

Five years of cardio-ankle vascular index (CAVI) and CAVI₀: How close are we to a pressure-independent index of arterial stiffness?

A. GIUDICI^{a,b}, A.W. KHIR^a, K.D. REESINK^b, T. DELHAAS^b, B.SPRONCK^{b,c}

Supplementary material

APPENDIX

1) Simplification of the Bramwell-Hill equation.

The Bramwell-Hill equation is defined as

$$\text{PWV} = \sqrt{\frac{1}{\rho \cdot \text{distensibility}}}, \quad (\text{A1})$$

with

$$\text{distensibility} = \frac{1}{A} \frac{dA}{dP} \quad (\text{A2})$$

Given $A = \frac{1}{4}\pi D^2$, distensibility can also be formulated in terms of diameter (D):

$$\text{distensibility} = \frac{1}{D^2} \frac{d(D^2)}{dP} = \frac{1}{D^2} \frac{d(D^2)}{dD} \frac{dD}{dP} = \frac{2}{D} \frac{dD}{dP} \quad (\text{A3})$$

When estimating distensibility from clinical data, however, commonly $\frac{dD}{dP}$ is estimated using a diastolic-to-systolic linearization ($dP \approx \text{SBP} - \text{DBP}$, $dD \approx D_s - D_d$):

$$\text{distensibility}_{D,\text{lin}} = \frac{2}{D_d} \frac{D_s - D_d}{\text{SBP} - \text{DBP}} \quad (\text{A4})$$

This linearization, together with Eq. A1 is what's used in CAVI.

Note: sometimes another linearization is chosen, using Eq. A2 and $dA \approx A_s - A_d$ (and again $dP \approx \text{SBP} - \text{DBP}$). The resulting metric is similar but *not* equal to $\text{distensibility}_{D,\text{lin}}$:

$$\begin{aligned} \text{distensibility}_{A,\text{lin}} &= \frac{1}{A_d} \frac{A_s - A_d}{\text{SBP} - \text{DBP}} = \frac{1}{D_d^2} \frac{D_s^2 - D_d^2}{\text{SBP} - \text{DBP}} = \frac{D_s + D_d}{D_d} \frac{1}{D_d} \frac{D_s - D_d}{\text{SBP} - \text{DBP}} \\ &= \frac{D_s + D_d}{2D_d} \text{distensibility}_{D,\text{lin}} \end{aligned} \quad (\text{A5})$$

As systolic diameter is by definition larger than diastolic diameter ($D_s > D_d$), in all cases, $\text{distensibility}_{A,\text{lin}} > \text{distensibility}_{D,\text{lin}}$.

2) CAVI and P_m

Eq. 1 is defined with respect to a generic pressure P_{ref} . If P_{ref} is set to the mid pressure P_m , Eq. 1 becomes:

$$P(D) = P_m e^{\beta_m \left(\frac{D}{D_m} - 1\right)}, \quad (\text{A6})$$

where D_m is the diameter at P_m and β_m is the value of β_0 when $P_{\text{ref}} = P_m$. Using Eq. A6, the derivative term in Eq. 3 becomes:

$$\frac{dP}{dD} = \frac{P_m \beta_m}{D_m} e^{\beta_m \left(\frac{D}{D_m} - 1\right)}. \quad (\text{A7})$$

If the derivative dP/dD is calculated at P_m (i.e., when $D = D_m$), Eq. A7 simplifies to

$$\frac{dP}{dD} = \frac{P_m \beta_m}{D_m}. \quad (\text{A8})$$

Then, substituting dP/dD in Eq. 3 with Eq. A8 and opportunely rearranging leads to the following relationship:

$$\beta_m = \frac{\text{PWV}^2 \cdot 2\rho}{P_m}. \quad (\text{A9})$$

Note that, unlike Kawasaki's β , β_m is linked to Hayashi's β_0 by the relationship

$$\beta_0 = \beta_m - \ln\left(\frac{P_m}{P_{\text{ref}}}\right). \quad (\text{A10})$$

3) Estimation of the haPWV-relevant pressure

We follow the assumption at the basis of CAVI and CAVI_0 : constant β_0 throughout the arterial tree and in particular in the heart-to-ankle and heart-to-brachial artery pathways. In this example, we will use a person with $\beta_0 = 8.50$, DBP = 80 mmHg and SBP = 120 mmHg. Further, we also assume that the length of the heart-to-ankle arterial pathway (L_{ha}) is 148 cm and that of the heart-to-brachial pathway (L_{hb}) is 41 cm [49]. The average pressure waveforms in [48] indicate that the pressure at the dicrotic notch is approximately

$$P_{\text{notch}} = 0.55 \cdot \text{DBP} + 0.45 \cdot \text{SBP}. \quad (\text{A11})$$

Hence, in this case $P_{\text{notch}} = 98$ mmHg. Inverting the CAVI_0 equation (Eq. 9) we obtain the following relationship:

$$\text{PWV} = \sqrt{\frac{\left[\beta_0 + \ln\left(\frac{\text{DBP}}{P_{\text{ref}}}\right)\right] \cdot \text{DBP}}{2\rho}}. \quad (\text{A12})$$

It is worth noting that the CAVI_0 formula is based on the derivative of the pressure-diameter relationship at diastolic pressure and, therefore, Eq. A11 determines PWV at DBP (PWV_{DBP}). In our person, $\text{PWV}_{\text{DBP}} = 6.48$ m/s ($\rho = 1050$ kg/m³). Further, Eq. A11 can be generalised to any pressure level P as follows

$$PWV = \sqrt{\frac{[\beta_0 + \ln(\frac{P}{P_{ref}})] \cdot P}{2\rho}}, \quad (A13)$$

so that the PWV at P_{notch} ($PWV_{P_{notch}}$) is 7.26 m/s. Therefore, tb and tba can be estimated as

$$tb = \frac{L_{hb}}{PWV_{P_{notch}}} \quad \text{and} \quad tba = \frac{L_{ha} - L_{hb}}{PWV_{DBP}} \quad (A14)$$

Substituting values in Eq. A14 leads to $tb = 56$ ms and $tba = 228$ ms. Therefore, PWV is calculated at P_{notch} over the first 56 ms of wave travel and at DBP for the remaining 228 ms. A “representative” haPWV pressure can finally be estimated using a weighted average:

$$P_{haPWV} = \frac{tb \cdot P_{notch} + tba \cdot DBP}{tb + tba}. \quad (A15)$$

For the proposed person, this amounts to:

$$P_{haPWV} = 0.91 \cdot DBP + 0.09 \cdot SBP = 84 \text{ mmHg}. \quad (A16)$$

Further, it can be shown that the “0.09” herein is only mildly affected by changes in the choice of the haemodynamic parameters, slightly increasing with increasing DBP and β_0 , and decreasing for higher pulse pressure.

4) Conceptual differences between haPWV, cfPWV, and baPWV

We would like to point out a conceptual difference between haPWV (and its derived indices CAVI/CAVI₀) and e.g., baPWV and cfPWV. Notably, a haPWV is “physically sound” in the sense that there is a physical pressure wave that arises at the heart and travels towards the ankles. This contrasts with e.g., baPWV, where there is no such wave *arising* at the brachial artery. **Figure A1** summarises the differences between haPWV and baPWV. This has an important consequence: when the brachial artery stiffens, this directly leads to a *lower* baPWV (Eq. A19, below). In haPWV, this effect will be much smaller, as only the *difference* between notch and diastolic wave speeds / transit times (TTs) will have an influence (Eq. A17; **Figure A1**). With stiffening, in general, both notch and diastolic TTs will decrease and likely their difference will also decrease. This would imply a (modest) *increase* in haPWV.

The transit time equations corresponding to haPWV, baPWV, and cfPWV are:

$$TT_{ha} = TT_{hy,notch} + \underbrace{TT_{yb,notch} - TT_{yb,dia}}_{\substack{\text{subtraction of TTs} \\ \text{from the same artery}}} + TT_{ya,dia}, \quad (A17)$$

$$TT_{ba} = \underbrace{-TT_{yb} + TT_{ya}}_{\substack{\text{subtraction of TTs} \\ \text{from different arteries}}}, \text{ and} \quad (A18)$$

$$TT_{cf} = \underbrace{-TT_{yc} + TT_{yf}}_{\substack{\text{subtraction of TTs} \\ \text{from different arteries}}}, \text{ respectively.} \quad (A19)$$

Points a, c, f, h, and y are defined in **Figure A1**. In addition to these “subtraction effects”, haPWV includes the proximal aorta, whereas this segment is excluded in baPWV and cfPWV. Finally, haPWV and baPWV include the lower leg segment, whereas this is excluded in cfPWV.

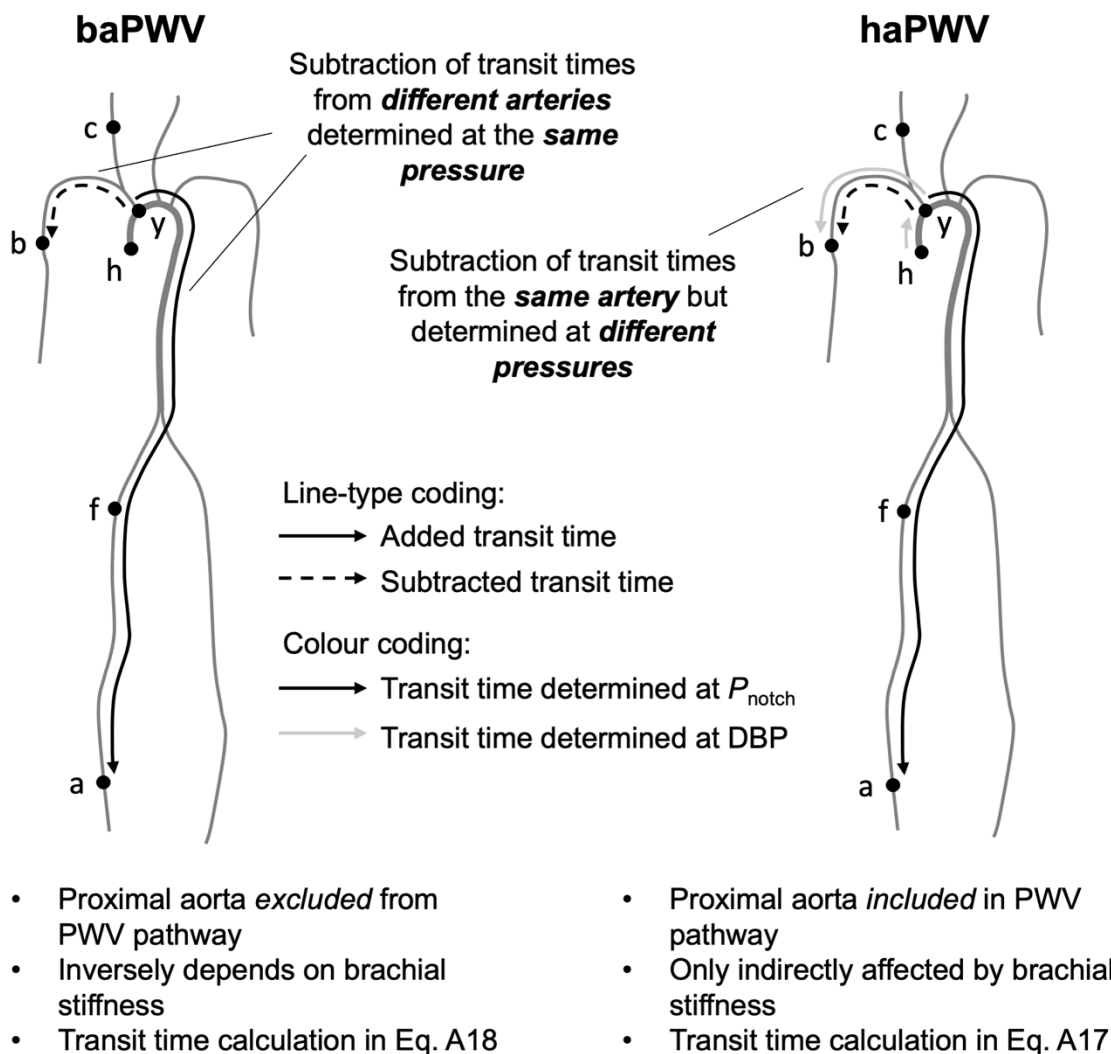


Figure A1 – Schematic representation of the differences between the brachial-ankle (baPWV) and the heart-ankle pulse wave velocities (haPWV). Three main elements differentiate the two techniques: 1) the haPWV-relevant pathway includes the proximal aorta which is excluded from the baPWV, 2) unlike heart-to-ankle, brachial-to-ankle is not a real arterial pathway and this affects the estimation of the transit time (see **Appendix 4**), and 3) while the baPWV transit time relies solely on the foot of the wave (i.e., at diastolic pressure), the determination of haPWV transit time is more complex and involves both foot and diastolic notch fiducial points. cfPWV is conceptually similar to baPWV, however, 1) it includes the carotid vs. the brachial artery, and 2) it excludes the femoral-to-ankle segment which is included in baPWV. a, b, c, f, ankle, brachial, carotid, and femoral measurement sites, respectively; h, heart; y, bifurcation between the aorta and brachiocephalic artery.