Abstract P3815 – Table 1. Associations between SNPs, GRS and BrS phenotype

SNP	Chromosome	Gene/nearest gene	Position	Without correction for E1784K		With correction for E1784K		Patients with E1784K mutation		Wild-type relatives	
				OR, 95% CI	P.chisq	OR, 95% CI	P.chisq	OR, 95% CI	P.chisq	OR, 95% CI	P.chisq
E1784K	3	SCN5A	Exon 28	12.96, 4.09–41.08	0.0000**	NA	NA	NA	NA	NA	NA
rs11708996	3	SCN5A	Intron	3.32, 1.58–6.97	0.0015**	1.44, 0.61–3.42	0.4016	1.25, 0.50–3.14	0.6397	3.40, 0.38–30.66	0.2754
rs10428132	3	SCN10A	Intergenic	1.82, 0.96–3.45	0.0657	2.75, 1.22–6.19	0.0148*	2.28, 0.96–5.39	0.0614	7.49, 0.73–76.46	0.0893
rs9388451	6	HEY2-NCOA7	Intergenic	0.86, 0.50–1.50	0.6032	0.70, 0.37–1.30	0.2580	0.71, 0.36–1.39	0.3151	0.60, 0.10–3.80	0.5902
rs41315485	3	SCN5A	3'UTR	2.12, 1.06–4.22	0.0327*	3.04, 1.31–7.07	0.0099*	3.48, 1.27–9.49	0.0149*	2.111, 0.43–10.33	0.356
BrS GRS	NA	NA	NA	1.57, 1.15–2.16	0.0049**	1.60, 1.10–2.32	0.0129*	1.46, 0.99–2.14	0.0564	3.53, 0.76–16.51	0.109

*p<0.05; **p<0.005.

ECG pattern and sudden death risk. Pathogenic variants in SCN5A are identified in 20% and common genetic variation has been associated. SCN5A-E1784K, which can manifest as a mixed variable phenotype, is the variant most commonly associated with BrS.

Purpose: To create a BrS genetic risk score (GRS) in families with E1784K to predict BrS.

Methods: 232 E1784K patients and 104 wild-type (WT) relatives were recruited from 15 centres internationally. Comprehensive clinical and pedigree data were collected. Only subjects who had either a spontaneous type 1 Brugada pattern or undergone sodium channel blocker provocation testing to confirm BrS status were included. Four single nucleotide polymorphisms (SNPs) associated with BrS were studied: rs11708996, rs10428132, rs9388451 and rs41315485. Single SNP associations and a combined GRS with BrS were determined using a logistic regression model and a ROC curve for the GRS.

Results: 94 E1784K patients and 26 WT relatives with known BrS status were included: mean age 31.1, range 0.3–67.3 years and 46/120 (38%) male. 66/94 (70%) E1784K patients had BrS (12 spontaneous; 54 drug-induced). 4/26 (15%) WT subjects were found to have BrS, all drug-induced. E1784K, rs11708996 and rs41315485 were significantly associated (Table 1). Following correction for E1784K, rs10428132, rs41315485 and GRS were associated. Associations were weaker when E1784K and WT subjects were separated but with similar trends. The C-statistic for GRS predicting BrS was 0.671. The optimal cut-off resulted in a positive predictive value of 95.0% and a negative predictive value of 48.7% (Fig. 1).

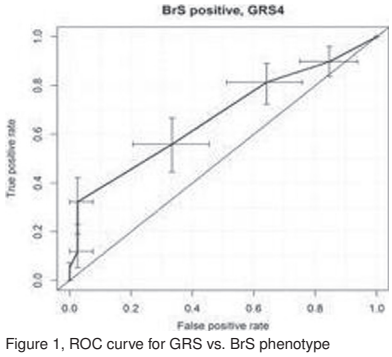

Figure 1, ROC curve for GRS vs. BrS phenotype

Conclusion: The GRS and rs41315485 are associated with BrS in E1784K families, validating that common genetic variation underlies BrS. Mutation status alone cannot exclude a drug-induced BrS phenotype in E1784K families. This has implications for cascade genetic screening and indicates the potential diagnostic role of a GRS for BrS phenotype in SCN5A families.

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P3816
New electrocardiographic risk score for the prediction of ventricular fibrillation in Brugada type 1 ECG pattern

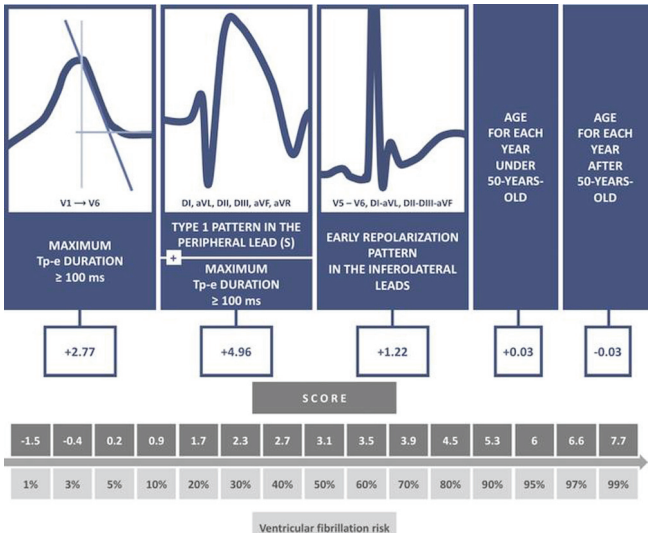
A. Deliniere[1], A. Baranchuk[2], J. Giai[3], D. Maucort-Boulch[3], P. Defaye[4], E. Marijon[5], O. Le Vavasseur[6], D. Dobreanu[7], A. Dacosta[8], E. Delacretaz[9], C. Kouakam[10], R. Eschalier[11], H. Burri[12], P. Winum[13], P. Chevalier[1]. *[1]Hospital Louis Pradel of Bron, Heart Rhythm Service, Lyon, France; [2]Queen's University, Department of Medicine, Kingston, Canada; [3]Civils Hospices of Lyon, Department of Biostatistics, Lyon, France; [4]University Hospital of Grenoble, Department of Cardiology, Grenoble, France; [5]European Hospital Georges Pompidou, Department of Cardiology, Paris, France; [6]North-West Hospital, Department of Cardiology, Villefranche-sur-Saône, France; [7]University of Medicine and Pharmacy of Tirgu-Mures, Physiology Department, Tirgu-Mures, Romania; [8]University Hospital of Saint-Etienne, Department of Cardiology, Saint-Etienne, France; [9]Cecil Cardiovascular Center, Lausanne, Switzerland; [10]Lille University Hospital, Department of Cardiovascular Medicine, Lille, France; [11]University Hospital Gabriel Montpied, Department of Cardiology, Clermont-Ferrand, France; [12]Geneva University Hospitals, Department of Cardiology, Geneva, Switzerland; [13]University Hospital of Nimes, Department of Cardiology, Nimes, France*

Background/Introduction: There is currently no accurate and reliable tool to quantify the risk of ventricular fibrillation (VF) in asymptomatic patients with Brugada (Br) type 1 electrocardiographic (ECG) pattern.

Purpose: To design a VF risk score based on ECG analysis in asymptomatic Br type 1 patients by validating the independence of known ECG risk factors and estimating their relative weight in the prediction process.

Method: In a multicenter international study, we retrospectively analyzed data from 137 patients (mean age 46.3±13.4, 122 males: 89.1%) with Br type 1 pattern, including 32 individual from published case reports. 60 patients (43.80%) presented VF or polymorphic ventricular tachycardia (VF group). A systematic review of the literature identified 10 ECG criteria for multivariate analysis. We performed a multivariate analysis with logistic regression to build a risk prediction model. The consistency of this model was verified by comparing to a Cox model and to another logistic model using the total number of ECG criteria.

Results: With univariate analysis, early repolarization pattern in the inferolateral leads (p=0.001), type 1 pattern in the peripheral leads (p<0.001), maximum Tp-e duration ≥100 ms (p<0.001) and QRS duration in lead V2 ≥120 ms (p=0.024) were significantly more common in the VF group. The cumulative number of ECG criteria was significantly higher in the VF group (3.68±1.37) compared to the control group (2.47±1.66, p<0.001). In multivariate analysis, three ECG criteria were significantly associated with an increased risk of VF: early repolarization pattern in the inferolateral leads (OR=3.397, CI95% 1.124–11.688, p=0.0379), maximum Tp-e duration ≥100 ms (OR=15.999, CI95% 4.355–103.882, p=0.0003) and maximum Tp-e duration ≥100 ms associated with type 1 pattern in the peripheral leads (OR 142.817, CI95% 22.821–1610.289, p=0.0000). Age after 50 was a protective factor (OR=0.972, CI95% 0.941–1.003, p=0.0791). The final logistic model determined a weight to each of these four criteria. The final score is correlated with the risk of VF with a relevant discrimination (AUC=0.84).



The final score

Conclusions: A simple risk score of VF in Br type 1 pattern based on 3 ECG criteria and age could be helpful for VF risk stratification in asymptomatic ECG type 1 Brugada patients. This score could provide a rationale for a prospective randomized interventional study that evaluates the AICD option in this population.

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P3817
Diagnostic yield of genetic testing in cardiac arrest survivors with or without clinical evidence of cardiac disease: A swiss experience

B. Asatryan[1], J. Seiler[1], H. Servatius[1], F. Noti[1], H. Tanner[1], L. Roten[1], R. Dillier[2], A.M. Saguner[3], S.A. Mueller[2], F. Duru[3], A. Auricchio[4], P. Ammann[5], T. Reichlin[6], H. Burri[7], A. Medeiros-Domingo[1]. *[1]Department of Cardiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [2]Triemli Hospital, Department of Cardiology, Zurich, Switzerland; [3]University Heart Center, Department of Cardiology, Zurich, Switzerland; [4]Cardiocentro Ticino, Department of Cardiology, Lugano, Switzerland; [5]Cantonal Hospital St. Gallen, Department of Cardiology, St. Gallen, Switzerland; [6]University Hospital Basel, Department of Cardiology, Basel, Switzerland; [7]Geneva University Hospitals, Department of Cardiology, Geneva, Switzerland*

Background: Cardiac arrest is often the first manifestation of a silent genetic