

# Blood Pressure-Adjusted Values of Markers of Arterial Stiffness: Three Brothers or also Others?

Hirofumi Tomiyama

Department of Cardiology, Tokyo Medical University, Tokyo, Japan

*See article vol. 26: 603-615*

Here, I would like to comment as a member of the editorial team of the Journal of Atherosclerosis and Thrombosis. Arterial stiffness, as assessed by pulse wave velocity (PWV), has been used as a risk marker for cardiovascular disease (CVD) and also as a marker for vascular damage<sup>1, 2)</sup>. Arterial stiffness comprises two components, namely functional arterial stiffness, which is affected by the blood pressure (BP), and structural arterial stiffness<sup>2)</sup>. Hemodynamic abnormalities related to increased arterial stiffness are thought to be risk factors for the development of CVD, and both functional and structural stiffness might have important roles as risk markers for CVD<sup>1, 2)</sup>. On the other hand, while structural arterial stiffness is thought to be associated with atherosclerotic vascular damage, elevated BP may disturb the assessment of the severity of structural arterial stiffness because elevated BP is associated with increased functional arterial stiffness. In this regard, the cardio-ankle vascular index (CAVI) has been proposed as a marker for arterial stiffness that is influenced to a lesser degree by BP (i.e., as a marker for structural arterial stiffness)<sup>3)</sup>. However, this parameter can also be influenced by BP<sup>4)</sup>. Recently, Spronck *et al.* proposed CAVI<sub>0</sub>, which is influenced to a lesser degree by BP as compared to CAVI, using a simulation model<sup>5)</sup>. Thus, two modified markers for arterial stiffness are now available. In this issue, based on the data from a large sample size (i.e., not a simulation model), Shirai *et al.* demonstrated differences in the associations of BP variables with CAVI and CAVI<sub>0</sub>; they showed that diastolic BP was differently associated with CAVI and CAVI<sub>0</sub><sup>6)</sup>. These findings need to be taken into account while measuring the values of BP-adjusted markers. However, there are several limitations. While PWV is a marker for segmental arterial

stiffness, the stiffness index-beta, the base concept for CAVI and CAVI<sub>0</sub>, is a marker for regional, and not segmental, arterial stiffness. In addition, the existence of a BP gradient in the arterial tree is well known<sup>1)</sup>; therefore, the use of brachial BP for calculating the BP-adjusted value of the segmental arterial stiffness has not yet been fully validated. Finally, it has not been fully clarified how closely the arterial stiffness values, adjusted and not adjusted for BP, reflect atherosclerotic vascular damage related to the development of CVD. Therefore, as mentioned in the scientific statement, “criteria for evaluation of novel markers of cardiovascular risk”<sup>7)</sup>, further study is needed to clarify whether the use of these modified markers (i.e., CAVI and CAVI<sub>0</sub>) can improve the risk prediction over that using the original marker (i.e., heart-ankle PWV). Notwithstanding, Dr. Spronck mentioned that measurement of these markers could be easily incorporated into the device used to measure CAVI<sup>8)</sup>. Therefore, clarification of the merits and demerits of these markers is needed before they can perhaps be applied in a complementary manner in clinical practice.

## Conflict of Interest

Clinical research funding (Teijin Pharma); Courses endowed companies (Omron Health Care company & Asahi Calpis Wellness company)

## References

- 1) Safar ME, Smulyan H. Hypertensive Cardiovascular Risk: Pulsatile Hemodynamics, Gender, and Therapeutic Implications. *Am J Hypertens*, 2017; 30: 947-953
- 2) Tomiyama H, Matsumoto C, Shiina K, Yamashina A. Brachial-Ankle PWV: Current Status and Future Directions as a Useful Marker in the Management of Cardio-

- vascular Disease and/or Cardiovascular Risk Factors. *J Atheroscler Thromb*, 2016; 23: 128-146
- 3) Saiki A, Sato Y, Watanabe R, Watanabe Y, Imamura H, Yamaguchi T, Ban N, Kawana H, Nagumo A, Nagayama D, Ohira M, Endo K, Tatsuno I. The Role of a Novel Arterial Stiffness Parameter, Cardio-Ankle Vascular Index (CAVI), as a Surrogate Marker for Cardiovascular Diseases. *J Atheroscler Thromb*, 2016; 23: 155-168
  - 4) Kubozono T, Miyata M, Ueyama K, Nagaki A, Otsuji Y, Kusano K, Kubozono O, Tei C. Clinical significance and reproducibility of new arterial distensibility index. *Circ J*, 2007; 71: 89-94
  - 5) Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Arterial stiffness index beta and cardio-ankle vascular index inherently depend on blood pressure but can be readily corrected. *J Hypertens*, 2017; 35: 98-104
  - 6) Shirai K, Suzuki K, Tsuda S, Shimizu K, Takata M, Yamamoto T, Maruyama M, and Takahashi K. Comparison of Cardio-Ankle Vascular Index (CAVI) and  $CAVI_0$  in Large Healthy and Hypertensive Populations. *J Atheroscler Thromb*, 2019; 26: 603-615
  - 7) Hlatky MA, Greenland P, Arnett DK, Ballantyne CM, Criqui MH, Elkind MS, Go AS, Harrell FE Jr, Hong Y, Howard BV, Howard VJ, Hsue PY, Kramer CM, McConnell JB, Normand SL, O'Donnell CJ, Smith SC Jr, Wilson PW; American Heart Association Expert Panel on Sub-clinical Atherosclerotic Diseases and Emerging Risk Factors and the Stroke Council. Criteria for evaluation of novel markers of cardiovascular risk: a scientific statement from the American Heart Association. *Circulation*, 2009; 119: 2408-2416
  - 8) Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Reply: Medical science is based on facts and evidence. *J Hypertens*, 2018; 36: 960-962