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**1 Ottobre**  
**2022**



## SINDROME DI BRUGADA NEL 2022

# TERAPIA FARMACOLOGICA

**Carla Giustetto**

Division of Cardiology, Department of Medical Sciences,  
University of Torino  
Città della Salute e della Scienza Hospital, Torino

# How to treat Brugada patients: Guidelines

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



**2015**

Quinidine or isoproterenol should be considered in patients with Brugada syndrome to treat electrical storms.	<b>IIa</b>	<b>C</b>
<u>Quinidine</u> should be considered in patients who qualify for an ICD but present a <u>contraindication</u> or <u>refuse it</u> and in patients who require treatment for supraventricular arrhythmias.	<b>IIa</b>	<b>C</b>

# Efficacy of Quinidine in High-Risk Patients With Brugada Syndrome

Bernard Belhassen, MD; Aharon Glick, MD; Sami Viskin, MD

25 pts. 56 ± 67 month f-up

Circulation 2004;110:1731-1737

## Hydroquinidine Therapy in Brugada Syndrome

Jean-Sylvain Hermida, MD,\* Isabelle Denjoy, MD,†‡ Jérôme Clerc, MD,\* Fabrice Extramiana, MD, Geneviève Jarry, MD,\* Paul Milliez, MD,† Pascale Guicheney, PhD,‡ Stefania Di Fusco, MD,† Jean-Luc Rey, MD,\* Bruno Cauchemez, MD,† Antoine Leenhardt, MD†

35 pts. 17 month mean f-up

J Am Coll Cardiol 2004;43:1853–60)

## Excellent Long-Term Reproducibility of the Electrophysiologic Efficacy of Quinidine in Patients with Idiopathic Ventricular Fibrillation and Brugada Syndrome

BERNARD BELHASSEN, M.D., AHARON GLICK, M.D., and SAMI VISKIN, M.D.

9 pts, 15 year mean f-up

PACE 2009; 32:294–301

## Long-term efficacy of low doses of quinidine on malignant arrhythmias in Brugada syndrome with an implantable cardioverter-defibrillator: A case series and literature review

Manlio F. Márquez, MD,\* Aimé Bonny, MD,† Eduardo Hernández-Castillo, MD,\* Antonio De Sisti, MD,\* Jorge Gómez-Flores, MD,\* Santiago Nava, MD,\* Françoise Hidden-Lucet, MD,† Pedro Iturralde, MD,\*

6 pts, 4 year mean f-up

Net, MD†

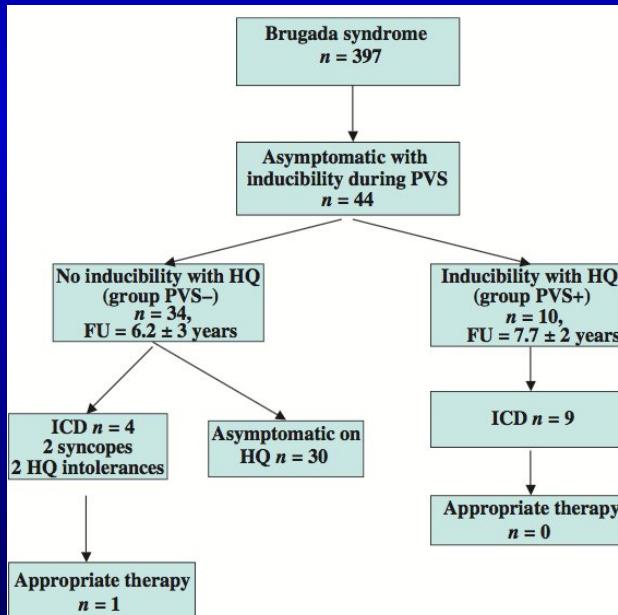
Heart Rhythm 2012;9:1995–2000

# Long-term follow-up of asymptomatic Brugada patients with inducible ventricular fibrillation under hydroquinidine

Europace 2014; 16:572–577

Abdeslam Bouzeman<sup>1</sup>, Sarah Traulle<sup>2</sup>, Anne Messali<sup>1</sup>, Fabrice Extramiana<sup>1,3</sup>,  
Isabelle Denjoy<sup>1,4</sup>, Kumar Narayanan<sup>5</sup>, Eloi Marijon<sup>5</sup>, Jean-Sylvain Hermida<sup>2</sup>,  
and Antoine Leenhardt<sup>1,3\*</sup>

## 44 asymptomatic type 1 Brugada patients with positive PVS



Overall annual rate of arrhythmic events: 1.04% (95% C.I. 0.00 – 2.21)

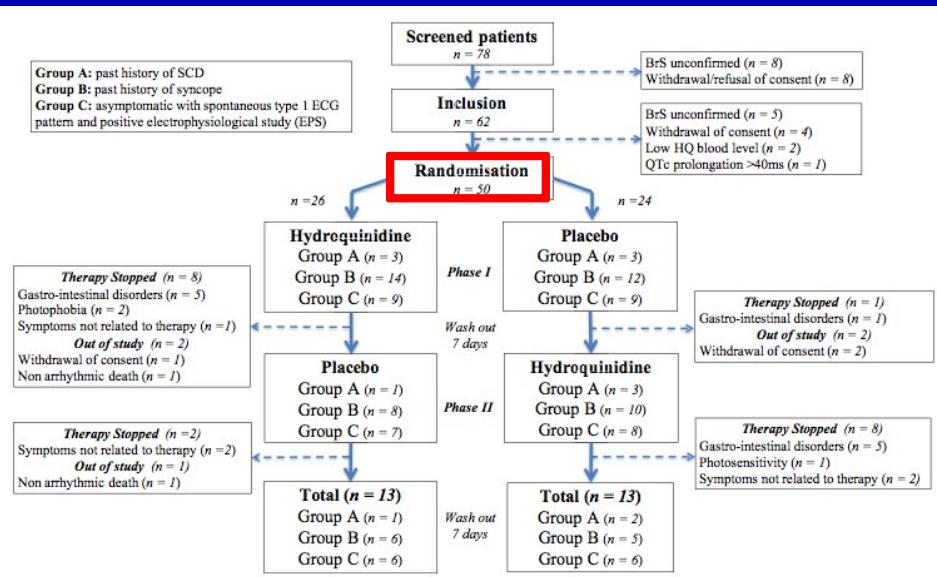
Mean follow-up 7.7+/- 2 yrs

Low rate of events in asymptomatic Brugada pts with inducible VF.  
Residual inducibility under HQ of limited value to predict events.

# The QUIDAM study: Hydroquinidine therapy for the management of Brugada syndrome patients at high arrhythmic risk

Heart Rhythm 2017; 14:1147–1154

Antoine Andorin, MD,\* Jean-Baptiste Gourraud, MD, PhD,\* Jacques Mansouriati, MD,<sup>†</sup>  
Swanny Fouchard, PhD,\* Hervé le Marec, MD, PhD,\* Philippe Maury, MD,<sup>‡</sup>  
Philippe Mabo, MD, PhD,<sup>§</sup> Jean-Sylvain Hermida, MD,<sup>¶</sup> Jean-Claude Deharo, MD,<sup>||</sup>  
Béatrice Delasalle, MS,\* Simon Esnault, MD,\* Nicolas Sadoul, MD,\*\*  
Jean-Marc Davy, MD, PhD,<sup>††</sup> Antoine Leenhardt, MD,<sup>††</sup> Didier Klug, MD,<sup>§§</sup>  
Pascal Defaye, MD,<sup>¶¶</sup> Dominique Babuty, MD, PhD,<sup>|||</sup> Frédéric Sacher, MD,\*\*\*  
Vincent Probst, MD, PhD\*



Multicenter randomized double-blind study with two 18-month crossover phases

F-up 36 m

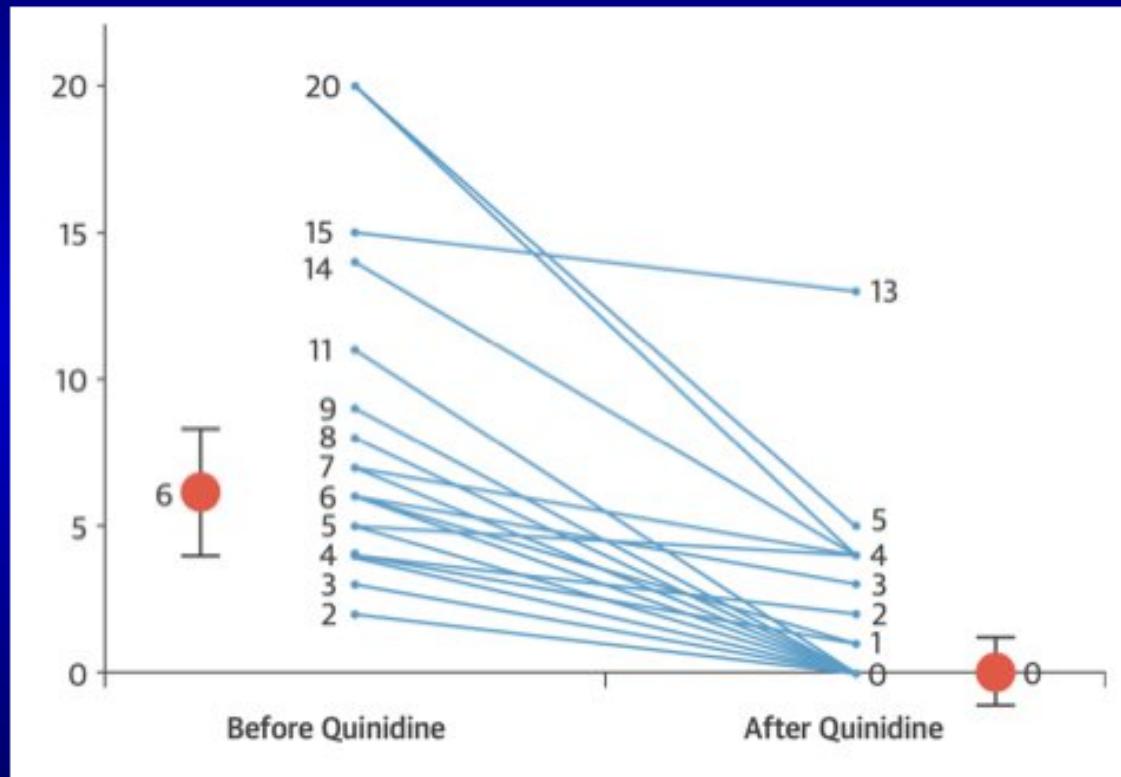
## Placebo

- € 1 ICD shock
- 1 self-terminating VF
- HQ
- € No arrhythmic events

HQ-related side effects leading to HQ discontinuation in 13 (26%) patients.

Frequent HQ-related side effects and rare arrhythmic events made it difficult to prove HQ efficacy

## Shock Reduction With Long-Term Quinidine in Patients With Brugada Syndrome and Malignant Ventricular Arrhythmia Episodes

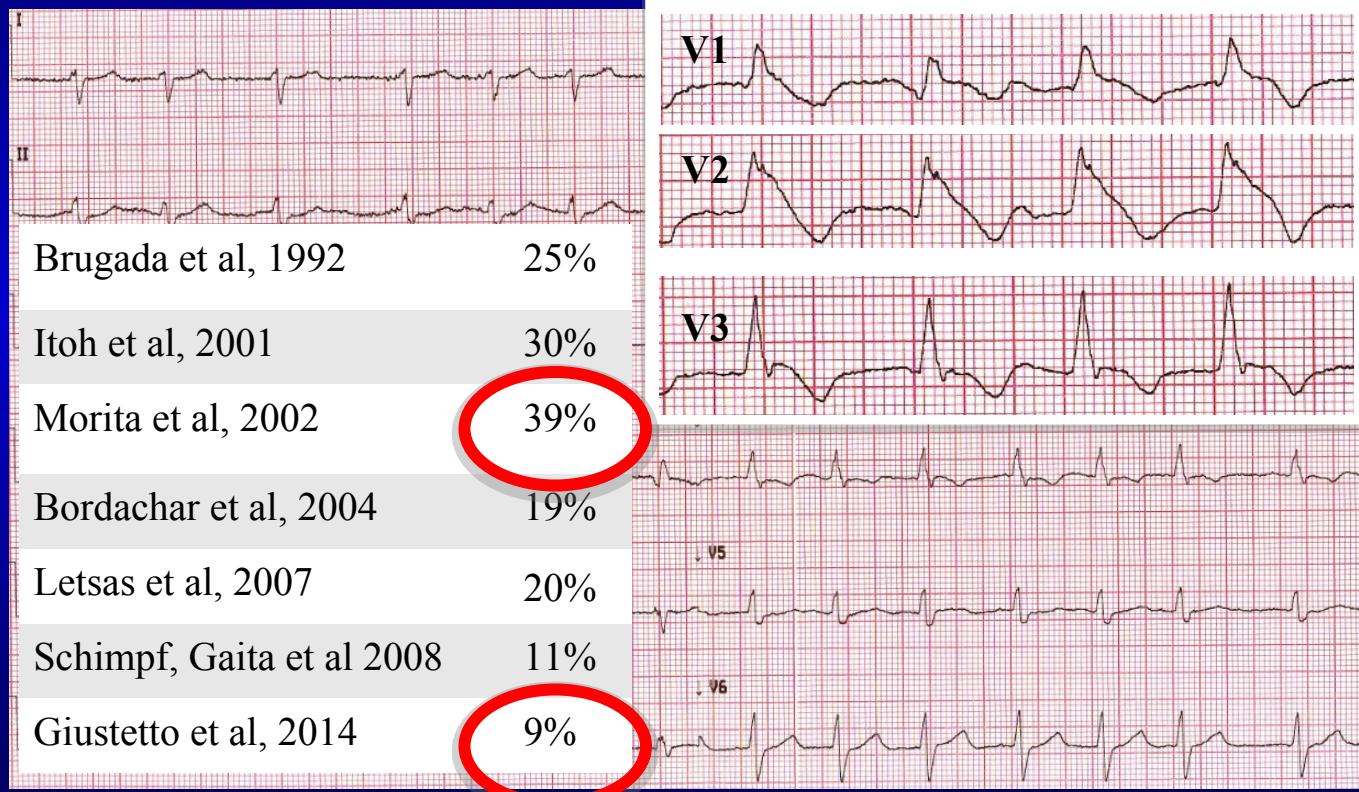


Out of 820 BrS pts with ICD, 29 (3.5%) received quinidine for recurrent VA

66% remained free of appropriate ICD shocks  
10 (34%) had recurrent shocks,  
4 after reduction/discontinuation  
of quinidine

Predictors of recurrent shock  
were discontinuation of quinidine  
and the number of shocks prior  
to quinidine initiation.

# Atrial fibrillation prevalence in subjects with Brugada ECG pattern



# Atrial fibrillation in a large population with Brugada electrocardiographic pattern: Prevalence, management, and correlation with prognosis

C. Giustetto, N. Cerrato, E. Gribaudo, C. Scrocco, D. Castagno, E. Richiardi, D. Giachino, F. Bianchi, L. Barbonaglia, A. Ferraro, M. Scaglione, R. Riccardi and F. Gaita.

*Heart Rhythm 2014; 11:259-65*



AF/AfI documented after  
diagnosis of Brugada



- ✓ younger
- ✓ spontaneous type 1 pattern
- ✓ aSD/syncope at diagnosis
- ✓ normal atrial dimensions
- ✓ ventricular arrhythmias at f-up

Pts with Brugada ECG unmasked by  
Class IC antiarrhythmic therapy given  
for AF/AfI



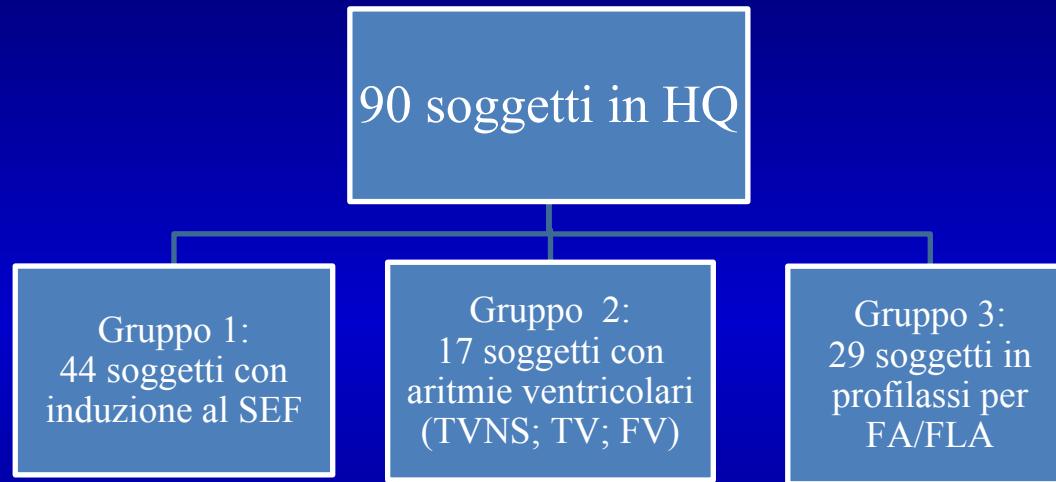
- ✓ higher mean age
- ✓ never spontaneous type 1 pattern
- ✓ asymptomatic
- ✓ enlarged left atrium
- ✓ NO ventricular arrhythmias at f-up

The genesis of AF/AfI is linked to  
ionic channel dysfunction

AF/AfI is linked to left atrial  
enlargement

# Registro Brugada della Regione Piemonte

1214 pts from 2001 to 2021



	Gruppo 1	Gruppo 2	Gruppo 3
<b>Età alla diagnosi</b>	$42 \pm 9$	$54 \pm 15$	$45 \pm 17$
<b>Sesso (M)</b>	88.6%	82.4%	65.5%
<b>Follow-up (mesi)</b>	84 (IQR 69 - 101)	100 (IQR 58 - 113)	81 (IQR 56 - 101)

Gruppo 1:

44 soggetti con SEF positivo per induzione di aritmie ventricolari

	pre HQ	In HQ	p value
Induzione al SEF	100%	4,7%	p<0.0001

## Gruppo 2:

17 soggetti con aritmie ventricolari spontanee (FV, TV, TVNS), 71% con ICD o loop recorder

	Pre HQ	In HQ	p value
Sincopi aritmiche	69%	0%	p=0.023
Sincopi vagali	56%	25%	p=0.023
Aritmie ventricolari	100%	13%	p=0.0005
Shock ICD	57%	0%	p=0.008
TAE/FA/FLA	38%	0%	p=0.031

## Gruppo 3: 29 soggetti in profilassi con HQ per FA/FLA

	Pre HQ	In HQ	p value
Cardiopalmo	83,9%	27,6%	p<0.0001
FA/FLA	100%	6,4%	p<0.0001

## Idrochinidina:

Dose media (g/die) 545,7 +/- 152,7

Idrochinidinemia 0,820 +/- 0,360

(mcg/ml) 0,820 +/- 0,360

QTc in V5 (ms) 427,73 +/- 38,288

Effetti collaterali 28,6%  
31,9%

Sospensione terapia 27,7%  
30,0%

## Idrochinidina:

Dose media (g/die)  $545,7^{+/-152,7}$  145

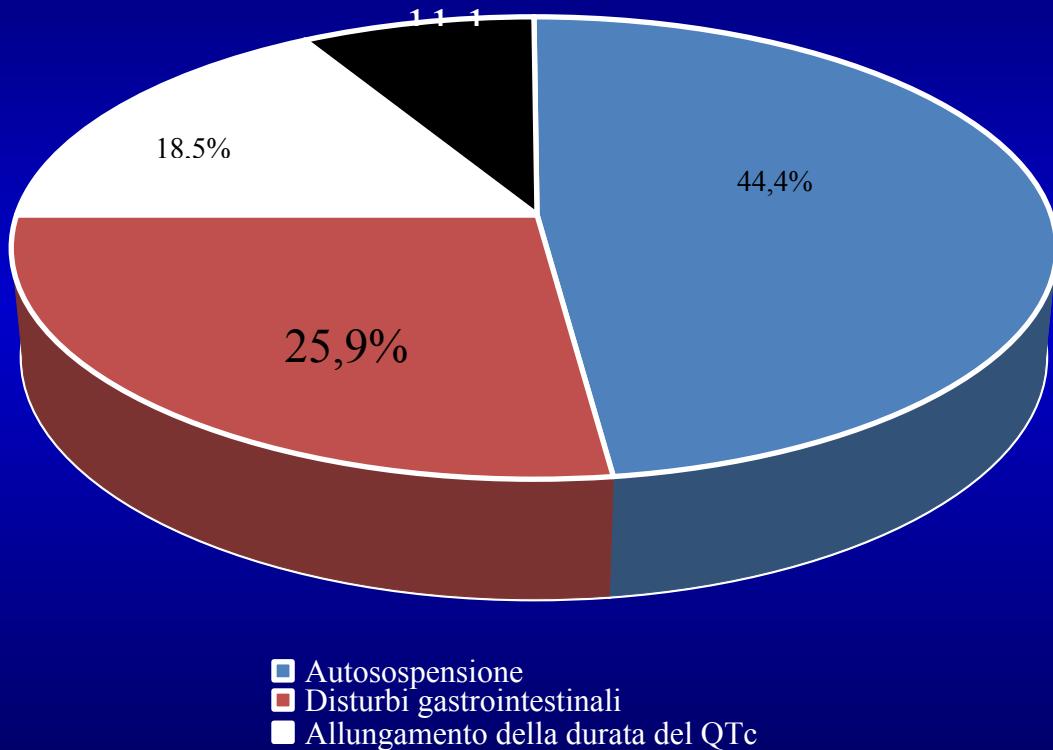
Idrochinidinemia (mcg/ml)  $0,820^{+/-0,360}$  0,360

QTc in V5 (ms)  $427,73^{+/-38,288}$  38

Effetti collaterali  $31,9\%$   


Sospensione terapia  $27,8\%$   


# Cause di sospensione dell'Idrochinidina:



## **CONCLUSIONI**

- L'Idrochinidina è altamente efficace nella riduzione dell'inducibilità di aritmie ventricolari allo studio elettrofisiologico (95%)
- Ha un'efficacia superiore all'85% nella prevenzione di eventi ventricolari spontanei
- E' altrettanto efficace nella profilassi della fibrillazione atriale/flutter in pazienti con pattern Brugada, in cui rappresenta il farmaco di scelta
- Complessivamente si è dimostrata ben tollerata ed efficace anche a lungo termine

# Brugada Syndrome: Treatment

## How we treat Brugada patients

