Hypertension Research (2017) 40, 429–431

www.nature.com/hr

COMMENTARY

The time is ripe to reevaluate the second derivative of the digital photoplethysmogram (SDPTG), originating in Japan, as an important tool for cardiovascular risk and central hemodynamic assessment

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Hypertension Research (2017) **40,** 429–431;doi:10.1038/hr.2016.175; published online 22 December 2016

The report by Inoue *et al.*[1] in the present issue of *Hypertension Research* is important in several respects.

Most importantly, it is the first report demonstrating the significant prognostic impact of the SDPTG-d/a index (the ratio of the height of the d wave to the a wave of the SDPTG), on the basis of long-term follow-up observation of a large general Japanese female population. Using a substantial follow-up totaling 39 732 person-years and including 327 deaths, 79 of which were cardiovascular, the authors successfully established a significant association between the SDPTG-d/a and cardiovascular mortality. This association was clearly independent of BP levels (either SBP or DBP), age and other prognostic factors.

The SDPTG is a pulse wave modality that was devised in the 1970s and has been clinically applied ever since, albeit mainly in Japan. In 1998, Takazawa *et al.*[2] introduced the SDPTG to an international audience, emphasizing its usefulness as an index of vascular aging, as well as its ability to reflect the central augmentation index (cAI) compared with simultaneously recorded direct ascending aortic pressure waveform data. Thus, the present data reported by Inoue *et al.*[1] reinforce the prognostic impact of aortic wave reflections (or augmentation), which are a determinant of central hemodynamics. The paper also strengthens the validity of the SDPTG-d/a as a central blood pressure (CBP)-related index or biosignal carrying central hemodynamic information. However, international clinical and research applications of the SDPTG have been limited, possibly because of a misconception that a peripheral fingertip volume pulse cannot properly convey central hemodynamic information.

For this reason, it would be worthwhile to review how a central aortic pressure wave transmits to the peripheral upper limb and determines the finger artery volume, which can be measured by digital plethysmography (PTG) for SDPTG derivation.

MODEL-BASED UNDERSTANDING OF PULSE WAVE TRANSDUCTION FROM THE AORTA TO FINGERTIP PTG

In this context, it is useful to envision the upper limb arteries as a physical system consisting of two components, one corresponding to a conduit (subclavian-radial arteries) and the other to a Windkessel (palm-finger arteries). The output from each component can be calculated from its input multiplied by the system function in the frequency domain,[3] that is, the complex ratio of output/input (usually plotted as gain and phase and referred to as a Bode diagram) for each harmonic component as a function of frequency. In the case of the upper limb arteries, the system function of the conduit component is an aorto-radial pressure transfer function that is well known and used as a generalized transfer function (GTF) to estimate CBP with the commercially available SphygmoCor device (AtCor Medical System, Sydney, Australia). Figure 1 shows a 'Japanized' GTF (GTF_J) modified for use in Japanese patients on the basis of simultaneous direct aortic pressure and radial tonometric waveform data recorded in 20 cardiac patients.[4] The aorto-radial GTF (the conduit system) gain is characterized as a feature of a band-pass filter. It is also similar to a typical frequency response of an underdamped fluid-filled catheter-manometer system, as discussed elsewhere.[5] The band-pass feature has a peak (or central) frequency at ~5 Hz, above which input signals expressed as power spectra (defined as squared signal amplitude) become as small as $<1/10\,000$ of the input level at zero frequency (corresponding to the squared MAP). This suggests that the higher-frequency input amplitude of central aortic pressure (P_{Ao}) is very small, that is, $<1\%$ of the MAP level (Figure 1, lower panel). This feature causes the GTF to function similarly to a high-pass filter, and the resultant output corresponding to the peripheral radial pressure (P_{Ra}) waveform is distorted to be early peaked according to the frequency-dependent amplification.

The conduit system output, P_{Ra}, is subsequently fed to the palm-finger Windkessel connected to the distal end of the conduit (that is, the radial artery). 'Windkessel' refers to a compliant chamber or reservoir whose analog electrical model is a CR (capacitor +resister) circuit that acts as an integrator or low-pass filter. The Windkessel is filled with

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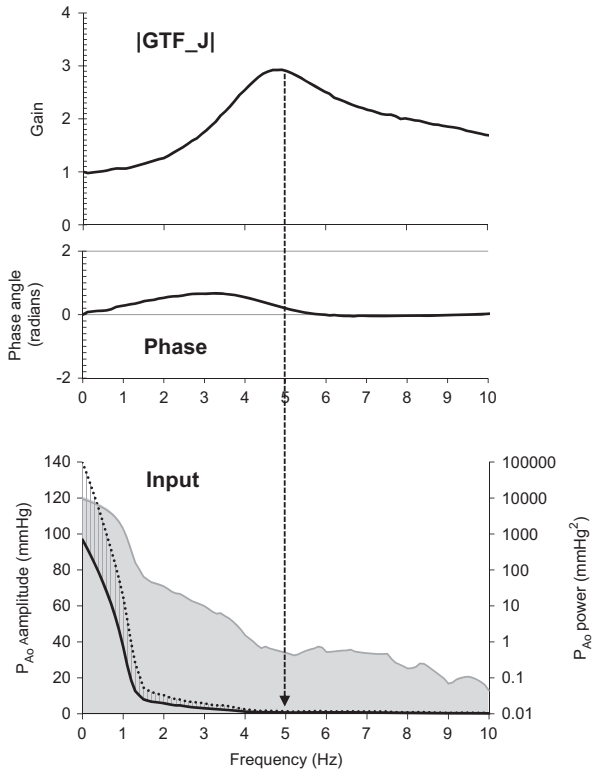

Figure 1 'Japanized' generalized pressure transfer function (GTF) between the aorta and the radial artery (GTF_J) and its input spectra. GTF_J was determined by modifying the SphygmoCor GTF to fit the characteristics of Japanese patients by frequency rescaling (unpublished data).[4] In the frequency domain, GTF is a complex function that can be shown as the gain (upper panel) and phase (middle panel) functions. The phase function is plotted after the elimination of linear delay due to a simple conduction time lag. The gain has a peak at ~5 Hz (arrow). The lower panel shows input signals (the frequency component amplitude of the P_{Ao}, denoted by a solid line) of the GTF. The pooled data analysis was based on micromanometric P_{Ao} measured invasively in 20 cardiac patients (unpublished data).[4] The dotted line indicates the input amplitude +1 s.d. The gray area plot representing input power spectra (squared amplitude) is also shown superimposed on the same coordinates, but its ordinate scale is logarithmic. Above the peak gain frequency, the input signals are considerably small.

blood flow depending on the instantaneous pressure gradient at the inlet of the system. The integral of the input blood flow minus the leak flow volume through the resistor determines blood volume in the system, similarly to how a capacitor is charged with an electrical quantity. Therefore, the volume change monitored as the PTG waveform is related to the integrated radial pressure waveform. The measured palm-finger Windkessel system function, that is, the P_{Ra}-PTG GTF, was reported by Millasseau *et al.*[6] in 2000. Because those authors might consider the causal direction of the transfer function to be PTG→pressure (P_{Ra}) to estimate the P_{Ra} waveform from PTG, the resultant GTF shows a band-pass or high-pass feature resembling an aorto-radial GTF. For the normal causal direction described above (pressure→PTG), the transfer function (TF) should be inverted. The TF becomes nearly counter-balanced with the aorto-radial GTF (Figures 2a and b). Hence, it may act as a low-pass filter, permitting at least partial compensation for the pressure wave propagation-induced distortion or amplification. Metaphorically, this TF may act as an inline damper for an underdamped pressure line (the conduit arteries), and thus the total system function (from aorta to fingertip PTG), which is the product of both component system functions, may have nearly all-pass or flat frequency characteristics (Figure 2c). Therefore, PTG not only appears similar to the CBP waveform but also can convey all central hemodynamic information.

UNRESOLVED ISSUES IN CBP ESTIMATION AND CBP-RELATED INDEXES

The primary purpose of CBP assessment is to obtain hemodynamic information specific to the central aorta, that is, the information that cannot be acquired from brachial cuff BP measurements. Because MAP, the DC (direct current) or static component of BP, is nearly common to central and peripheral BPs, CBP estimation is not necessary to assess MAP.[5] All the features specific to CBP are related to the dynamic components of BP modifiable by pressure wave propagation, which are chiefly attributable to wave reflection dynamics.[7] In addition, there is a major unresolved issue relating to the inaccuracy of cuff BP measurements, which are essential to calibrate the pressure waveforms to estimate CBP.[5] Furthermore, there are also unresolved problems related to the limited generalizability of GTF or the inability to individualize.[8,9] These issues, which have proven difficult to elucidate or resolve for clinicians as well as researchers, may prevent the clinical application of CBP assessment.

Therefore, a reasonable way to avoid these issues is to take advantage of the CBP/augmentation-related indexes, such as the cAI and pulse pressure amplification acquired as peripheral AI (pAI), because these indexes can be assessed without absolute BP values.

UNACKNOWLEDGED ADVANTAGES OF THE SDPTG

Like the cAI and pAI, the SDPTG-d/a is useful as a CBP/augmentation-related index.[1,2] Further, the SDPTG-d/a has several advantages over AIs. As mentioned above, the pressure pulse wave signal transduction acts as a low-pass filter characterized as the aforementioned P_{Ra}-PTG GTF (Figure 2b). This phenomenon results in an effective reduction of higher frequency noise or an improved signal-to-noise ratio of PTG, which is advantageous to stably derive a noiseless waveform of the SDPTG. The mathematical differentiation to derive the SDPTG acts as a high-pass (low-cut) filter to effectively eliminate from PTG its offset (static or DC component), which includes no information specific to CBP or central hemodynamics.

Though there is still controversy in regard to the exact mechanism, AIs have been reported to lose their age-dependency after the sixth decade of life, especially in women.[10–13] In contrast, Inoue *et al.* have shown that the SDPTG-d/a data maintain their age-dependency (Figure 2 in their paper), in agreement with data reported by Takazawa *et al.*[2] and Tabara *et al.*[13] This finding suggests that the SDPTG-d/a may provide additional and more useful information about cardiovascular aging than AIs. In turn, the SDPTG-d/a may provide not only information that has been reported to be equivalent to cAI, an index related to

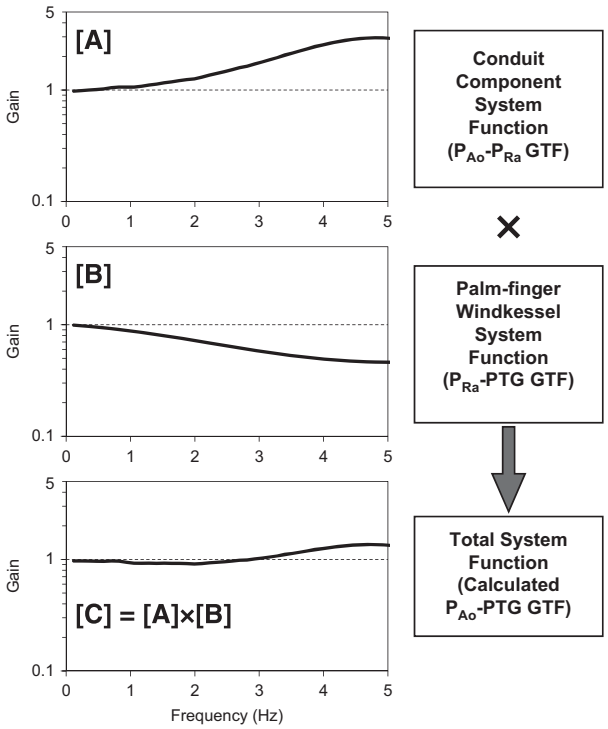

Figure 2 Pulse wave propagation from the central aorta to fingertip PTG characterized as two component system functions (GTFs). For simplicity, only the gains (absolute value of complex TF; the scale is logarithmic) of GTFs are plotted over the frequency range (~5 Hz), where significant input power exists. The upper panel shows the 'Japanized' aorto-radial GTF (GTF_J) [A], essentially the same as in Figure 1, which is the system function of the conduit component system. In the displayed frequency range, GTF_J (GTF [A]) exhibits marked high-pass characteristics. The middle panel shows the GTF [B] of the Windkessel component system, which is the pressure (P_{Ra}) input/volume (PTG) output GTF (P_{Ra}-PTG GTF). This GTF is plotted on the basis of a quartic polynomial model fitted to the reported data (normalized so that the DC gain is unity),[6] which acts as an integrator or a low-pass filter. This feature may at least partially compensate for the pressure transmission-induced amplification/distortion based on the GTF [A], thus resulting in the GTF [C] showing nearly all-pass characteristics. GTF [C] is obtained as a complex product of GTFs [A] and [B], and represents the total pulse wave transduction from the P_{Ao} to fingertip PTG.

augmentation amplitude, but also information specific to the second derivative, which represents the shape of an augmentation peak of the PTG waveform (reflecting CBP waveform); that is, the SDPTG-d/a can reflect more detailed features of central aortic augmentation.

Finally, the ease and low-cost features of SDPTG may facilitate the routine clinical assessment of central hemodynamics or vascular function.

Given all of the aforementioned reasons, the study by Inoue *et al.*[1] indicates that the time is ripe for reevaluation of the SDPTG as an important biosignal processing modality that can provide information about cardiovascular risk and central hemodynamics.

CONFLICT OF INTEREST

The author declare no conflict of interest.

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