

Sudden Cardiac Death in the Young

Case presentation

January 2022

K. M., 21 y/o, male, BMI 31

Syncopal episode while driving a baggage cart at the airport

no prodrome, caused mild accident while driving his cart into a baggage conveyer belt no obvious traumatic injuries

Previous personal and medical history:

no relevant prior medical history, no cardiovascular risk factors

GI infection up until 1 day prior to syncopal event

Family history:

Negative for syncope, seizures or sudden cardiac death

K. M., 21 y/o, male, syncope

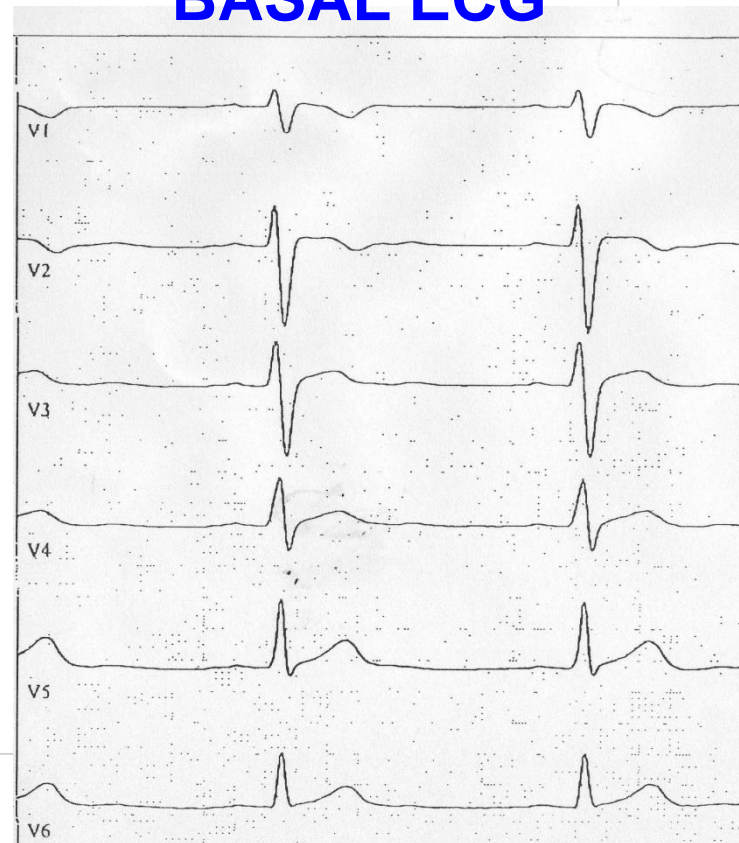
Intra-hospital clinical assessment

Basal ECG is displayed on the right.

**Echocardiogram, 24-hour Holter ECG
monitoring, stand up test and exercise
stress test were normal.**

No evidence for ACS, pulmonary embolism,
myocarditis, structural heart disease,
orthostatic hypotension, bradycardia or
sustained tachycardia recorded.

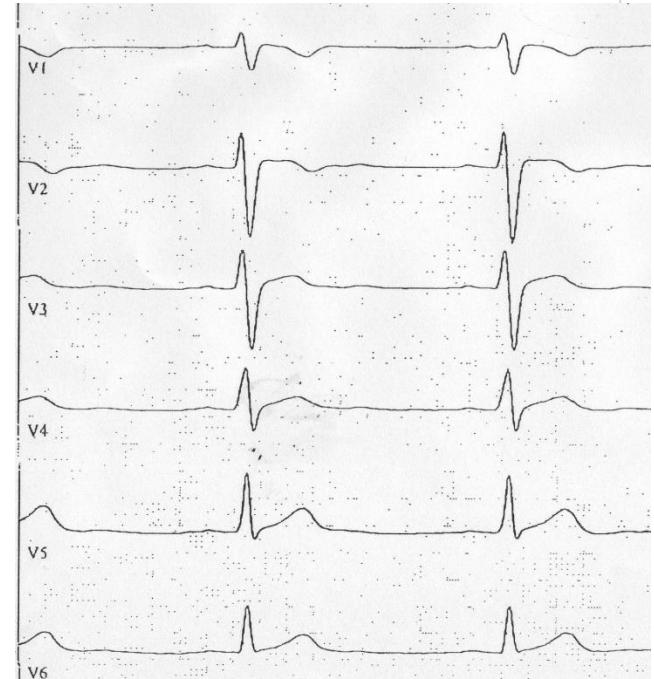
BASAL ECG



K. M., 21 y/o, male, BMI 31

Based on these findings, what would be your next step?

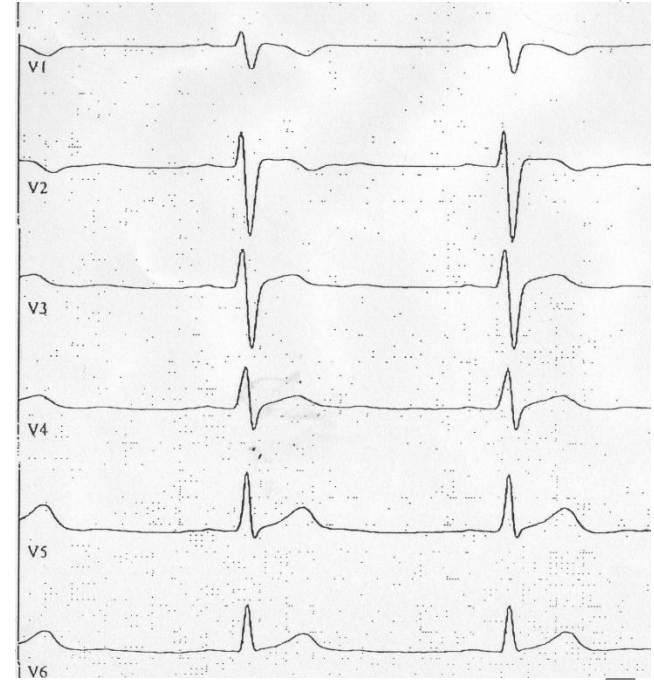
1. No need for further tests
2. Cardiac Magnetic Resonance
3. Electrophysiological Study
4. Coronary Angiogram
5. Sodium Challenging provocative test



K. M., 21 y/o, male, BMI 31

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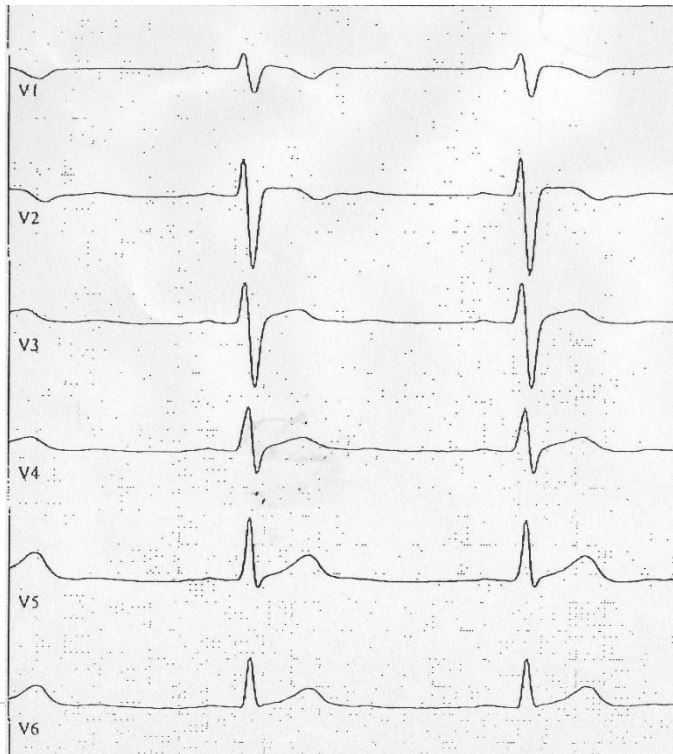
1. No need for further tests
2. Cardiac Magnetic Resonance
3. Electrophysiological Study
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5. **Sodium Challenging provocative test**



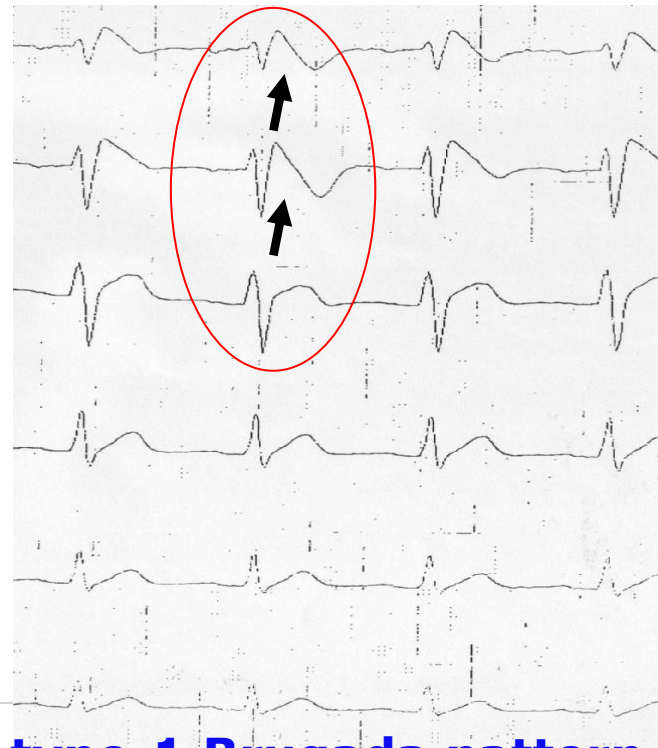
The patient experienced a syncope suspicious for arrhythmic origin. The ECG shows an IRBBB with a <1 mm saddle-back ST-segment elevation that rise the suspicious of Brugada Syndrome Therefore an Ajmaline test should be performed

Ajmaline test

Basal ECG: type-2 Brugada pattern



After Ajmaline 1 mg/kg ev



type-1 Brugada pattern

Brugada Syndrome ECG

According to the *HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes*, which one of the following statement is correct?

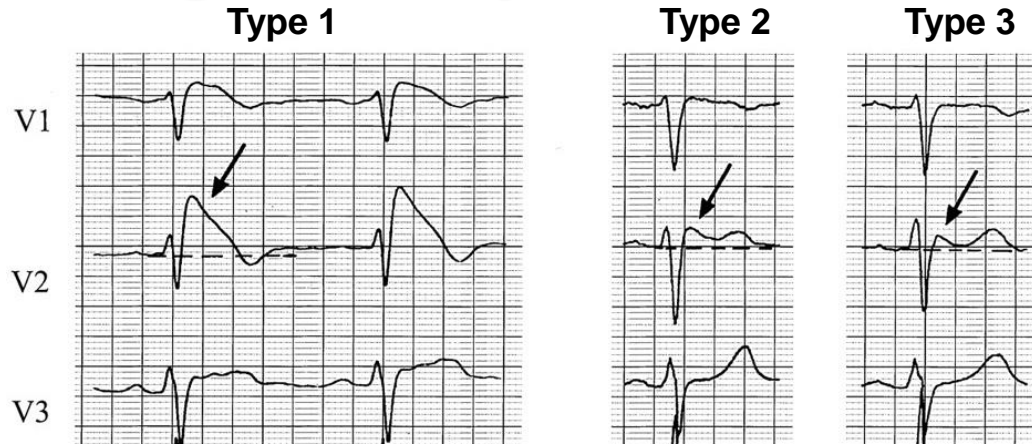
1. ST-segment elevation ≥ 2 mm **in at least 2 right precordial leads** placed in a standard position occurring spontaneously
2. ST-segment elevation ≥ 2 mm **in at least 2 right precordial leads** placed in a standard position (4th intercostal space) or a superior position (2nd or 3rd intercostal space) occurring spontaneously
3. ST-segment elevation ≥ 2 mm **in ≥ 1 right precordial lead** placed in a standard position (4th intercostal space) or a superior position (2nd or 3rd intercostal space) occurring spontaneously
4. None of the above

Brugada Syndrome ECG

According to the *HRS/EHRA/APHRS Expert Consensus Statement on the Diagnosis and Management of Patients with Inherited Primary Arrhythmia Syndromes*, which one of the following statement is correct?

1. ST-segment elevation ≥ 2 mm in at least 2 right precordial leads placed in a standard position occurring spontaneously
2. ST-segment elevation ≥ 2 mm in at least 2 right precordial leads placed in a standard position (4th intercostal space) or a superior position (2nd or 3rd intercostal space) occurring spontaneously
3. ST-segment elevation ≥ 2 mm in ≥ 1 right precordial lead placed in a standard position (4th intercostal space) or a superior position (2nd or 3rd intercostal space) occurring spontaneously
4. **None of the above**

Brugada Syndrome ECG



DIAGNOSTIC PATTERN: TYPE-1 ECG, COVED-TYPE ECG ST-segment elevation ≥ 2 mm in ≥ 1 right precordial lead (V1, V2) which are placed in a standard (4th intercostal space) or a superior position (2nd or 3rd intercostal space) occurring either spontaneously or after provocative drug test with intravenous administration of Class I antiarrhythmic drugs

Brugada Syndrome

DIAGNOSIS

Brugada Syndrome

BEFORE

- Brugada Typ-I-ECG (spontaneous, with fever or medication or provocative drug test using class I antiarrhythmic drugs)

AND

- one or more of the following criteria:
 - documented VF
 - polymorphic VT
 - positive family history for SCD ≤ 45 y/o
 - Type I-ECG in 1st degree relatives
 - inducible VT/VF during EP study
 - syncope
 - nocturnal gasping

Circulation 2005

NOWADAYS

RULE OUT:

Atypical RBB
LVH, ARVC,
Early Repolarization,
Acute pericarditis
Acute MI, Prinzmetal angina
Acute stroke,
Pulmonary embolism,
Dissecting aortic aneurysm,
Central and autonomic nervous system abnormalities
Hyperkalemia, Hypercalcemia,
Pectus excavatum,
Hypothermia

Europace 2017

SHANGHAI SCORE SYSTEM

	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

*One item from this category must apply. †Only award points once for highest score within this category. Score (requires at least 1 electrocardiographic (ECG) finding): >3.5 points: probable and/or definite Brugada syndrome (BrS); 2 to 3 points: possible BrS; <2 points: nondiagnostic. Reproduced with permission from Antzelevitch et al (6).

SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia.

Brugada Syndrome ECG or phenocopy?

- **Type-1 Brugada Pattern: Coved pattern**

The following characteristics are present in the right precordial leads (V1-V2)

1. An ascending and quick slope with a high takeoff that is $\geq 2\text{mm}$ at the end of the QRS complex followed by a concave or rectilinear down-sloping ST.

Note: there have been cases with a coved pattern that has a high takeoff between 1 and 2 mm.

2. There is no clear r` wave

3. The high takeoff often does not correspond with the J point

4. At 40 ms of high takeoff, the decrease in amplitude of ST is $\leq 4\text{mm}$.

5. Note: in RBBB and athletes, it is much higher

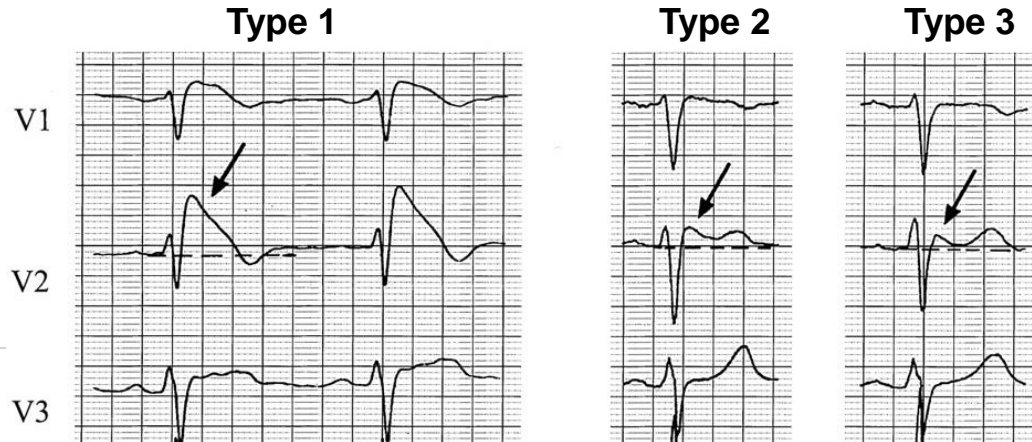
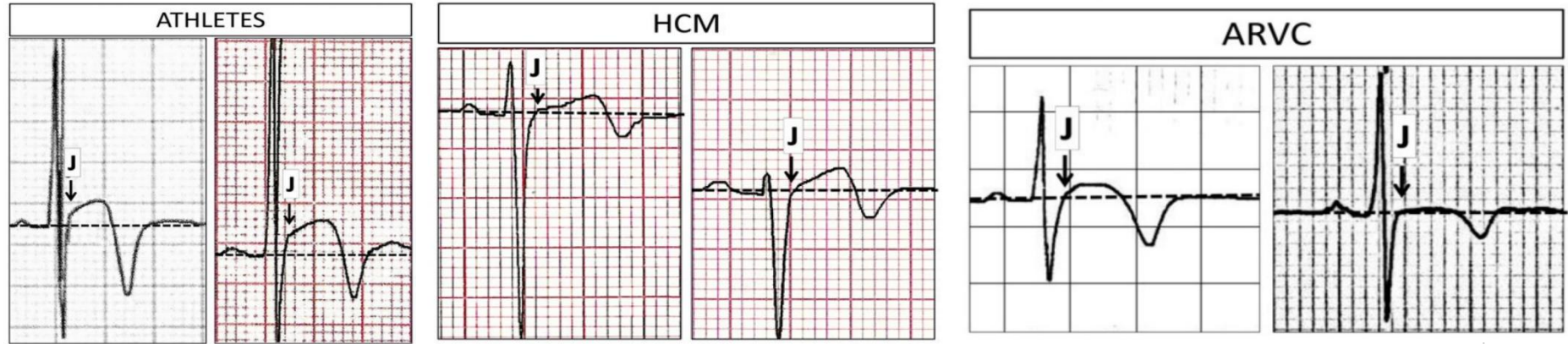
6. ST at the high takeoff is greater than the ST at 40 ms and greater than the ST at 80 ms

7. ST is followed by a negative and symmetric T wave

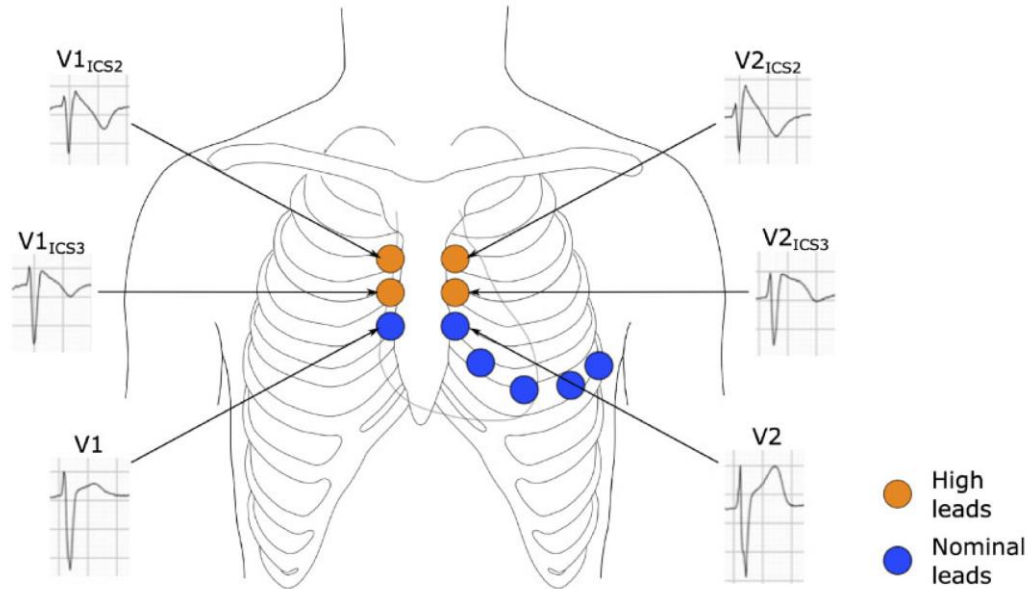
8. The duration of QRS is longer  <http://www.brugadaphenocopy.com>

T-Wave inversion in anterior leads: differential diagnosis

ECGs (Ableitung V₃)



DETECTING TYPE-1 BRUGADA ECG PATTERN: STANDARD AND HIGH INTERCOSTAL SPACES LEADS POSITION



Brugada Syndrome

Which one of the following is not a marker of increased risk of arrhythmic events in Brugada Syndrome?

1. Spontaneous BrS Type-1 ECG pattern
2. Early repolarization pattern
3. Syncopal episode
4. Family history of sudden cardiac death

Brugada Syndrome

Which one of the following is not a marker of increased risk of arrhythmic events in Brugada Syndrome?

1. Spontaneous BrS Type-1 ECG pattern
2. Early repolarization pattern
3. Syncopal episode
4. **Family history of sudden cardiac death**

Brugada Syndrome

ARRHYTHMIC RISK

The risk of lethal or near-lethal arrhythmic episodes among previously asymptomatic patients with Brugada Syndrome

- 8% event rate at 33 ± 39 months of follow-up, 547 pts

Brugada et al 2003

- 1% event rate after 40 ± 50 months, 123 pts

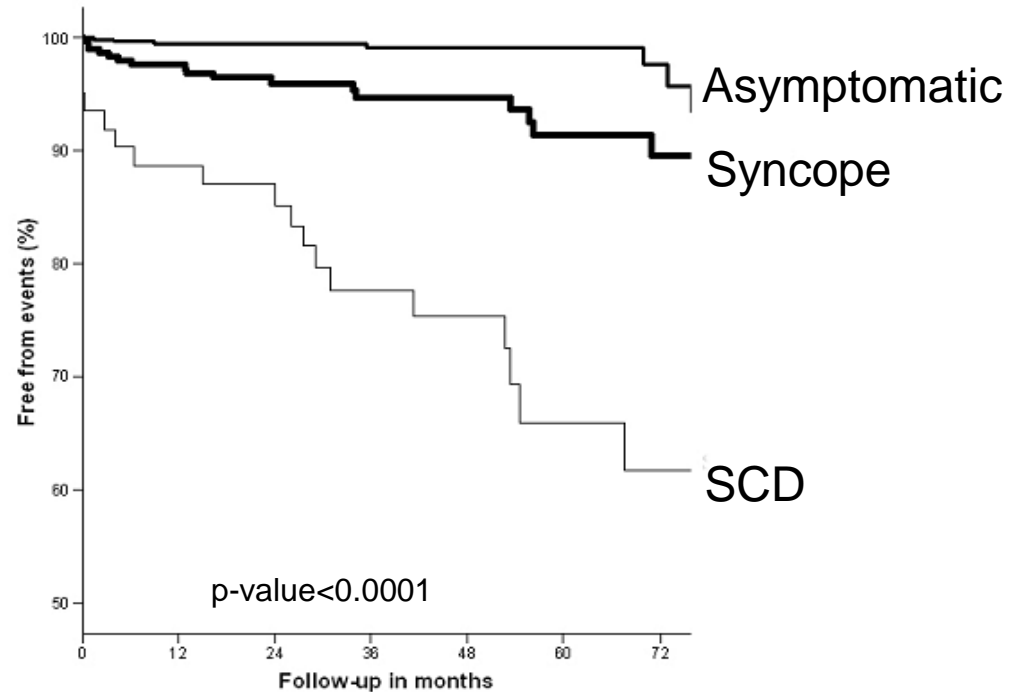
Eckardt et al. 2004

- 1.5% event rate at 31 months of follow-up, 478 pts

Probst et al. 2010

Markers for arrhythmic events

Brugada Syndrome: Risk of Arrhythmic Events by Symptoms (FINGER Registry, n=1029)



syncopal events that are defined as „probable arrhythmia related“ indicate unfavorable prognosis in patients with spontaneous type I Brugada ECG

Markers for arrhythmic events

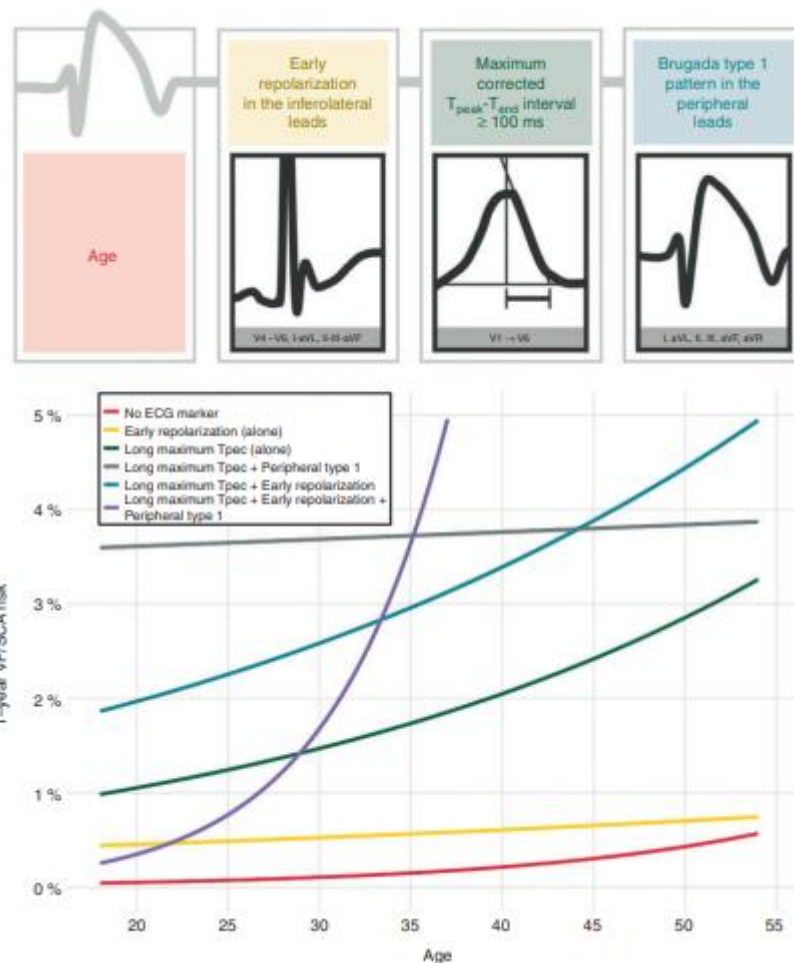
In patients with a spontaneous Brugada type 1 pattern (BrT1), the combination of

-a corrected $T_{peak}-T_{end}$ interval ≥ 100 ms

-an early repolarization pattern

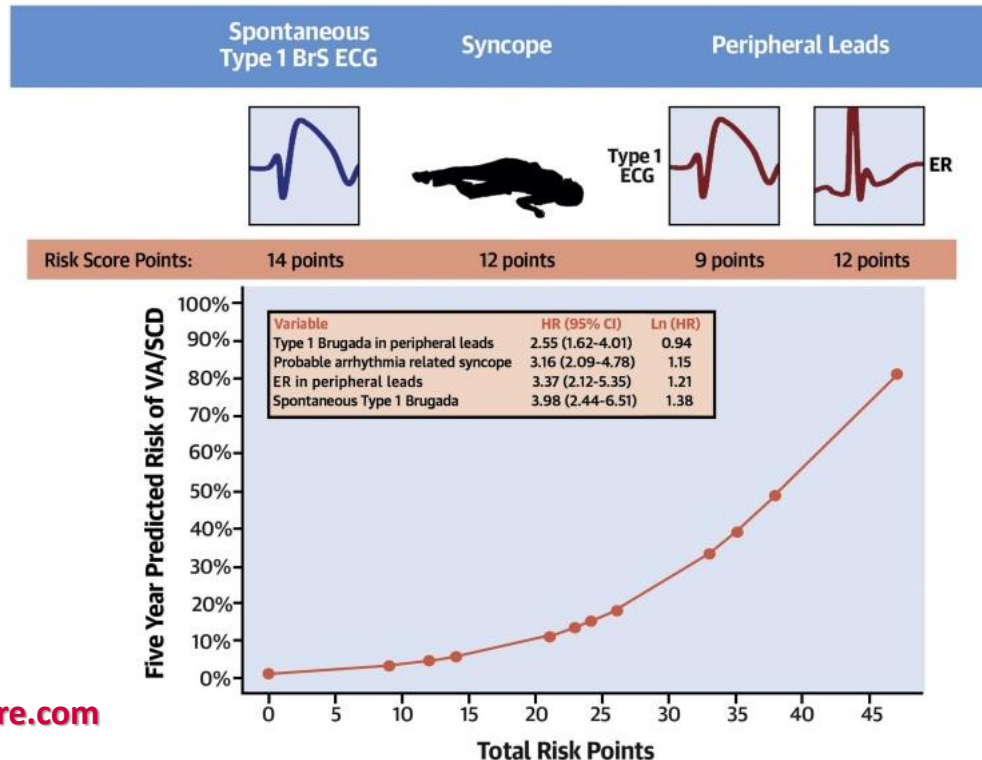
-and a peripheral BrT1

was highly predictive of VF occurrence



Markers for arrhythmic events

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



<http://brugadariskscore.com>

Brugada Syndrome

GENETICS

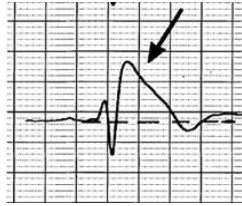
Genetics of Brugada Syndrome: new strategy



ESC

Council
Cardiovascular Genomics

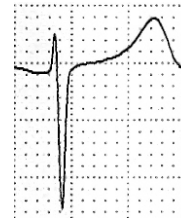
Genome Wide Association Study



N=312

Type-I BrS index cases

Case-control



N=1115

General population

600 000 SNPs (Axiom chip)

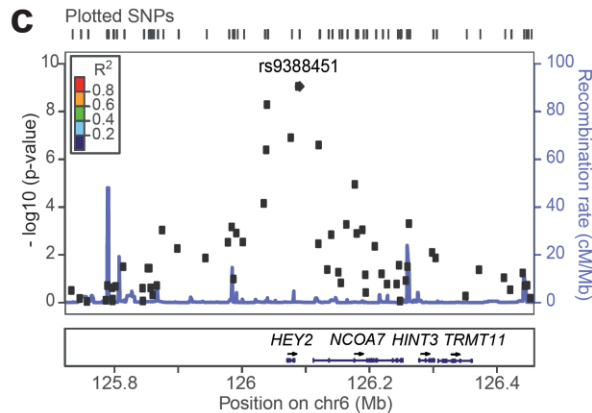
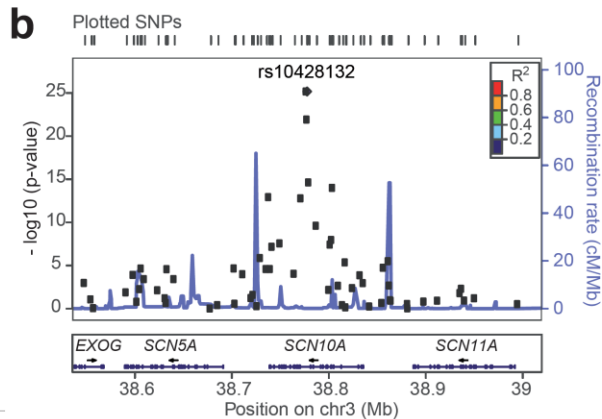
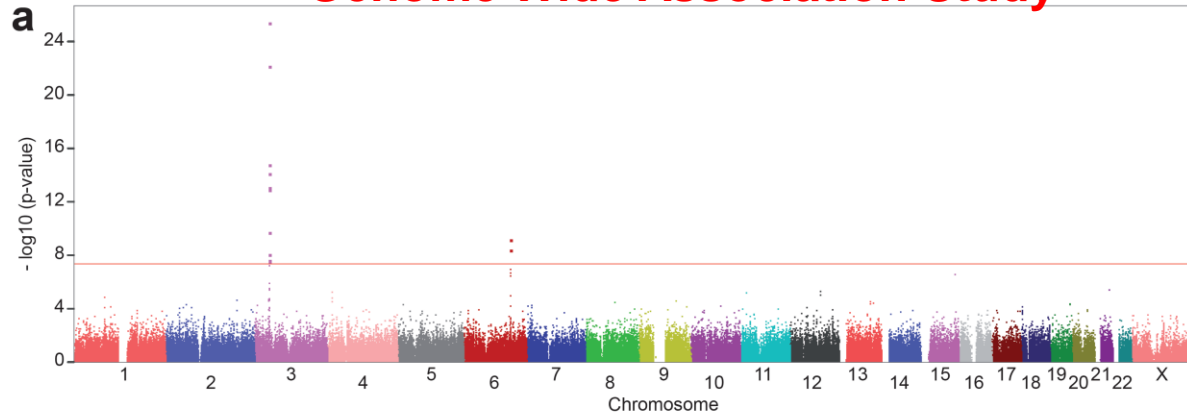
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ESC

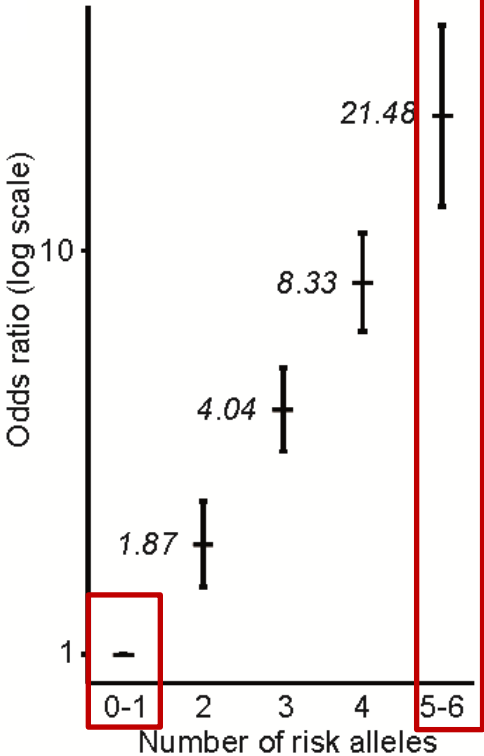
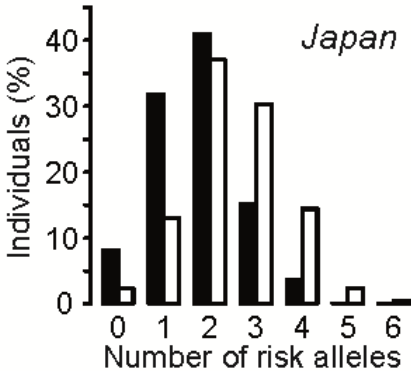
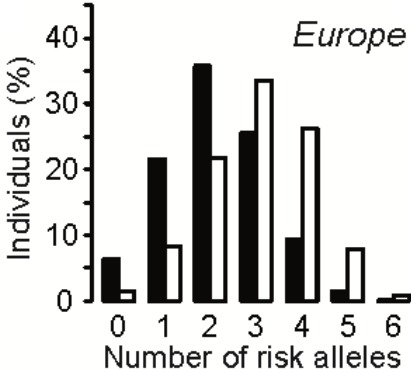
Council
Cardiovascular Genomics

Genome Wide Association Study

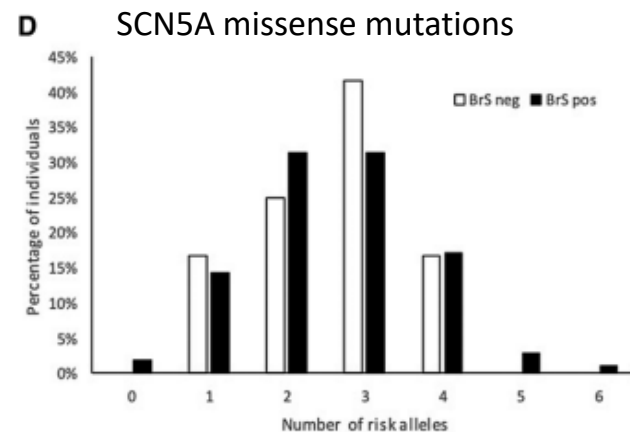
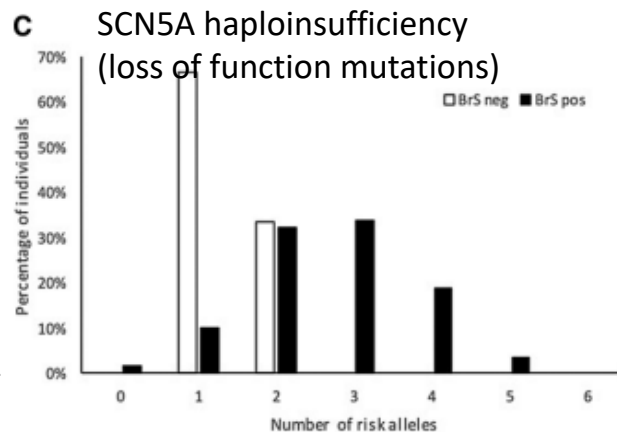
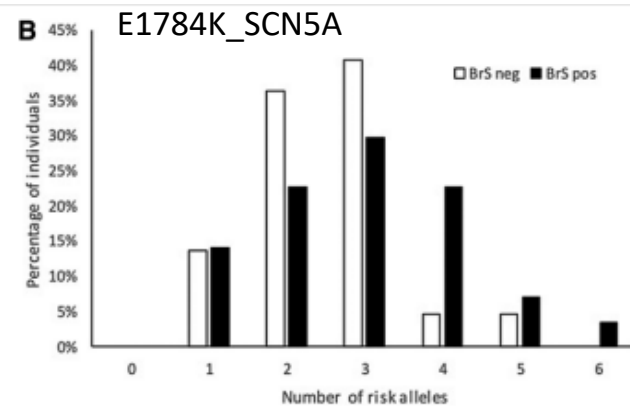
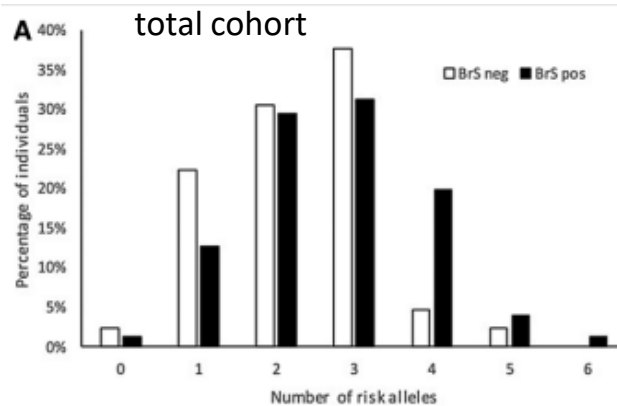
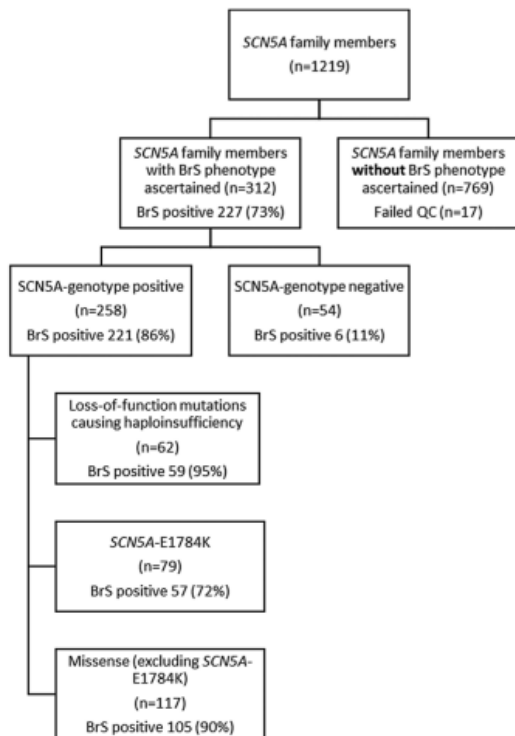


Cumulative effect of alleles at the three loci on susceptibility to BrS

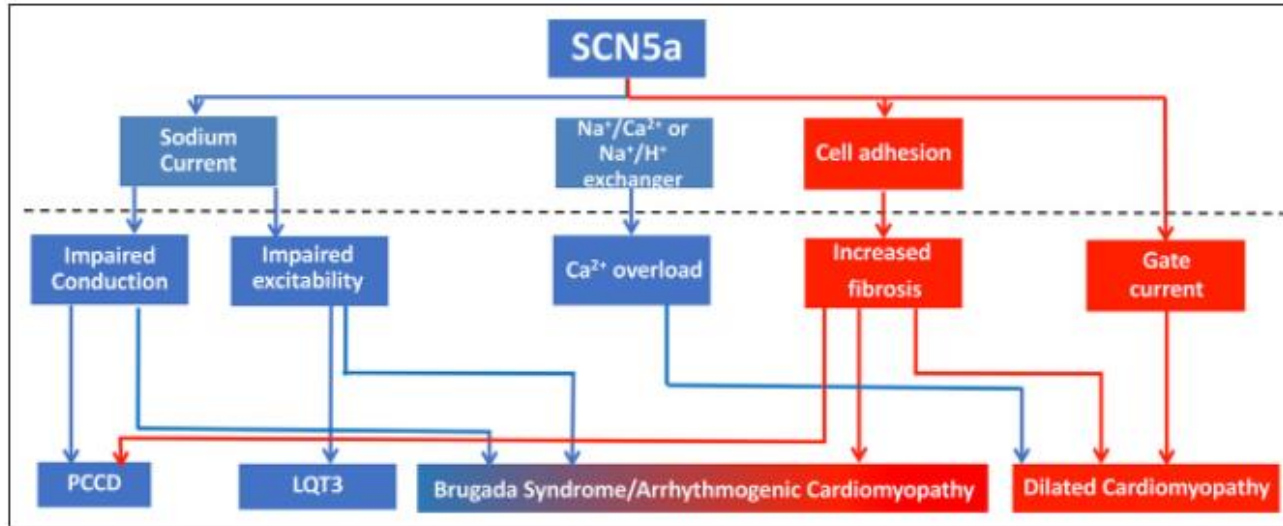
Controls
BrS cases



SCN5A Mutation type and a genetic risk score associate variably with Brugada syndrome phenotype in SCN5A families

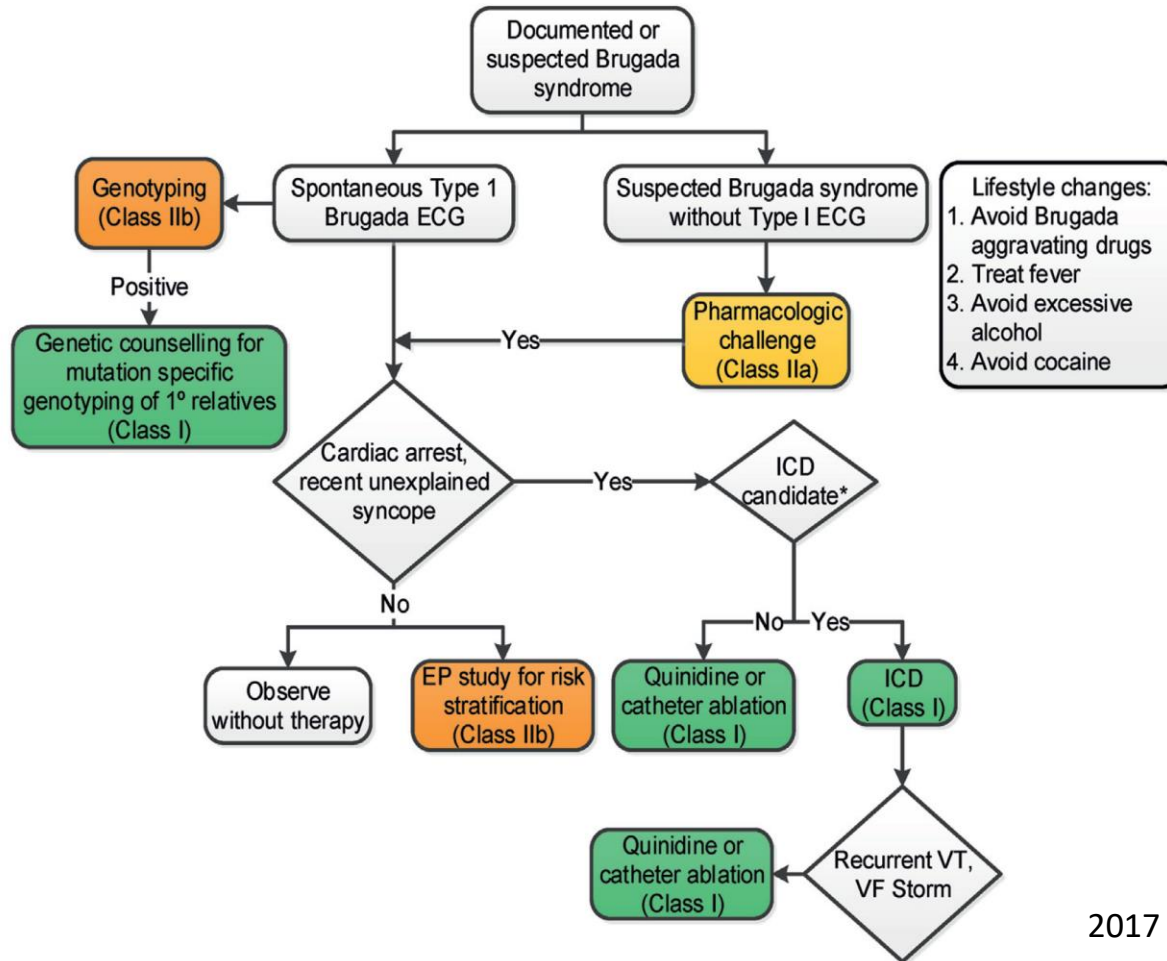


Genetic testing and risk prediction in Brugada Syndrome?



Genetic testing and genetic risk scores are promising for Brugada syndrome
Importance of genetic counselling regarding disease complexity

Brugada syndrome: Risk stratification and prevention of SCD



I suspect it is a Brugada: What should I do? - Summary:

- **Definite diagnosis – high lead placement, rule out phenocopies (www.brugadaphenocopy.com), Shanghai diagnosis score**
- **Lifestyle recommendations including drugs, fever, excessive alcohol (www.brugadadrugs.org)**
- **syncopal events that are defined as „probable arrhythmia related“ indicate unfavorable prognosis in patients with spontaneous type I Brugada ECG**
- **Combination of advanced age, early repolarization in inferolateral leads, Tpeak-Tend interval \geq 100ms and Brugada Typ 1 ECG in peripheral leads indicates high risk**
- **Risk score of syncope, spontaneous Brugada type 1 ECG, Type 1 ECG and/or early repolarization pattern in peripheral leads predicts 5 year risk of VA/SCD (<http://brugadariskscore.com>)**
- **Growing role for genetic testing after counselling**

Take home messages:

- **A careful medical evaluation is mandatory for every patient presenting unexplained syncope**
- **In the presence of an unexplained syncope, a detailed familial history should be obtained, which is not always directly suggestive of an inherited cardiac condition**
- **Challenge the ECG of your patient and perform pharmacological test in case of doubt**
- **Perform a deep phenotyping of the index case and the family members**
- **Genetic testing and counselling should be offered to patients and their relatives**
- **A negative genetic test do not rule out a Brugada syndrome, which is not a pure monogenic disorder in many cases**
- **Molecular autopsy could be considered after sudden cardiac death in the young**