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REPLY

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Reply by Casella et al. to letter regarding article, incidence of ventricular arrhythmias related to COVID infection and vaccination in patients with Brugada syndrome: Insights from a large Italian multicenter registry based on continuous rhythm monitoring

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Overall, our population included a large and nonselected cluster of patients previously diagnosed with Brugada syndrome (BrS). That said, 50.3% of patients in our analysis (164/326 patients) had a spontaneous Brugada type 1 electrocardiogram (ECG). It is well-demonstrated that patients with a spontaneous Brugada type 1 ECG have a worse arrhythmic prognosis than patients with drug-induced Brugada type 1 ECG.[2] Previous data from large meta-analyses reported an arrhythmic risk three to four times higher in asymptomatic patients with a spontaneous Brugada type 1 ECG.[3,4] In addition, 20.1% of patients presenting with a spontaneous type 1

ECG also had a history of documented ventricular fibrillation/sudden cardiac death (VF/SCD), thus representing an even higher risk population. In our population, 10.4% of patients had a previous history of VF/SCD documented. Patients with a history of severe ventricular arrhythmias or aborted SCD are considered at high risk, with an estimated recurrence rate of arrhythmic events of 48% over 10 years.[5]

Among the group of patients with drug-induced Brugada type 1 ECG (162/326 patients, 49.7%), who are generally considered at lower risk than subjects with spontaneous type 1 ECG, 23.4% had a positive programmed electrical stimulation (PES). Although we acknowledge that the role of PES in the risk stratification of asymptomatic patients remains controversial, it may still have a role in selected patients.[6,7]

Considering only the implantable cardioverter-defibrillator (ICD) carriers (202/326 patients), the overall number of patients that presented with ventricular arrhythmias in our population was comparable between patients deemed at high risk and those at low risk. During COVID infection, 1.4% of patients with drug-induced Brugada type 1 had ventricular arrhythmias compared to 1.5% of patients with spontaneous Brugada type 1. After the first and booster vaccine dose, no sustained ventricular arrhythmias were recorded in patients with drug-induced Brugada type 1 and spontaneous Brugada type 1. After the second dose of vaccine, one VT episode was recorded in the group of patients with spontaneous Brugada type 1 and one in the group of patients with drug-induced Brugada type 1.

What surprised us the most was the peculiar timing of ICD interventions. Indeed, in the two patients that received ICD therapies (1 anti–tachicardia pacing and 1 shock), these episodes were not related to acute infection or vaccine-related hyperpyrexia but happened in the last window of the study observation (6 months after COVID infection or 1-month after the last dose of vaccine). Moreover, one of the two episodes was in a patient with drug-induced Brugada type 1 ECG, and the other was in a subject with spontaneous Brugada type 1 ECG and positive PES.

In our opinion, the added value of our study was the extensive use of remote device monitoring and the vast amount of data collected and analyzed to assess the arrhythmic burden, which strengthen our findings. Finally, in this real-world analysis, we found that most BrS patients followed the recommendations given for fever treatment and pretreatment. This may reconcile the apparent discrepancy between the heterogeneous risk profile and the low observed incidence of ventricular arrhythmia in our population.

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