Editorial comment

Abnormal hemodynamic responses to exercise as a marker of end-organ damage in the "high-normal" blood pressure state

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Both American and European guidelines for hypertension diagnosis ad management emphasize the clinical relevance of the hemodynamic condition characterized by blood pressure values ranging from 120 to 139 mmHg for systolic and from 80 to 89 for diastolic[1,2]. The two guidelines, however, differ each other in the definition (and in the related implications) they provide to this category of blood pressure values. Indeed, while European guidelines make use of the term "high-normal blood pressure state"[2], the American ones define this condition as "pre-hypertension", implying that this clinical state represents, in temporal terms, the step of the disease development immediately preceding the occurrence of an overt hypertensive state[1]. The American "view" has been criticized because 1) the progression of this blood pressure category to hypertension is much less frequent than thought[3-5], and 2) the anxiety over the term may generate the need for frequent medical visits and laboratory examinations, favoring via behavioral and emotional influences the development and progression of the hypertensive state itself[3-7].

In the present issue of the Journal, Fazio et al.[8] publish the results of an intriguing study aimed at investigating in a group of "pre-hypertensive" individuals the association between the systolic blood pressure response to dynamic exercise (bicycle ergometry) and the presence of cardiac and vascular target organ damage. Although the above-mentioned reasoning suggests that the term "high-normal" blood pressure should better reflect this blood pressure category, the study results appear to be clinically relevant and, in some instance, provocative. They indeed show that, in a noticeable fraction of subjects displaying "high-normal" blood pressure values, an abnormal blood pressure response to exercise represents a marker of the presence of early alterations in cardiac and vascular structure and function, namely an increase in left ventricular wall thickness, a greater left ventricular relaxation time, and an augmented systemic arterial stiffness value.

Exercise, blood pressure and cardiovascular outcome

The study by Fazio et al. represents a step forward in the research area on the relationship between blood pressure response to exercise and cardiovascular outcome. Indeed there has been considerable interest over the last decades in the extent to which blood pressure response to exercise may reflect prognosis[9-12]. Overall the studies show an inconsistent relationship between blood pressure responses to exercise and fatal cardiovascular events, although some of the better designed and controlled studies do indicate a significant, positive relationship between an abnormal systolic blood pressure response to exercise and cardiovascular morbidity and mortality. It is likely that the non-uniformity of the results depends on two major factors. First, in any population of normotensive or hypertensive subjects, there is a very close interdependence of resting and maximal exercise blood pressure

values. This interdependence (which is highly variable from one study to another) may represent an explanation of the relationship between exercise blood pressure and cardiovascular events because it reflects the well-defined link between resting blood pressure and clinical outcome. This consideration also applies to the study of Fazio et al.[8], whose results also show the presence of a close direct relationship between blood pressure values measured at rest and the hemodynamic responses to exercise. The second consideration refers to a methodological issue that the authors take into account in their study[8], namely the unsatisfactory reproducibility of the hemodynamic responses to exercise and more in general to stressors. As discussed in previous studies and editorials by our group[13-15], one of the problems to be faced in the evaluation of the hemodynamic responses to physical stressors concerns the poor reproducibility of the blood pressure (particularly systolic) and heart rate responses to these maneuvers in each individuals. In some instances the differences between the hemodynamic responses to two different exercise tests performed in the same subjects within a short time period (30 to 60 min of interval) may be so marked as to display coefficients of variation in the responses approaching values close even to 50%[14]. The poor reproducibility of the hemodynamic responses to physical stressors can be partially overcome by repeating several times in the same individual the exercise test and averaging the results obtained. This would allow to achieve more "solid" data, which may more faithfully reflect the hemodynamic responses to physical stress in a given individual[14,15].

Factors influencing prognosis in the hypertensive state

The already mentioned European Society of Hypertension-European Society of Cardiology guidelines for hypertension diagnosis and management indicate, along with markers of organ damage, a list of factors useful for stratifying prognosis of the hypertensive state (Table I)[2]. Do the results of the present study suggest that systolic blood pressure responses to exercise should be a variable useful in risk stratification? The answer is a negative one for two main reasons. First the study is not based on a prospective design, thus making impossible to assess the prognostic value of a given variable. Second, the markers of end-organ damage assessed in the present study are 1) alterations in left ventricular structure and 2) arterial stiffness. Because according to European guidelines only left ventricular thickness represents a marker of end-organ damage[2], the study's conclusions are based on a single "surrogate" endpoint. In practical terms this implies that future prospective studies will be needed to strengthen the interesting findings of the present study by longitudinal assessing the relationships between peak exercise blood pressure responses and different target organ damage.

Table I. Risk factors for cardiovascular disease used for stratifying prognosis in hypertensive patients according to European Society of Hypertension-European Society of Cardiology guidelines[2].

Age (men > 55 years, women > 65 years)
Family history of premature cardiovascular diseases
Resting systolic and diastolic blood pressure
Dyslipidemia
Cigarette smoking
Abdominal obesity

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