

Letters

TO THE EDITOR

The Role of Inflammation and Gender Differences in the Pathogenesis of Cardiac Arrhythmias



We have recently read with great interest the review paper by Lazznerini et al¹ entitled “Fir(e)ing the Rhythm: Inflammatory Cytokines and Cardiac Arrhythmias.”

From a pathophysiological point of view, the review by the authors appears to be illuminating for clinicians who are directly interested every day in managing these types of patients, such as those affected by Brugada syndrome (BrS). Many studies have long shown that inflammatory cytokines may directly or indirectly facilitate different arrhythmias through multiple systemic effects. Furthermore, a significant role also seems to have the gender-dependent inflammatory response and the resulting potential proarrhythmic response.²

From the authors, it would be interesting to understand if hormonal factors may also correlate with the mechanisms reported and whether these hormone-dependent factors are equally decisive in the proarrhythmic response to cytokines. For example, regarding patients with BrS, the existence of gender-attributable differences in the prevalence and arrhythmic risk profile is widely accepted. Although only 30% of the available publications regarding BrS include gender-related information and current findings are based on studies conducted mainly in the male population, women diagnosed with BrS appear less likely to experience arrhythmic events.^{3,4} Such differences are not exclusively due to the influence of sex hormones but may result from a complex interplay of gender, proinflammatory cytokine response, age-dependent genetic factors, and other variables involved in the modulation,

expression, and function of cardiac ion channels. Nevertheless, due to the low number of published data on female patients, current guidelines on the management and risk stratification of patients with BrS do not differ in their recommendations according to gender.^{5,6}

Considering the importance that these new data can bring to deepen knowledge about determinants and precipitants factors of cardiac arrhythmias, the review of the authors represents an interesting input because, in our opinion, further insights are still needed to elucidate the pathophysiological mechanisms underlying these gender differences, possibly also related to a different hormone-dependent proinflammatory response.

*Gregory Dendramis, MD
Pedro Brugada, MD, PHD

*ARNAS Ospedale Civico Di Cristina Benfratelli
Piazza Nicola Leotta 4
90127 Palermo, Italy

E-mail: gregorydendramis@libero.it

<https://doi.org/10.1016/j.jacbts.2023.02.019>

© 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

REFERENCES

1. Lazznerini PE, Abbate A, Boutjdir M, et al. Fir(e)ing the rhythm: inflammatory cytokines and cardiac arrhythmias. *J Am Coll Cardiol Basic Trans Science*. 2023;8(6):728–750.
2. Villareal RP, Woodruff AL, Massumi A. Gender and cardiac arrhythmias. *Tex Heart Inst J*. 2001;28:265–275.
3. Berthome P, Tixier R, Briand J, et al. Clinical presentation and follow-up of women affected by Brugada syndrome. *Heart Rhythm*. 2019;16:260–267.
4. Benito B, Sarkozy A, Mont L, et al. Gender differences in clinical manifestations of Brugada syndrome. *J Am Coll Cardiol*. 2008;52:1567–1573.
5. Martínez-Barrios E, Arbelo E, Cesar S, et al. Brugada syndrome in women: what do we know after 30 years? *Front Cardiovasc Med*. 2022;9:874992.
6. Dendramis G, Brugada P. Lights and shadows of subcutaneous implantable cardioverter defibrillator in Brugada syndrome. *Heart Rhythm*. 2023;20:274–281.