

Brugada syndrome and COVID-19 vaccines

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Brugada syndrome (BrS) is a hereditary cardiac disease predisposing to sudden cardiac death in patients with structurally normal heart. Fever has been reported not only to unmask the type 1 Brugada electrocardiogram (ECG) pattern¹ but also to trigger ventricular arrhythmias.² In the Survey on Arrhythmic Events in Brugada Syndrome (SABRUS) registry, the fever-related arrhythmic events (AEs) are the first manifestation of the disease in the majority of BrS patients and frequently occur in asymptomatic patients without spontaneous type 1 ECG pattern; moreover, the 77% of children and 27% of adults with fever-induced AEs presented SCN5A pathogenic variants.³ Sodium channel function seems either less expressed or rapidly inactivated at higher temperatures, thus sensitizing patients to develop life-threatening arrhythmias, as also confirmed by further studies.⁴

COVID-19 clinical presentation is characterized by fever in about 92.8% of adults and 43.9% of children.⁵

Moreover, beyond the acute respiratory distress, severe cardiac complications, such as myocarditis, heart failure, and arrhythmias may complicate the clinical course of the disease.⁴ Due to these reasons, patients with either structural heart diseases or primary arrhythmia syndromes disclose a higher risk of COVID-19 related mortality.⁶ Thus, a rapid diagnosis, isolation, and intensive clinical management is crucial for BrS patients with COVID-19.⁷ Even if BrS patients share the COVID-19 infection risk of the whole population, based on the increased fever-induced arrhythmic risk, they should be considered belonging to frail category for the COVID-19 vaccination program.

Brugada syndrome patients with spontaneous pattern are burdened by an increased risk of fever-related AEs compared to those with drug-induced pattern (0.5–0.8%/year vs. 0–0.35%/year); moreover, BrS children (<16 years of both genders) exhibit a considerable risk of AEs, up to 67% of fever-induced AEs occurred in 5 years old or younger children, while AEs are rare in the elderly BrS patients (>70 years).³ No data are actually available on the fever response to antipyretic drugs among BrS population.

COVID-19 vaccines approved by the European Medicines Agency (EMA) include two different platforms: mRNA (Comirnaty—BioNTech/Pfizer, COVID-19 Vaccine Moderna) and adenoviral vectored (COVID-19 Vaccine Janssen, Vaxzevria—AstraZeneca). All of them are burdened by several side effects, particularly fever. Though, data on fever onset, which usually occurs within the first 2 days, are biased by antipyretic medications use (Comirnaty—BioNTech/Pfizer 1st dose 28% and 2nd dose 45%; Janssen 26.7% in patients aged 18–59 and 10% aged >60 years; no data available for Moderna and Vaxzevria—AstraZeneca).^{8–11}

In our opinion, BrS patients should be managed at hospital vaccination centres so that adequate management proportionate to their arrhythmic risk could be guaranteed, allowing greater safety and avoiding delays in vaccinations (Figure 1).

We suggest for all BrS patients a prophylaxis with paracetamol 1000 mg every 6 h, acetaminophen 1000 mg every 6 h, ibuprofen 600 mg every 6 h, or other antipyretics, with dosage adjustment according to age, weight, kidney, and liver function, within the first 24–48 h, in order to reduce the risk of fever onset. Moreover, they should perform a daily fever self-monitoring. In case of fever unresponsive to antipyretic medications, BrS patients should be monitored at the emergency department till fever resolves, especially when they show an increased arrhythmic risk for the younger age, the spontaneous type 1 ECG pattern and/or SCN5A pathogenic variant.

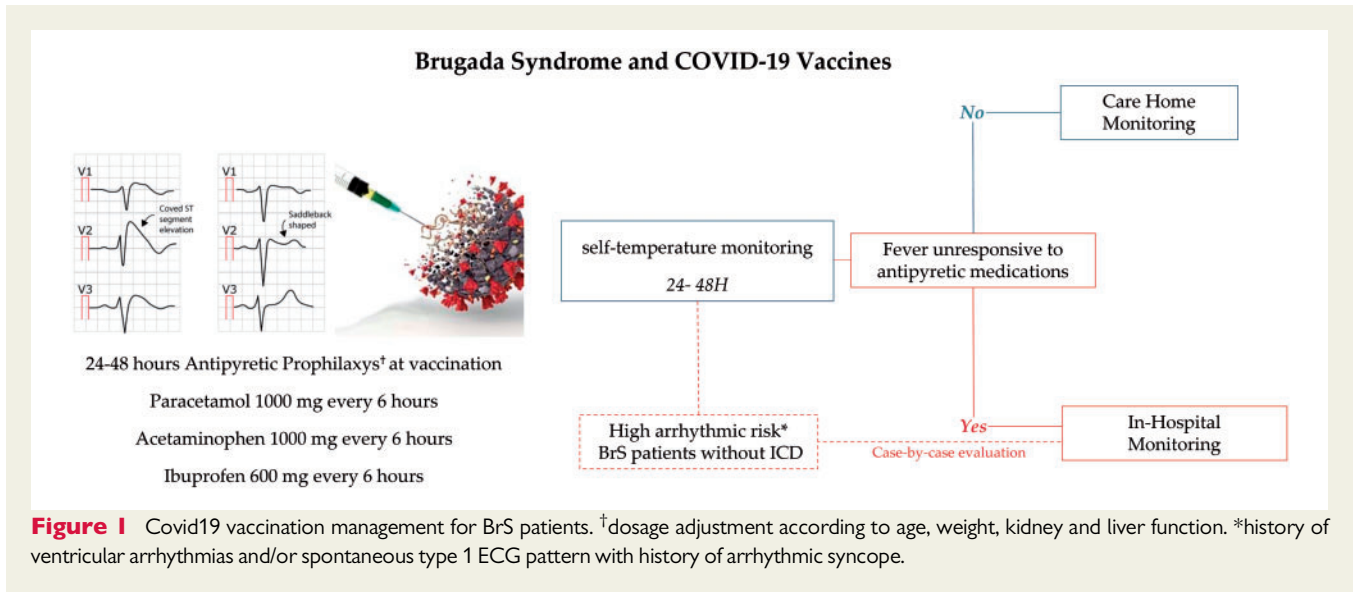
Brugada syndrome patients with high arrhythmic risk for the history of ventricular arrhythmias or spontaneous type 1 ECG pattern with a history of arrhythmic syncope may be considered for hospitalization following the COVID-19 vaccination, even without fever occurrence, especially if they are not implantable cardiac defibrillator recipients. However, in this latter subgroup, a case-by-case evaluation should be performed also considering the patients' age and how previously responded to vaccination and fever. In conclusion, we do believe that the achievement of herd immunity may protect this special population as well.

Conflict of interest: none declared.

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