**COMMENT**

# Functionally-important arterial properties that can be determined from 24-hour ambulatory blood pressure measurements in hypertensive patients

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The arterial vessels deliver blood enriched with oxygen and nutrients from the heart to each cell in the body tissues, according to local needs. This is accomplished via a vast number of capillaries (typically 5–10 μm diameter), in which carbon dioxide and waste are exchanged for oxygen and nutrients by diffusion through the capillary wall, before returning to the heart via the venous system. While blood is ejected into the aorta in pulses following the contraction of the left ventricle, diffusion at the capillary level is most effective for non-pulsatile blood flow, where the capillary transit time required by red blood cells (RBCs) to cross the capillary length matches the time required for effective diffusion [1]. Thus, cushioning the pulsatile flow is an important function of the arterial vessels [2]. The said input and output requirements are satisfied by the following mechanical properties of the arterial vessels, where the basic physiological concepts pertaining to the present views are illustrated in Fig. 1 here.

1. *Resistance to flow* is generated by the arterioles (mean lumen diameter ~100 μm) that provide and control blood flow to the capillaries of an individual tissue. This is done by actively changing the tone in smooth muscles located in the arteriolar wall that acts to vary the lumen diameter, controlled by neural activity and metabolic mechanisms. This resistance, as seen from the heart side, is the "total peripheral resistance" (TPR) defined by the ratio between the mean arterial pressure

and the cardiac output. TPR is also proportional to blood viscosity, where the concentration and deformability of RBCs play an important role, especially at the level of arterioles and capillaries, causing blood viscosity to vary with flow rate and under some conditions, e.g., diabetes mellitus [3].

2. *Arterial compliance* provides a measure for the distensibility of the artery (in the radial direction) in response to the ventricular ejection that leads to temporal storage of blood during the systole and its release during the diastole. The higher the compliance, the larger the stored blood volume. The combined effect of TPR and compliance cushions the pulsatility of arterial pressure and flow, similar to the rectifying effect of a capacitor connected in parallel to a resistor on a series of pulses. This so-called "two-element Windkessel model" [4] explains the pulse waveform—fast pressure increase during the systole followed by gradual, typically exponential pressure decay during the diastole (Fig. 1B here). Therefore, TPR and compliance are basic mechanical properties of the arteries that determine blood pressure (BP) variation in response to the left-ventricular ejection in an individual. It is important to mention that for both normal and high arterial pressures, the increase of arterial volume (or cross-sectional lumen area or diameter) in response to a given increase in arterial pressure is reduced upon elevating the pressure (Fig. 1C here). It means that the arterial wall becomes stiffer, i.e., less compliant upon increasing the arterial pressure from DBP to SBP during the systole [5]. This behavior is explained by the elastin and collagen fibers in the arterial wall that respond differently to stretch: while elastin fibers behave like a simple elastic spring, collagen fibers are recruited via smooth muscles in response to the increased stretch, generating stiffness

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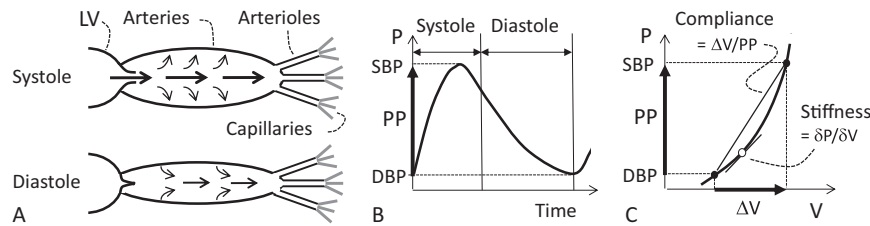    P.O.B. 53221, Jerusalem 9153101, Israel

**Fig. 1** Basic physiologically-relevant concepts: **A** A schematic illustration of the blood flow from the heart towards the periphery, including the arterioles that generate and control the total peripheral resistance (TPR) to the flow, and the capillaries. During the systole, some of the blood ejected from the left ventricle (LV) is stored by the elastic arteries that expand in response to the arterial pressure. During the diastole, which starts after the closure of the aortic valve, the stored blood is gradually released towards the periphery by the elastic recoil of the arterial wall. **B** The arterial pressure (*P*) waveform, resulting from the events described in (**A**). P peaks at the systole, reaching the systolic BP (SBP), and then decays during the diastole until reaching the diastolic BP (DBP). **C** The usually-curved relationship between *P* and blood volume *V* (also stands for cross-sectional lumen area or lumen diameter) [5]. During the systole, *P* and *V* increase by the pulse pressure PP and $\Delta$V, respectively, where compliance is defined by the ratio $\Delta$V/PP. Upon increasing PP, the curved *P–V* relationship causes compliance to decrease. Stiffness is defined for any *P* value by the tangent slope, i.e., the ratio between virtually small variations ($\delta$) in *P* and *V* (marked by the line through the unfilled circle). Here, stiffness increases upon increasing *P*.

that increases dynamically with the wall stretch [6]. Stiffness can be defined at a given pressure (or volume) point and thus varies during the systole (see the legend of Fig. 1C here). Compliance, which can be viewed as the reciprocal value of stiffness is defined, for the purpose of this comment, by the ratio between the overall changes in volume and pressure during the systole, frequently estimated by [stroke volume]/PP. Compliance is expected to decrease with increasing PP or V (Fig. 1C here). This physiological description may underlie the known association of PP with aging and CV risk [7]. We may conclude that measuring TPR and compliance may provide clinically valuable information about the functional state of the arterial vessels. In the present study, Aristizábal-Ocampo et al. [8] described and tested a new method for estimating the "hemodynamic profile" of hypertension in terms of total peripheral resistance (TPR), and total arterial compliance (Ct) (a modified version of the said definition) from the data of 24-h ambulatory BP measurement (24-h ABPM) obtained using the oscillometric method. This was done without the need for pulse waveform or cardiac output measurements. The method is based on the two-element Windkessel model combined with phenomenological models for the systolic time and Ct that were justified by comparison with experimental data. A step-by-step determination of Ct and TPR from 24-h ABPM was described in Table 2 [8]. The method also estimated the stroke volume and thus, the cardiac output (equals [Stroke volume]·[Heart rate]). Using the mean 24-h ambulatory systolic BP (SBP), diastolic BP (DBP), and pulse pressure (PP), hypertension (HT) was defined as [SBP ≥ 130 mmHg or DBP ≥ 80 mmHg] and normotension (N) by [SBP < 130 mmHg and DBP < 80 mmHg]. Taking PP = 50 mmHg as an additional threshold, the

authors defined the following HT subtypes: "isolated diastolic hypertension" (IDH) by [DBP ≥ 80 mmHg and SBP < 130 mmHg]; "systolic-diastolic HT" (SDH) by [SBP ≥ 130 mmHg, and DBP ≥ 80 mmHg], which was further split into the subtypes "divergent systolic-diastolic HT" (D-SDH) for PP ≥ 50 mmHg and "non-divergent systolic-diastolic HT" (ND-SDH) for PP < 50 mmHg, and "isolated-systolic HT" (ISH) by [SBP ≥ 130 mmHg and DBP < 80 mmHg]. The authors showed that the following BP subtypes series N, IDH, ND-SDH, D-SDH, and ISH appeared as non-overlapping domains that completely fill a plane defined by the axes PP and DBP (Fig. 2 [8]).

In this cross-sectional study, the hemodynamic profile was determined for the said BP subtypes in 7434 patients with suspected HT undergoing 24-h ABPM without pharmacological treatment, including 5523 hypertensive patients and 1950 normotensive controls. Age (mean ± SD) was 46.2 ± 13.0 years and 54.8% were male.

The main findings of this study were that different BP subtypes could be characterized by different pairs of the hemodynamic parameters TPR and Ct determined by the present method, as presented in detail in Figure 3 and Table 1 [8], and in a compact way in Fig. 2A here. Divergent systolic-diastolic HT (D-SDH) and isolated systolic HT (ISH) were characterized by high TPR and low compliance, while normotension (N) and isolated diastolic HT (IDH) were characterized by low TPR and high compliance. Non-divergent systolic-diastolic HT (ND-SDH) were characterized by intermediate values of TPR and compliance. These findings support the researchers' view that both Ct and TPR may be responsible for the observed BP subtype in an individual patient. Quantitative support for this view is found in Fig. 2B and C here, showing that TPR correlated with SBP by $r = 0.990$ ($p < 0.001$), and
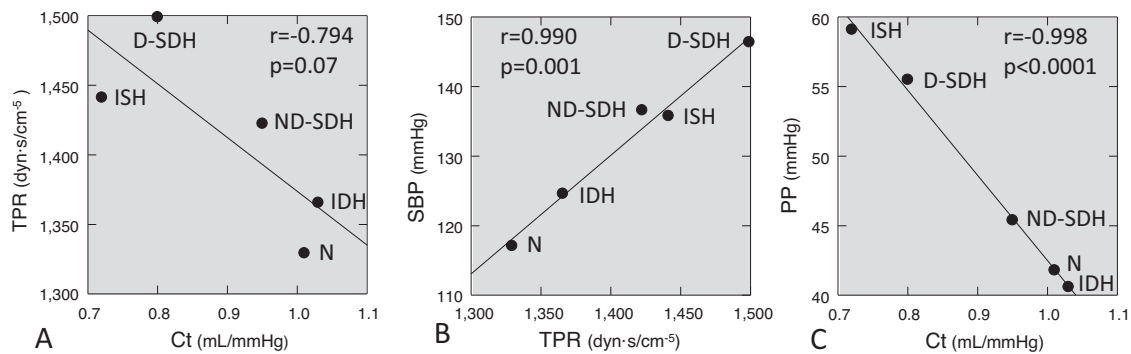
**Fig. 2** Plots of relationships between **A** total peripheral resistance (TPR) and total arterial compliance (Ct) determined merely from 24-h ambulatory BP measurements for the for patients having normal BP (N) and hypertension (HT) subtypes [8], **B** mean systolic BP (SBP) and TPR, and **C** mean pulse pressure (PP) and Ct, for the said normal and hypertension subtypes including isolated diastolic HT (IDH), non- divergent systolic-diastolic HT (ND-SDH), isolated systolic HT (ISH), and divergent systolic–diastolic HT (D-SDH), as defined in the text. The data were taken from Table 1 of the present study [8]. Pearson correlation coefficient $r$ is marked. The lines and the $p$ values were obtained using linear regression.

compliance correlated with PP by $r = -0.998$ ($p < 0.001$). Stiffness defined as 1/Ct was correlated with PP by $r = 0.992$ ($p < 0.001$). Since DBP equals SBP minus PP, DBP can be expressed by a linear combination of TPR and compliance. The very high correlation between PP and compliance may be rationalized by the pressure depen- dence of compliance deduced from Fig. 1C here. TPR and compliance did not correlate significantly (Fig. 2A here), which may reflect their contribution by different arterial vessels. The finding that for all BP subtypes the mean cardiac index (the ratio between cardiac output and body surface) was stable within ±5% of the total mean (Table 1 [8]) may suggest that the function of the observed varia- tions between BP subtypes and the associated variations in TPR and compliance is to provide appropriate blood supply to the tissues despite changes due to aging, lifestyle, obe- sity, etc. However, this possibility requires further analysis. In addition, the fact that PP depends on heart rate [9] suggests that the sensitivity of TPR and compliance with heart rate should be evaluated. This study has high clinical impact due to the possibility of evaluating the functionality of the arterial system in addition to the 24-h BP profile merely by using standard 24-h ABPM.

## Compliance with ethical standards

**Conflict of interest** The author declares no competing interests.

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