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Top Stories: Clinical

Top stories on Brugada syndrome

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Ever since its early descriptions in the late 80s and early 90s of the previous century, Brugada syndrome (BrS) has been surrounded by debates. Is it therefore not surprising that a continuous flow of research papers (250–300 per year during the last decade) deal with these aspects of this intriguing disease.

Progression of structural abnormalities in BrS over time

Although BrS was originally considered a "channelopathy," subtle *structural* changes have been consistently demonstrated in the right ventricular outflow tract (RVOT). Now, Australian researchers demonstrate with repeated magnetic resonance imaging (MRI) scans that these structural abnormalities worsen over time.[1] Eighteen patients with asymptomatic BrS (drug-induced BrS in 9) who had normal results in a cardiac MRI study performed $\geq$3 years previously underwent second MRI. Although all volumetric indices remained within the normal range, there was a significant increase in right ventricular end-systolic volume and a nonsignificant trend toward reduction in right ventricular ejection fraction.[1] Late gadolinium enhancement, never seen at baseline, was now apparent in 4 patients (22%) (Figure 1A).

Structural abnormalities in BrS are not limited to the RVOT

A recent study of 22 patients with BrS (20 symptomatic) who underwent extensive epicardial mapping revealed areas of abnormal activity suggesting local fibrosis, not only (as expected) in the RVOT but also in the epicardial surface of the left ventricle in almost half (10 of 22) of the patients.[2] These patients more often had a pathogenic *SCN5A* variant and had a longer arrhythmia history. These data clearly underscore the current prevailing notion that BrS is not a pure electrical disease but more a discrete localized cardiomyopathy.

Ablation of areas with structural abnormalities prevents ventricular fibrillation recurrence

Earlier studies suggest that targeting these structural changes with radiofrequency (RF) ablation in the most affected area (RVOT epicardial layer) normalizes the electrocardiogram (ECG) and reduces the risk of ventricular fibrillation (VF) recurrence. Now, the Brugada Ablation of VF Substrate Ongoing study[3] reports on 159 patients with high-risk BrS (all with spontaneous VF, recurrent in 80%) who were treated with RF targeting all abnormal epicardial signals.[3] There was a dramatic reduction in spontaneous VF events during a period of 48 $\pm$ 29 months; 81% and 96% of patients remained free of VF after single and repeated RF procedures. Absence of a type 1 Brugada ECG, with or without drug provocation at the end of the ablation procedure, was the only predictor of VF-free survival.[3]

Role of the sodium channel blocker challenge test in the diagnosis of BrS

A sodium channel blocker challenge test (SCBT) for diagnosing BrS has been advocated for years, as well as for asymptomatic individuals with an incidental type 2–3 ECG. Since the 2013 EHRA/HRS consensus document, BrS was diagnosed in both patients with a spontaneous type 1 ECG and those with only a drug-induced ECG. Yet, we know for years that the prognosis of the latter group is considerably better. This is now emphasized by a comprehensive review of the role of the SCBT.[4] For asymptomatic patients with a spontaneous type 1 ECG, the average annual event rate was 0.88% but only 0.29% when revealed by a SCBT (Figure 1B).[4] Considering that many of these patients are nowadays subjected to invasive ablation procedures, it is important to get more insight into the specificity and sensitivity of the SCBT. Real data here are scarce, but cumulative data suggest that the sensitivity is good but the specificity is actually moderate at best. This essentially means that a

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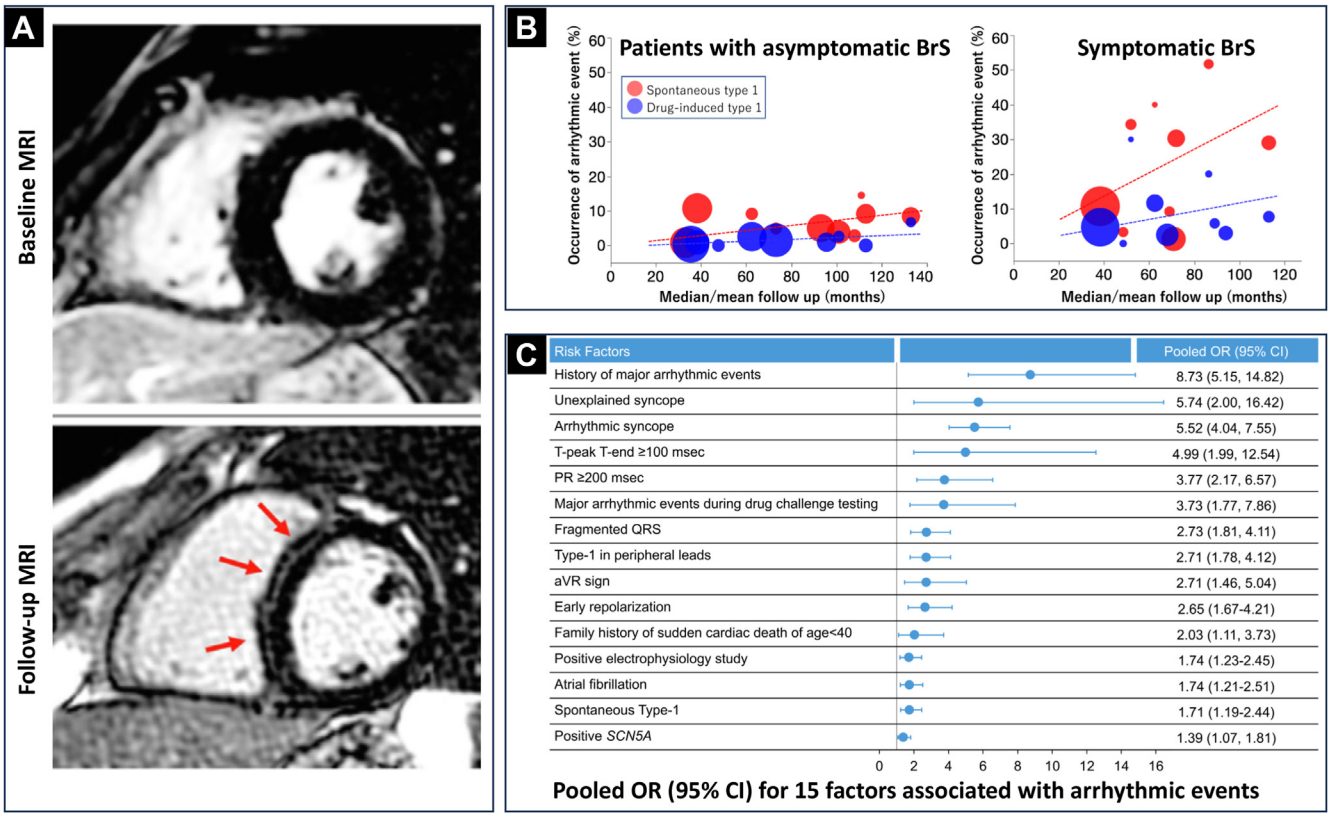

Figure 1
Top stories on Brugada syndrome (BrS). **A:** Worsening of structural abnormalities over time. Late gadolinium enhancement was absent in baseline magnetic resonance imaging (MRI) (*top panel*) but fairly extensive during follow-up (*lower panel*). Reproduced from Isbister et al.[1] **B:** Bubble plot of the prognosis of asymptomatic (*left panel*) and symptomatic (*right panel*) BrS. The bubble size represents the number of patients; *red bubbles* represent patients with a spontaneous type 1 electrocardiogram (ECG) and *blue bubbles* patients with only a drug-induced type 1 ECG. Reproduced from Wilde et al, by permission of Oxford University Press.[4] **C:** Fifteen factors significantly associated with arrhythmic events in BrS and their pooled odds ratio (OR) with 95% confidence interval (CI). Reproduced from Rattanawong et al.[5]

drug-induced ECG does not equal the diagnosis of BrS. We therefore proposed to be more cautious with the SCBT and not to test asymptomatic individuals with a type 2 ECG.[4]

New risk prediction score in BrS

Our ability to estimate future risk remains limited for asymptomatic patients. An extensive review of the existing literature, with a pooled analysis of 67 studies comprising 7358 patients with BrS, was recently reported.[5] For the whole group, including symptomatic (37%) and asymptomatic (63%) patients, as well as patients with a spontaneous (70%) or drug-induced type 1 ECG, a new risk score (Predicting Arrhythmic evenT [PAT]) was constructed on the basis of risk factors suggested to be significant by the meta-analysis results (Figure 1C). As the end point of interest was predicting the *first* arrhythmic event, the history of arrhythmic events was excluded from the score. Ultimately, 9 factors formed the PAT score, 7 of which are derived from the ECG. This score, which was validated in a relatively small internal and external cohort, showed 95.5% sensitivity and 89.1% specificity for predicting the *first* major arrhythmic event in the overall cohort of patients with BrS. The PAT score performed better than the currently used Sieira and Shanghai scores. An accompanying editorial criticizes lumping together patients with a spontaneous and those with a drug-induced type 1 ECG because the risk for these subgroups differs markedly and demands for prospective external validation.

This brief overview highlights a few of the many studies in the BrS space in the last year. Not surprisingly, controversies have not been resolved but progress is made step by step.

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