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ISSN: 2329-9126

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June 2014



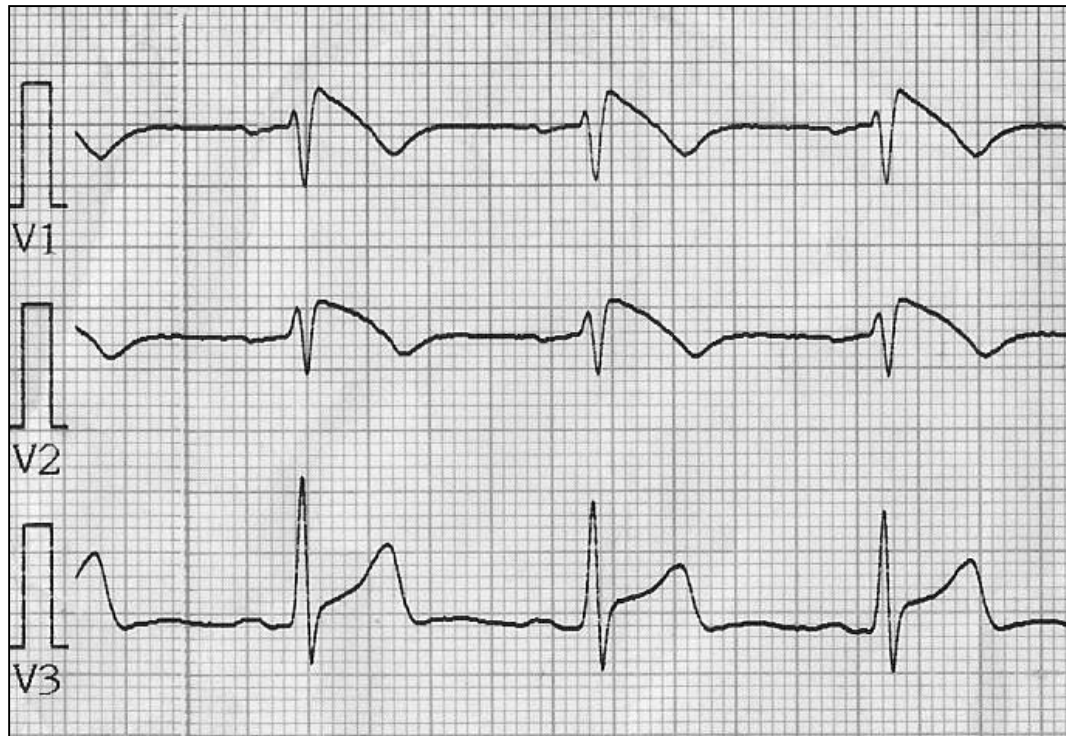


Journal of General Practice-Open Access



ISSN: 2329-9126

Brugada Phenocopy: Update 2014

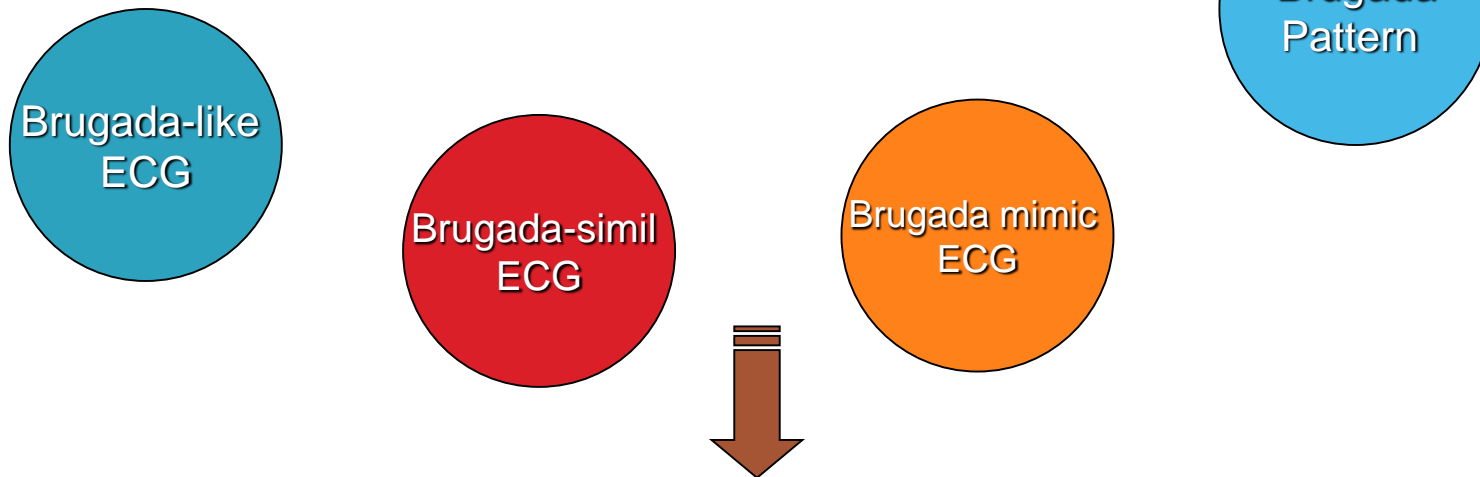




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Phenocopy: Definition

“an environmental condition that imitates (copies) one produced by a gene”



BRUGADA PHENOCOPY



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Brugada Phenocopy: New Terminology and Proposed Classification

ANE 2012

Adrian Baranchuk, M.D., F.A.C.C., F.R.C.P.C.,* Timothy Nguyen, B.Sc.,*
Min Hyung Ryu, B.Sc.,* Francisco Femenía, M.D.,† Wojciech Zareba, M.D., Ph.D.,‡
Arthur A.M. Wilde, M.D., Ph.D.,§ Wataru Shimizu, M.D., Ph.D.,¶
Pedro Brugada, M.D., Ph.D.,** and Andrés R. Pérez-Riera, M.D., Ph.D.††

1. Spontaneous Type-1 or type-2 ECG Brugada pattern
2. Underlying cause *justifying* the ECG abnormality
3. ECG **normalization** once the underlying cause is corrected
4. Lack of clinical features suggesting BrS (syncope/ aborted sudden death)
5. NEGATIVE Sodium channel blocker test (Fleca/Ajma/Procainamida)
6. Whenever possible NEGATIVE genetics (not mandatory!!!)
7. No surgical procedure involving the RVOT in the last 96 Hrs (**new!!!**)
8. Proper ECG filters (**new!!!**)



Why *negative genetics* is NOT a mandatory requisite?

- a) Because only 25-30% of cases true Brugada Syndrome (BrS) depict positive genetics!!!
- b) Therefore, **NEGATIVE** genetics do not rule out BrS



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READERS' COMMENTS

Brugada Phenocopy: Redefinition and Updated Classification

Anselm, Baranchuk. Am J Cardiol 2012

Updated summary of Brugada phenocopies*

Category	Number of Patients (Number of Case Reports)	Age (years), Mean (Range)	Men/Women	ECG Type	Presence of Structural Heart Disease
Metabolic conditions	14 (14)	51.9 ± 17.8 (28–89)	13/1	13 type 1, 5 type 2, 4 variable	0 yes, 14 no
Mechanical Compression	6 (5)	45.7 ± 18.5 (19–66)	3/3	6 type 1, 0 type 2, 0 variable	3 yes, 3 no
Ischemia	4 (4)	60.0 ± 6.7 (55–68)	2/2	4 type 1, 1 type 2, 1 variable	1 yes, 3 no
Myocardial and pericardial disease	8 (6)	46.2 ± 13.9 (28–72)	5/3	5 type 1, 4 type 2, 2 variable	2 yes, 6 no
ECG modulation [†]	1 (1)	55 (55)	0/1	0 type 1, 1 type 2, 0 variable	0 yes, 1 no
Miscellaneous	2 (2)	22.5 ± 0.7 (22–23)	1/1	2 type 1, 1 type 2, 1 variable	1 yes, 1 no

* Adapted from Baranchuk et al.²

[†] Updated category of Brugada phenocopy on the basis of inappropriate ECG high-pass filtering¹

García-Niebla, Bayés de Luna Am J Cardiol 2012

Updates to the classification were needed...



Brugada Phenocopy in the context of pulmonary embolism

Anselm, Baranchuk. Int J Cardiol 2013

Category

- i. Metabolic conditions
- ii. Mechanical compression
- iii. Ischemia & pulmonary embolism^a
- iv. Myocardial & pericardial disease
- v. ECG modulation
- vi. Miscellaneous

^a Updated category of Brugada Phenocopy to include pulmonary embolism.

Let's avoid confusion...



Useful definitions to remember

Brugada Syndrome

Types 1 & 2 ECG pattern,
Symptoms,
Aborted SD,
Family history
Sodium channel blocker
test is POSITIVE

Brugada ECG Pattern

Types 1 & 2 ECG pattern,
(defined as per 3er
Consensus, JE 2012)

Brugada Phenocopy

Spontaneous
Types 1 & 2 ECG pattern
Underlying cause
ECG resolution upon
Resolution of underlying
cause
Sodium channel blocker
test is NEGATIVE



New morphological classification 2014

1. Type-1: ECG identical to true type-1 Brugada ECG pattern
2. Type-2: ECG identical to true type-2 Brugada ECG pattern

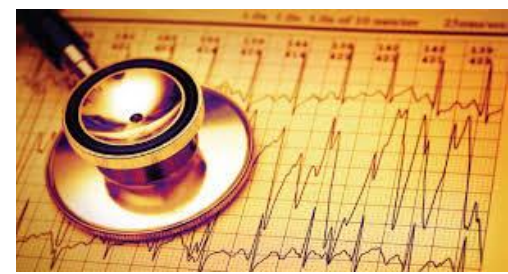
Sub-types

A: All conditions for BrP are met

B: Not all aconditions for BrP are met

C: Not all conditions are necessary (i.e. ECG modulation)

ECG Modulation)



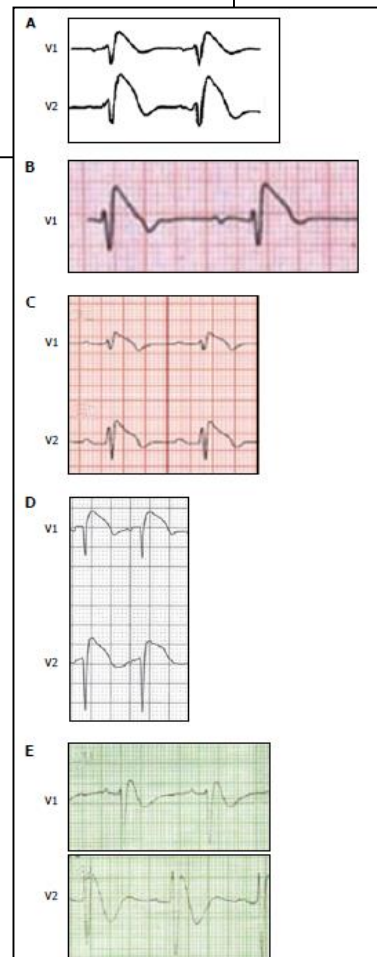
Brugada phenocopy: A new electrocardiogram phenomenon

Daniel D Anselm, Jennifer M Evans, Adrian Baranchuk

World J Cardiol 2014

Type-1 BrP

- A. True BrS ECG (covered)
- B. Acute inferior MI w/RV involvement
- C. Hyperkalemia & acidosis
- D. Acute pulmonary embolism
- E. Hypokalemia (hypokalemic periodic paralysis)





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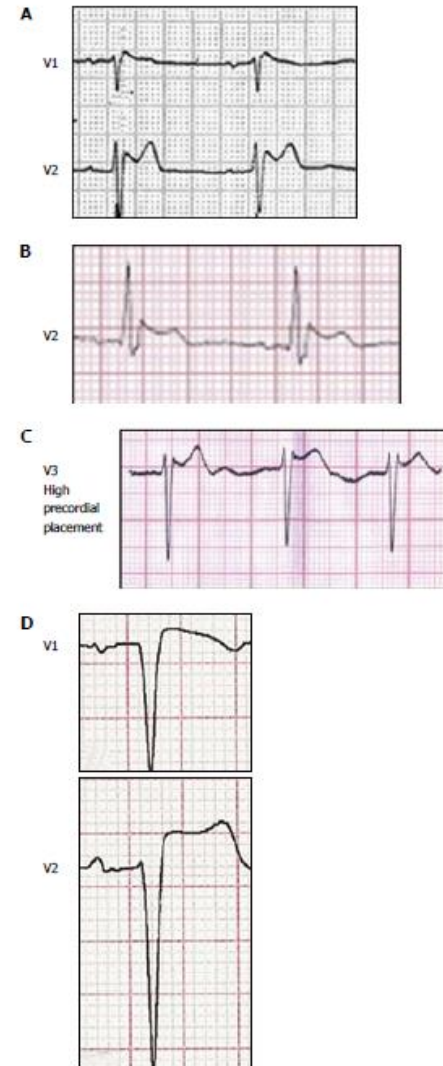
Brugada phenocopy: A new electrocardiogram phenomenon

Daniel D Anselm, Jennifer M Evans, Adrian Baranchuk

World J Cardiol 2014

Type-2 BrP

- A. True BrS ECG (saddleback)
- B. Electrocutation
- C. Pectus excavatum
- D. ECG w/high pass filter





Proof of Concept: Steps to validate a new ECG Phenomenon

1. Visibility
2. Physiopathology speculation
3. Clinical Reproducibility
4. Experimental model

A red double-line oval encircles the text "Experimental model" in the list. A red double-line arrow originates from the bottom right of this oval and points downwards towards the text "We are at this point".

We are at this point

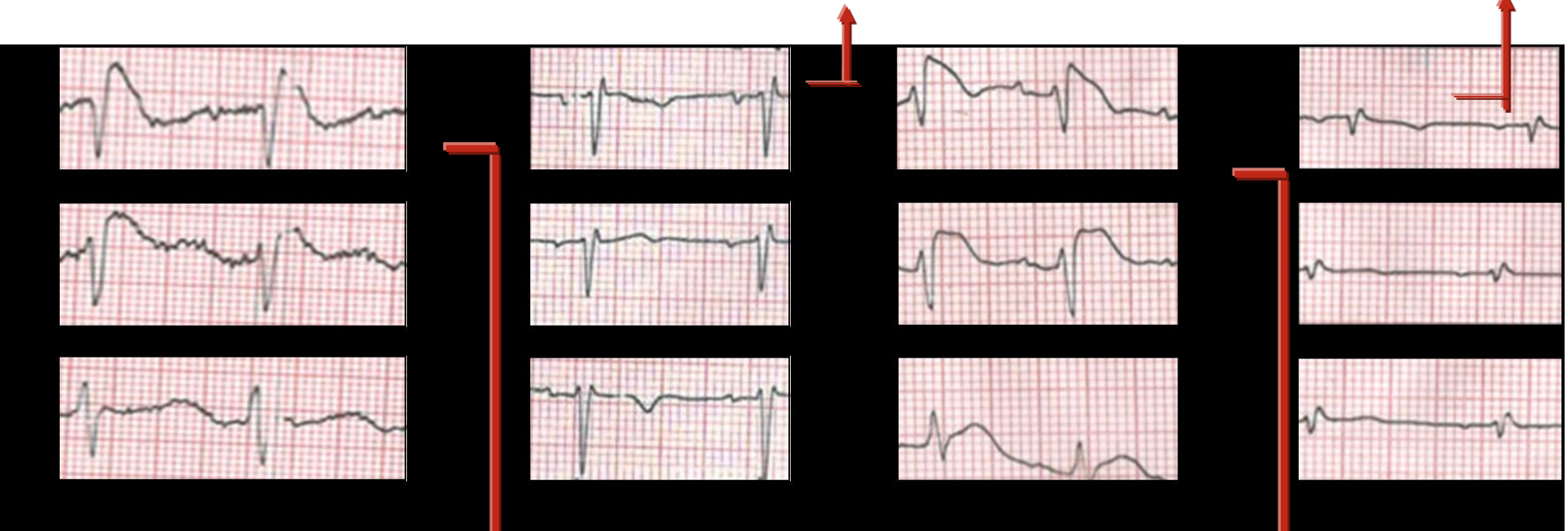


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Proof of Concept: Clinical reproducibility

K= normal

K= normal



ANE 2014

K= 1.5meq/l

K= 2.5meq/l

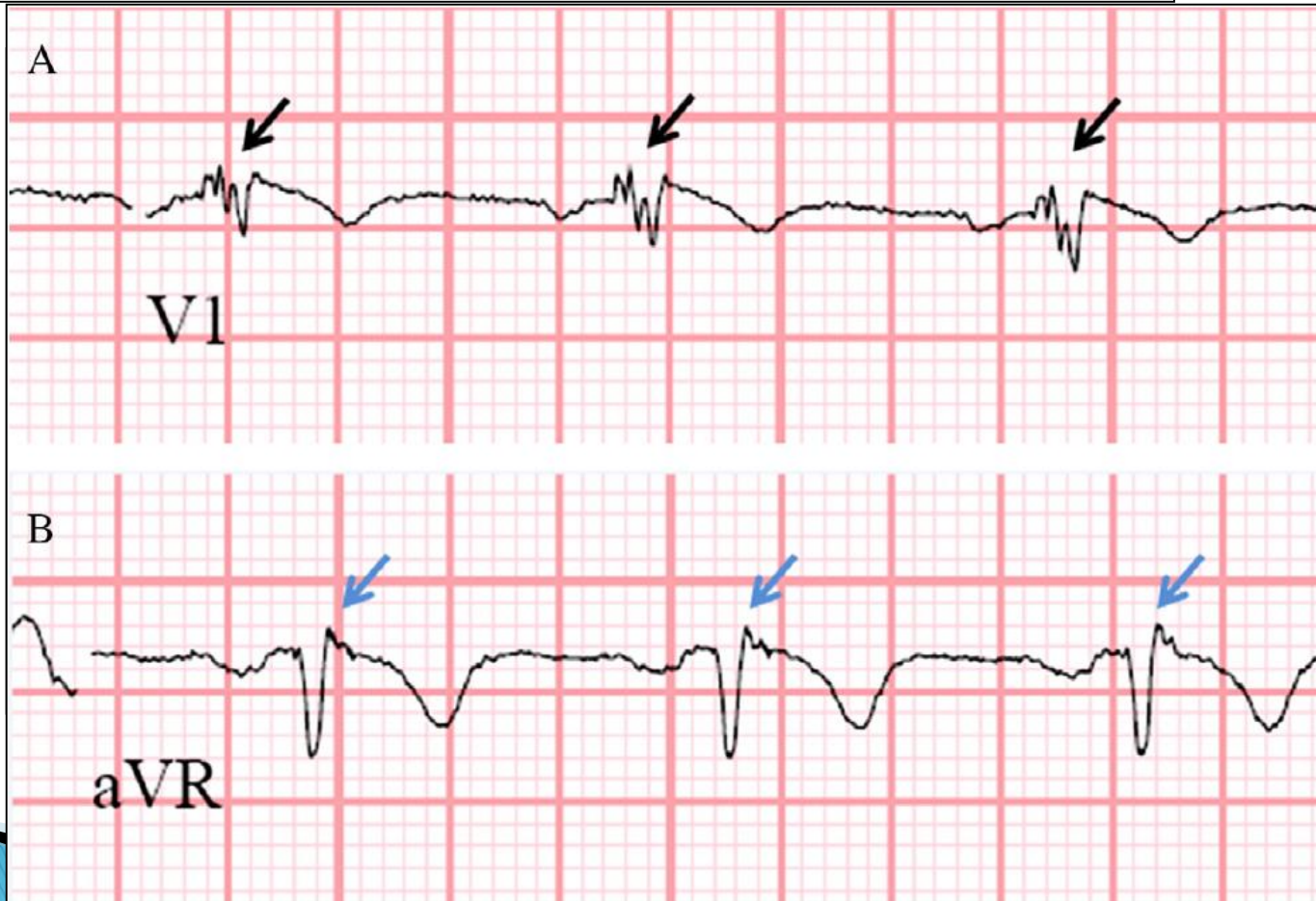
Brugada Phenocopy Clinical Reproducibility Demonstrated by Recurrent Hypokalemia



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Electrocution-induced Brugada phenocopy

Jing Gennie Wang, William F. McIntyre, Waitak Kong, Adrian Baranchuk

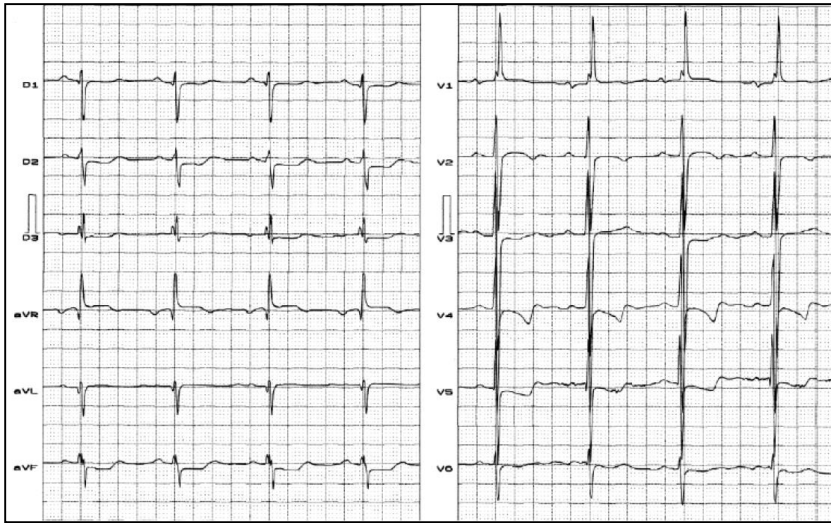


This case shows 2 possible dangerous signs: 1. fQRS, 2. aVR sign

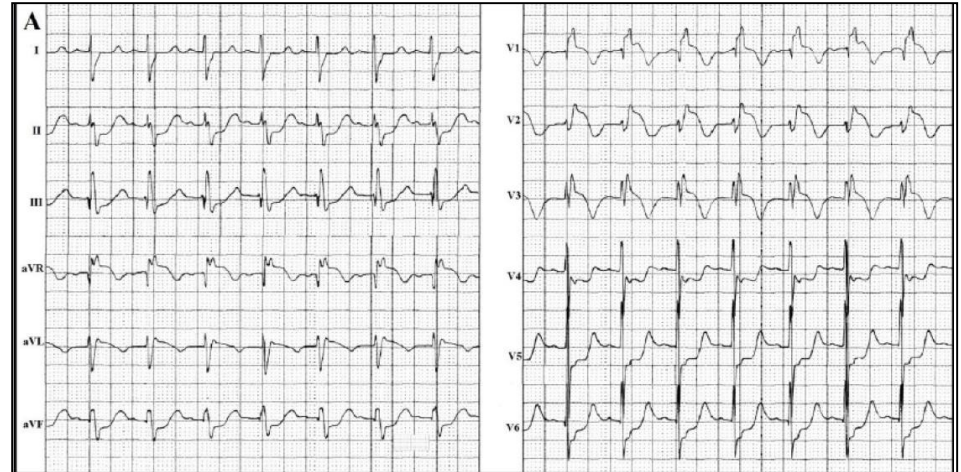
Brugada Phenocopy in a patient with surgically repaired Pentalogy of Fallot

Anselm, Baranchuk. RIA 2012

Pre-op ECG

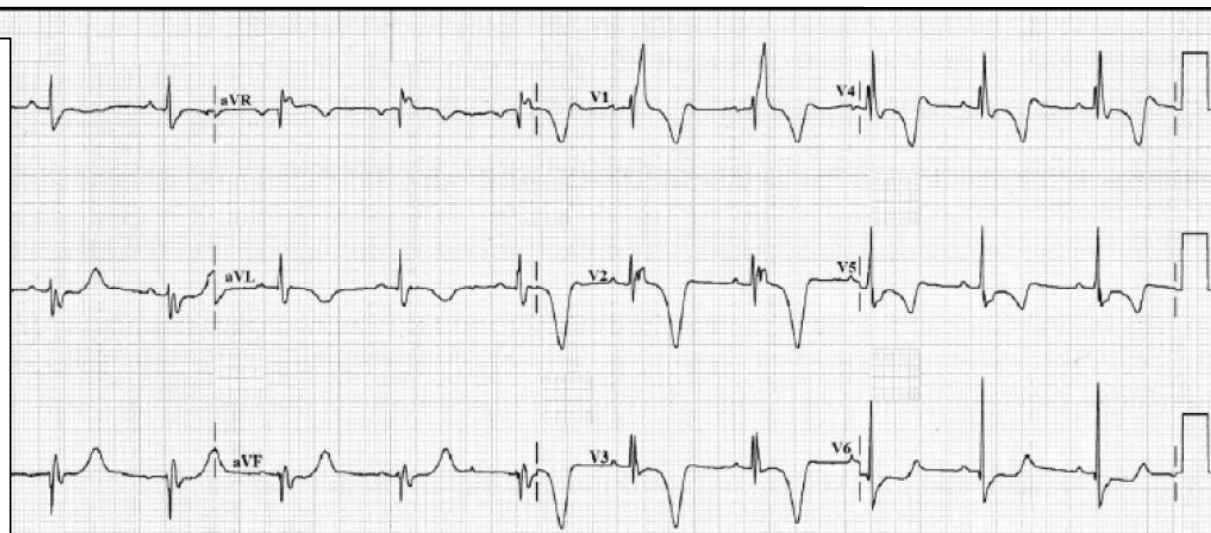


Immediate Post-op ECG



3 months post-op

Immediate post-op ECG shows Brugada Phenocopy. Three months later, ECG evolves with typical ECG changes associated with Fallot. From this case we learnt that surgical manipulation of the RVOT could produce a Brugada Phenocopy



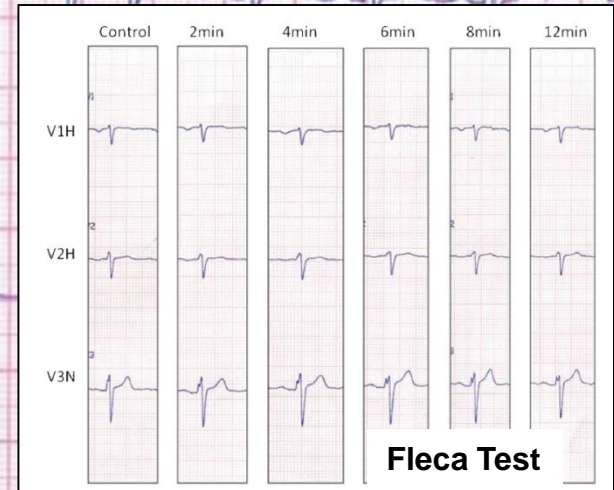
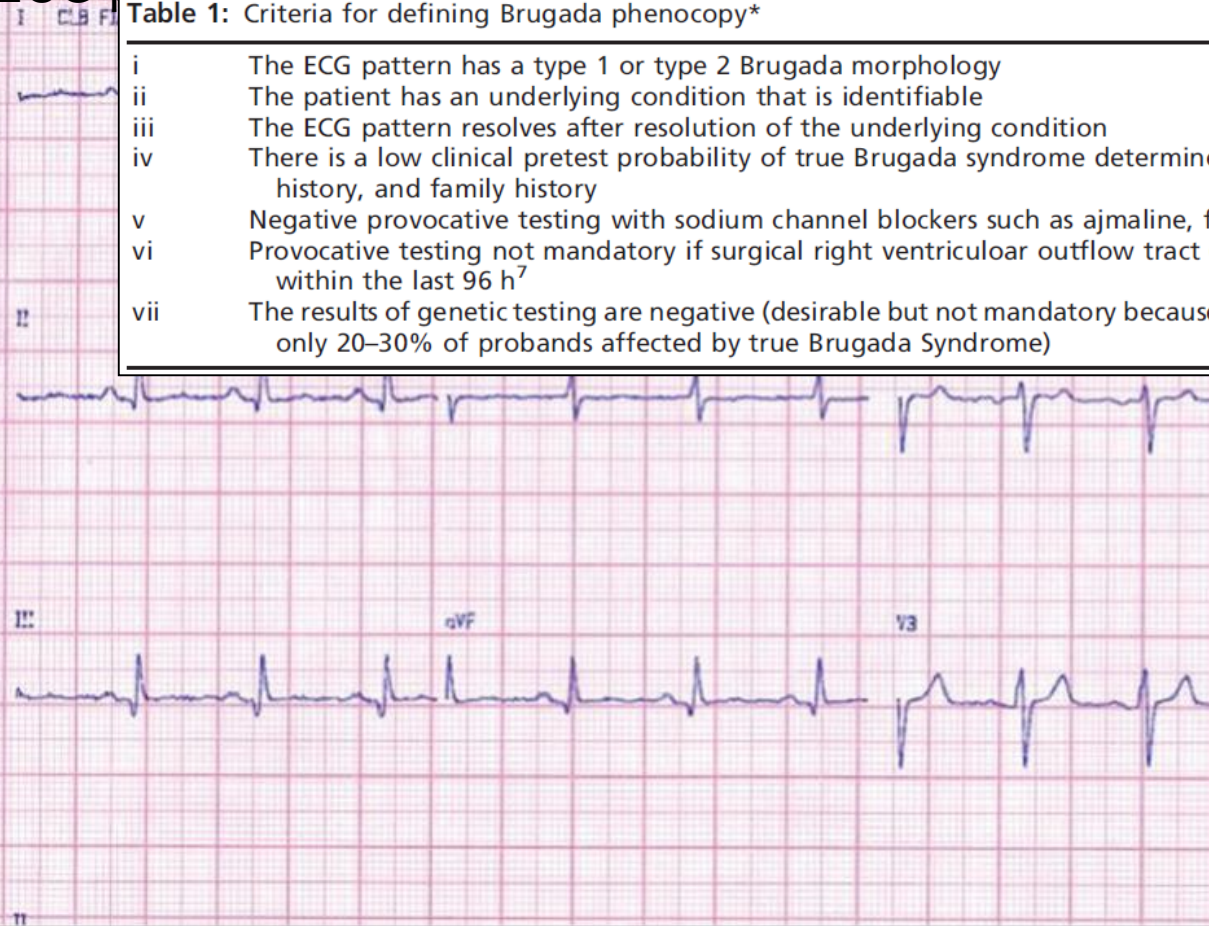
Brugada Phenocopy Induced by Acute Inferior ST-segment Elevation Myocardial Infarction with Right Ventricular Involvement

Anselm, Baranchuk. Inn Card Rhythm Manag 2013

ECG post-streptokinase

Table 1: Criteria for defining Brugada phenocopy*

- i The ECG pattern has a type 1 or type 2 Brugada morphology
- ii The patient has an underlying condition that is identifiable
- iii The ECG pattern resolves after resolution of the underlying condition
- iv There is a low clinical pretest probability of true Brugada syndrome determined by lack of symptoms, medical history, and family history
- v Negative provocative testing with sodium channel blockers such as ajmaline, flecainide, or procainamide
- vi Provocative testing not mandatory if surgical right ventriculoar outflow tract (RVOT) manipulation has occurred within the last 96 h⁷
- vii The results of genetic testing are negative (desirable but not mandatory because the SCN5A mutation is identified in only 20–30% of probands affected by true Brugada Syndrome)



Fleca Test



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Clarification needed RE:

Brugada Phenocopy & ischemia vs. Brugada Syndrome & ischemia

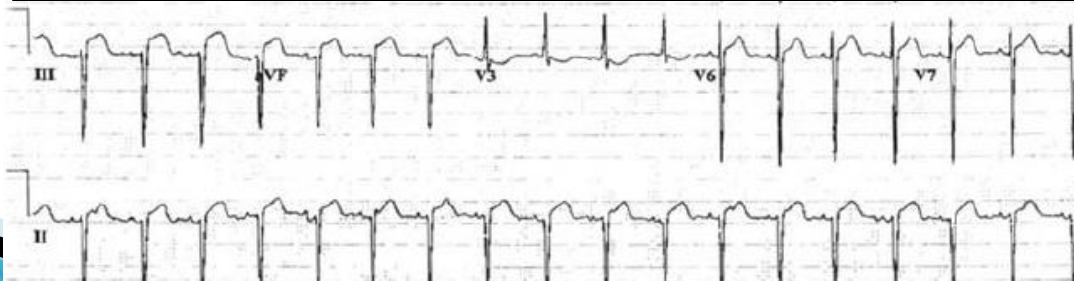
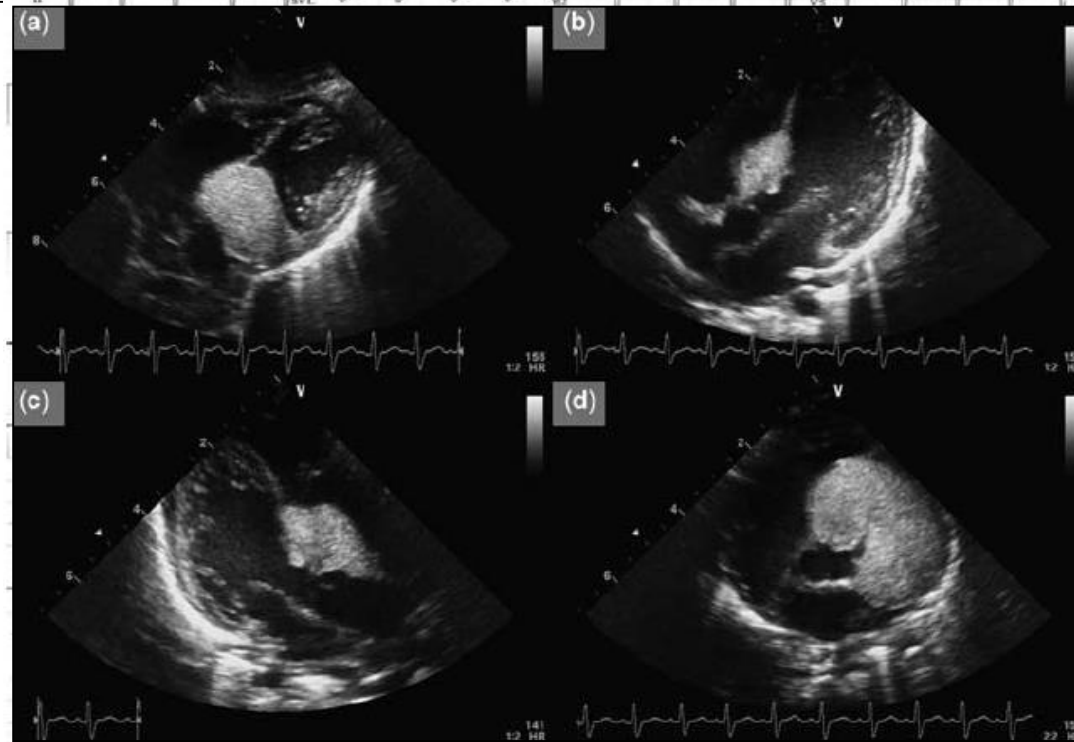
- Prior case is a Brugada Phenocopy, given a **NEGATIVE** FLECA test.
 - **WARNING!**: Ischemia can “modulate” gradients between epicardium and endocardium unmasking or aggravating a true Brugada Syndrome (in such case, Fleca test would be **POSITIVE**).
- (see studies by Di Diego & Antzelevich)

Rhabdomyoma as a Brugada

Timothy Nguyen

presenting

Cardiol Young 2011



Fenocopia de Brugada: un nuevo concepto

Dres. Juan Cruz López-Diez¹, Adrian Baranchuk FACC FRCPC²

REVISTA ESPAÑOLA DE
CARDIOLOGÍA

Brugada Phenocopy emerging as a new concept
Re: Hyperkalemia Mimicking a Pattern of Brugada Syndrome.

Comentario editorial

Rev Urug Cardiol 2013; 28: 26-28

Categoría *Número de* *Edad (años)* *Hombre/Mujer* *Patrón* *Presencia de*

Possible Brugada Phenocopy Induced by Hypokalemia in a Patient with Congenital Hypokalemic Periodic Paralysis

Daniel D. Anselm¹, Natalia Rodriguez Genaro², Adrian Baranchuk¹



About Brugada Phenocopy: Brugada Phenocopy with a Flecainide Overdose: A Pharmacological Dose Effect?



Enfermedad miocárdica o pericárdica	8	46.9 ± 12.0	5/3	5 tipo 1, 4 tipo variable	2-6
Modulación electrocardiográfica				1, 1 tipo variable	0-1
Misceláneas				1, 1 tipo variable	1-1

Confirmed Brugada phenocopy in the setting of hypopituitarism





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Other authors using the term Brugada Phenocopy

- [Brugada phenocopy emerging as a new concept. Response.](#)

Recasens L, Meroño O, Bazan V, Ribas N.

Rev Esp Cardiol (Engl Ed). 2013 Sep;66(9):756. doi: 10.1016/j.rec.2013.05.003.

Epub 2013 Jul 10. No abstract available.

- ["About Brugada phenocopy": Brugada phenocopy with a flecainide overdose: a pharmacological dose effect?](#)

Chubb H, Cooklin M, Rosenthal E.

J Cardiovasc Electrophysiol. 2014 Mar;25(3):E1. doi: 10.1111/jce.12373. Epub

2014 Feb 20. No abstract available.

- [Brugada phenocopy or Brugada ECG pattern in patients characterized by early repolarization pattern and additional arrhythmogenic right ventricular cardiomyopathy.](#)

Peters S.

Int J Cardiol. 2014 Mar 1;172(1):278. doi: 10.1016/j.ijcard.2013.12.241. Epub

2014 Jan 10. No abstract available.



Future directions

1. Internatioanl registry via website ready to be launched (www.brugadaphenocopy.com)
2. Natural history paper (you maybe contacted...)
3. New electrocardiographic features to be applied to all Brugada Phenocopies (some of them may dissapear...)



Future directions

Experimental model

1. Hyperkalemic model
2. Hypokalemic model
3. RV stretch model



Conclusions & Questions

1. Brugada Phenocopies are Frequently observed
2. Proper recognition avoids decision making errors
3. Brugada ECG patterns unmasked by Sodium channel blockers are true Brugadas
4. We proved clinical reproducibility (Proof of Concept)
5. What's the natural history of this condition?
6. Is there a genetic predisposition?
7. Can we reproduce these patterns in the Lab?

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- [Journal of General Medicine: Open Access](#)
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- 2nd International Conference on Nursing & Healthcare



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