Response to “The Putative Role of Vitamin D in Essential Hypertension: Stepping Into the Light?”

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To the Editor: In their letter, “The Putative Role of Vitamin D in Essential Hypertension: Stepping Into the Light?,” Gkaliagkousi et al. seem to question the use of traditional circulating biomarkers such as soluble intercellular adhesion molecule (sICAM), C-reactive protein (CRP), and homocysteine (Hcy) for the evaluation of endothelial dysfunction. They point out the latest position statement1 and recent European Society of Hypertension guidelines5 as a source of information on methods for the evaluation of endothelial dysfunction. It is obvious, however, that guidelines do not explicitly define which biomarkers should be used, and the position statement presents different methods for evaluating endothelial function, including the measurement of biomarkers we used,1 with the special focus on emerging biomarkers.

We strongly disagree with Gkaliagkousi et al’s criticism because we measured the circulating biomarkers that are widely and commonly used by others as determinants of endothelial dysfunction.4,6 Serum biomarkers of the endothelial origin reflect endothelial function; higher levels are thought to mirror the endothelial activation or damage.4 It has been reported that activated endothelial cells show enhanced expression and release of cell-surface adhesion molecules. sICAM-1 concentration correlates with its cell expression and was confirmed recently to be a sensitive marker of inflammatory vascular activation in hypertensive adolescents.7 Within the past 10 years the association between CRP and other inflammatory markers (including sICAM-1, Hcy) with prehypertension, hypertension, and arterial stiffness has been demonstrated.3 CRP is not only a biomarker of inflammation but, as recently unraveled,4 also actively and directly participates in the development of the endothelial dysfunction, which stands in stark contrast to the criticism of Dr Gkaliagkousi.

Besides an array of traditional biomarkers, several modern but expensive methods may be used to assess the endothelial status: imaging methods and measurement of endothelial progenitor cells, circulating endothelial cells, and endothelial-derived microparticles (EMPs).4 Interestingly, a recent study6 demonstrated that sICAM-1 correlated significantly with EMPs measured by flow cytometry, which unequivocally substantiates its use as a surrogate marker of endothelial dysfunction. The emerging evidence suggests that blood EMPs may serve as specific markers and contributors to pathology; however, their accurate quantification is a substantial challenge. EMPs and ECPs (endothelial progenitor cells) may be attractive biomarkers, but their measurement by multicolor flow cytometry or proteomic analysis by mass spectrometry is not widely available. Furthermore, progress in standardization of measurement of the emerging biomarkers is crucial to establish their clinical interest for the assessment of endothelial dysfunction.

In the recent European Society of Hypertension guidelines, the term “BP variability” obviously refers to visit-to-visit blood pressure variability or blood pressure variability assessed by ambulatory blood pressure measurement. The mathematical definition of “variation” describes a function that relates the values of one variable to those of other variables, and in this sense we assessed variables of significance for the prediction of systolic blood pressure variation that was adjusted for possible confounders. In fact, both terms “variation” and “variability” are used interchangeably, which does not necessarily have to be correct because the R2 value explains the variability in the statistics.

25-Hydroxyvitamin D might mediate various biological effects, and it regulates physiological functions such as the expression of adhesion molecules and endothelium-dependent vasoconstriction. The endothelial dysfunction was associated with 25(OH)D deficiency; moreover, 25(OH)D deficiency was propounded to promote endothelial dysfunction. We presented potential mechanisms relating to the role of 25(OH)D and its influence on the endothelial dysfunction in hypertension. The putative causal relationships remain to be elucidated.

DISCLOSURE

The authors declared no conflict of interest.
REFERENCES


