ELECTRA - COMMENT GERER LE PATIENT ASYMPTOMATIQUE

Syndrome de Brugada

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Marseille 20/05/2022

Centre de Référence des Maladies Cardiaques Héréditaires ou Rares

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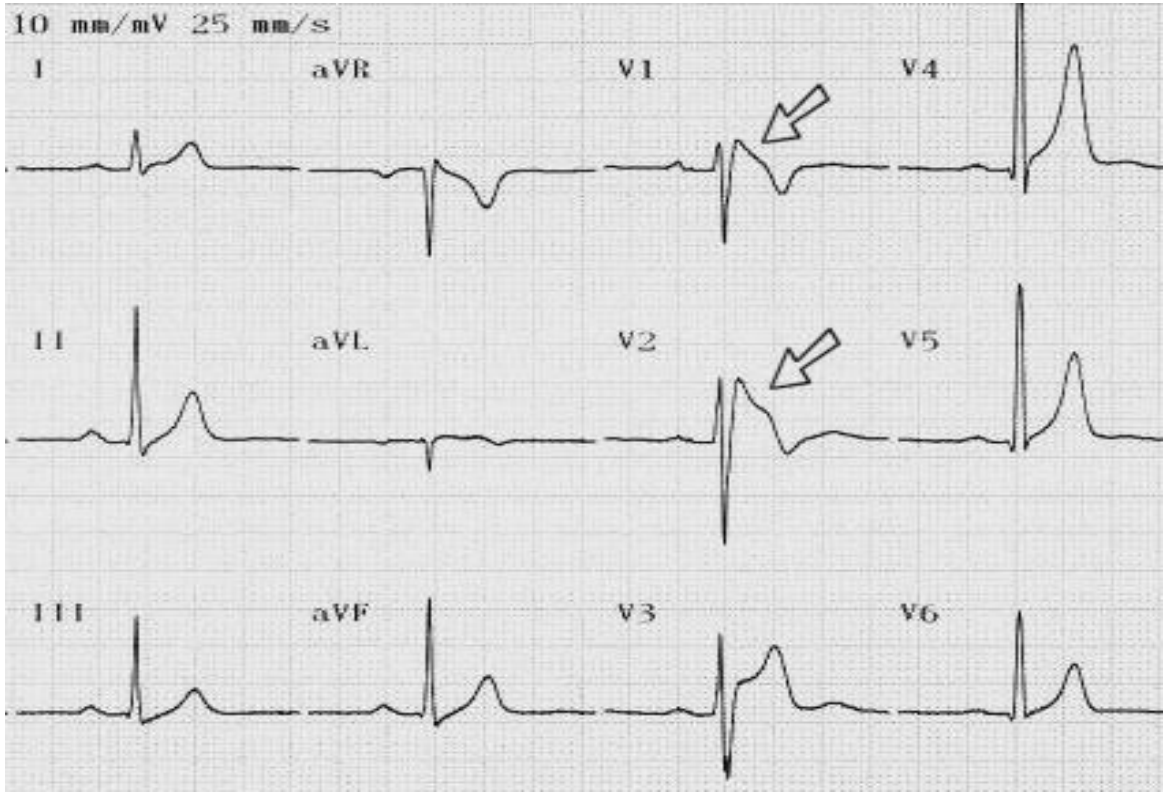
Liens d'intérêts

• Bayer	honoraires, prise en charge congrès
• Microport	prise en charge congrès
• Mylan	honoraires
• Sanofi	honoraires, consultant, étude clinique, prise en charge congrès

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Syndrome de Bugada



Maladie rare (5/10 000 chez l'adulte)
Prédominance masculine (9/10)
Age moyen 41 ±15 ans

Substrat d'arythmies ventriculaires

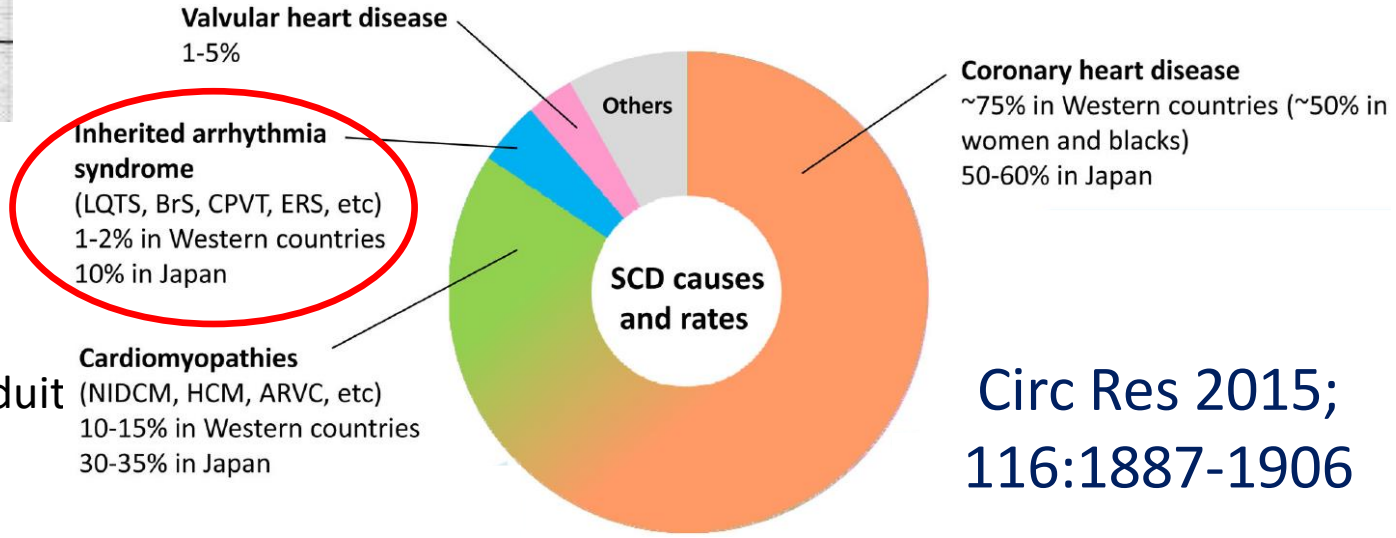
- Syncopes
- Arrêts cardiaques récupérés / Morts subites
  - <4% de l'ensemble de mort subite
  - Mais jusqu'à 20 des MS sur cœur « sain »

Recommendations	Class[a]	Level[b]
Brugada syndrome is diagnosed in patients with ST-segment elevation with type 1 morphology ≥2 mm in one or more leads among the right precordial leads V1 and/or V2 positioned in the second, third, or fourth intercostal space, occurring either spontaneously or after provocative drug test with intravenous administration of sodium channel blockers (such as ajmaline, flecainide, procainamide or pilsicainide).	I	C

Sus-décalage ST

- type 1
- ≥ 2 mm
- V1V2V3 ou V1V2 Hautes
- spontané ou pharmaco-induit

Eliminer phénocopie



Circ Res 2015; 116:1887-1906

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

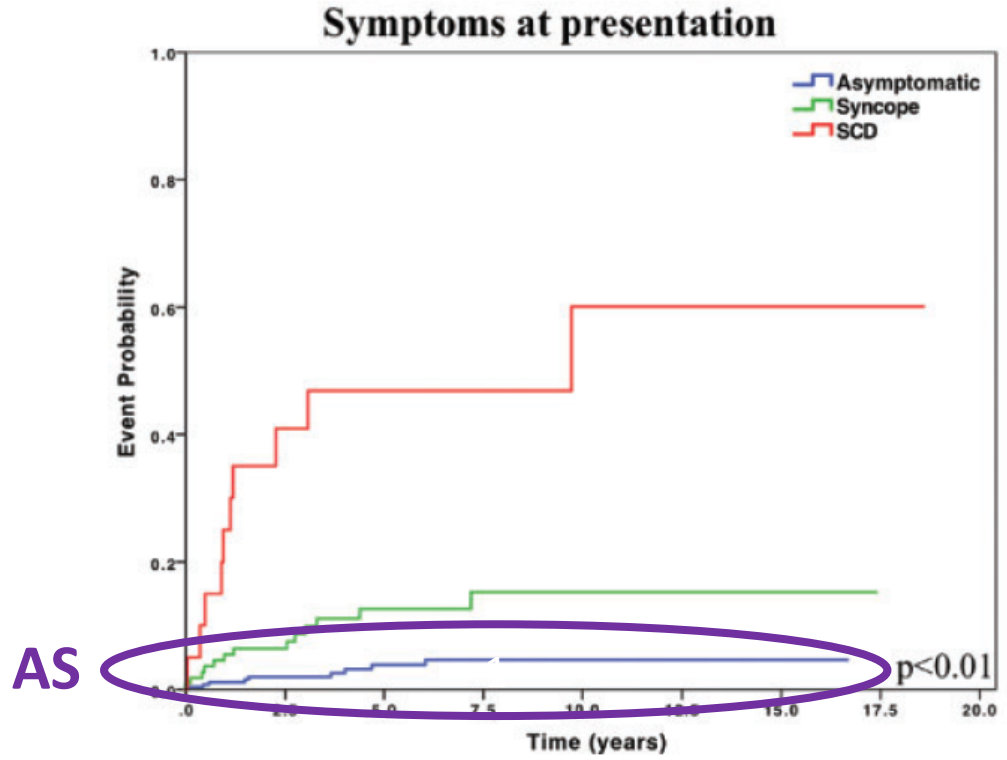
The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC)

Recommendations	Class[a]	Level[b]	Ref.[c]
ICD implantation is recommended in patients with a diagnosis of Brugada syndrome who (a) Are survivors of an aborted cardiac arrest and/or (b) Have documented spontaneous sustained VT.	I	C	451
ICD implantation should be considered in patients with a spontaneous diagnostic type I ECG pattern and history of syncope.	IIa	C	451

Syndrome de Brugada
Symptomatique = ICD

A score model to predict risk of events in patients with Brugada Syndrome

Juan Sieira[1]*, Giulio Conte[1], Giuseppe Ciconte[1], Gian-Battista Chierchia[1], Ruben Casado-Arroyo[1], Giannis Baltogiannis[1], Giacomo Di Giovanni[1], Yukio Saitoh[1], Justo Juliá[1], Giacomo Mugnai[1], Mark La Meir[2], Francis Wellens[2], Jens Czapla[2], Gudrun Pappaert[1], Carlo de Asmundis[1†], and Pedro Brugada[1†]



Asymtopmatic	269	194	137	99	64	22	9	3
Syncope	111	85	50	31	21	10	7	
SCD	20	10	4	4	3	2	1	1

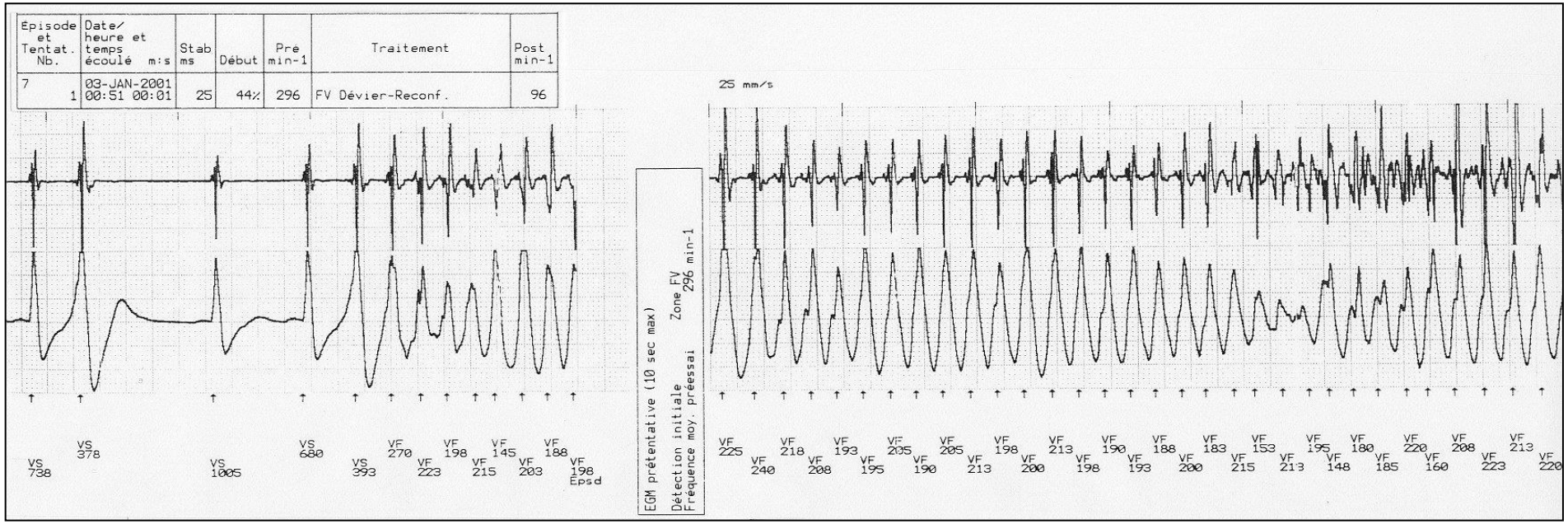
Eur Heart J. 2017;38:1756-1763

Homme 33 ans en 2000

Coup de poing sternal – Douleur thoracique – SAU
Sus-décalage ST V1-V2 – Coronarographie normale

Diagnostic de Brugada (type 1 spontané)
Asymptomatique – SVP positive – SCN5A négatif – Pas d'histoire familiale
→ Décision DAI (2000)

Consultation de suivi
Asymptomatique
03/01/2001 nuit



FV réduite par choc endo en 2001 et 2008
Pas de récidive depuis sous hydroquinidine

2002 : Homme 60 ans – Mort subite au repos (1er évènement)
Diagnostic rétrospectif ECG Brugada spontané – variant SCN5A
3 fils ont le variant SCN5A

1er Fils	2ème Fils	3ème Fils
40 ans	35 ans	30 ans
Asymptomatique	Asymptomatique	Asymptomatique
Type 1 intermittent	Type 1 intermittent	Type 1 intermittent
SVP positive	SVP positive	SVP positive
DAI	**DAI**	**DAI**
Pas de complication	Rupture sonde *2 Chocs inappropriés	Pas de complication
FV réduite par dernier choc endo Pendant sommeil / hyperthermie	Pas d'évènement	Pas d'évènement

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risk score Brugada Syndrome

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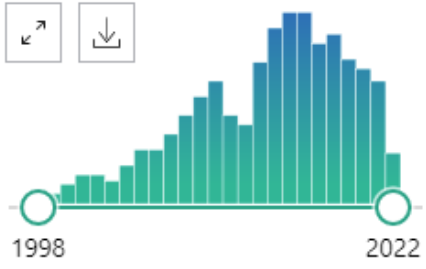
622 results

Page 1 of 63

RESULTS BY YEAR



TEXT AVAILABILITY

- Abstract
- Free full text
- Full text

ARTICLE ATTRIBUTE

1 The Genetics of **Brugada Syndrome**.

Cite

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Cerrone M, Costa S, Delmar M.

Annu Rev Genomics Hum Genet. 2022 May 13. doi: 10.1146/annurev-genom-112921-011200. Online ahead of print.

PMID: 35567276 Review.

Brugada syndrome is a heritable channelopathy characterized by a peculiar electrocardiogram (ECG) pattern and increased **risk** of cardiac arrhythmias and sudden death. ...The limited monogenic inheritance has pointed toward new perspectives on the possible comp ...

2 Performance of Multiparametric Models in Patients With **Brugada Syndrome**: A Systematic Review and Meta-Analysis.

Cite

Share

Wei HT, Liu W, Ma YR, Chen S.

Front Cardiovasc Med. 2022 Apr 14;9:859771. doi: 10.3389/fcvm.2022.859771. eCollection 2022.

PMID: 35497979 Free PMC article.

BACKGROUND: Multiparametric models have shown better **risk** stratification in **Brugada syndrome**.

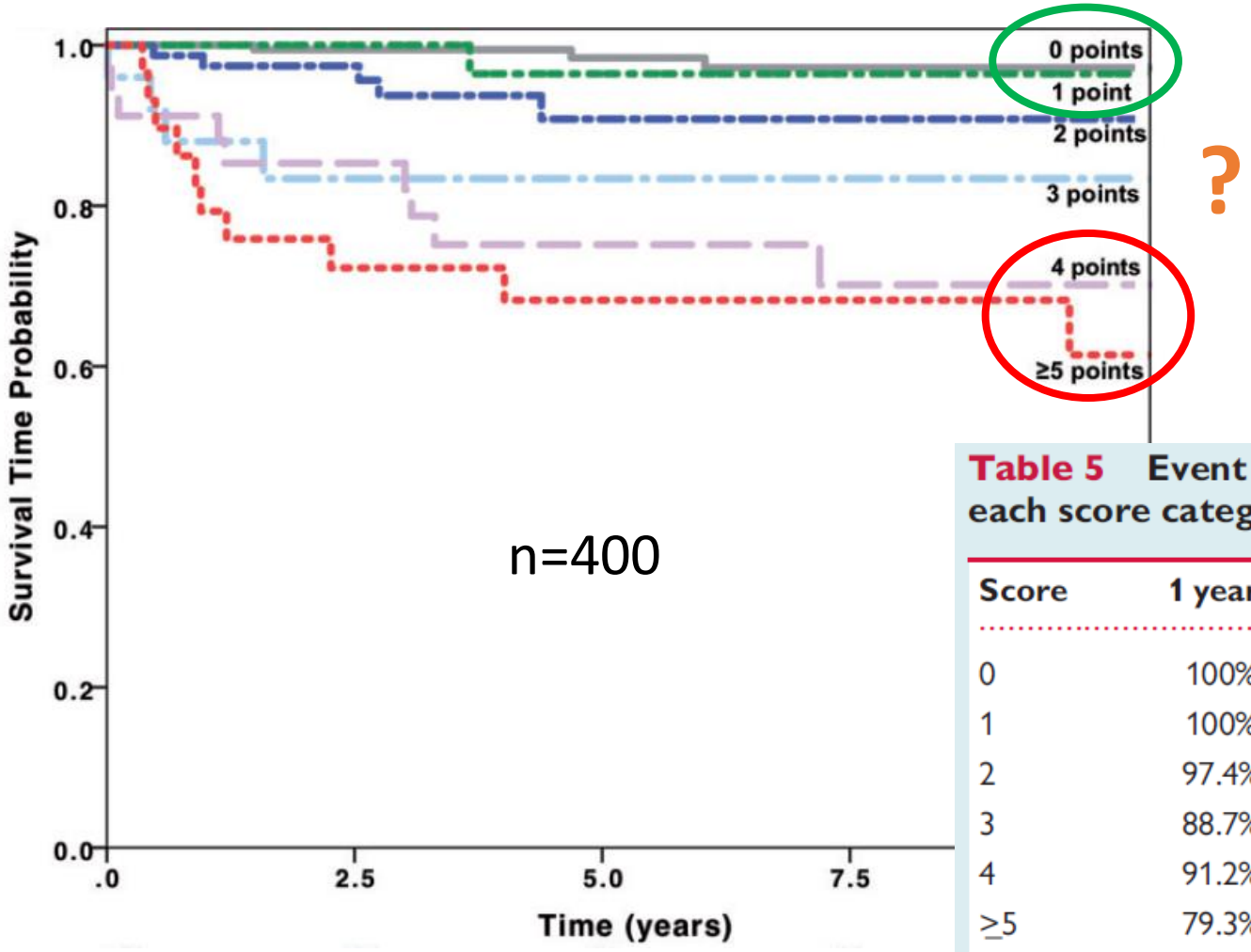
Stratification du risque et décision DAI difficile en cas de BS asymptomatique

A score model to predict risk of events in patients with Brugada Syndrome

Juan Sieira[1]*, Giulio Conte[1], Giuseppe Ciconte[1], Gian-Battista Chierchia[1], Ruben Casado-Arroyo[1], Giannis Baltogiannis[1], Giacomo Di Giovanni[1], Yukio Saitoh[1], Justo Juliá[1], Giacomo Mugnai[1], Mark La Meir[2], Francis Wellens[2], Jens Czapla[2], Gudrun Pappaert[1], Carlo de Asmundis[1†], and Pedro Brugada[1†]

Eur Heart J. 2017; 38:1756-1763

Risk factor	Points
Spontaneous type I	1
Early familial SCD	1
Inducible EPS	2
Syncope	2
SND	3
SCD	4



?

n=400

Table 5 Event free survival at 1, 5, and 10 years, in each score category

Score	1 year	5 years	10 years	*P*-value
0	100%	98.4%	97.2%	
1	100%	96.4%	96.4%	0.79
2	97.4%	90.8%	90.8%	0.02
3	88.7%	83.4%	83.4%	<0.01
4	91.2%	75.2%	70.1%	<0.01
≥5	79.3%	68.2%	61.4%	<0.01

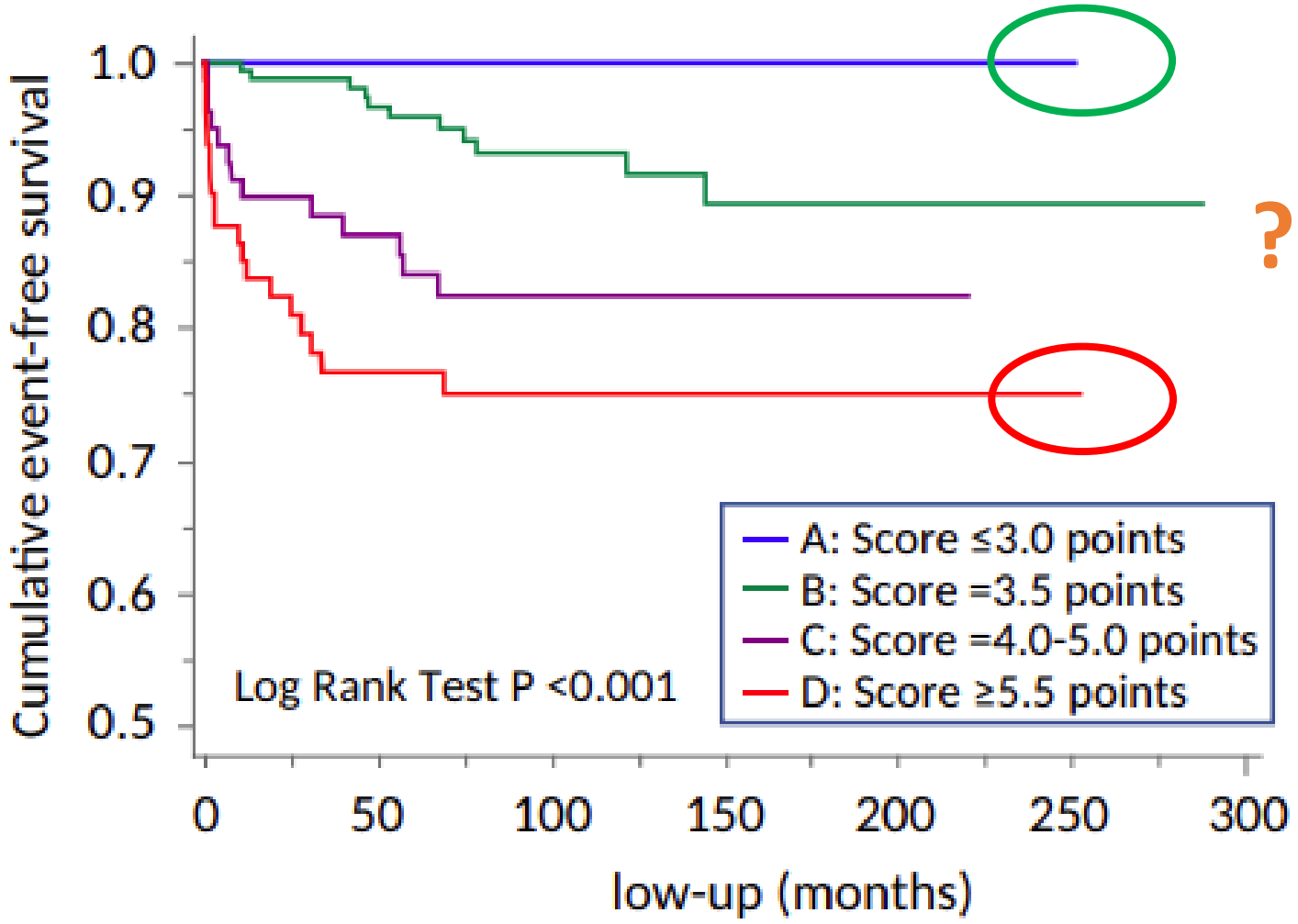
Shanghai Score System for Diagnosis of Brugada Syndrome

Validation of the Score System and System and Reclassification of the Patients

JACC EP. 2018;4:724–30

TABLE 1 Proposed Shanghai Score System for Diagnosis of Brugada Syndrome (6)

	Points
I. ECG* (12-lead/ambulatory)	
A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5
B. Fever-induced type 1 Brugada ECG pattern at nominal or high leads	3
C. Type 2 or 3 Brugada ECG pattern that converts with provocative drug challenge	2
II. Clinical history†	
A. Unexplained cardiac arrest or documented VF/polymorphic VT	3
B. Nocturnal agonal respirations	2
C. Suspected arrhythmic syncope	2
D. Syncope of unclear mechanism/unclear etiology	1
E. Atrial flutter/fibrillation in patients <30 yrs without alternative etiology	0.5
III. Family history	
A. First- or second-degree relative with definite BrS	2
B. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first- or second-degree relative	1
C. Unexplained SCD <45 yrs in first- or second-degree relative with negative autopsy	0.5
IV. Genetic test result	
A. Probable pathogenic mutation in BrS susceptibility gene	0.5



Score (requires at least 1 ECG finding)

≥ 3.5 points: Probable/definite BrS

2–3 points: Possible BrS

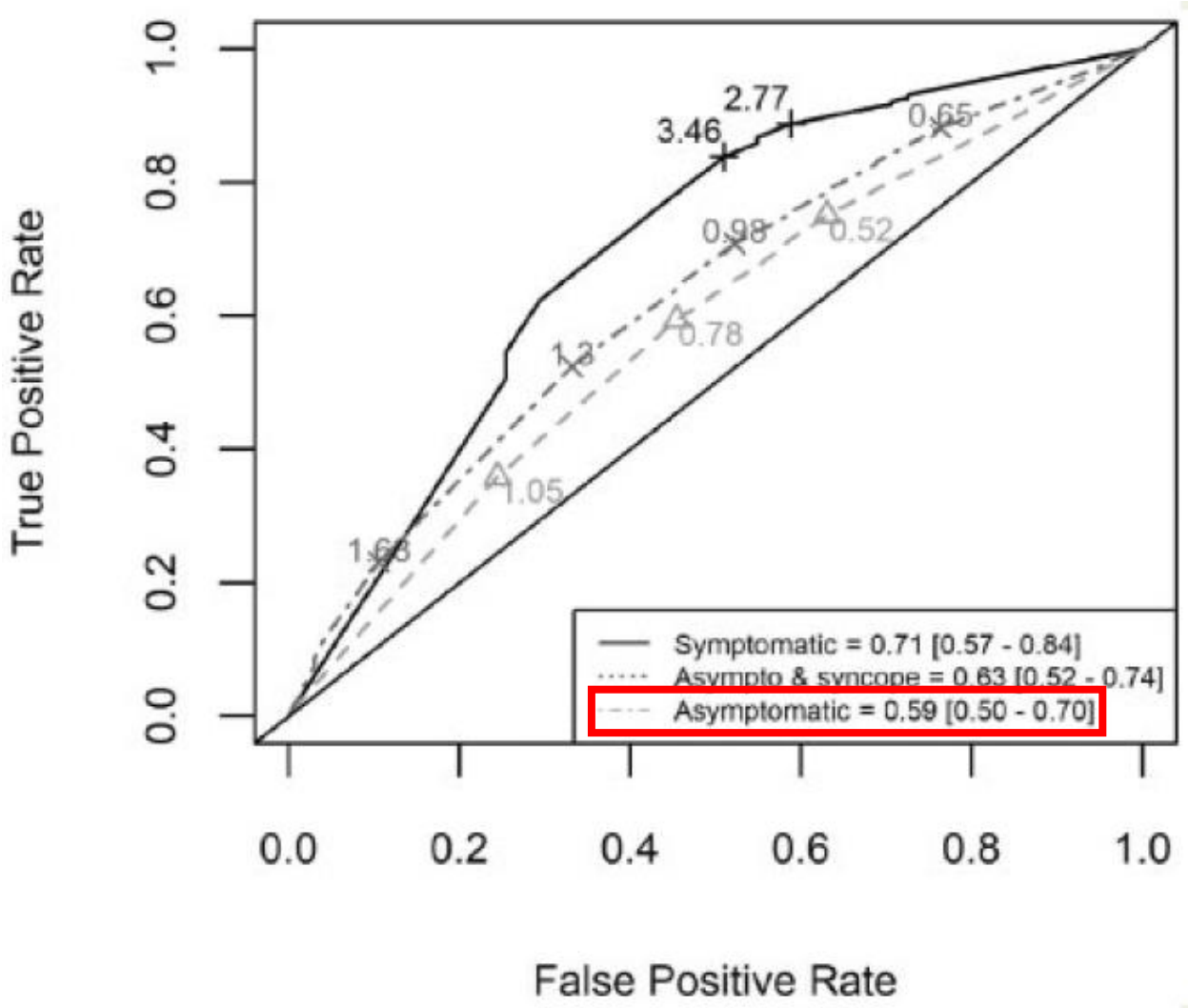
< 2 points: Nondiagnostic

Robustness and relevance of predictive score in sudden cardiac death for patients with Brugada syndrome

Vincent Probst[1†], Thomas Goronflot[2†], Soraya Anys[3†], Romain Tixier[4], Jean Briand[5], Pauline Berthome[3], Olivier Geoffroy[6], Nicolas Clementy[7], Jacques Mansourati MD[8], Laurence Jesel[9], Jean-Marc Dupuis[10], Paul Bru[11], Florence Kyndt[1], Matthieu Wargny[2], Béatrice Guyomarch[1], Aurélie Thollet[1], Philippe Mabo[5], Pierre-Antoine Gourraud[2], Nathalie Behar[5], Frédéric Sacher[4], and Jean-Baptiste Gourraud[1]*

Eur Heart J. 2021; 42:1687-1695

Capabilities of Sieira and Shanghai scores to predict an event within 10 years of inclusion (n=461)



"In the largest cohort of Brs patient ever described, risk scores do not allow stratifying the risk of arrhythmic event in intermediate-risk patient".

Brugada syndrome: ECG risk markers

Prolonged PR interval
Ventricular conduction delay
SA ECG parameters - QRS fragmentation
S-wave D1
QRS vector magnitude

Spontaneous Type 1 - Type 1 burden
Low voltage Type 1 - Post exercise STE
Type 1 aVR or inferior leads
Early repolarization pattern
Horizontal ST segment - Tpeak-Tend - TWA

Atrial Fibrillation
Low T/R ratio…

Combination of parameters

Uchimura, JCE 2014 / Maury, Am J Cardiol 2013 / Probst, Circulation 2010 / Sieira, Eur Heart J 2017 / Extramiana, JECG 2010 / Morita, JCE 2018 / Nagase, JAHA 2018 / Morita H, Circ 2008 / Take, Indian pacing and elec 2012 / Tokioka, JACC 2014
Subramian M et al, JEelectrocardiology 2019 / Morita, JCE 2018 / Priori, JACC 2012 / Subramian, JCE 2017 / Makimoto, JACC 2010 / Kawata H, Heart rythm 2013 / Takagi, Heart Rythm 2013 / Kaneko, Arrythmia electrophysiol 2014 / Morita, JCE 2018 / Tokioka, JACC 2014 / Deliniere, JECG 2020 / Delinière, Europace 2019 / Kamakura, Arrythmia electrophysiol 2009 / Takagi, Heart Rythm 2013 / Ragab, Am J Cardiol 2019 / Juntilla, J cardiovasc Electrophysiol 2008 / Giustetto, IJC 2020 / Huang, 2009 / Tada, JCE 2008 / Nademanee, Circulation 1997 / Antzelevitch C, EJCI 2001 / Maury, Heart Rythm 2012 / Morita, JCE 2018 / Subramian M, J electrocardiology 2019 / Delinière, Europace 2019 / Zumhagen, Europace 2016 / Fish, JCE 2008 / Tada, JCE 2008 / Yoshioka, Circulation 2013 / Uchimura, JCE 2014 / Rollin, Heart Rythm 2013 / Deliniere, JCE 2020 / Delinière, Europace 2019 / Calo, JACC 2016 / Subramian M, J electrocardiology 2019 / Giustetto, IJC 2020 / Calo, JACC 2016 / Deliniere, JCE 2020 / Babai, Heart Rythm 2007 / Maury, Am J Cardiol 2013…

A Primary Prevention Clinical Risk Score Model for Patients With Brugada Syndrome (BRUGADA-RISK)

JACC EP. 2021;
7:210-222

n=1110

TABLE 4 HRs From Cox Regression Models and Derived Points Per Risk Factor

	Separate Univariate Models			Multivariate Model				
	HR	95% CI	p Value	HR	95% CI	p Value	Log(HR)	Score
Age at diagnosis	1.00	0.99-1.01	0.90					
Male	0.99	0.64-1.51	0.95					
Probable arrhythmia-related syncope	5.92	4.05-8.63	<0.001	3.71	2.41-5.70	<0.001	1.15	12
Diagnosis by family screening of SCD	3.31	1.85-5.91	<0.001	4.56	2.39-8.71	<0.001		
Spontaneous type 1 Brugada ECG pattern	5.93	3.71-9.48	<0.001	3.80	2.31-6.24	<0.001	1.38	14
SCN5A mutation	1.19	0.71-1.99	0.52					
Positive programmed ventricular stimulation (induction of polymorphic VT or VF)	1.46	0.83-2.54	0.19					
VERp <200 ms	0.88	0.42-1.86	0.74					
SND	1.01	0.32-3.20	0.99					
AF/atrial flutter	0.91	0.44-1.86	0.79					
ER in peripheral leads	6.07	4.12-8.94	<0.001	3.42	2.17-5.41	<0.001	1.21	9
Type 1 Brugada ECG pattern in peripheral leads	6.86	4.69-10.04	<0.001	2.33	1.48-3.67	<0.001	0.94	12
aVR sign	1.62	1.04-2.52	0.03					
Significant S-wave in lead I	1.25	0.84-1.87	0.27					
QRS interval >120 ms in V_2	1.26	0.75-2.11	0.39					
QRS fragmentation	1.09	0.61-1.95	0.77					

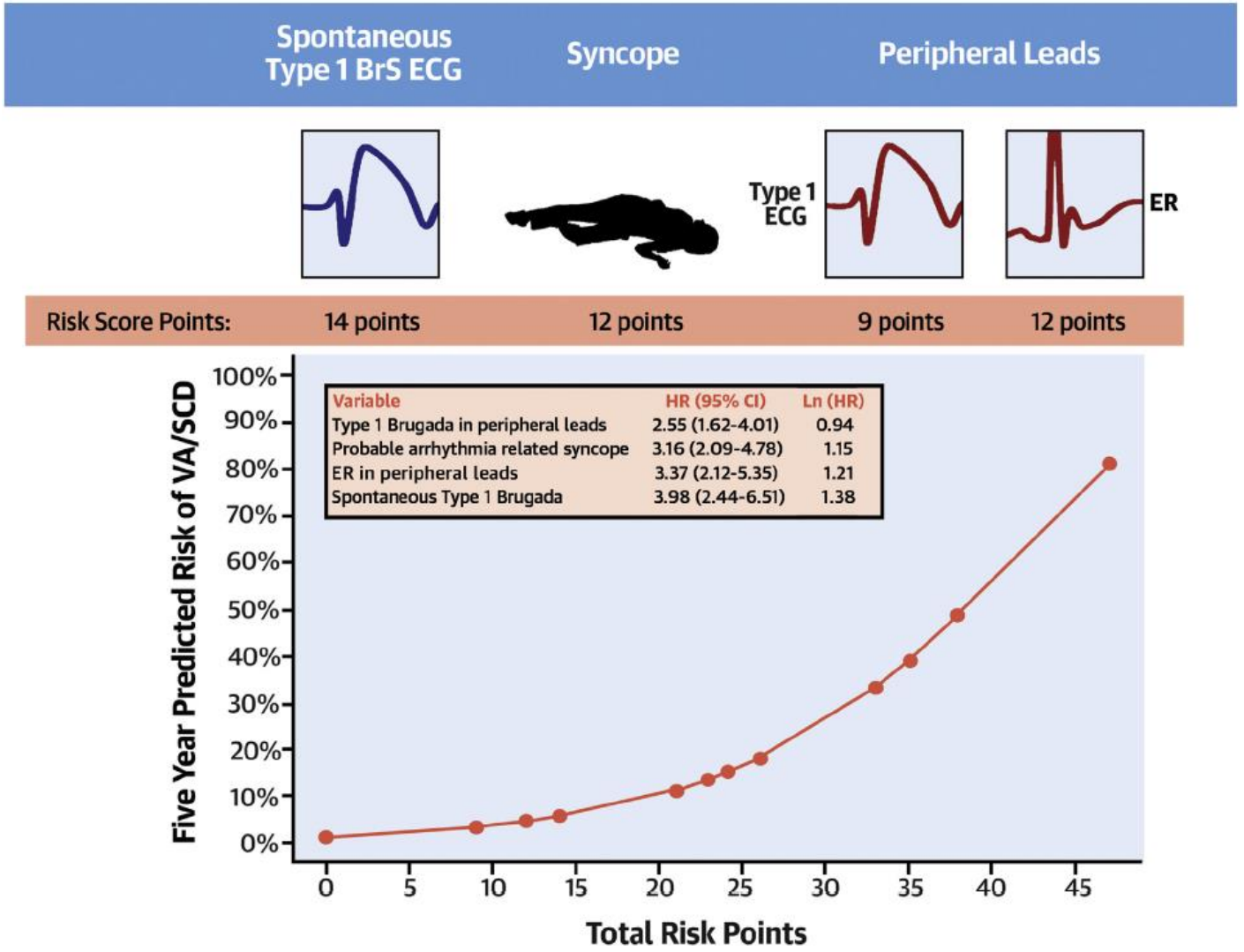
CI = confidence interval; HRs = hazard ratios; other abbreviations as in Tables 1 and 3.

A Primary Prevention Clinical Risk Score Model for Patients With Brugada Syndrome (BRUGADA-RISK)

JACC EP. 2021; 7:210-222

TABLE 5 Risk Factors, Scores, and Average 5-Year Predicted Risks of VA/SCD

Type 1 Brugada ECG Pattern in Peripheral Leads	Probable Arrhythmia-Related Syncope	ER in Peripheral Leads	Spontaneous Type 1 BRS ECG Pattern	Score Points	Average Risk of VA/SCD, %
0	0	0	0	0	1.5
1	0	0	0	9	3.6
0	1	0	0	12	4.9
0	0	1	0	12	4.9
0	0	0	1	14	5.9
1	1	0	0	21	11.5
1	0	1	0	21	11.5
1	0	0	1	23	13.9
0	1	1	0	24	15.2
0	1	0	1	26	18.3
0	0	1	1	26	18.3
1	1	1	0	33	33.4
1	1	0	1	35	39.1
1	0	1	1	35	39.1
0	1	1	1	38	48.8
1	1	1	1	47	80.7

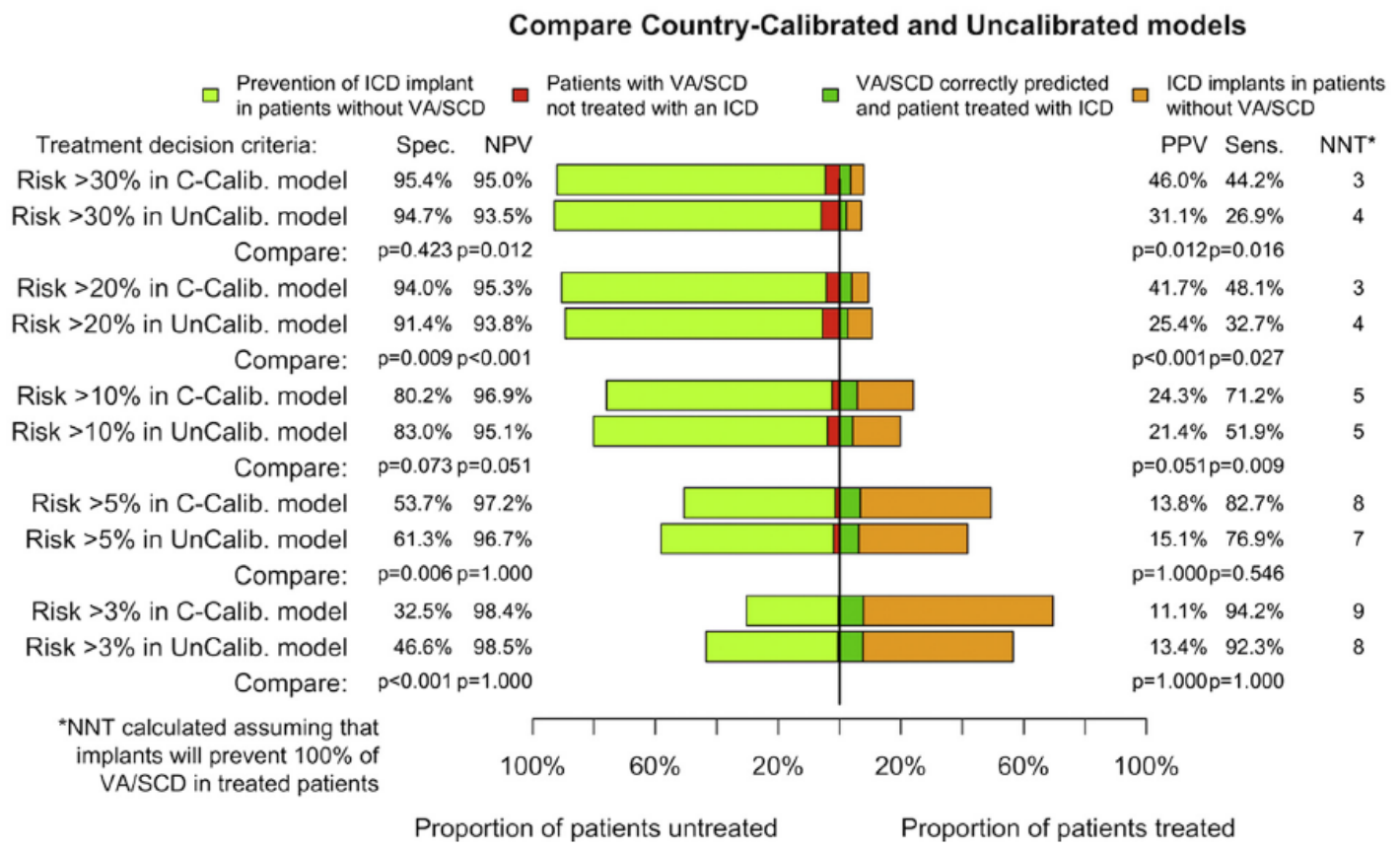


Honarbakhsh, S. et al. J Am Coll Cardiol EP. 2021;7(2):210-22.

A Primary Prevention Clinical Risk Score Model for Patients With Brugada Syndrome (BRUGADA-RISK)

JACC EP. 2021;
7:210-222

FIGURE 3 Impact of the Risk Prediction Model on Clinical Decision-Making



The bars represent the proportion of patients who would have received an implantable cardioverter-defibrillator (ICD) **(right of 0)** and those who would have not **(left of 0)** at specific risk thresholds. Each of the 2 proportions is further divided into patients with and without ventricular arrhythmia (VA)/sudden cardiac death (SCD) events at the end of the 5-year follow-up. Sensitivity (Sens.), Specificity (Spec.), positive predictive values (PPVs), and negative predictive values (NPVs) are also presented for the model when applied at the different risk levels. The figure also shows the differences in these parameters whether the risk score model is used calibrated (C-Calib) or uncalibrated (UnCalib).

PROGRAMMED STIMULATION AND GENETIC TESTING. Due to the controversial nature of programmed ventricular stimulation as a risk factor for VA/SCD in BrS (2,6,18,20,24), it is not strongly recommended in clinical guidelines (10); only 406 patients (37%) in the current cohort underwent programmed ventricular stimulation as in other published studies (24), and 66% underwent SCN5A mutation testing, compatible with previous studies (6,23). Thereby, the findings from these investigations were not included in the

Programmed Ventricular Stimulation for Risk Stratification in the Brugada Syndrome

A Pooled Analysis

Jakub Sroubek, MD, PhD; Vincent Probst, MD, PhD; Andrea Mazzanti, MD; Pietro Delise, MD; Jesus Castro Hevia, MD; Kimie Ohkubo, MD; Alessandro Zorzi, MD; Jean Champagne, MD; Anna Kostopoulou, MD; Xiaoyan Yin, PhD; Carlo Napolitano, MD, PhD; David J. Milan, MD; Arthur Wilde, MD; Frederic Sacher, MD, PhD; Martin Borggrefe, MD, PhD; Patrick T. Ellinor, MD, PhD; George Theodorakis, MD; Isabelle Nault, MD; Domenico Corrado, MD, PhD; Ichiro Watanabe, MD; Charles Antzelevitch, PhD; Giuseppe Allocca, MD; Silvia G. Priori, MD, PhD; Steven A. Lubitz, MD, MPH

Circulation. 2016; 133:622-630

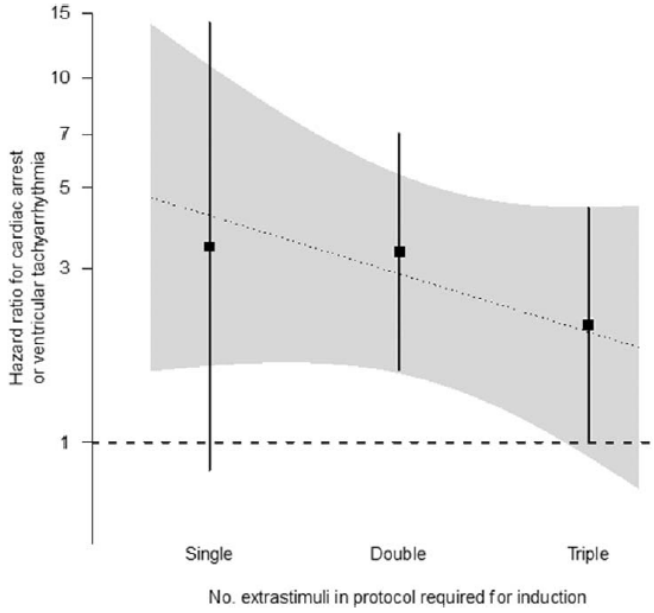
Characteristic	
Subjects, n	1312
Study, n (%)*	
Castro Hevia et al[19]	62 (5)
Champagne et al[20]	23 (2)
Delise at al[26]	228 (17)
FINGER[23]	575 (44)
Kostopoulou et al[22]	18 (1)
Ohkubo et al[21]	50 (4)
PRELUDE[9]	308 (23)
Zorzi et al[27]	48 (4)

Table 2. Annual Incidence Rates of Cardiac Arrest or Ventricular Tachyarrhythmia Among 1312 Individuals Included in the Analysis

	Spontaneous Type 1 ECG Pattern	Drug-Induced Type 1 ECG Pattern
Syncope at presentation		
Events, n/person-y	34/1056	10/693
Overall	3.22 (2.23–4.50)	1.44 (0.69–2.65)
Induced arrhythmia	5.60 (2.98–9.58)	1.96 (0.40–5.73)
No induced arrhythmia	2.55 (1.58–3.89)	1.29 (0.52–2.67)
Asymptomatic at presentation		
Events, n/person-y	17/1630	4/1506
Overall	1.04 (0.61–1.67)	0.27 (0.07–0.68)
Induced arrhythmia	1.70 (0.73–3.35)	0.45 (0.01–2.49)
No induced arrhythmia	0.78 (0.36–1.47)	0.23 (0.05–0.68)

Table 3. Risk of Sudden Cardiac Arrest or Ventricular Tachyarrhythmia With Different Definitions of Arrhythmia Induction

Definition of Induced Arrhythmia	Total, n*	Induced, n (%)	Events Among Induced/Not Induced, n	Age, Sex, Cohort Adjusted: HR (95% CI) Relative to Those Not Induced	Age, Sex, Cohort Adjusted: *P* Value	Age, Sex, Cohort, ECG, and Presenting Symptom Adjusted: HR (95% CI) Relative to Those Not Induced	Age, Sex, Cohort, ECG, and Presenting Symptom Adjusted: *P* Value
Single extrastimulus	1312	22 (2)	3/62	1.99 (0.52–7.68)	0.32	2.39 (0.62–9.21)	0.20
Up to double extrastimuli	1312	253 (19)	25/40	2.87 (1.60–5.12)	<0.001	2.66 (1.44–4.89)	0.002
Up to triple extrastimuli	1247	527 (42)	40/25	2.75 (1.52–4.98)	<0.001	2.66 (1.44–4.92)	0.002



2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC)

Recommendations	Class[a]	Level[b]
The following lifestyle changes are recommended in all patients with a diagnosis of Brugada syndrome: (a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org) (b) Avoidance of excessive alcohol intake and large meals (c) Prompt treatment of any fever with antipyretic drugs.	I	C

Recommendations	Class[a]	Level[b]
Quinidine should be considered in patients who qualify for an ICD but present a contraindication or refuse it and in patients who require treatment for supraventricular arrhythmias.	IIa	C
ICD implantation may be considered in patients with a diagnosis of Brugada syndrome who develop VF during PVS with two or three extrastimuli at two sites.	IIb	C

BrugadaDrugs.org
Safe drug use and the Brugada syndrome

https://www.brugadadrugs.org/

Drugs to be avoided

Drugs preferentially avoided

Potential anti-arrhythmic drugs

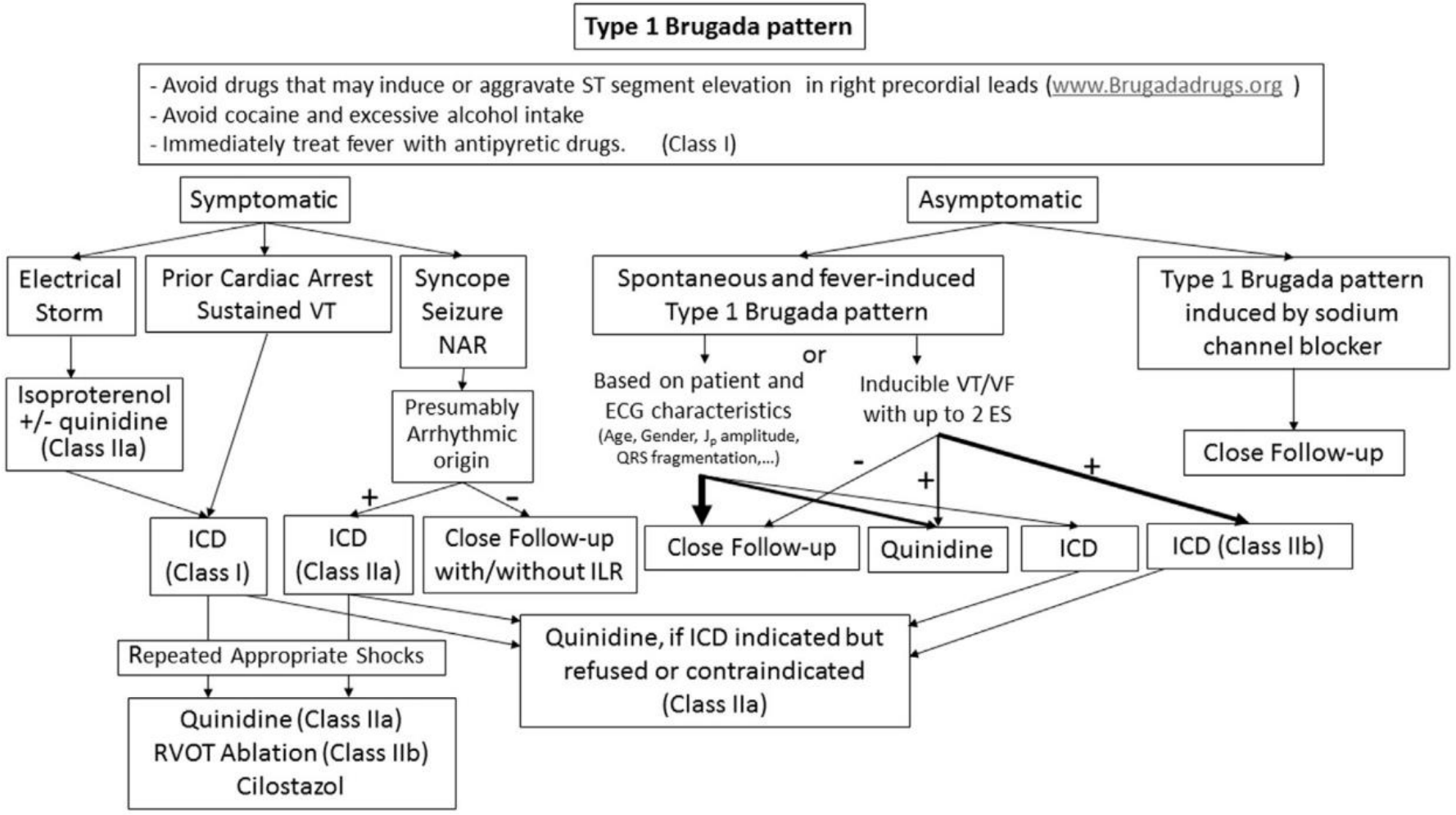
Diagnostic drugs

Patient letter

J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge ☆, ☆☆

Charles Antzelevitch, PhD, FHRS[a,*], Gan-Xin Yan, MD, PhD[b], Michael J. Ackerman, MD, PhD[c], Martin Borggrefe, MD[d], Domenico Corrado, MD, PhD[e], Jihong Guo, MD[f], Ihor Gussak, MD, PhD[g], Can Hasdemir, MD[h], Minoru Horie, MD[i], Heikki Huikuri, MD[j], Changsheng Ma, MD[k], Hiroshi Morita, MD, PhD[l], Gi-Byoung Nam, MD, PhD[m], Frederic Sacher, MD, PhD[n], Wataru Shimizu, MD, PhD[o], Sami Viskin, MD[p], Arthur A.M. Wilde, MD, PhD, FHRS[q,r]

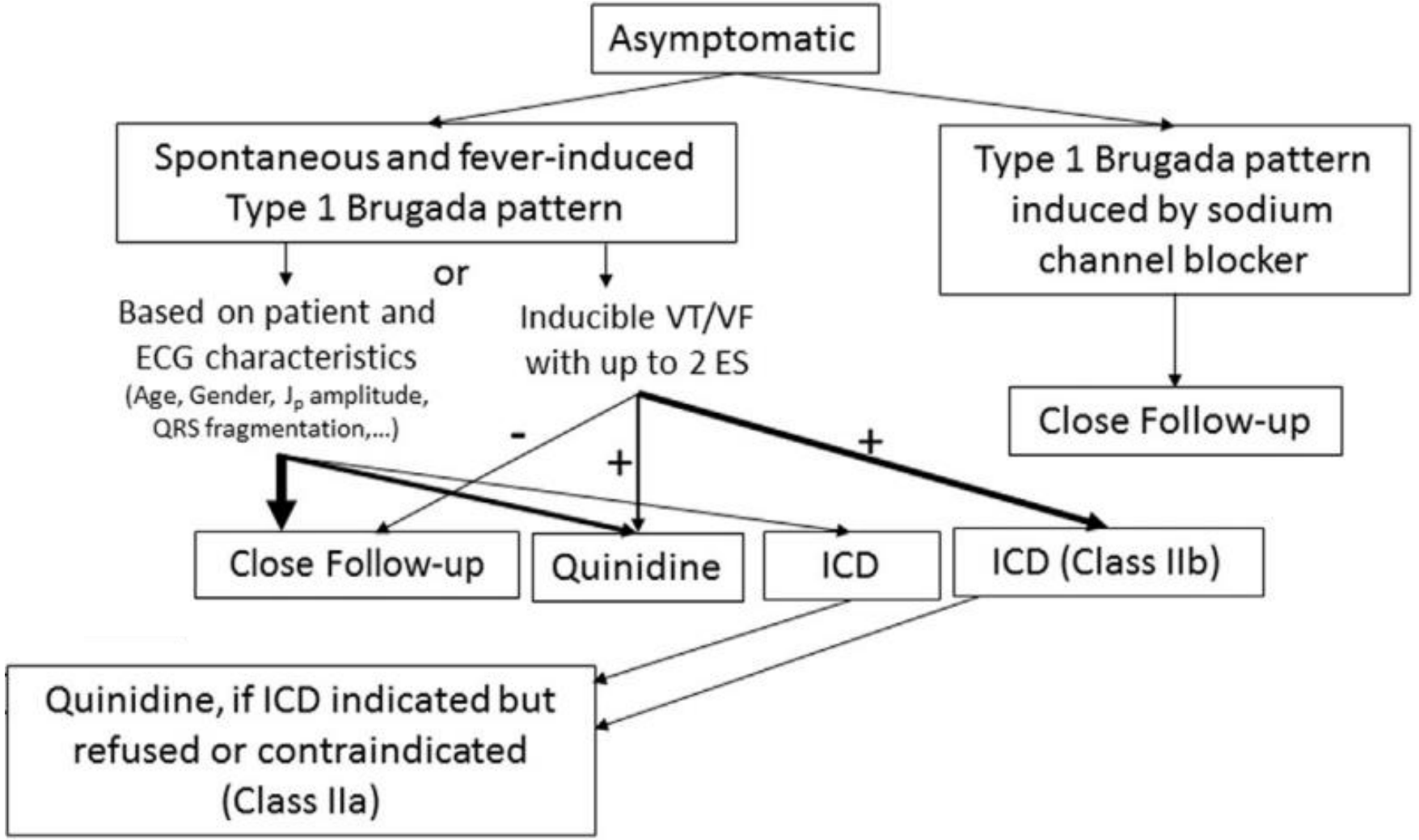
Journal of Arrhythmia. 2016;32:315-39



J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge☆,☆☆

Charles Antzelevitch, PhD, FHRS[a,*], Gan-Xin Yan, MD, PhD[b], Michael J. Ackerman, MD, PhD[c], Martin Borggrefe, MD[d], Domenico Corrado, MD, PhD[e], Jihong Guo, MD[f], Ihor Gussak, MD, PhD[g], Can Hasdemir, MD[h], Minoru Horie, MD[i], Heikki Huikuri, MD[j], Changsheng Ma, MD[k], Hiroshi Morita, MD, PhD[l], Gi-Byoung Nam, MD, PhD[m], Frederic Sacher, MD, PhD[n], Wataru Shimizu, MD, PhD[o], Sami Viskin, MD[p], Arthur A.M. Wilde, MD, PhD, FHRS[q,r]

Journal of Arrhythmia. 2016;32:315-39



European Heart Rhythm Association (EHRA)/ Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) Expert Consensus Statement on the state of genetic testing for cardiac diseases

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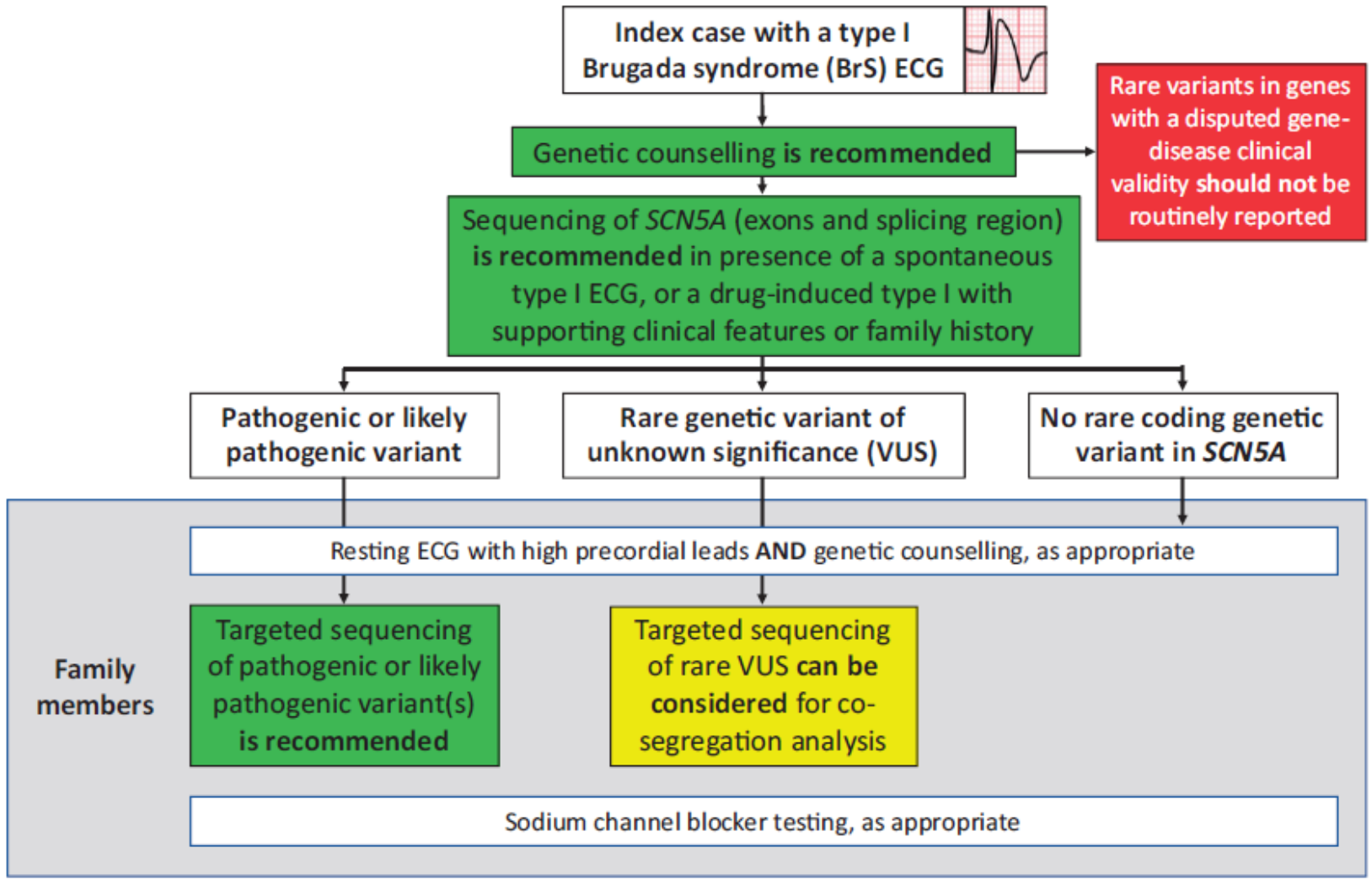

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