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Increased parathyroid hormone concentration as a biomarker of atrial fibrillation in severe aortic stenosis: Editorial comment

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Related article
by Olasińska-Wiśniewska et al.

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The interesting study by Olasińska-Wiśniewska et al. [1] published in this issue of the *Polish Heart Journal* focuses on the role of parathyroid hormone (PTH) as a biomarker of atrial fibrillation (AF) in older patients with aortic stenosis and heart failure. In a sample of 106 individuals with a median age of 77 years, the authors found that patients with a history of paroxysmal or persistent AF were more likely to have higher PTH levels than those with no AF. These findings support the vision of PTH as a polyhedric molecule with functions that go beyond the osteometabolic and renal ones.

In the last decades, several studies highlighted a relationship between hyperparathyroidism and cardiovascular disorders [2]. In particular, individuals with primary hyperparathyroidism (PHPT) were more likely to also present with arterial hypertension, chronic heart failure, ischemic heart disease, and cerebrovascular atherosclerosis, especially in advanced age [3]. In addition, Iwata et al. [4] found that mild PHPT and PTH levels were associated with subclinical calcification of the aortic valve, irrespective of serum calcium concentrations. Of note, in that study, the relationship of PTH with aortic valve calcification was stronger than other well-established cardiovascular risk factors, such as arterial hypertension, hyperlipidemia, excess weight, or smoking habits [4].

As far as AF onset is concerned, the role of PTH has not been fully clarified, although it may be supported by direct and indirect mechanisms. Regarding the direct effects, PTH could act on vascular cells, increasing calcium influx and resulting in vasoconstriction and hypertension, which are risk factors for AF [5]. In addition, PTH can affect cardiomyocytes and lead to cardiac remodeling, which can promote AF development. Among the indirect pathways, it is well-known that PTH may alter the renin–angiotensin–aldosterone system by stimulating aldosterone secretion and, consequently, impact blood pressure [5]. Moreover, growing evidence shows that higher PTH concentrations are associated with a persistent mild inflammatory status by prompting interleukin-6 production [6]. This leads to an increased synthesis of acute-phase proteins, which seem to be involved in AF pathogenesis [6, 7]. Overall, these alterations can result in functional and structural cardiac remodeling of the left atrium through mechanisms of fibrosis, myolysis, and apoptosis [7]. Moreover, considering the cardiac electrical system, PTH and PTH-induced cytokines can increase the vulnerability to AF by acting on calcium homeostasis, raising the arrhythmogenicity of pulmonary vein cardiomyocytes [7]. The PTH chronotropic and proarrhythmic effects may thus develop into atrial electromechanical delay, an early AF marker [8].

In addition to the possible role as a risk factor for AF, recent studies suggest that high PTH levels may be associated with a worse prognosis and increased risk of AF-related complications [9]. In a nationwide study, AF patients with PHPT had a risk of ischemic stroke and death increased by 1.4 and 1.32-fold, respectively, compared with their matched controls with AF but no PTH alterations [9]. Of note, in this study, PHPT patients had a higher risk of ischemic events even after taking into account other traditional stroke risk factors, suggesting that mechanisms under this effect include not only cardiovascular but also coagulation system alterations [9].

When assessing the effects of PTH at the systemic level, one cannot fail to consider vitamin D. Like PTH, vitamin D also has a role in the regulation of the inflammatory response and the renin–angiotensin–aldosterone system, and its deficiency has been related to vascular changes, cardiac dysfunctions, and electrical remodeling [10]. These effects may increase individual vulnerability to cardiovascular diseases, such as AF. Accordingly, in several studies, low vitamin D levels emerged as one of the critical factors influencing the incidence of AF, especially after cardiac surgery [11]. The results of 2 systematic reviews and meta-analyses [10, 12] confirmed that vitamin D deficiency could influence the development of AF. Nonetheless, the observational design of most of the available studies on the matter makes it difficult to evaluate the independent and causal relationship between vitamin D and AF risk.

Moreover, only a few works investigated the interplay between PTH and vitamin D in influencing AF onset. Among these, a study from our group [13] underlined that high PTH, especially when combined with low vitamin D levels, was associated with an increased risk of AF in older adults. This strengthens the need to assess further how these hormones can interact with each other to influence AF development.

In conclusion, growing evidence supports the role of PTH as a factor influencing the onset of AF. This suggests that the evaluation of patients with high PTH levels should not only be addressed to the traditional skeletal and renal systems but could also benefit from an assessment of cardiovascular health. In turn, further studies are needed to verify whether including PTH among routine tests may improve stratifying the risk of AF in patients with pre-existent cardiovascular diseases. In this context, the early detection of subclinical cardiac dysfunctions may help recognize at-risk patients and optimize their cardiovascular health outcomes.

Article information

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