



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA
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di Confindustria
Auditorium
della Tecnica

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30 Settembre
1 Ottobre
2022

SINDROME DI BRUGADA NEL 2022

**STRATIFICAZIONE DEL RISCHIO:
DALL'ASINTOMATICO TIPO 1 AL PAZIENTE CON PATTERN TIPO 2**

Pasquale Crea

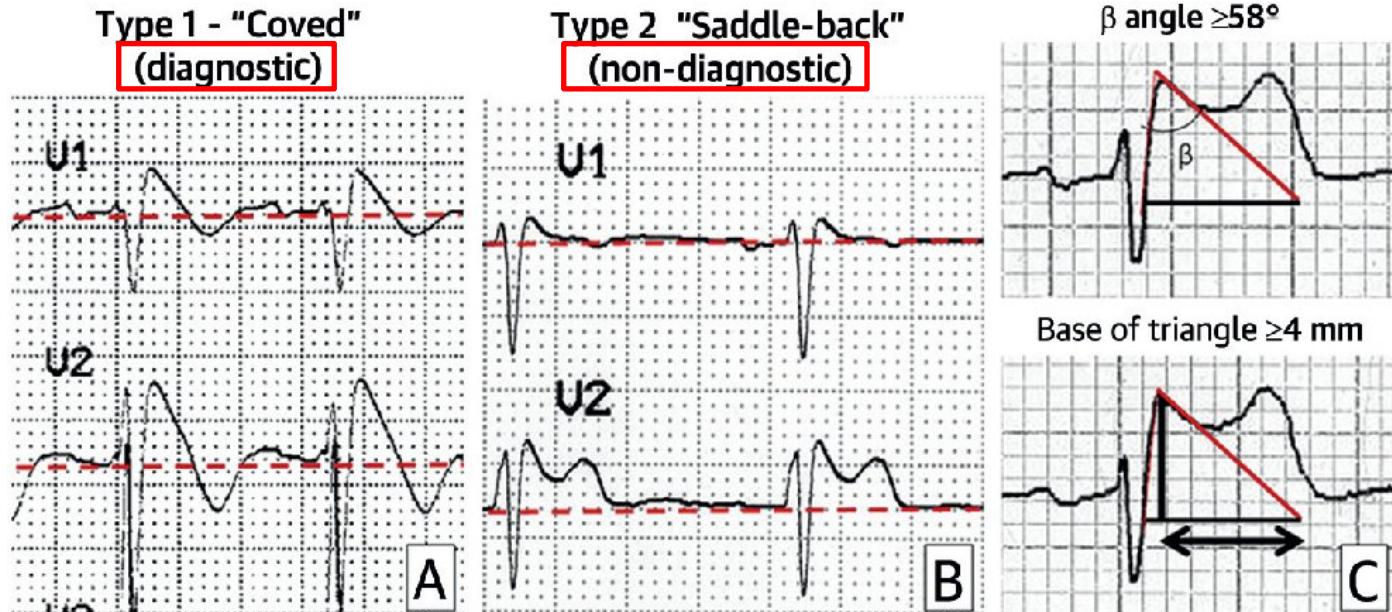




Present Status of Brugada Syndrome

JACC State-of-the-Art Review

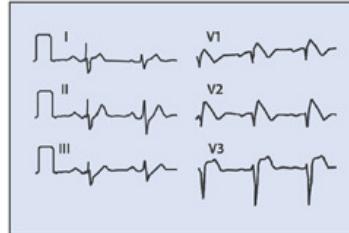
Josep Brugada, MD, PhD,^{a,b,c,*} Oscar Campuzano, BSc, PhD,^{c,d,e,*} Elena Arbelo, MD, PhD,^{a,c}
Georgia Sarquella-Brugada, MD, PhD,^{b,e} Ramon Brugada, MD, PhD^{c,d,e,f}



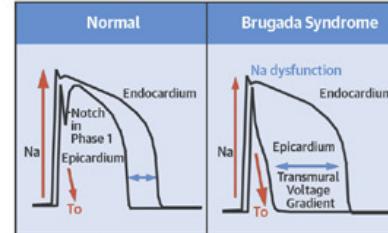


CENTRAL ILLUSTRATION: Main Characteristics of Brugada Syndrome

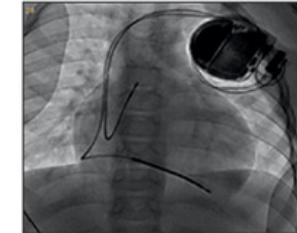
Brugada Syndrome



Coved type ST-segment in V1-V2

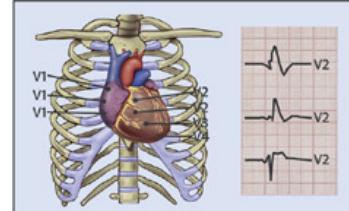


Loss of function of sodium channels

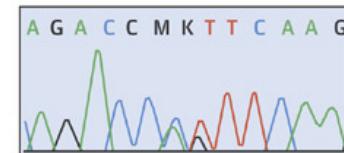


ICD is standard therapy,
epicardial radiofrequency ablation
a promising one

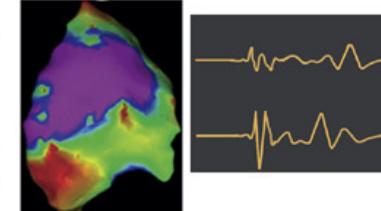
Diagnosis



Pathophysiology

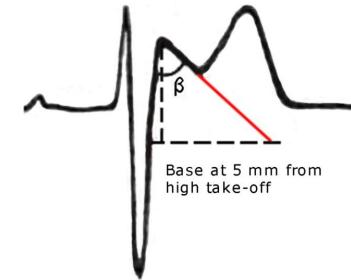


Management



Brugada, J. et al. J Am Coll Cardiol. 2018;72(9):1046-59.

Type 2 (Saddle back pattern)

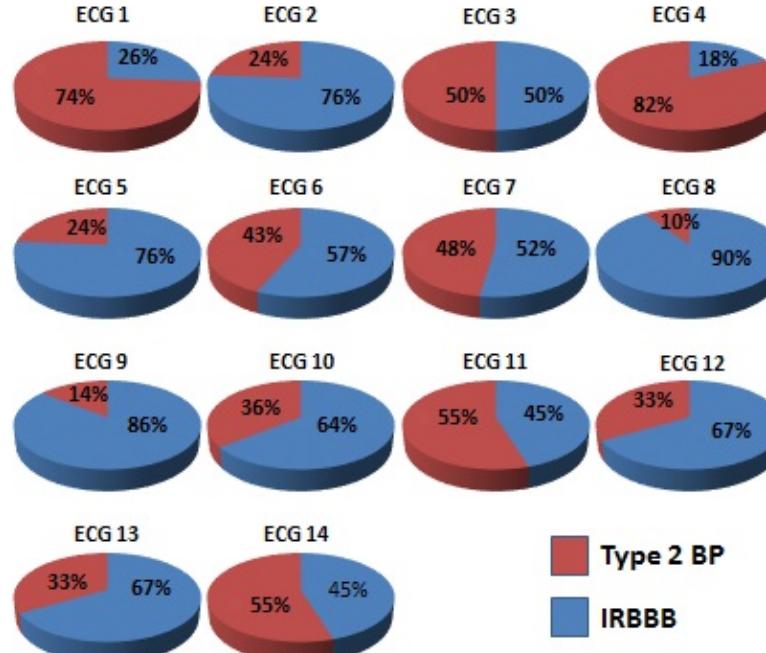


- High take-off of r' (that not necessary coincides with J point) ≥ 2 mm
 - The descending arm of r' coincides with the beginning of ST
 - Minimum ST elevation ≥ 0.05 mv
 - Positive T wave in V2 (T peak $>$ ST minimum > 0) and of variable morphology in V1.
 - The duration of QRS is longer in BP type 2 than in other cases with r' in V1 and there is a mismatch between V1 and V6
 - The characteristics of triangle formed by r' allow to define different criteria useful for diagnosis
 - a) β angle $> 58^\circ$ (Chevallier 2011).
 - b) duration of the base triangle of r' at 5 mm from the high take-off > 3.5 mm (Serra 2012)
- Bayes de Luna et al: *J Electrocardiol*, 2012;45:433-442





Diagnosis of type 2 Brugada pattern: insights from a pilot survey

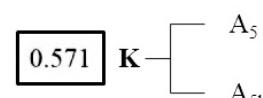
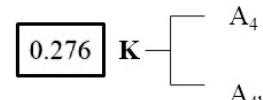
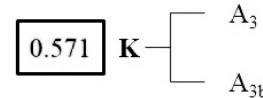
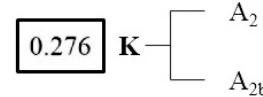
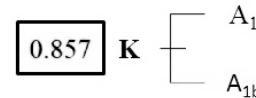


Crea et al. Minerva 2021

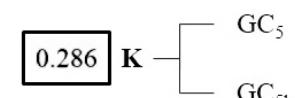
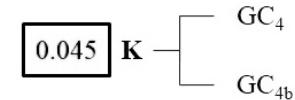
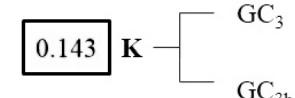
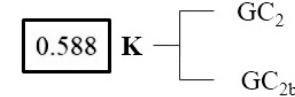
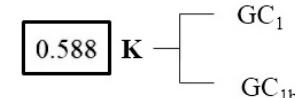


Intra-observer agreement

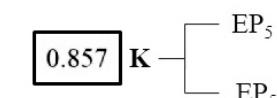
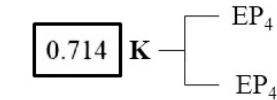
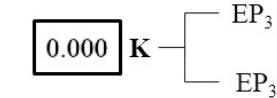
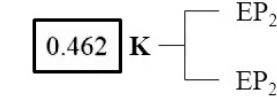
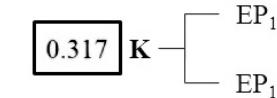
Arrhythmologists



General Cardiologists



EP Fellows

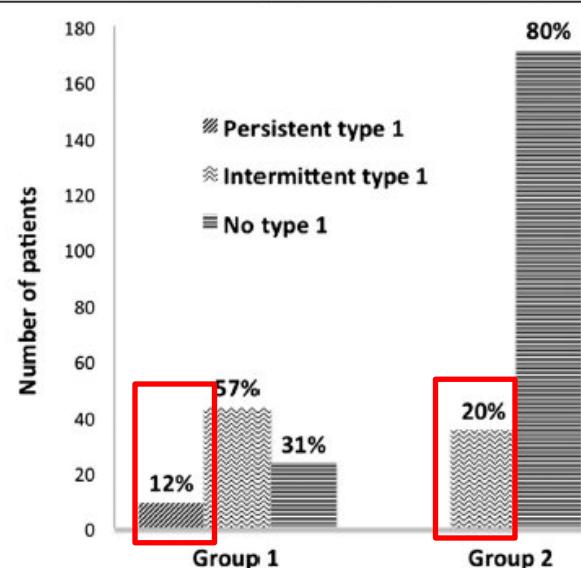




Prevalence of Type 1 Brugada Electrocardiographic Pattern Evaluated by Twelve-Lead Twenty-Four-Hour Holter Monitoring



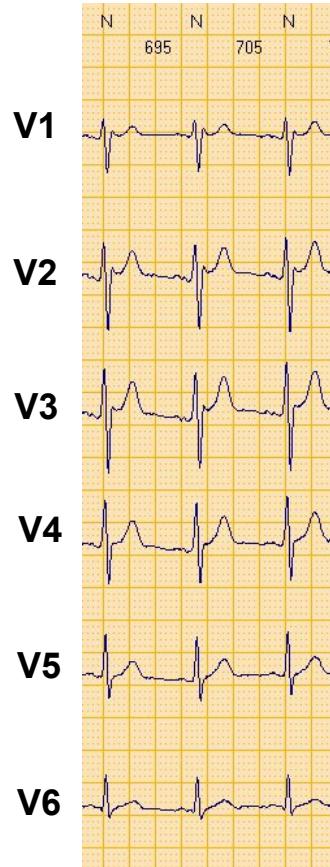
Natascia Cerrato, MD^a, Carla Giustetto, MD^{a,*}, Elena Gribaudo, MD^a, Elena Richiardi, MD^b, Lorella Barbonaglia, MD^c, Chiara Scrocco, MD^a, Domenica Zema, MD^a, and Fiorenzo Gaita, MD^a



electrocardiograms (BrECGs) are considered to be a risk factor; however, it is instead, considered a risk factor; however, it is rECG fluctuations. The aim of this study was to evaluate with Br, the real prevalence of type 1 BrECG (12L-Holter) and its correlation with the time of day. In 51 patients. Seventy-five (30%) patients exhibited type 1 BrECG (group 1) and 176 (70%) had only drug-free BrECG. BrECG was defined as “persistent” (>85% of the day). In group 1, 12% showed persistent type 1 at least once, 31% never had type 1; in group 2, none had type 1, and 80% never showed type 1. To evaluate the time of day, two periods in the day were considered. Type 1 BrECG was more frequently detected in the afternoon (52%, p <0.001). In conclusion, in patients with type 1 Brugada syndrome, type 1 BrECG can be detected more frequently during the day. Follow-up with periodic ECGs and this has been shown to be effective. 12L-Holter recording might avoid 20% of the use of sodium channel blockers, which are not without side effects. © 2015 Elsevier Inc. All rights reserved.



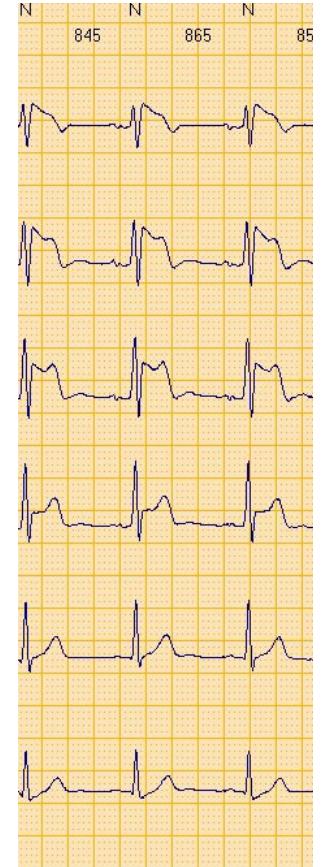
10 AM



3 PM



5 PM



7 AM





Read My Lips

A Positive Ajmaline Test Does Not Always Mean You Have Brugada Syndrome*

Sami Viskin, MD, Raphael Rosso, MD

Drug Provocation Testing in Brugada Syndrome

A Test of Uncertain Significance*

Albert Y. Sun, MD^{a,b}

In the end, the conclusion from this study and those before it regarding SCB testing for Brugada syndrome is that we currently have a test of uncertain significance, a test of uncertain significance in a syndrome full of value of uncertain significance. This, however, should not be confused with a test without value. With future testing focusing on dose-dependent effects, long-term outcomes, and correlation with genotypes, we may find that we all have a Brugada pattern threshold. Those persons with a lower threshold may indeed comprise a group for which we are more willing to risk using lifesaving measures such as medications, ablation, or implantable cardioverter-defibrillators. Ultimately, as the study by Cheung et al. (10) highlights, the more we collaborate, the more we will move forward.



«Tutti sono asintomatici prima di diventare sintomatici per la prima volta»

J. Brugada



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EDITORIAL COMMENT

Will I Die From Brugada Syndrome?

The Rummination of Risk Stratification*

Sami Viskin, MD, Aviram Hochstadt, MD, Arie Lorin Schwartz, MD, Raphael Rosso, MD

Brugadaphobia is a term we need to come to terms with (1). The typical individual diagnosed with Brugada syndrome (BrS) nowadays is an otherwise healthy and asymptomatic young male patient, on whom an electrocardiogram (ECG) was performed for no good reason and was found to have “electrocardiographic imperfections” in his right precordial leads. At this stage, and without really understanding the consequences of this next step, he entered the path “to rule out BrS” by undertaking an ajmaline/flecainide challenge test that was graded positive. By now, and mainly for “historical reasons” (2), he is diagnosed with BrS (3).

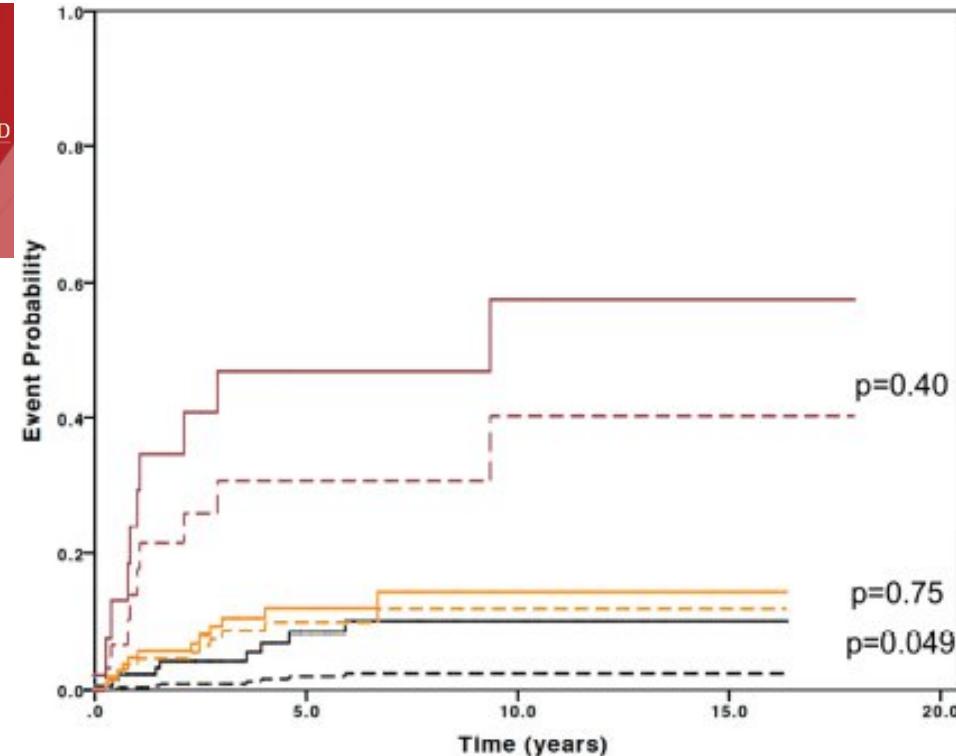


Long-term prognosis of drug-induced Brugada syndrome

Juan Sieira, MD • Giuseppe Ciccone, MD, PhD • Giulio Conte, MD, PhD • ... Kristel Wauters, MD
Gudrun Pappaert, RN • Pedro Brugada, MD, PhD • Show all authors

Published: May 04, 2017 • DOI: <https://doi.org/10.1016/j.hrthm.2017.04.044> • Check for updates

- SCD Spontaneous
- - SCD Induced
- Syncope Spontaneous
- - Syncope Induced
- Asymptomatic Spontaneous
- - Asymptomatic Induced





EDITORIAL COMMENTARY | VOLUME 14, ISSUE 10, P1434-1435, OCTOBER 01, 2017

Risk of arrhythmic events in drug-induced Brugada syndrome

Najim Lahrouchi, MD • Mario Talajic, MD • Rafik Tadros, MD, PhD  Published: June 27, 2017 • DOI: <https://doi.org/10.1016/j.hrthm.2017.06.033> • 

Table. Summary of event rate in spontaneous and drug-induced Brugada syndrome in PRELUDE, FINGER and Sieira et al.

Study	Median follow-up in months [IQR]	Number of BrS patients			Ventricular arrhythmia event rates			Hazard ratio [CI]
		Spont.	Drug-induced	Asx drug-induced	Spont.	Drug-induced	Asx drug-induced	
PRELUDE ⁹	34 [NR]	171	137	107	7.6%	0.7%	0%	4.2 [1.4-12.8]
FINGER ¹⁰	31.9 [14-54.4]	468	561	386	2.3%/year	1.07%/year	0.35%/year	2.1 [1.2-3.6]
Sieira et al. ⁸	62.5 [28.9-115.6]	78	343	244	2.3%/year	1.1%/year	0.4%/year	2.8 [1.5-5.9]

Asymptomatic patients with drug-induced BrS now represent a large proportion of BrS cases seen in clinical practice (58% in Sieira et al.8). **One should highlight that the absolute risk of arrhythmic events (including ICD therapies) in this subgroup is very low across studies (<0.4%/year; Table). This risk is somewhat higher but not too far from that of SCD in the general adult population (>0.1%/year).**



Cardiac arrest and Brugada syndrome: Is drug-induced type 1 ECG pattern always a marker of low risk?☆☆☆

Pietro Delise ^{a,*}, Giuseppe Allocca ^b, Nadir Sitta ^b, Federico Migliore ^c, Federica Dagradi ^d, Carla Spazzolini ^d, Luigi Sciarra ^e, Valeria Carinci ^f, Domenico Corrado ^c, Leonardo Calò ^e, Peter J. Schwartz ^{d,**}

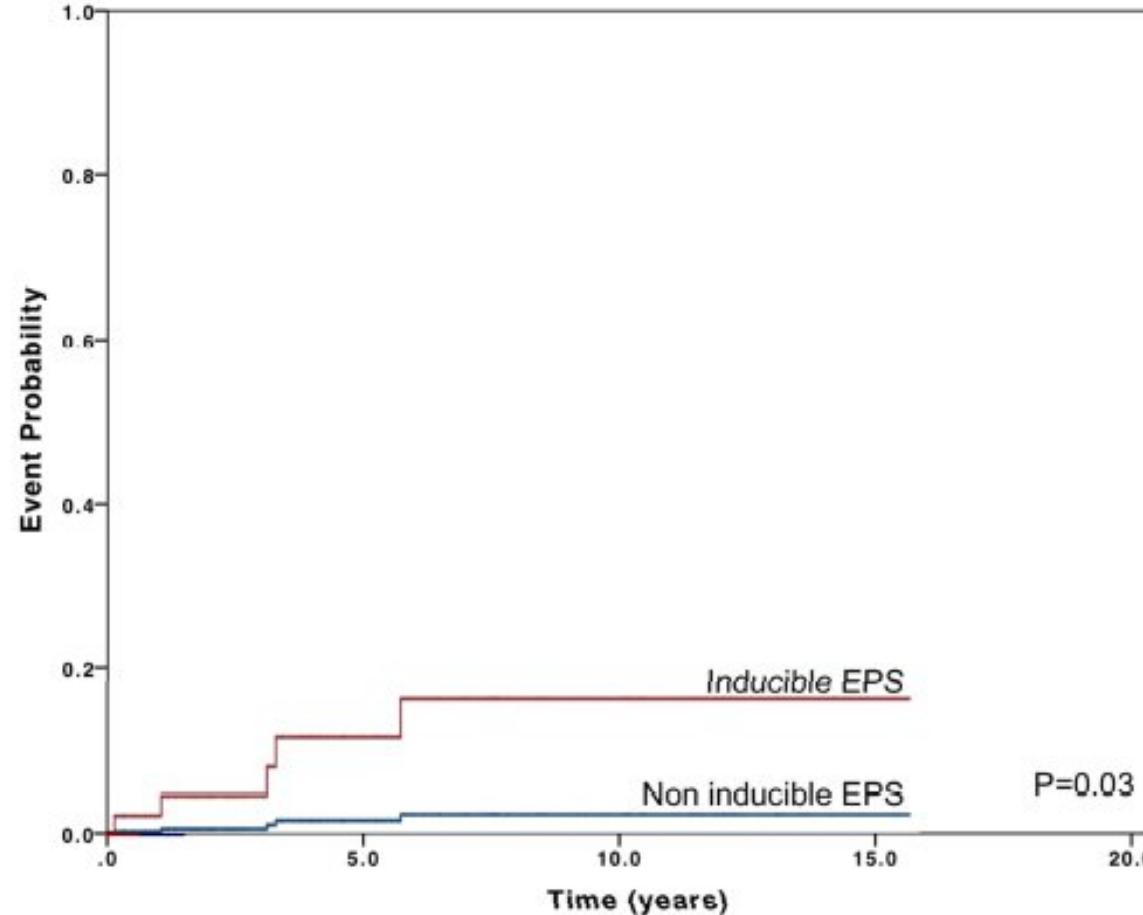
A B S T R A C T

Background: Patients diagnosed as affected by Brugada syndrome (BrS) on the basis of a drug-induced type 1 ECG pattern (type1) are regarded as at low risk for cardiac arrest. We tested whether this assumption matches reality.

Methods: The study population included 26 patients from our group and 217 patients from three studies published between 2002 and 2013, all of them with aborted cardiac arrest (ACA) and in whom a previously unrecognized type1 (spontaneous or drug-induced) was discovered after the event, thus leading to the diagnosis of BrS.

Results: Among our 26 patients, a drug-induced type1 was detected in 11 (42%) and only 1/11 showed a spontaneous pattern during follow-up; of 6 patients with syncope before ACA, 4 (67%) had only a drug-induced pattern. ICD shocks rates were similar in both spontaneous and drug-induced groups (57% and 45%). Early on, year 2002, the percentage of drug-induced type1 after ACA was much lower (14%) and has progressively increased to approximately 50%.

Conclusions: If drug-induced type1 carries low arrhythmic risk, it should seldom be the only marker for BrS after an ACA. In studies on patients after an unexpected ACA, a drug-induced type1 leads to the diagnosis of BrS more often than anticipated. This contrasts with prospective studies focusing on patients already diagnosed as BrS and which consider drug-induced type1 as a marker of low risk. Contrary to current views, it is possible that not all patients with a drug-induced BrS type1 are at low risk of future events.



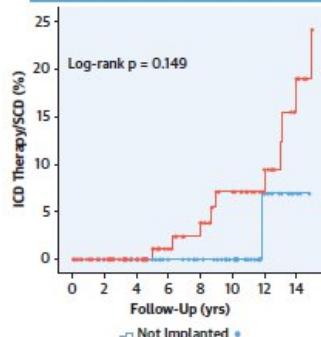


Electrophysiological Study Prognostic Value and Long-Term Outcome in Drug-Induced Type 1 Brugada Syndrome

The IBRYD Study

Vincenzo Russo, MD, PhD,^{a,*} Pia Clara Pafundi, MSc, PhD,^{b,*} Alfredo Caturano, MD,^{b,*} Gregory Dendramis, MD,^{c,*} Andrea Ottonelli Ghidini, MD,^d Vincenzo Ezio Santobuono, MD, PhD,^e Luigi Sciarra, MD,^f Pasquale Notarstefano, MD,^g Maria Antonietta Rucco, MD,^h Emilio Attena, MD,ⁱ Roberto Floris, MD,^j Emanuele Romeo, MD,^k Berardo Sarubbi, MD, PhD,^l Gerardo Nigro, MD, PhD,^a Antonio D'Onofrio, MD,^l Leonardo Calò, MD,^f Martina Nesti, MD^g

226 Drug-Induced Type 1 BrS Patients
Followed for a Median Time of 106 Months



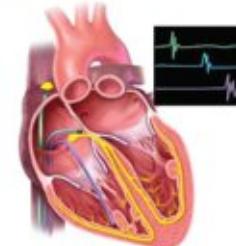
No difference in a composite of appropriate ICD therapy and sudden cardiac death between ICD vs. non-ICD recipients

142 ICD Recipients



Low arrhythmic risk
(appropriate shock 0.38%/yr)
High prevalence of ICD-related complications (14.8%)

Electrophysiological Study



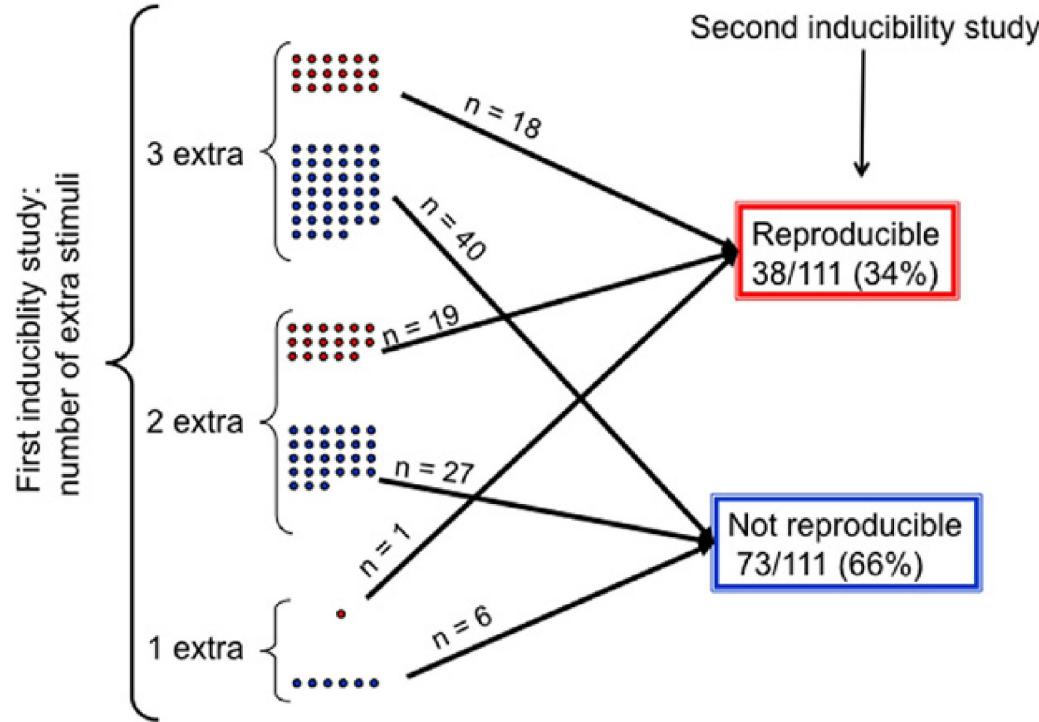
BrS patients with syncope
High negative predictive value (95%)
Low positive predictive value (9.6%)

BrS patients without syncope
High negative predictive value (100%)
Low positive predictive value (8.9%)



Risk Stratification in Brugada Syndrome

Results of the PRELUDE (PRogrammed EElectrical stimUlation preDictive valuE) Registry





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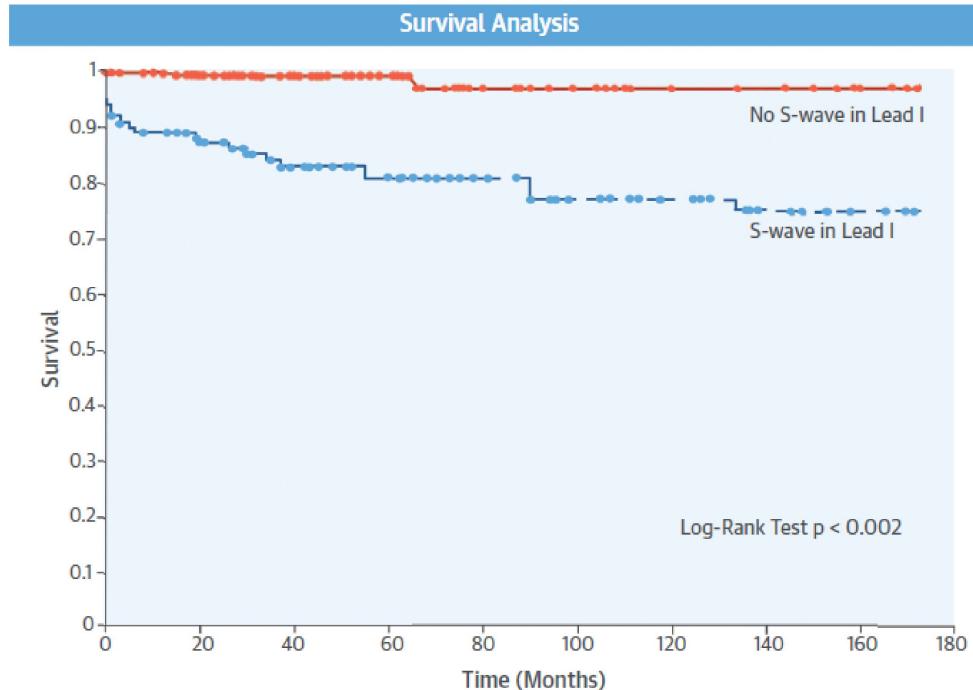
A New Electrocardiographic Marker of Sudden Death in Brugada Syndrome

The S-Wave in Lead I



Leonardo Calò, MD,^a Carla Giustetto, MD,^b Annamaria Martino, MD,^a Luigi Sciarra, MD,^a Natascia Cerrato, MD,^b Marta Marziali, MD,^a Jessica Rauzino, MD,^c Giulia Carlino, MD,^d Ermenegildo de Ruvo, MD,^a Federico Guerra, MD,^e Marco Rebecchi, MD,^a Chiara Lanzillo, MD, PhD,^f Matteo Anselmino, MD,^b Antonio Castro, MD,^f Federico Turreni, MD,^f Maria Penco, MD,^d Massimo Volpe, MD,^c Alessandro Capucci, MD,^e Fiorenzo Gaita, MD^b

CENTRAL ILLUSTRATION Brugada Syndrome: A New Marker of Sudden Death



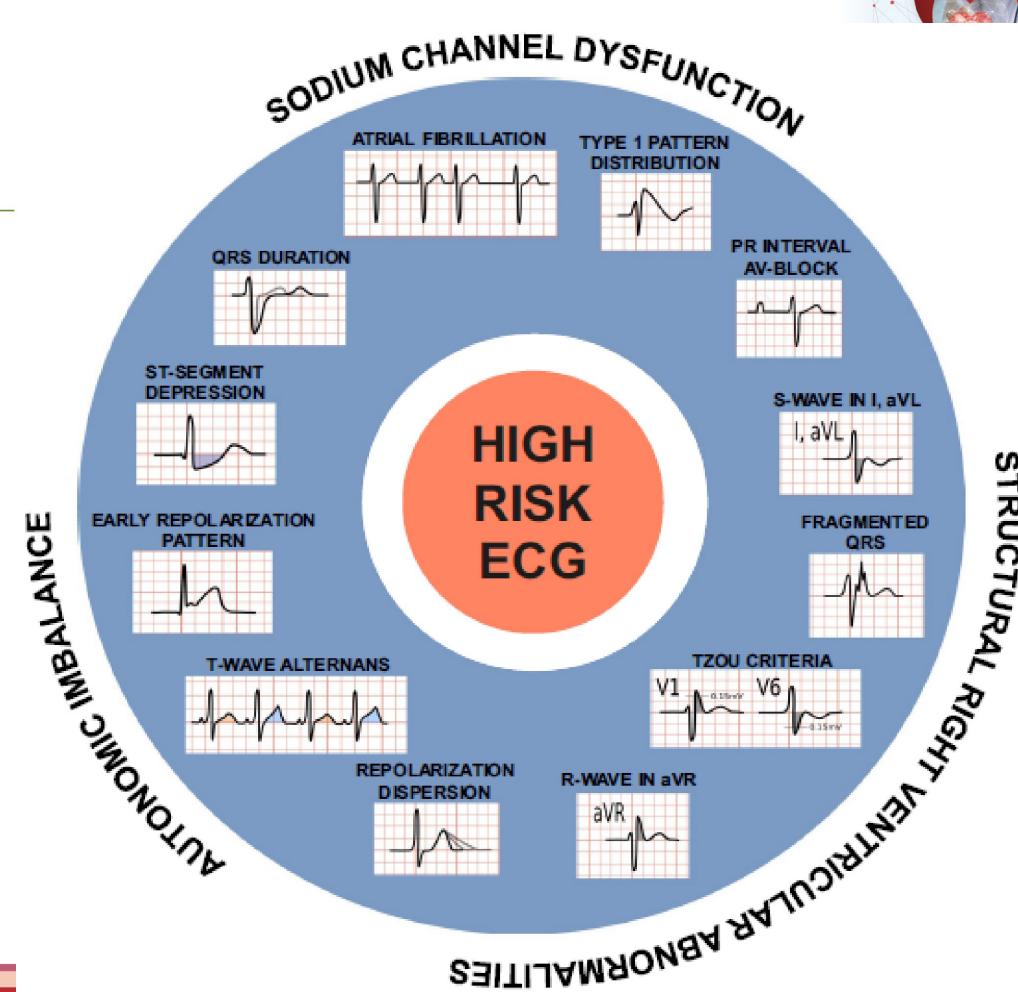


Journal of the American Heart Association

SYSTEMATIC REVIEW AND META-ANALYSIS

Standard ECG in Brugada Syndrome as a Marker of Prognosis: From Risk Stratification to Pathophysiological Insights

Francesco Vitali, MD*; Alessandro Brieda , MD*; Cristina Balla , MD, PhD; Rita Pavasini , MD; Elisabetta Tonet, MD; Matteo Serenelli, MD; Roberto Ferrari, MD, PhD; Pietro Delise, MD; Claudio Rapezzi, MD, PhD; Matteo Bertini , MD, PhD





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VOL. 7, NO. 2, 2021

CLINICAL ELECTROPHYSIOLOGY: CHANNELOPATHIES

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

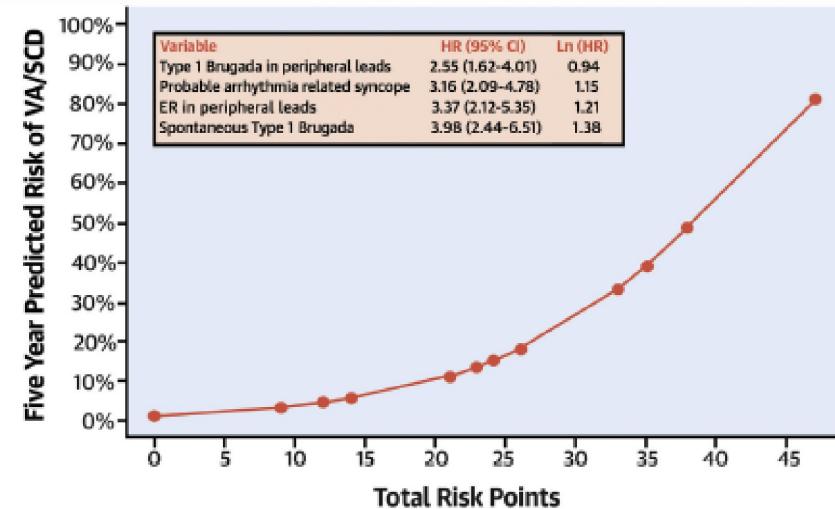


Spontaneous Type 1 BrS ECG Syncope Peripheral Leads



Risk Score Points:	14 points	12 points	9 points	12 points
--------------------	-----------	-----------	----------	-----------

Variable	HR (95% CI)	Ln (HR)
Type 1 Brugada in peripheral leads	2.55 (1.62-4.01)	0.94
Probable arrhythmia related syncope	3.16 (2.09-4.78)	1.15
ER in peripheral leads	3.37 (2.12-5.35)	1.21
Spontaneous Type 1 Brugada	3.98 (2.44-6.51)	1.38



2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death



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Axel Verstraet (Belgium), Maurizio Volterrani (Italy).

¹Representing the Association for European Paediatric and Congenital Cardiology (AEPC).

Recommendations for management of patients with Brugada syndrome



ESC
(1)

Recommendations	Class	Level
Diagnosis		
It is recommended that BrS is diagnosed in patients with no other heart disease and a spontaneous type 1 Brugada ECG pattern.	I	C
It is recommended that BrS is diagnosed in patients with no other heart disease who have survived a CA due to VF or PVT and exhibit a type 1 Brugada ECG induced by sodium channel blocker challenge or during fever.	I	C
Genetic testing for SCN5A gene is recommended for probands with BrS.	I	C
BrS should be considered in patients with no other heart disease and induced type 1 Brugada pattern who have at least one of: <ul style="list-style-type: none">🎬 arrhythmic syncope or nocturnal agonal respiration🎬 a family history of BrS🎬 a family history of SD (< 45 years old) with a negative autopsy and circumstance suspicious for BrS.	IIa	C



European Heart Journal (2015) **36**, 2793–2867
doi:10.1093/euroheartj/ehv316



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)

Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC)

ESC GUIDELINES

Diagnosis of Brugada Syndrome

Recommendations	Class ^a	Level ^b	Ref. ^c
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	This panel of experts

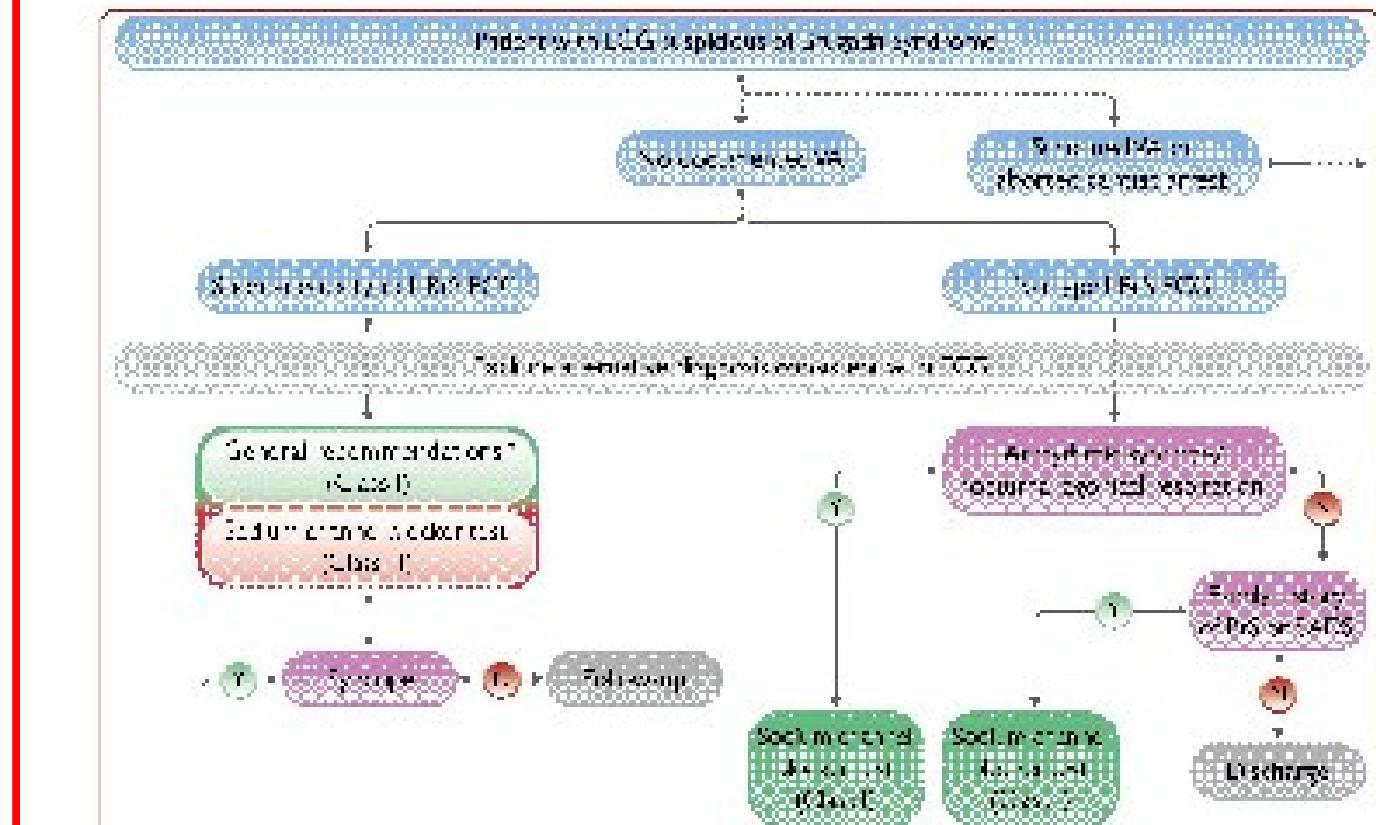
^aClass of recommendation.

^bLevel of evidence.

^cReference(s) supporting recommendations.

Figure 33 Part One

Algorithm for the management of patients with Brugada pattern ECG



Recommendations for management of patients with Brugada syndrome



ESC
(4)

Recommendations	Class	Level
<i>Risk stratification, prevention of SCD, and treatment of VA (continued)</i>		
Catheter ablation of triggering PVCs and/or RVOT epicardial substrate should be considered in BrS patients with recurrent appropriate ICD shocks refractory to drug therapy.	IIa	C
PES may be considered in asymptomatic patients with a spontaneous type I BrS ECG.	IIb	B
ICD implantation may be considered in selected asymptomatic BrS patients with inducible VF during PES using up to 2 extrastimuli.	IIb	C
Catheter ablation in asymptomatic BrS patients is not recommended.	III	C

Sami Viskin, MD

Algoritmo Brugada - Messina



1) Arresto cardiaco, Sincope aritmica → ICD

2) SINCOPI:
di ndd

SEF+ → ICD

SEF - → Raccomandazioni * e Follow-up** (loop recorder)

3) ASINTOMATICI:

Tipo 1 spontaneo → >45 yo → Raccomandazioni * e Follow-up**

<45 yo → SEF → + → ICD

Tipo 1 indotto → Holter 24 h/12 D → - → Raccomandazioni * e Follow-up**

Raccomandazioni *
e Follow-up**

*Raccomandazioni = Farmaci da evitare e pronto controllo febbre; ECG parenti I grado
 ** Follow-up=Visita, ECG e Holter 12D annuale



CONCLUSIONI

- *La variabilità intrinseca del Pattern di Brugada rende spesso difficile la diagnosi*
- *La diagnosi di Sindrome di Brugada non è dettata dal solo ECG*
- *La diagnosi di Sindrome di Brugada ha un impatto psicologico importante*
- *Un approccio primariamente clinico è fondamentale nella stratificazione del rischio*

Sono contento delle ultime linee guida