

PLACE

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA
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di Confindustria
Auditorium
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2022

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30 Settembre
1 Ottobre
2022

Sindrome di Brugada nel 2022

Diagnosi, farmaci e condizioni da evitare.
Loop recorder in quali pazienti?

Palmisano Pietro, FAIAC

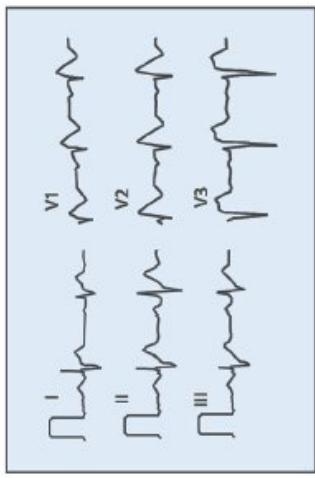


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Azienda Ospedaliera Card. G. Panico Tricase (Le)

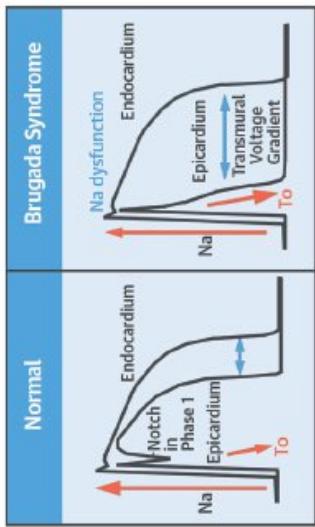


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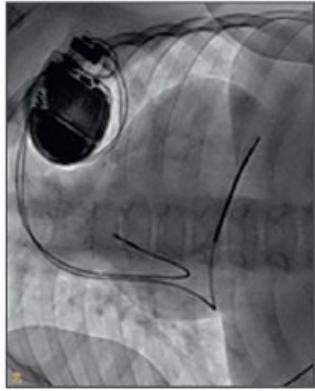
Sindrome di Brugada: caratteristiche



Coved type ST-segment in V1-V2

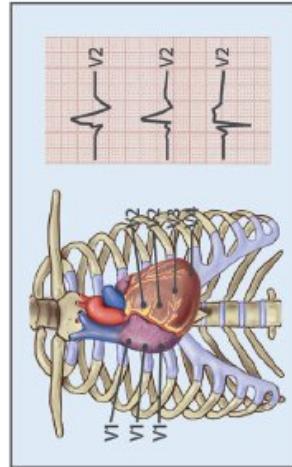


Loss of function of sodium channels

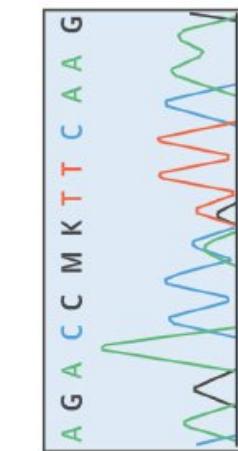


ICD is standard therapy,
epicardial radiofrequency ablation
a promising one

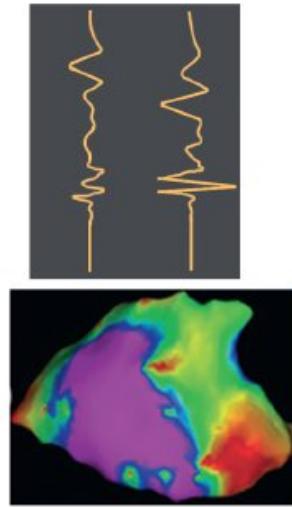
Diagnosis



Pathophysiology



Management

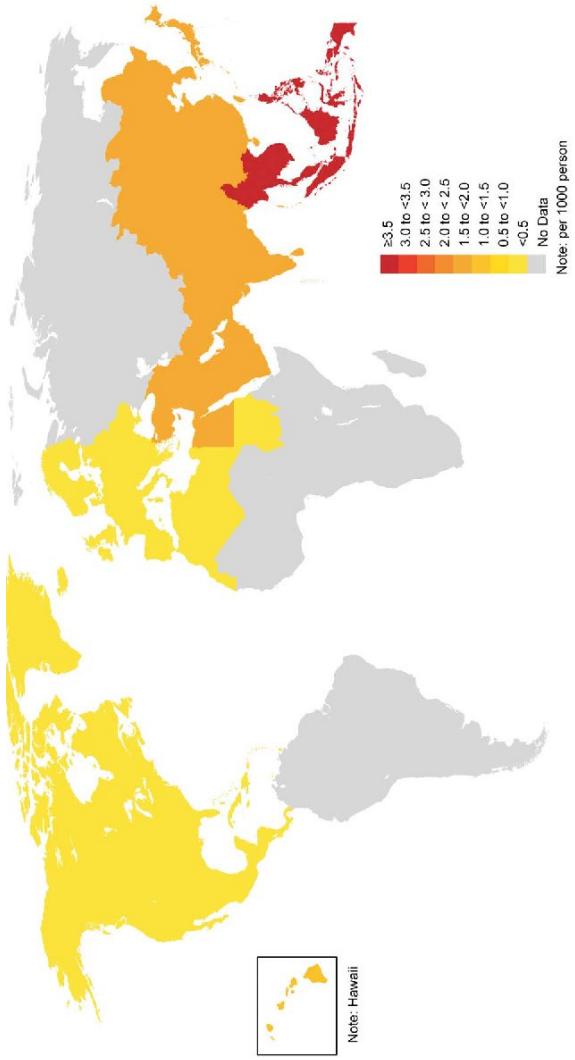


Brugada J, et al. J Am Coll Cardiol 2018;72:1046–59.



Sindrome di Brugada: epidemiologia

- Prevalenza: **0.5-5:1000**
- Incidenza del pattern ECG: **1,2-8‰**
- Responsabile del **4-12%** delle morti improvvise
- **>20%** delle morte improvvise in cuori strutturalmente sani
- Rischio di eventi nei maschi **8-10 volte superiore** rispetto alle donne



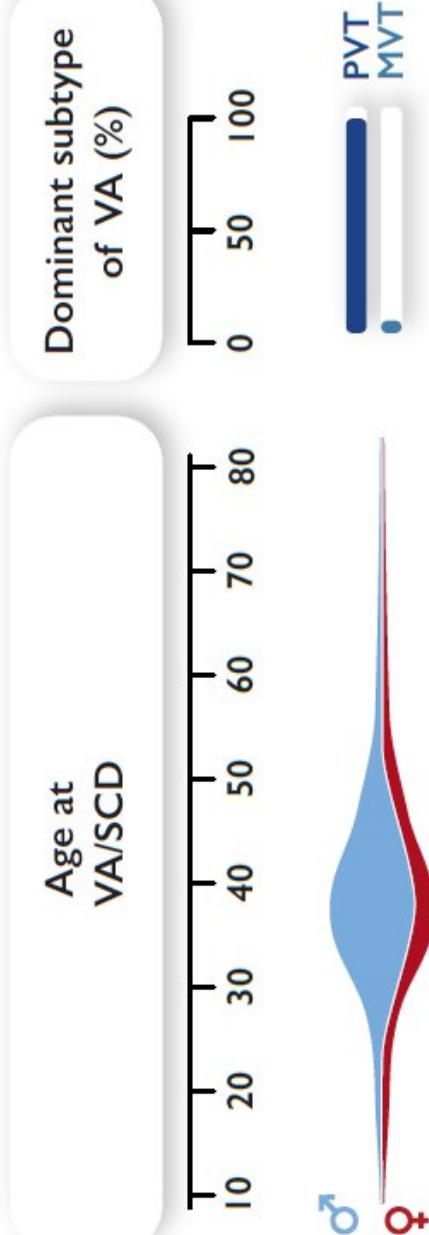
Quan XQ, et al. Medicine 2016;95:e5643.
Brugada J, et al. J Am Coll Cardiol 2018;72:1046-59.

Sindrome di Brugada: clinica

Genetic risks and triggers
for VA/SCD

Age at
VA/SCD

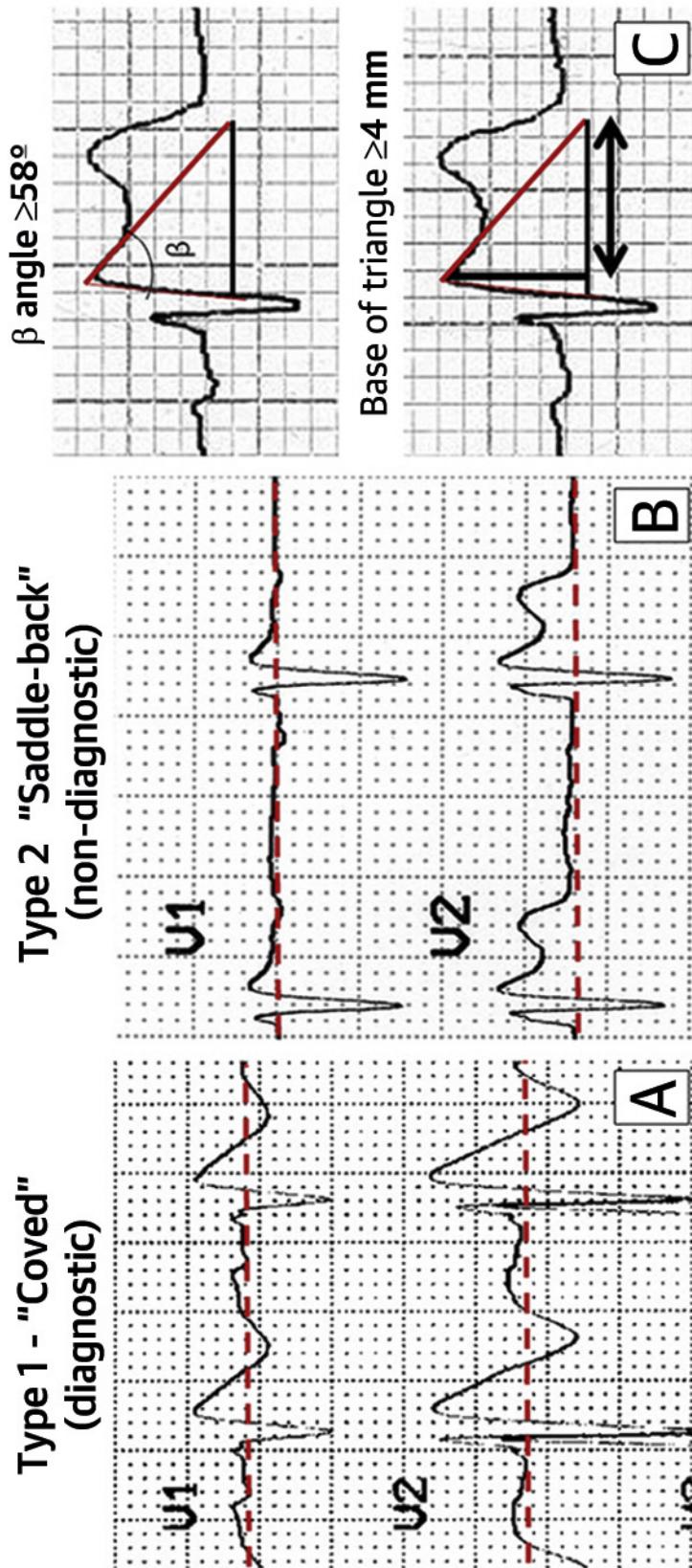
Dominant subtype
of VA (%)



2022 ESC guidelines on ventricular arrhythmias.



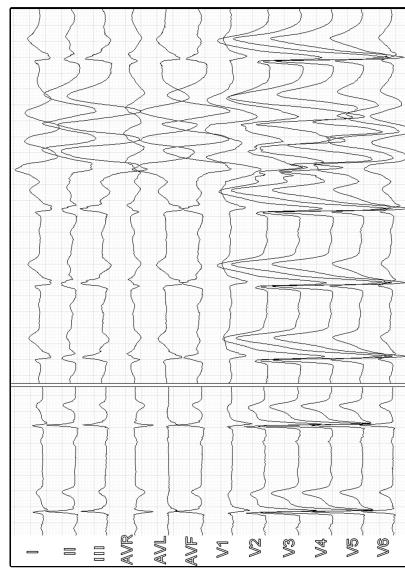
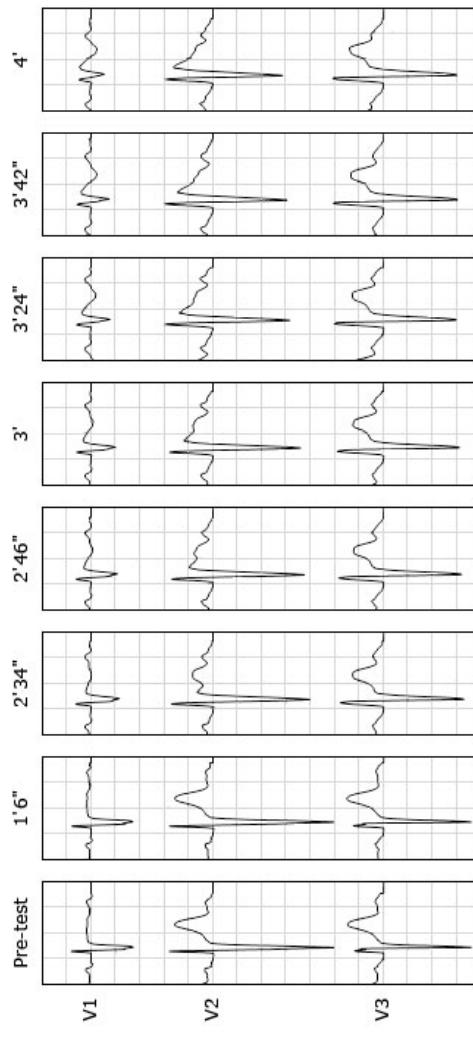
Sindrome di Brugada: patterns ECG



Brugada J, et al. J Am Coll Cardiol 2018;72:1046–59.



Sindrome di Brugada: test farmacologici



Drug	Dosage	Route of administration
Ajmaline	1 mg/kg over 5 minutes	IV
Flecainide	2 mg/kg over 10 minutes	IV
	400 mg	PO
Procainamide	10 mg/kg over 10 minutes	IV
Pilsicainide	1 mg/kg over 10 minutes	IV

- Somministrazione e.v. di ajmalina o flecainide o procainamide in corso di monitoraggio ECG continuo
- Test positivo: comparsa di pattern tipo 1 in almeno una derivazione
- L'allargamento del QRS >130%, frequenti extrasistoli ventricolari, aritmie ventricolari complesse sono criteri di interruzione
- Il monitoraggio ECG continuo deve essere mantenuto fino a ritorno dell'ECG alla morfologia basale
- 25% di falsi negativi
- Falsi positivi

Brugada J, et al. J Am Coll Cardiol 2018;72:1046-59.
2022 ESC guidelines on ventricular arrhythmias.

Sindrome di Brugada: criteri diagnostici

Fino al 2013:

- Pattern ECG tipo 1
- +
- Manifestazioni cliniche:
 - arresto cardiaco resuscitato
 - TV polimorfa documentata
 - storia di sинcope non vasovagale
 - storia familiare di morte improvvisa giovanile (<45 anni)

Antzelevitch C, et al. Circulation 2005;111:659-70.



Sindrome di Brugada: criteri diagnostici

HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes

Silvia G. Priori, MD, PhD, (HRS Chairperson)¹, Arthur A. Wilde, MD, PhD, (EHRA Chairperson)²,
Minoru Horie, MD, PhD, (APHRS Chairperson)³, Tongkeun Cho, MD, PhD, (APHRS Chairperson)⁴,
Elijah R. Behr, MA, MBBS, MD, FRCP⁵, Charles Berul, MD, FHRS, CCS⁶, Nico Blom, MD, PhD^{7,*},
Josep Brugada, MD, PhD⁸, Chern-En Chiang, MD, PhD⁹, Heikki Huikuri, MD¹⁰, Prince Kannankeril, MD^{11,†},
Andrew Kahn, MD, FHRS¹², Antoine Lenhardt, MD¹³, Arthur Moss, MD¹⁴, Peter J. Schwartz, MD¹⁵,
Wataru Shimizu, MD, PhD¹⁶, Gordon Tomaselli, MD, FHRS^{17,†}, Cynthia Tracy, MD^{18,%}

3. Brugada Syndrome (BrS) Expert Consensus Recommendations on Brugada Syndrome Diagnosis

1. BrS is diagnosed in patients with ST-segment elevation with type 1 morphology ≥ 2 mm in ≥ 1 lead among the right precordial leads V₁, V₂, positioned in the 2nd, 3rd or 4th intercostal space occurring either spontaneously or after provocative drug test with intravenous administration of Class I antiarrhythmic drugs.
2. BrS is diagnosed in patients with type 2 or type 3 ST-segment elevation in ≥ 1 lead among the right precordial leads V₁, V₂ positioned in the 2nd, 3rd or 4th intercostal space when a provocative drug test with intravenous administration of Class I antiarrhythmic drugs induces a type I ECG morphology.

Priori SG, et al. Heart Rhythm. 2013 Dec;10(12):1932-63.



Sindrome di Brugada: criteri diagnostici

ESC European Society of Cardiology <https://doi.org/10.1093/eurheartj/ehac262>

ESC GUIDELINES

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

Developed by 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 the Association for European Paediatric and Congenital Cardiology (AEPC)

It is recommended that BrS is diagnosed in patients with no other heart disease and a spontaneous type 1 Brugada ECG pattern. [974-976](#)

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. [135,136,975,981,982](#)

BrS should be considered in patients with no other heart disease and induced type 1 Brugada pattern who have at least one of:

- 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.

BrS may be considered as a diagnosis in patients with no other heart disease who exhibit an induced type 1 Brugada ECG. [136,973,975,978,984,985](#)

Recommendations	Class ^a	Level ^b
Diagnosis		



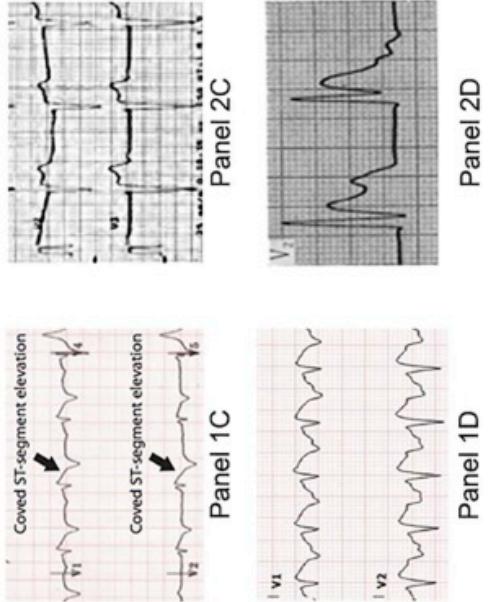
2022 ESC guidelines on ventricular arrhythmias.

Fenocopie Brugada

- Ischemia miocardica
- Embolia polmonare acuta
- Compressione meccanica del tratto di efflusso destro
- Blocco di branca destra
- Ipotrofia ventricolare sinistra
- Pectus excavatum
- Displasia aritmogena del ventricolo destro

Fattori modulanti:

- Bradicardia e ipertono vagale
- Bloccanti dei canali del Na
- Propofol
- Antidepressivi triciclici
- Fluoxetina
- Litio
- Trifluoperazina
- Antistaminimi
- Cocaína



Brugada J, et al. J Am Coll Cardiol 2018;72:1046–59.



Sindrome di Brugada: criteri diagnostici

Recommendations	Class ^a	Level ^b
Diagnosis		
It is recommended that BrS is diagnosed in patients with no other heart disease and a spontaneous type 1 Brugada ECG pattern. ⁹⁷⁴⁻⁹⁷⁶	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. ^{135,136,975,981,982}	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
BrS may be considered as a diagnosis in patients with no other heart disease who exhibit an induced type 1 Brugada ECG. ^{136,973,975,978,984,985}	IIb	C

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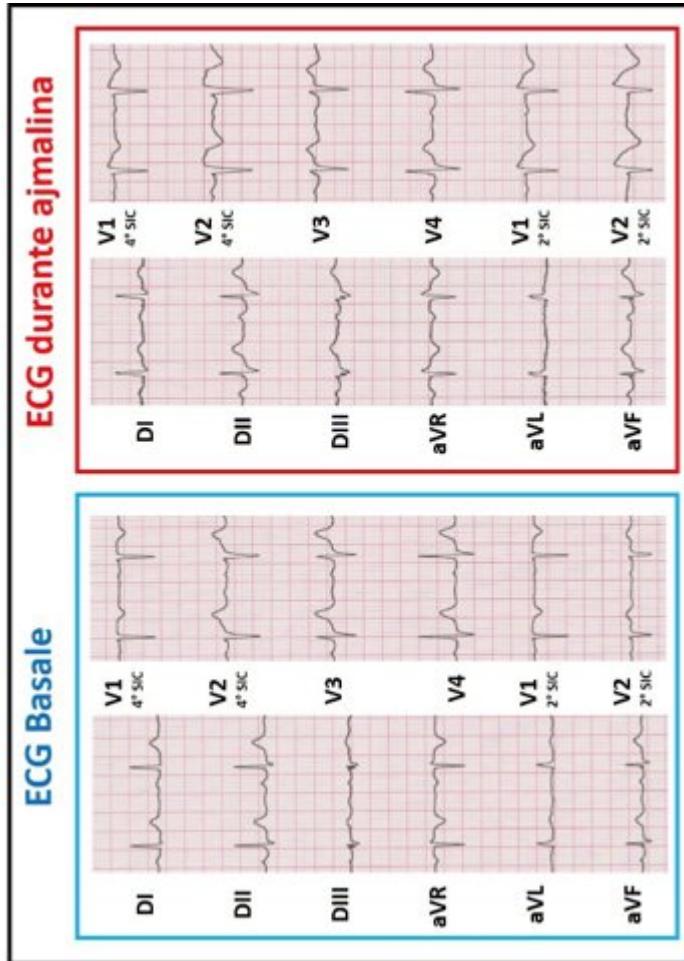
ESC European Society of Cardiology (<https://doi.org/10.1093/eurheartj/ehac262>)

ESC GUIDELINES



2022 ESC guidelines on ventricular arrhythmias.

Bassa specificità del pattern Brugada tipo 1 farmaco-indotto



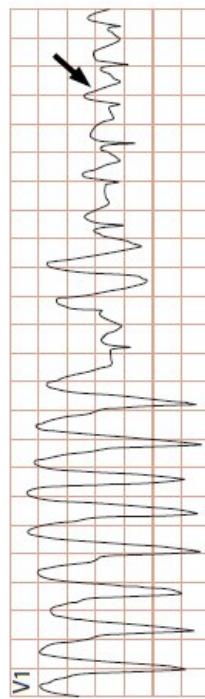
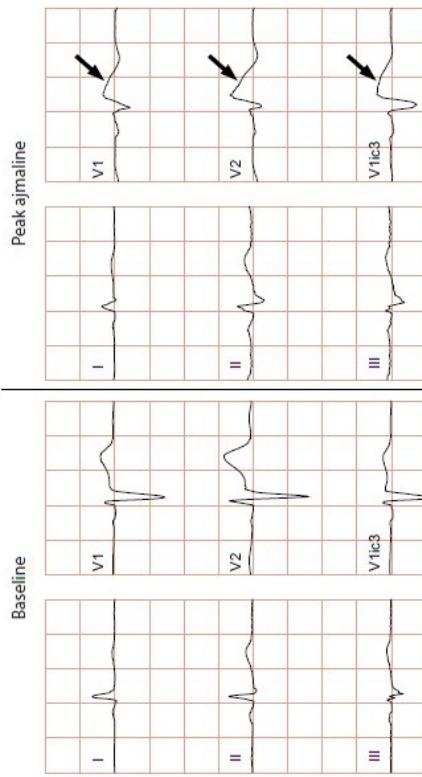
- Prevalenza nella popolazione sana: **2-4%**
- Prevalenza nei pazienti con vie accessorie AV: **16%**
- Prevalenza nei pazienti con TRNAV: **27%**

Adler A, et al. Heart Rhythm 2016;13:299–310.
Hasdemir C, et al. Pacing Clin Electrophysiol. 2018 Sep;41(9):1078-1092.
Hasdemir C, et al. Heart Rhythm. 2015 Jul;12(7):1584-94.

Sindrome di Brugada: fattori modulanti e precipitanti

- Ipertono vagale, bradicardia
- Febbre
- Farmaci e sostanze che possono indurre un pattern tipo 1 e provocare aritmie ventricolari maligne

General recommendations
<p>The following is recommended in all patients with BrS:</p> <ul style="list-style-type: none">(a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org).(b) Avoidance of cocaine, cannabis, and excessive alcohol intake.(c) Treatment of fever with antipyretic drugs.



2022 ESC guidelines on ventricular arrhythmias.
Postema PG, et al. Heart Rhythm. 2009 Sep;6(9):1335-41.
Brugada J, et al. J Am Coll Cardiol 2018;72:1046-59.



BrugadaDrugs.org

Safe drug use and the Brugada syndrome



Q

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Drugs to be avoided

Drugs preferentially avoided

Potential anti-arrhythmic drugs

Diagnostic drugs

Patient letter

- **Class I:** There is evidence and/or general agreement that a given drug is potentially arrhythmic in Brugada syndrome patients.
- **Class IIa:** There is conflicting evidence and/or divergence of opinion about the drug, but the weight of evidence/opinion is in favor of a potentially arrhythmic effect in Brugada syndrome patients.
- **Class IIb:** There is conflicting evidence and/or divergence of opinion about the drug, and the potential arrhythmic effect in Brugada syndrome patients is less well established by evidence/opinion.
- **Class III:** There is no or very little evidence and/or general agreement that a drug is potentially arrhythmic in Brugada syndrome patients. You can find a list of these drugs on this page.



Sindrome di Brugada: quali farmaci evitare

Table 1 Drugs to be avoided by Brugada syndrome patients

Drug category	Drug (generic)	Recommendation
Antiarrhythmic drugs	Ajmaline ²⁶⁻²⁹	Class I
	Flecainide ³⁰⁻³⁴	Class I
	Pilsicainide ³⁵⁻³⁸	Class I
	Procainamide ^{17,26,39,40}	Class I
	Propafenone ⁴¹⁻⁴⁵	Class IIa
	Amitriptyline ⁴⁶⁻⁴⁹	Class IIa
	Clomipramine ^{50,51}	Class IIa
	Desipramine ⁵²⁻⁵⁵	Class IIa
	Lithium ^{52,56}	Class IIa
	Loxapine ^{47,57}	Class IIa
Anesthetic drugs	Nortriptyline ^{55,58,59}	Class III
	Trifluoperazine ^{47,60}	Class IIa
	Bupivacaine ⁶¹⁻⁶⁴	Class IIa
	Propofol ^{62,65-67}	Class IIb
	Acetylcholine ^{17,68,69}	Class IIa
	Alcohol (toxicity) ^{47,70,71}	Class IIb
	Cocaine ⁷²⁻⁷⁵	Class IIa
Other substances	Ergonovine ^{68,76}	Class IIb

Table 2 Drugs preferably avoided by Brugada syndrome patients

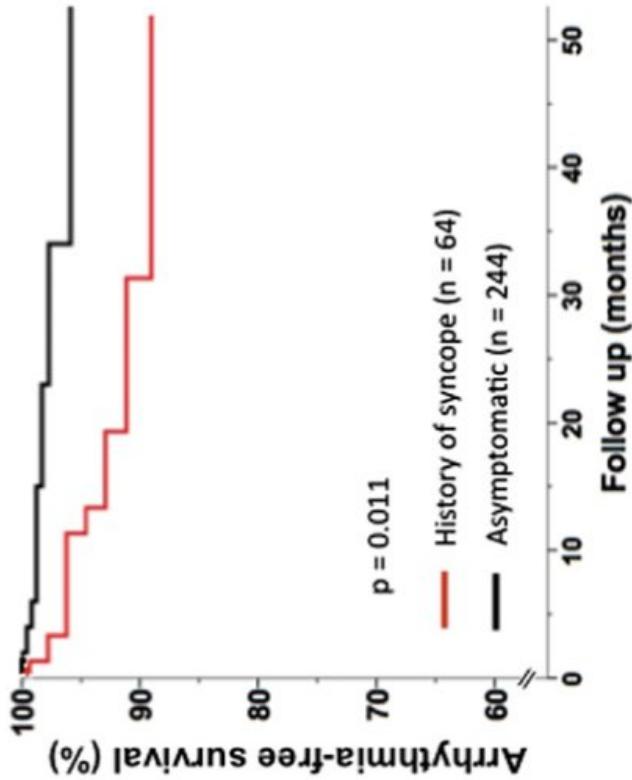
Drug category	Drug (generic)	Recommendation
Antiarrhythmic drugs	Antiarrhythmic drugs	
	Amiodarone ⁷⁷⁻⁷⁹	Class IIb
	Cibenzoline ⁸⁰⁻⁸²	Class IIb
	Disopyramide ^{14,17,83-85}	Class IIb
	Lidocaine ^{17,86*}	Class IIb
	Propranolol ^{17,18,70,87,88}	Class IIb
	Verapamil ^{17,89,90}	Class IIb
	Carbamazepine ^{91,92}	Class IIb
	Cyamemazine ^{47,93}	Class IIb
	Doxepin ^{48,94}	Class IIb
Psychotropic drugs	Fluoxetine ^{47,51}	Class IIb
	Imipramine ⁹⁵	Class IIb
	Maprotiline ^{46,96}	Class IIb
	Perphenazine ^{46,97}	Class IIb
	Phentytoin ^{98,99}	Class IIb
	Thioridazine ¹⁰⁰	Class IIb
	Diltiazem ^{1,101-103}	Class III
Antianginal drugs	Nicorandil ^{1,104}	Class III
	Nifedipine ^{1,105}	Class III
	Nitroglycerine ^{1,106,107}	Class III
	Sorbidnitrate ^{1,89,108}	Class III
	Dimenhydrinate ¹⁰⁹⁻¹¹¹	Class IIb
Other substances	Edrophonium ^{17,18}	Class IIb
	Indapamide ¹¹²	Class IIb



Postema PG, et al. Heart Rhythm.
2009 Sep;6(9):1335-41.



Impatto prognostico della sincope



- Rischio di eventi aritmici nei pazienti asintomatici:
5%^{1,2}
- La sincope inspiegata aumenta
il rischio di eventi di 4 volte³
- **1/3 dei pazienti con S. di Brugada presenta sincope**⁴

¹⁾ Sieira J, et al. Arrhythm Electrophysiol Rev 2016;5:164–169.

²⁾ Nishizaki M, et al. Circ J 2010;74:2464–2473.

³⁾ Priori SG, et al. J Am Coll Cardiol 2012;59:37–45.

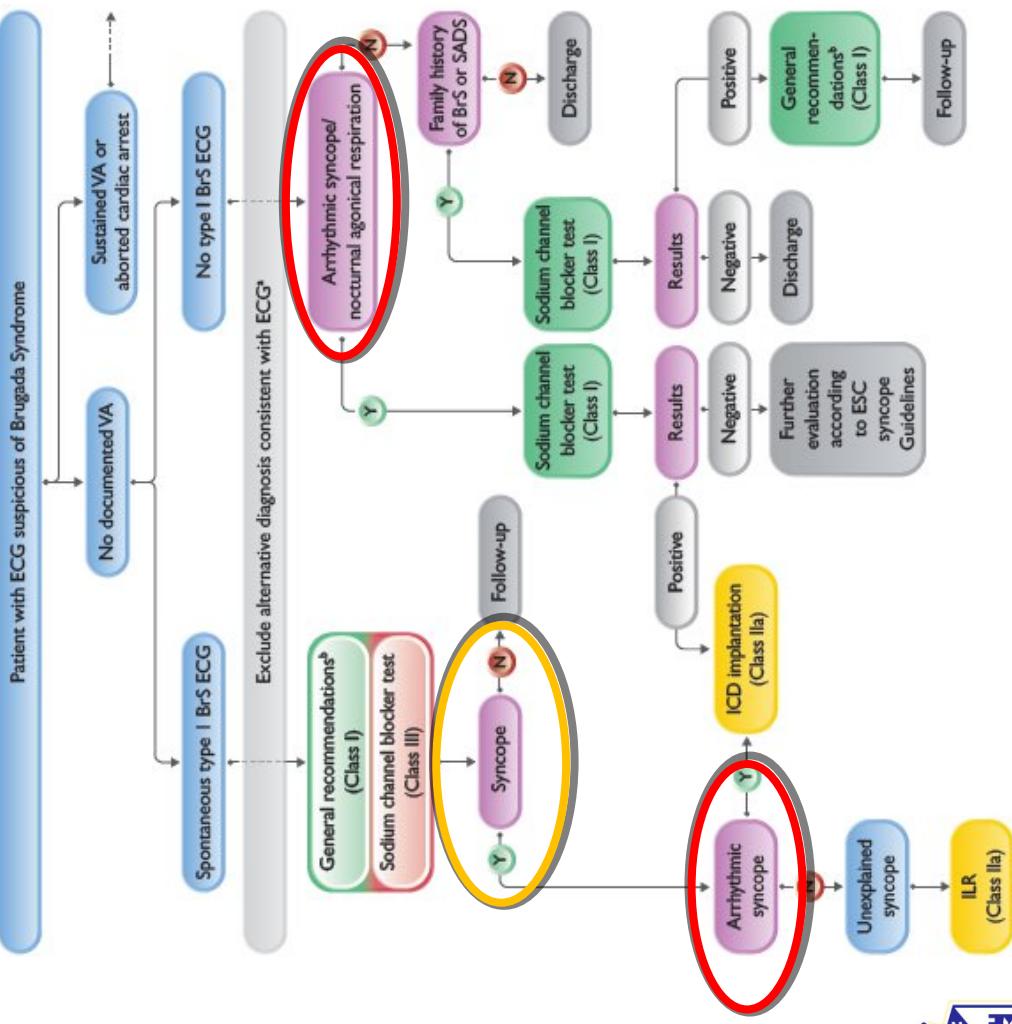
⁴⁾ Mascia G et al. Europace 2021;23:996–1002.



La sincope nella stratificazione del rischio del paziente con Brugada

“Sincope aritmica”

...fattori scatenanti, prodromi, sintomi di accompagnamento...

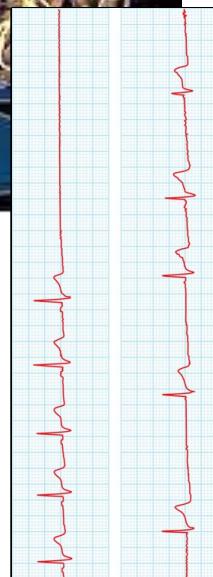


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Sincope Vasovagale nel paziente con Brugada

- Il 35-40% dei pazienti con SB ha una risposta positiva al Tilt Test, il significato prognostico di tale suscettibilità vagale è sconosciuto^{1,2}
- Una disfunzione autonomica cardiaca è presente nel 46% dei pazienti con pattern Brugada tipo 1 ed è un marker di aritmie ventricolari³
- Nei pazienti con SB vi è un riduzione segmentale dell'uptake di norepinefrina a livello della parete inferiore e settale del ventricolo sinistro⁴



1) Yokokawa M et al. J Cardiovasc Electrophysiol. 2010 Feb;21(2):186-92.

2) Leitsas et al. PACE 2008;31:418-421.

3) Babaee Bigi et al. Europace 2008;10:821-824.

4) Wichter et al. Circulation. 2002;105:702-706.

Loop recorder: in quali pazienti?

Cardiology

Electrophysiology and Arrhythmia: Research Article

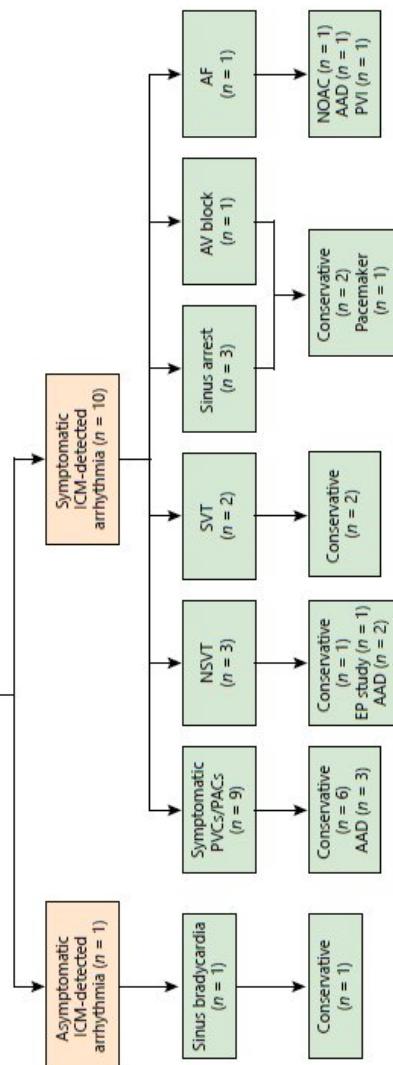
Received December 5, 2018
Accepted February 5, 2020
Published online April 22, 2020



Outcome of Insertable Cardiac Monitors in Symptomatic Patients with Brugada Syndrome at Low Risk of Sudden Cardiac Death

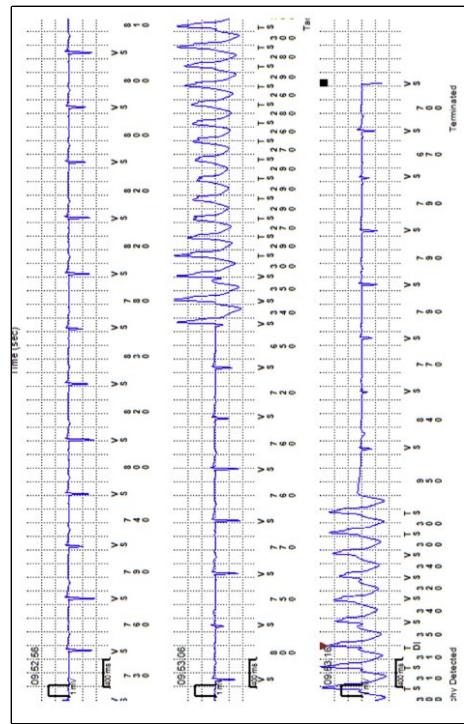
Rafi Sakhi^a Amira Assa^a Dominic A.M.J. Theuns^a Judith M.A. Verhagen^b
Tomas Szilsi-Torok^a Jolien W. Roos-Hesselink^a Sing-Chien Yap^a
^aDepartment of Cardiology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands;
^bDepartment of Clinical Genetics, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands

Durante un follow-up mediano di **32 mesi** il loop recorder ha permesso di raggiungere una **diagnosi nel 55% dei pazienti** (nel **42%** dei pazienti con sincope inspiegata)

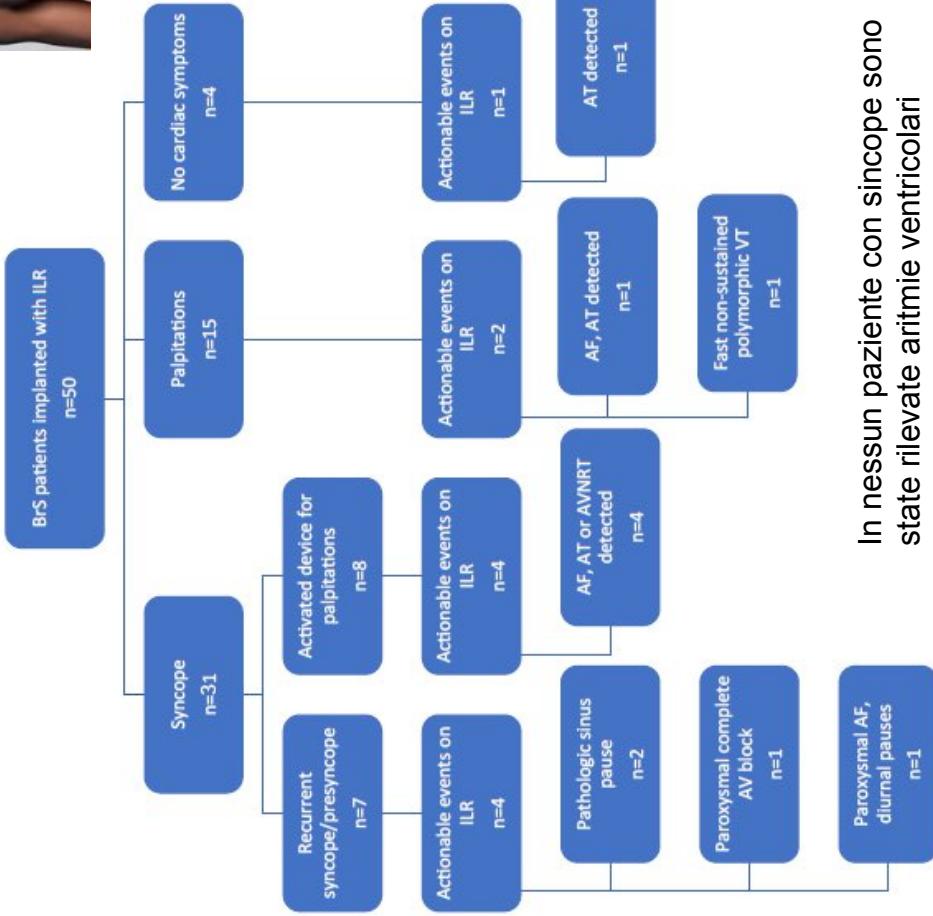


Aritmie ventricolari rilevate nel 9% dei pazienti con sincope inspiegata

Sakhi R et al. Cardiology 2020;145:413–420.



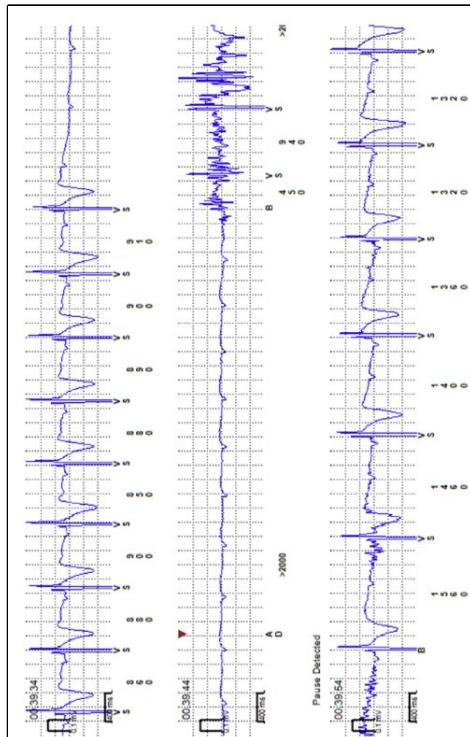
Loop recorder: in quali pazienti?



In nessun paziente con sincope sono state rilevate aritmie ventricolari



Durante un follow-up mediano di **18 mesi** il loop recorder ha permesso di raggiungere una **diagnosi nel 36% dei pazienti** (nel **48%** dei pazienti con sincope spiegata)



Scrocco C et al. Heart Rhythm 2022;19:70–78.

Role of subcutaneous implantable loop recorder for the diagnosis of arrhythmias in Brugada syndrome: A United Kingdom single-center experience

Chiara Scrocco, MD,* Yael Ben-Haim, MD,* Brian Devine, MSc,† Maite Tome-Esteban, MD, PhD,* Michael Papadakis, MBBS, MD, MRCP,* Sanjay Sharma, BSC(Hons), MD,* Peter W. Macfarlane, DSC,* Elijah R. Beir, MA, MBBS, MD*

From the *Cardiovascular Clinical Academic Group St. George's, University of London and St. George's, University Hospitals NHS Foundation Trust, London, United Kingdom, and †Institute of Health & Wellbeing, University of Glasgow, Glasgow, United Kingdom.

Loop recorder: in quali pazienti?

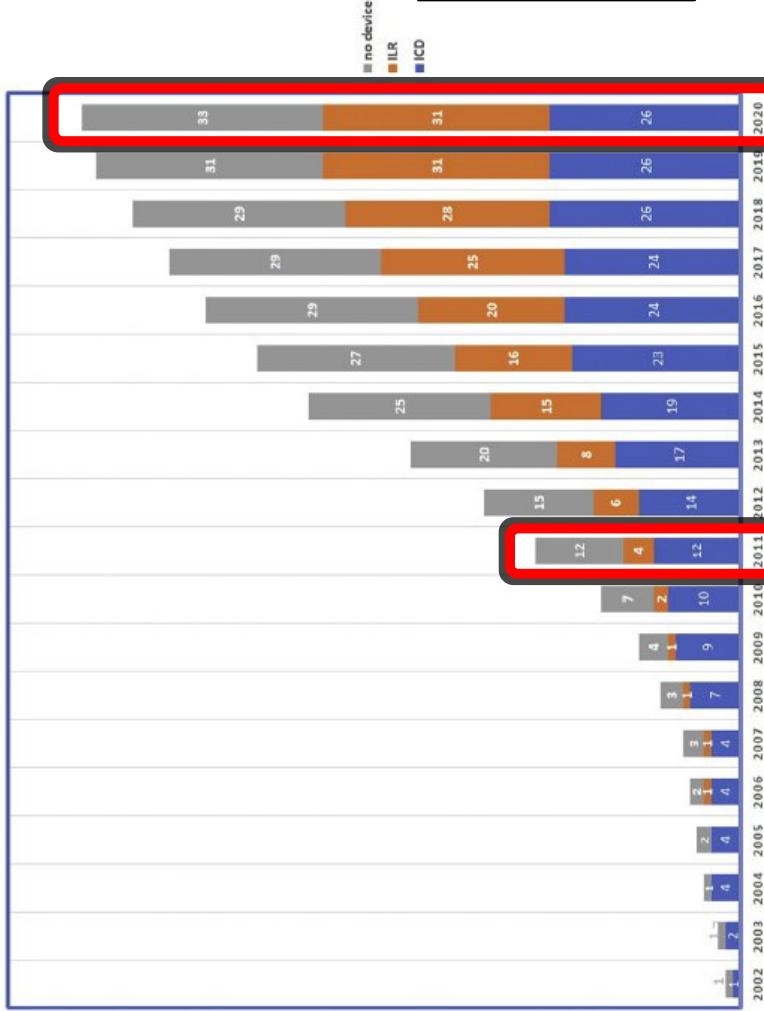
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From the *Cardiovascular Clinical Academic Group St. George's, University of London and St. George's, University Hospitals NHS Foundation Trust, London, United Kingdom, and †Institute of Health & Wellbeing, University of Glasgow, Glasgow, United Kingdom.

Conclusion

Implantable cardiac monitor devices are useful to guide diagnosis in symptomatic BrS subjects deemed at insufficient risk for SCD to require immediate ICD implantation. Recurrent syncope, including unexplained episodes in subjects without spontaneous type 1 pattern and with negative EPS, often is secondary to conduction and sinus nodal dysfunction.



2020:

ICD 29%
ILR 34%

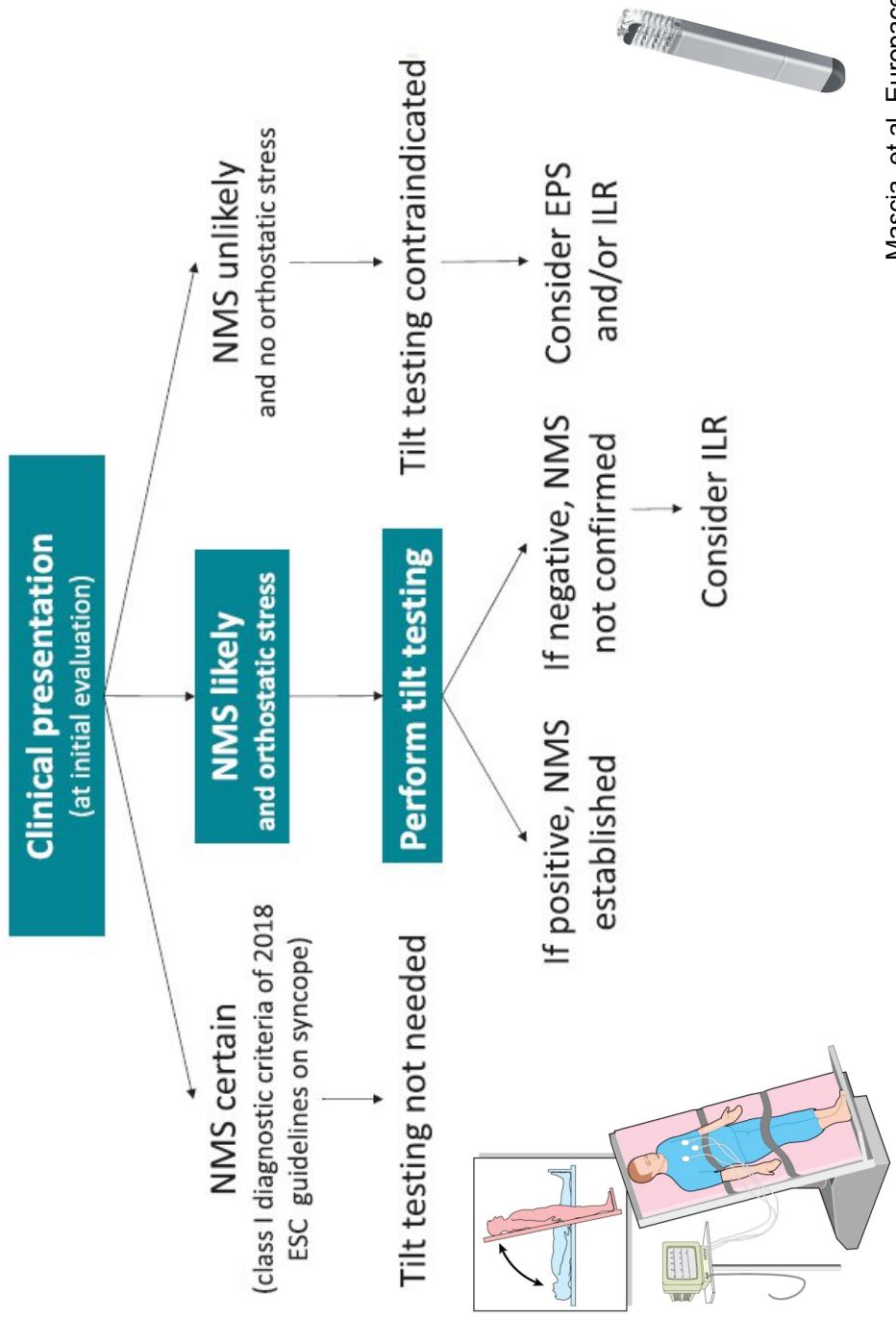
2011:

ICD 43%
ILR 14%



Scrocco C et al. Heart Rhythm 2022;19:70–78.

Gestione del paziente con Brugada e sincope



Mascia, et al. Europace 2021;23:996–1002.



Loop recorder: in quali pazienti? Le Linee Guida



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