomenon. Indeed, the fact that arteries stiffen with age, and that such changes are associated with an increased incidence of major cardiovascular events, is now established beyond doubt [1–4]. However, the influence of arterial stiffening on the interaction between the heart and large vessels, and on atherosclerosis, is less well understood. Early researchers used pulse contour analysis of peripheral pressure waveforms to obtain information about arterial stiffness [5,6], but their results were mainly qualitative, and pulse contour analysis was largely abandoned by practicing clinicians in favour of conventional sphygmomanometry.

With the increased longevity of modern societies and the recognition that arterial stiffness is an independent predictor of cardiovascular risk in selected populations, the factors underlying vascular stiffness have assumed major importance. In particular, there has been interest in the association between stiffness and cardiovascular risk factors, such as diabetes and hypertension in individuals without manifest atheroma [7]. It has become clear that arterial stiffness is not solely determined by structural elements within the vessel wall and distending pressure, but that there is also functional regulation by the sympathetic nervous system [8] and endothelial-derived NO [9]. This suggests that functional abnormalities, such as endothelial dysfunction, may underlie some of the large artery stiffening found in individuals with cardiovascular disease and risk factors, and thus may potentially be reversible [10]. Moreover, assessment of arterial stiffness in such individuals may aid risk stratification.

It is against this background that several groups have focused on the development of simple reproducible methods to assess arterial stiffness in clinical practice [11]. In this issue of Clinical Science, Millasseau et al. [12], in a series of elegant studies, describe the use of pulse contour analysis to derive quantitative data concerning large arterial stiffness in the hope of providing new insights into ventricular vascular interaction. Using the established technique of photoplethysmography [13,14], they have devised a reproducible parameter termed ‘stiffness index’ by measuring the time delay between direct and reflected waves in the digital volume pulse [12]. Since this measure will be determined, to a large extent, by velocity of the arterial waveform in the aorta and large arteries, it is perhaps unsurprising that they were able to demonstrate a significant correlation between the stiffness index and carotid-femoral pulse wave velocity (PWV). In addition, both stiffness index and carotid-femoral PWV were, as expected, independently correlated with age and mean arterial pressure. Nevertheless, their results are important, as they suggest that stiffness index may be used as a valid surrogate for aortic PWV. Since digital pulse contour analysis is simple, operator-independent and relatively inexpensive, it may be, as the authors suggest [12], suitable for use in large clinical studies. However, several relatively simple commercial systems are available to measure PWV directly. Thus any perceived benefit of the stiffness index must be weighed against the fact that it is an indirect measure, as the authors [12] themselves note; indeed path length is not measured directly, instead height is used as a surrogate. Such limitations may not be important, but it is becoming increasingly clear that small changes in PWV may still be physiologically meaningful [9]. Indeed, in humans, femoral PWV changes by only 5% per decade [2]. Therefore, although Millasseau et al. [12] report only a ‘modest’ change in stiffness index and PWV following administration of glyceryl trinitrate, the potential importance of such a change should not be underestimated.

As the authors discuss [12], in addition to the stiffness index, other parameters have been shown to correlate with PWV, including central augmentation index (Alx), derived by from the radial artery waveform using a validated transfer function [15,16]. The timing of the start of wave reflection (T0) can also be derived from the ascending aortic waveform, and provides a surrogate of aortic PWV [17,18]. Interestingly, recent data [19], from the same cohort of patients with end-stage renal failure referred to by Millasseau et al. [12], demonstrates that central Alx and PWV are both independent predictors of mortality, despite the fact that the majority of subjects were receiving a wide variety of vasoactive drugs [20].

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Blood pressure varies throughout the arterial tree [21], and the normal amplification of pulse pressure towards the periphery depends on a number of factors, including age and mean pressure [22]. Interestingly, central rather than peripheral pulse pressure seems to predict mortality in patients with end-stage renal failure [23], and carotid intima-media thickness in healthy men [24]. Therefore, it appears that in order to fully assess the impact of disease processes and drugs on large arteries, perhaps both aortic PWV and AIx should be assessed, together with central blood pressure.

There is no doubt that the assessment of arterial stiffness will make a major contribution to the improved management of cardiovascular disease in the clinical arena and should be included in all future large intervention studies. However, the choice of technique will be influenced by ease of use, cost and other less rationally chosen factors [25]. The race is on, and the technique of digital pulse contour analysis, as described by Millasseau et al. [12], is an important addition to the field. It is, however, robust outcome data that is likely to determine the eventual winner.

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