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COMMENTARY

Left atrial enlargement and blood pressure variability in untreated hypertensive patients

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Left atrial enlargement (LAE) is a marker of left ventricular pressure and volume overload.[1,2] It is a common feature that is present in ~30% of patients with arterial hypertension, even in the absence of mitral valve disease.[3,4] A relationship between LAE and circulating levels of brain natriuretic peptide has been documented in patients with heart failure and preserved systolic function, as well as in hypertensive patients with asymptomatic diastolic dysfunction.[5,6] Recently, LAE has been proven to be associated with ischemic stroke and cardiovascular diseases, and the association is independent of diagnosed atrial fibrillation.[7,8] Furthermore, some studies have found that LAE might be a more sensitive indicator of cardiovascular disease than left ventricular remodeling.[6,9] However, most previous studies that described a relationship between LAE and arterial hypertension included both treated and untreated patients, and did not separate early stage from long-standing hypertension. Thus, it has not yet been determined whether LAE may be considered a specific marker of heart damage, independent of the presence of left ventricular hypertrophy and the effects of antihypertensive therapy.

Blood pressure (BP) variability has been a hot topic in recent years.[10,11] Rothwell *et al.*[12] showed that visit-to-visit variability in systolic BP was a strong predictor of stroke, and the association was independent of the mean systolic BP. Measurements of BP variability have included various time periods, so the conclusions drawn from the data obtained by these measurements are also quite variable. According to the length of the time period, BP variability has been divided into yearly changes, seasonal variation, visit-to-visit variation, day-to-day variation, diurnal changes, ambulatory BP variation (defined by the s.d. of each measurement) and beat-by-beat variation.[13] All of the different BP variabilities from short-term (beat-by-beat) to long-term (yearly) were associated with organ damage, as well as with the risk of cardiovascular events.[10,11] Home or ambulatory BP monitoring (ABPM) may therefore be used to complement conventional office measurements, thereby improving the prognostic value. Of particular relevance is the ability of 24-h ABPM to quantify the degree of BP variability over 24-h periods, as 24-h BP variability has been shown to be a significant and independent risk factor for cardiovascular morbidity and mortality.[11,14] Twenty-four-hour BP variability is indeed strongly associated with clinical outcomes, and the ability of ABPM to provide a quantification of BP throughout a 24-h period during the individual's normal daily routine is one of the reasons for its high prognostic value. Although a relationship between mean BP levels and left ventricular mass index (LVMi) has been consistently reported, the relationship between 24-h BP variability and LVMi or LAE in patients in the early stages of hypertension remains poorly understood. In this issue of *Hypertension Research*, Cipollini *et al.*[15] report that daily BP variability is significantly and independently associated with increased LAE in 167 newly diagnosed and untreated hypertensive patients.

The authors evaluated daily BP variability by monitoring each patient's 24 h-ABPM, which was calculated as the weighted mean standard deviation (SD) of both systolic and diastolic daytime and nighttime BPs (wSD). The mean of the day and night s.d. values were corrected for the number of hours included in each of these subperiods, according to the following formula: wSD = ((daytime SD×10)+nighttime SD× 6))/16.[16] This approach is considered advantageous to calculating a single s.d. over 24 h because it eliminates the influence of the day–night change in BP. Cipollini *et al.*[15] found that LVMi was significantly related to mean 24-h systolic BP variability, as expressed by ws.d., in men only. In contrast, left atrial dimension index (LADi) was related to either mean 24-h systolic or mean 24-h diastolic BP variability in both genders. Furthermore, the relationship between LADi and either systolic or diastolic BP viability, as measured by ws.d., was confirmed by a multiple regression analysis after adjusting for other covariates. In contrast, LVMi was not found to be independently associated with BP variability using this same model. Thus, Cipollini *et al.*[15] clearly showed that daily BP viability is an independent risk factor for LAE, but not for left ventricular hypertrophy, in newly diagnosed hypertensive patients.

What is the trigger for LAE in the early stages of hypertension? Most recently, Lee *et al.*[17] reported that LAE, expressed as an increase in left atrial volume index, simply reflects the duration and severity of raised left atrial pressure, and is independently associated with response to exercise in hypertensive patients, but not in normotensive control subjects. Tsioufis *et al.*[18] have shown that in patients with newly diagnosed essential hypertension without left ventricular hypertrophy, left atrial volume is positively associated with office BP, ambulatory BP, LVMi and plasma levels of brain natriuretic peptide. Although it still remains unclear

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whether both ventricular hypertrophy and LAE share the same pathogenesis, Fang *et al.*[19] reported that each of the clinical correlates of the metabolic syndrome, such as obesity, hypertension, diabetes and dyslipidemia, were associated with an increase in left atrial size and an impairment of both left atrial and ventricular function. Furthermore, Cipollini *et al.*[15] demonstrated that LAE is strongly associated with left ventricular diastolic dysfunction, and that increased 24-h systolic and diastolic BP variability might be related to LAE in patients with newly diagnosed arterial hypertension. This association was independent of the presence of left ventricular hypertrophy or dysfunction. An increase in atrial dimension is a major risk factor for the future development of atrial fibrillation. Therefore, scientific societies should recommend a more comprehensive evaluation of left atrial size based on volume rather on a single linear dimension to improve the effects of echocardiography in risk stratification.[3,4]

Because daily BP variability is largely dependent on physiological BP drops during the night, the issue of whether BP variability and heart damage are related in newly diagnosed hypertension becomes more complex. Nocturnal drops in BP might be protective against myocardial hypertrophy or remodeling, so the absence of nocturnal drops in BP, as in non-dipping status, has been considered to be an independent risk factor for left ventricular hypertrophy, as well as for cardiovascular events.[20] However, Cipollini *et al.*[15] showed that, although only left ventricular hypertrophy appears to be independently associated with non-dipping status, LAE is not related to non-dipping status. These results suggest that the ws.d. is largely independent from the extent of nocturnal drops in BP in newly diagnosed hypertensive patients.

As noted above, BP variability is associated with LAE, even in newly diagnosed hypertensive patients. Further studies are needed to better understand the pathophysiology of initial heart damage in patients with arterial hypertension to aid in diagnosis, prevention and therapy.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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