



## EDITORIAL COMMENT

# Early detection by non-invasive methods of predisposition to atrial remodeling in hypertension<sup>☆</sup>



## Predisposição para remodelagem auricular na hipertensão arterial - deteção precoce por meios não invasivos

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Hypertension (persistently high blood pressure levels) is one of the main cardiovascular risk factors. It causes pressure overload that leads to the structural and electrical alterations known as atrial remodeling.<sup>1,2</sup> The consequences are seen at various levels, especially in increased risk for atrial fibrillation (AF), which worsens with increasing age.<sup>3</sup> AF has a significant impact on cardiac output and is associated with a 4-5-fold higher risk of cardioembolic ischemic stroke,<sup>4,5</sup> as well as a considerably higher risk of death.<sup>6</sup>

Interatrial electromechanical delay and prolonged total atrial activation time have been linked to a higher incidence of AF.<sup>3,7,8</sup> Increased atrial conduction time is an indication of structural and electrical remodeling, which left atrial (LA) size and LA volume index are not.<sup>1,9</sup>

Increased left ventricular (LV) mass index is associated with prolonged interatrial conduction time and LA electromechanical coupling interval.<sup>1</sup> The severity of LV hypertrophy appears to be one of the factors associated with the onset of AF.

It has been demonstrated that pharmacological treatment that reduces blood pressure (BP) and hence LV mass makes AF less likely to occur.<sup>10–12</sup>

Data from the Framingham Heart Study show a relation between LA size as determined by echocardiography and systolic BP and pulse pressure (PP).<sup>13</sup> At the same time, there is evidence of a link between higher PP and increased incidence of AF in hypertension.<sup>14</sup> PP has been shown to be a better predictor of AF risk than mean arterial pressure or aortic distensibility.<sup>15,16</sup>

There is a good correlation between P-wave duration obtained in a single surface electrocardiographic (ECG) lead and the maximum duration of atrial electrograms; it also correlates with inter- and intra-atrial conduction times.<sup>17</sup>

P-wave dispersion, the difference between maximum and minimum P-wave duration recorded in multiple ECG leads in sinus rhythm, has been studied as an indicator of AF risk in populations with and without cardiovascular disease and in conditions including hypertension, ischemic heart disease, valve disease, congenital heart defects and heart failure.<sup>17</sup>

In hypertensive patients, P-wave dispersion may help identify LV hypertrophy and LV diastolic dysfunction, both of which lead to morphological and hemodynamic alterations in the left atrium that increase the risk of AF. Raised intra-atrial pressures and ischemia promote atrial remodeling, with disorganization of myocardial fibers and fibrosis, dilatation and electrical instability.<sup>17,18</sup>

Among the factors tending to increase P-wave dispersion and atrial fibrosis is elevation of angiotensin II and catecholamines.<sup>18</sup>

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Treatment targeting the renin-angiotensin-aldosterone system (RAAS) with perindopril in hypertensives led to a decrease in P-wave dispersion,<sup>17</sup> an effect also seen in a similar study using quinapril.<sup>17</sup>

In hypertensive patients, increased P-wave dispersion and maximum P-wave duration reflect instability and heterogeneity of atrial conduction, which may be a result of the morphological and hemodynamic alterations undergone by the left atrium as a consequence of hypertension.<sup>18</sup>

Heart failure with reduced LV ejection fraction (LVEF) predisposes to the onset of AF. In a study of patients with non-ischemic dilated cardiomyopathy, P-wave dispersion was much higher than in the control group.<sup>19</sup> This increased P-wave dispersion may be explained by hemodynamic variations resulting from LV dysfunction and associated neurohormonal activation affecting the left atrium.

Camsari et al. found a significant correlation between P-wave dispersion and LVEF in patients with heart failure. Both sympathetic activity and the RAAS are stimulated in heart failure, and this influences P-wave duration and dispersion, both of which were reduced following treatment with metoprolol in their study.<sup>20</sup>

For patients with symptomatic heart failure despite optimized drug treatment, in sinus rhythm and with LVEF  $\leq 35\%$ , QRS  $\geq 130$  ms and complete left bundle branch block, cardiac resynchronization therapy (CRT) improves LV function and reduces neurohormonal activation. It has also been shown to contribute to reverse atrial remodeling and thus to improvement in atrial function.<sup>21,22</sup>

In a study of 46 patients with heart failure with reduced LVEF, after three months of CRT, maximum P-wave duration, P-wave dispersion and LA diameter were decreased and LVEF was increased.<sup>22</sup> Maximum P-wave duration and P-wave dispersion were positively correlated with reduction in LA diameter and negatively correlated with improvement in LVEF.

P-wave terminal force in lead V1 (PTFV1) is the product of the amplitude and duration of the terminal negative phase of the P wave in lead V1 in mm $\times$ ms. It is a marker of cardiovascular prognosis and there is evidence that when increased it indicates increased risk of AF.<sup>23,24</sup> Abnormal PTFV1, defined as  $\geq 40$  mm $\times$ ms, was shown to be an independent predictor of cardiac death or hospitalization for heart failure in patients with prior myocardial infarction,<sup>23</sup> while another study, in patients with increased LV mass, showed that PTFV1  $\geq 40$  mm $\times$ ms was associated with increased risk for ischemic stroke.<sup>25</sup>

In their study published in this issue of the *Journal*, Çimen et al. examine early changes in atrial conduction times and P-wave dispersion in 157 patients with essential hypertension, no significant cardiac structural alterations, and elevated PP ( $\geq 60$  mmHg).<sup>26</sup> Atrial electromechanical delay (EMD) was assessed by tissue Doppler echocardiography and P-wave dispersion by electrocardiography. The authors show that elevated PP was associated with increased atrial EMD and P-wave dispersion.

Detection of early alterations, by non-invasive and easily accessible means, that could help prevent structural and electrical remodeling and thus reduce the risk of AF is of the utmost importance. The study by Çimen et al. in this issue is another contribution to this goal.

## Conflicts of interest

The author has no conflicts of interest to declare.

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