signature type I ECG was present in 160 mutation carriers (BrS-ECG+; 53%). In 42 families, we found 33 individuals affected by BrS but with a negative genotype (mutation-negative BrS-ECG+). Among them, 5 patients have an ECG suggestive of BrS but without the complete signature type I ECG. Among these 33 mutation-negative BrS-ECG+ individuals, 3 (9%), belonging to 3 different families, had a spontaneous type I ECG, whereas 28 had a type I ECG only after the administration of sodium channel blockers. Three of these 33 individuals (9%) had also experienced syncope. Mutation carriers had, on average, longer PR (190 ± 36 ms vs 154 ± 29 ms, p<0,0001) and QRS (107 ± 19 vs 92 ± 29 ms, p<0,0001) intervals than noncarriers, demonstrating that these mutations exerted functional effects.
Conclusion: Our results suggest that SCN5A mutations are not directly causal to the occurrence of a BrS-ECG+ and that genetic background may play a powerful role in the pathophysiology of BrS. These findings are consistent with the notion that the pathophysiology of BrS includes various elements beyond mutant sodium channels.

BS-513-04

BURDEN AND CLINICAL CHARACTERISTICS OF THAI BRUGADA SYNDROME PATIENTS CARRYING RARE *SCN5A* VARIANTS OF UNCERTAIN SIGNIFICANCE

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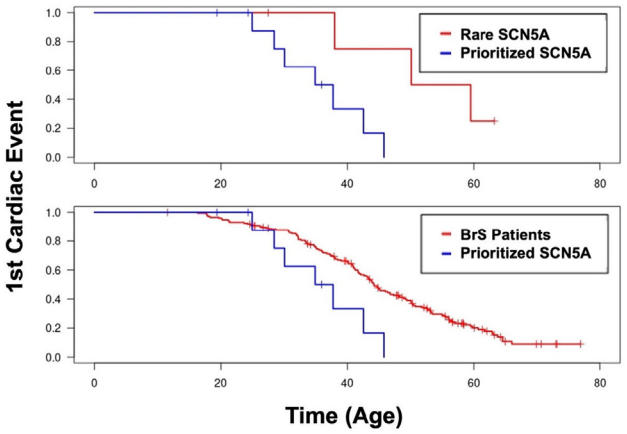
Background: Loss-of-function variants in the sodium channel α-subunit (*SCN5A*) are associated with Brugada Syndrome (BrS). As Southeast Asians are understudied, the detected variants often lack supporting evidence and are absent in current clinical databases. This creates a challenge as variant interpretation resulted in over 90% of rare variants detected being classified as variants of uncertain significance (VUS) according to ACMG guideline.
Objective: To investigate the burden of rare *SCN5A* variants in Thai BrS patients and to examine the clinical characteristics of BrSpatients with rare *SCN5A* variants.
Methods: Burden testing was performed on 196 cases and 394 controls. Rare variants, with allele frequency in gnomAD database (AF < 0.001), were included. Testing was further performed on variants prioritized with CADD score, a measure of variant deleteriousness (CADD>25). Clinical characteristics of Brugada Syndrome patients with rare *SCN5A* variants were assessed.
Results: Rare *SCN5A* variants are associated with Thai BrS cases (p= 0.04, 8.16% vs 3.04%). An enrichment of prioritized variants was observed in BrS cases (p= 2.31x10-(5), 5.61% vs 0.5%). No significant differences were found in clinical characteristics of patients with and without rare *SCN5A* variants. However, patients with prioritized *SCN5A* variants (n=11) showed significantly earlier age-onset of first cardiac event when compared to patients with rare *SCN5A* variants (p < 0.02, upper figure) and other BrS cases in the cohort (p < 0.01 lower figure).
Conclusion: BrS patients carrying *SCN5A* variants predicted to be deleterious show earlier age-onset of first cardiac event. The variable clinical characteristic in patients with rare *SCN5A* and prevalence of rare *SCN5A* variants in controls suggests that interpreting rare variants must be done with caution, especially in understudied populations where supporting evidence is limited. Further studies are needed for using prioritized *SCN5A* variants to aid in the diagnosis or prognostication of patients with BrS.



ABSTRACT CA-530:
Delivering Durable Lesions: Utilizing Surrogates to Guide Ablation in the Atrium and Ventricle

Friday, April 29, 2022
2:15 PM - 3:15 PM

CA-530-01

USE THE FORCE: ADEQUATE CATHETER CONTACT FORCE IS CRITICAL FOR HIGH QUALITY LESIONS GUIDED BY ABLATION INDEX

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Background: Ablation Index (AI) is a measure used to estimate lesion size based on power, contact force (CF), and lesion duration. Ideally, AI-guided titration of lesion duration corrects for variations in contact force. Impedance drop is a validated measure that correlates well with lesion formation. Therefore, analysis of the relationship between AI, CF, and impedance drop may offer insight into possible residual influences of CF on lesion formation.
Objective: To investigate and characterize the impact of CF on impedance drop during AI-guided ablation.
Methods: We retrospectively reviewed atrial fibrillation ablation cases (AFAs) performed at a single center. We examined the correlation between CF and Impedance drop within narrow ranges of AI (17 groups). In a secondary analysis, we matched lesion pairs with high and low CF (< 10 g and > 20 g) for stability, AI, lesion location, and power. Matched pairs were compared using a t-test.
Results: There were 13444 lesions with AI between 320 and 530 from 91 AFAs. For lesions that had a low AI (< 402.3), we observed mostly no residual correlation between contact force and impedance drop (Fig 1). For lesions with high AI (> 402.3), we observed a consistent significant correlation between CF and impedance drop (Fig 1).
In the matched sample, the high CF group had a greater impedance drop when compared to the low CF group: 8.5 ±5.3 vs 7.0 ±4.0 Ohms p < 0.01 (Figure 2), despite having similar AI. When examining the subset of matched pairs with AI < 400, we observed no significant difference in impedance drop between the high and low CF groups: 6.7 ±4.7 vs 6.5 ±4.1 Ohms (p = 0.6). When examining the matched pairs with AI > 400, we again