Editorial Comment

Reference Values of Arterial Stiffness–Related Indexes Derived from Pulse Wave Analysis

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The development of arterial applanation tonometry with modern pulse wave analysis (PWA), which includes estimation of central hemodynamic parameters based on the generalized pressure transfer function (GTF) included in the SphygmoCor® system, has enabled the noninvasive evaluation of systemic arterial stiffness. Since the 1990s, this method had been applied to clinical studies and large-scale clinical trials, such as the Conduit Artery Function Evaluation (CAFE) substudy of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) (*1*). However, the absence of reference values for these parameters has prevented the use of PWA in routine clinical practice.

The study of Wojciechowska *et al*. published in this journal (*2*) provided preliminary threshold values of arterial stiffness indexes, including peripheral as well as central augmentation indexes (AI's), that were acquired using the SphygmoCor® system, and determined by analyzing their distribution characteristics in a normal reference population of white Europeans. Although this was a pioneering study, care should be taken when interpreting the results due to the methodological issues described below.

Chen *et al*. (*3*) extensively evaluated the use of GTF to estimate central aortic pressure waveform. Their study justified the application of the estimated central waveform only for the acquisition of systolic blood pressure and pulse pressure, and vascular compliance, if clinically acceptable accuracy were to be assured. The report also indicated the difficulty of estimating the central AI in the waveform reconstructed by the use of GTF. In contrast to systolic peak pressure and diastolic pressure decay, which are mostly determined by the lower frequency characteristics of GTF, the estimation of AI is related to higher frequency characteristics. As shown in this and the other reports (*4*), the variance of the pressure transfer function is larger for higher frequencies, which are essential to reproduce central AI precisely. Needless to say, as the GTF cannot be individualized, if the condition of the subject differs from the average condition in the reference population, there is no guarantee that the estimated aortic pressure waveform is identical with the actually measured one. Therefore, GTF-based estimation of the central AI is not accurate enough to replace the actual central AI. A similar criticism of GTF-based analysis also appeared in a more recent report by Millasseau *et al*. (*5*).

GTF can be regarded as a filter function, *per se*, exhibiting an all-pass characteristic over the frequencies up to 8–10 Hz plus a band-pass characteristic with a peak at 3–5 Hz (*3*, *4*). This implies that the central pulse waveform is transmitted to peripheral sites with a certain distortion, but without any loss of the information it has carried. Therefore central information relating to AI is also preserved in the peripheral pulse waveform. In the case of the GTF method, peripheral and central waveform data can be regarded as the input and output of the inverse filter (GTF^{-1}), respectively. Theoretically, as the output signal cannot carry more information than the input signal, estimated central AI can be a useful clinical marker but cannot be more informative than peripheral AI.

Consequently, it is understandable that central AI estimated by the GTF method has proven to be a useful clinical parameter or correlate of systemic arterial function and cardiovascular risk. However, a useful "clinical" risk marker should not be confused with a precise estimate of the central waveform. Furthermore, the inverse filtering may amplify individual dif-

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ferences in pressure transfer characteristics, so that if a reflection peak is detectable in the peripheral pulse waveform, GTF-based central waveform estimation may have no advantage (*5*).

The study of Wojciechowska *et al*. (*2*) is welcomed for its provision of objective reference values for clinical decisions using PWA. However, it cannot be guaranteed that the reference value for central AI proposed in this study is applicable if a different device or GTF acquired from a different reference population is used for central AI estimation instead of the SphygmoCor® system.

Additionally, although the SphygmoCor® system has become a widely accepted device for PWA, there is still room for further improvement. The accuracy of waveform data acquired using this device might be dependent on the skill of the operator, because a tonometry sensor is operated manually and recorded data are selected subjectively. It would thus be a substantial improvement if automated sensor operation and data handling could be introduced in PWA.

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