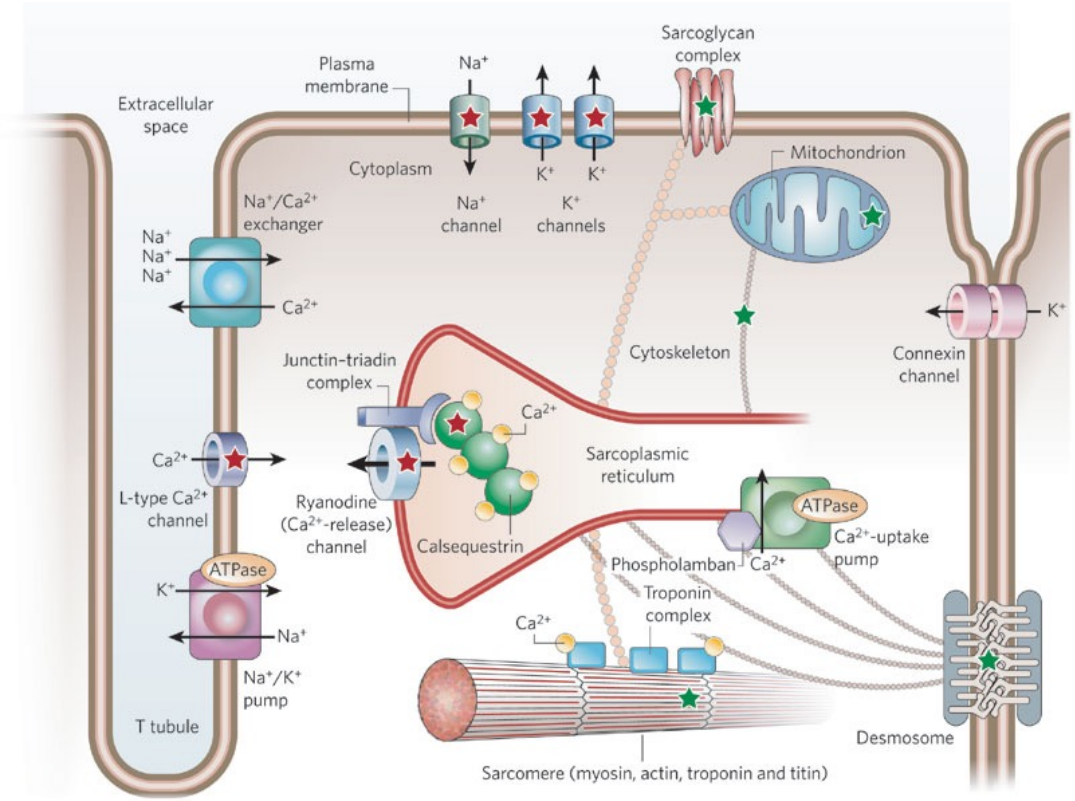
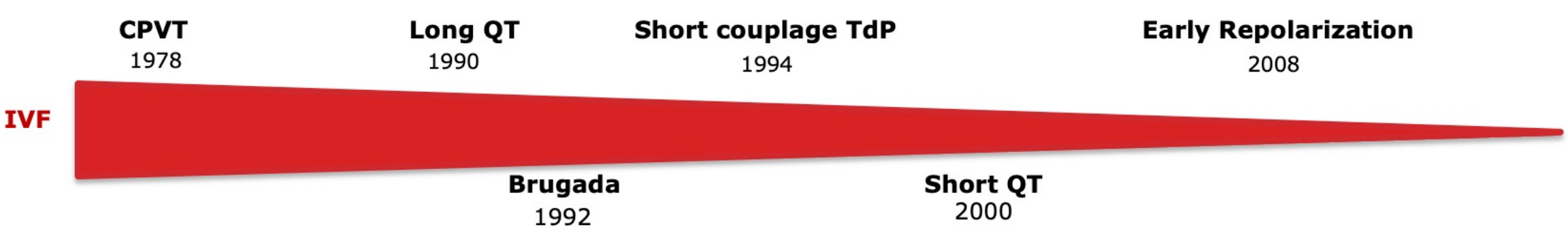
CANALOPATHIES



Victor WALDMANN

Hôpital Européen Georges Pompidou — Hôpital Necker

Spectre des Diagnostics

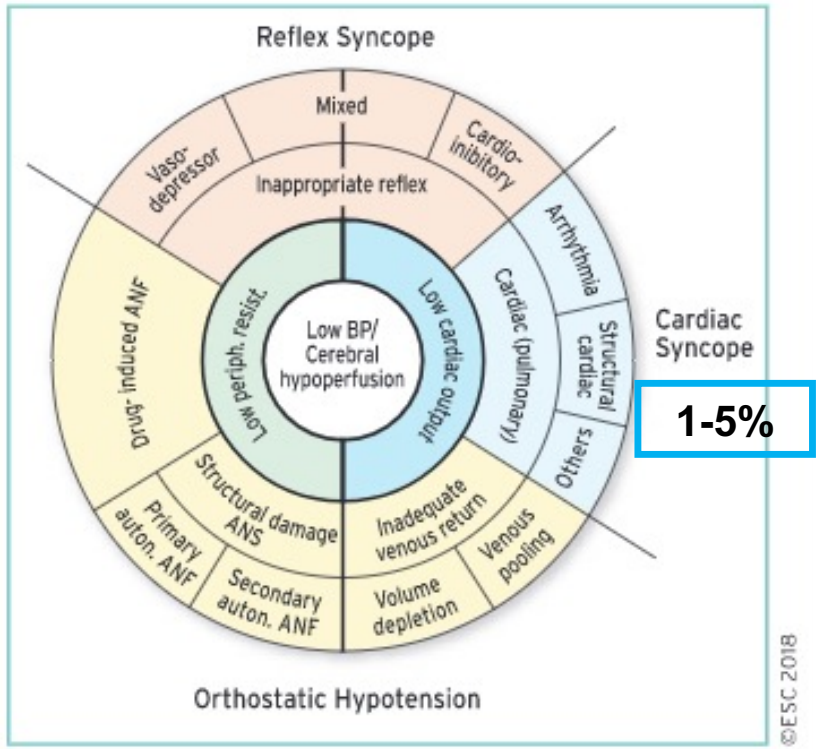


IVF: Idiopathic Ventricular Fibrillation

Evoquer le Diagnostic

Symptomes	**Syncope / Noyade / Comitialité**
Circonstances	**Effort / Emotion / Fièvre**
Famille	**Histoire familiale de mort subite** **—** **Surdité congénitale**

SYNCOPES



1-5%

CARDIAQUES

- ***Bradycardies***

Dysfonction sinusale, BAV

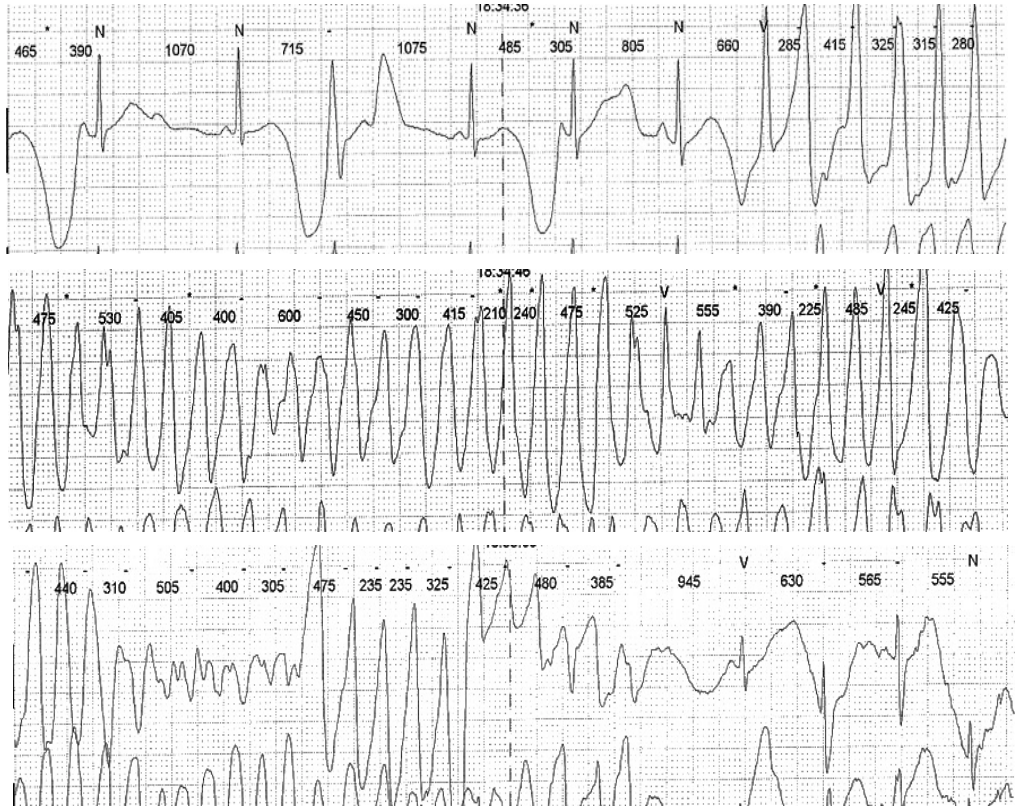
- ***Tachycardies***

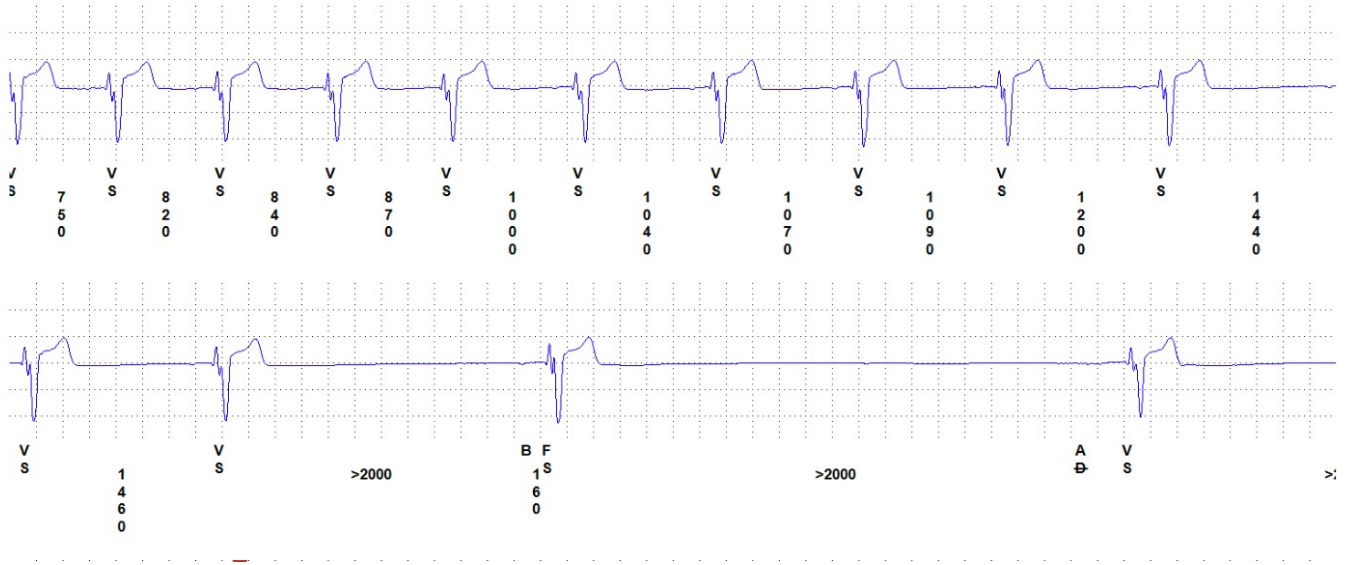
Ventriculaire >> supraventriculaire

- ***« Mécaniques »***

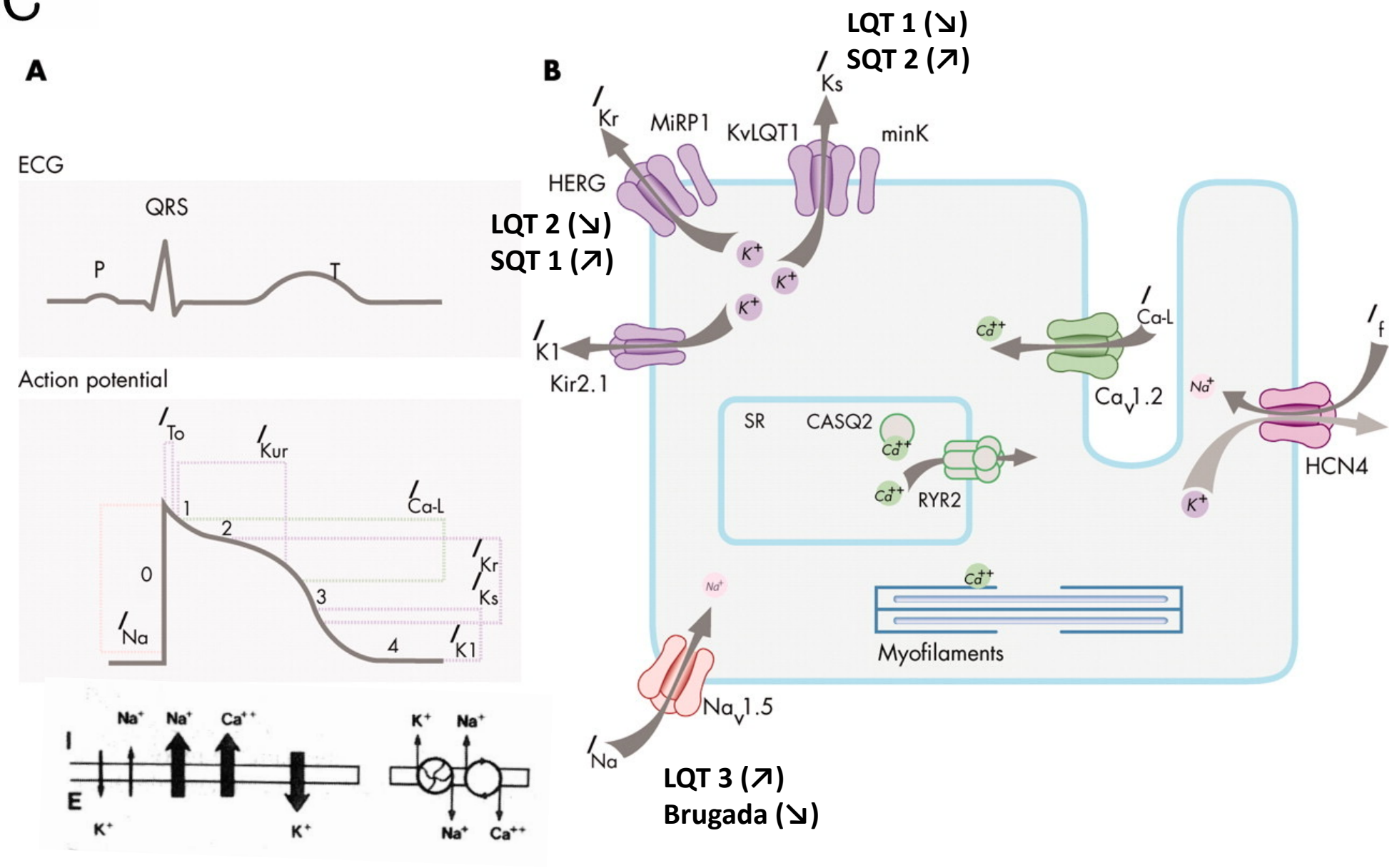
Sténose aortique, EP, CMH…

TDR Ventriculaire vs. Syncope Vagale





Les Canalopathies



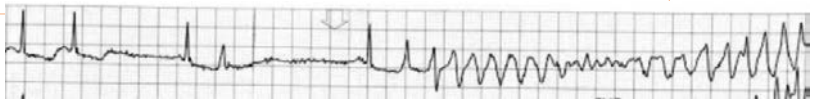
QT LONG

PHYSIOPATH

17 gènes connus – 1/2500
Mutation identifiée dans 75%:
LQTS1 KCNQ1 (effort ++, natation)
LQTS2 KNCH2 (émotion ou bruit)
LQTS3 SCN5A (repos ou sommeil)
Autosomique dominant (95%)

PRONOSTIC

Taux mort subite annuel 0.3-0.9%
5% par an si antécédent de syncope
LQT3 et QTc > 500 ms à haut risque



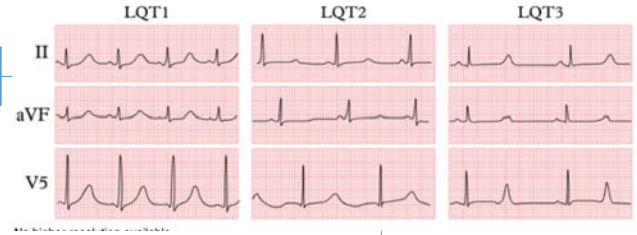
« Short-long-short »

DAI PREVENTION Iaire

ESC European Society of Cardiology
ESC GUIDELINES

TV malgré B-bloquants
Syncope

DIAGNOSTIC

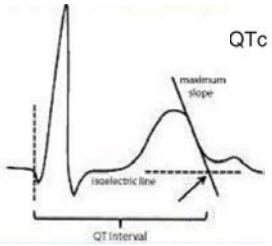


QTc ≥ 480 ms
Score > 3
Mutation positive
QTc > 460 ms + syncope inexpliquée

Variable	Points
Electrocardiogram	
QTc ms* ≥480	3
460-470	2
450 (males)	1
Torsade de pointes	2
T wave alternans	1
T wave notches in 3 leads	1
Bradycardia†	0.5
Clinical history	
Syncope	
With stress	2
Without stress	1
Congenital deafness	0.5
Family history‡	
Family members with confirmed LQTS§	1
Unexplained sudden death in first-order family members <30 years	0.5

Bazett

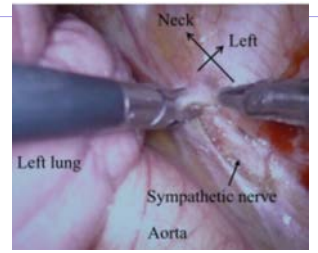
$$QTc\ interval = \frac{QT\ interval}{\sqrt{RR\ interval}}$$



D2 ++ ou V5

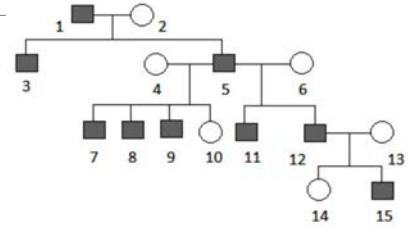
PERSPECTIVES

Dénervation
Flecaine ou mexiletine LQTS3
Stratification guidée par génétique



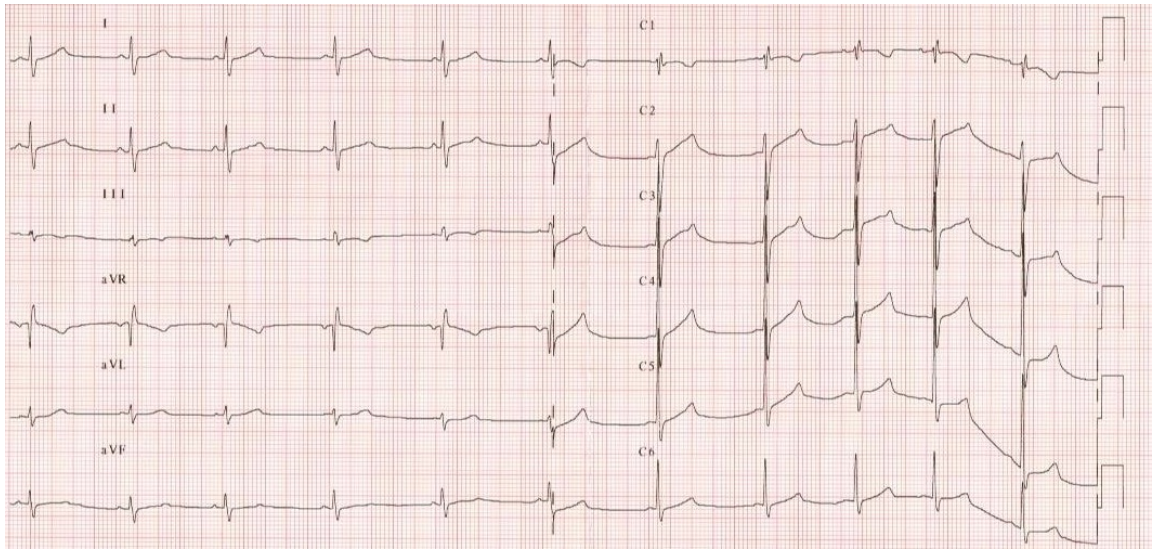
PRISE EN CHARGE

Médicaments contre indiqués
B-bloquants ++ (IIa pour porteur sain)
Restriction sportive
Dépistage familial
Orage rythmique: +/- SEES



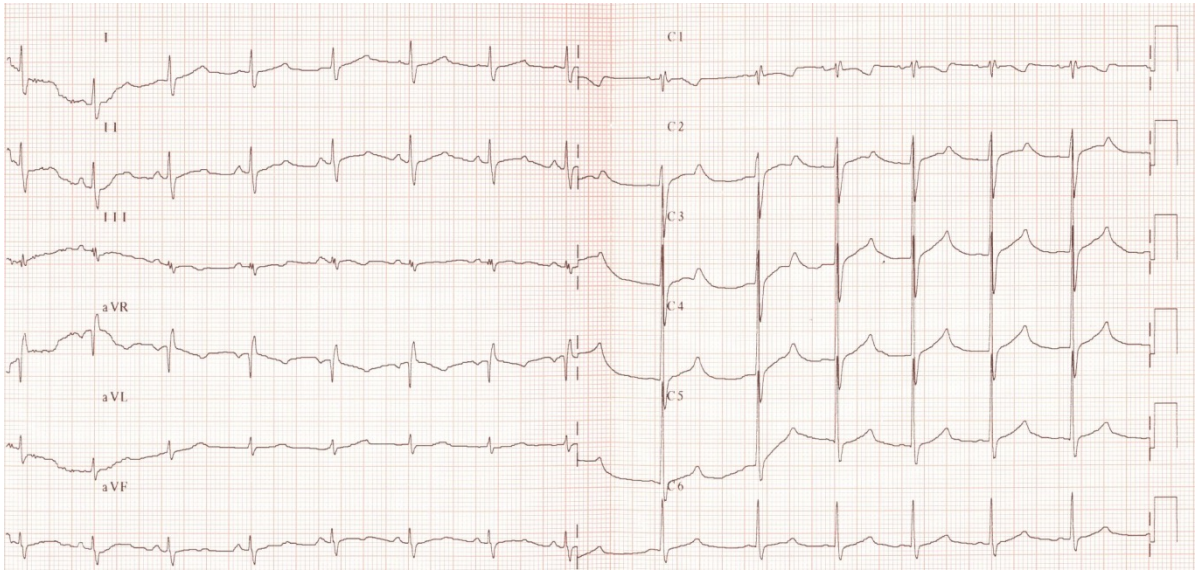
CREDIBLEMEDS®
https://crediblemeds.org/

QT LONG

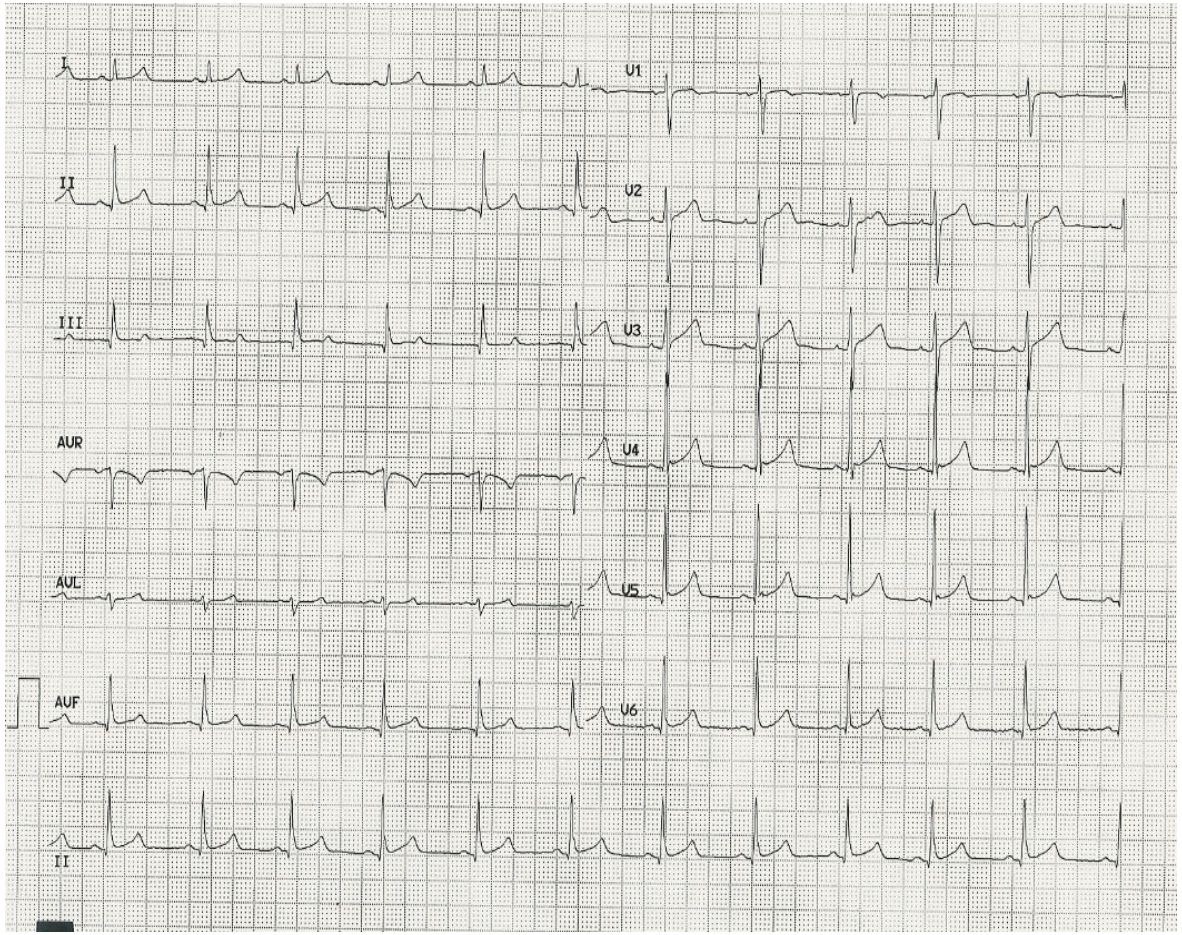


ECG allongé : QTc 440ms

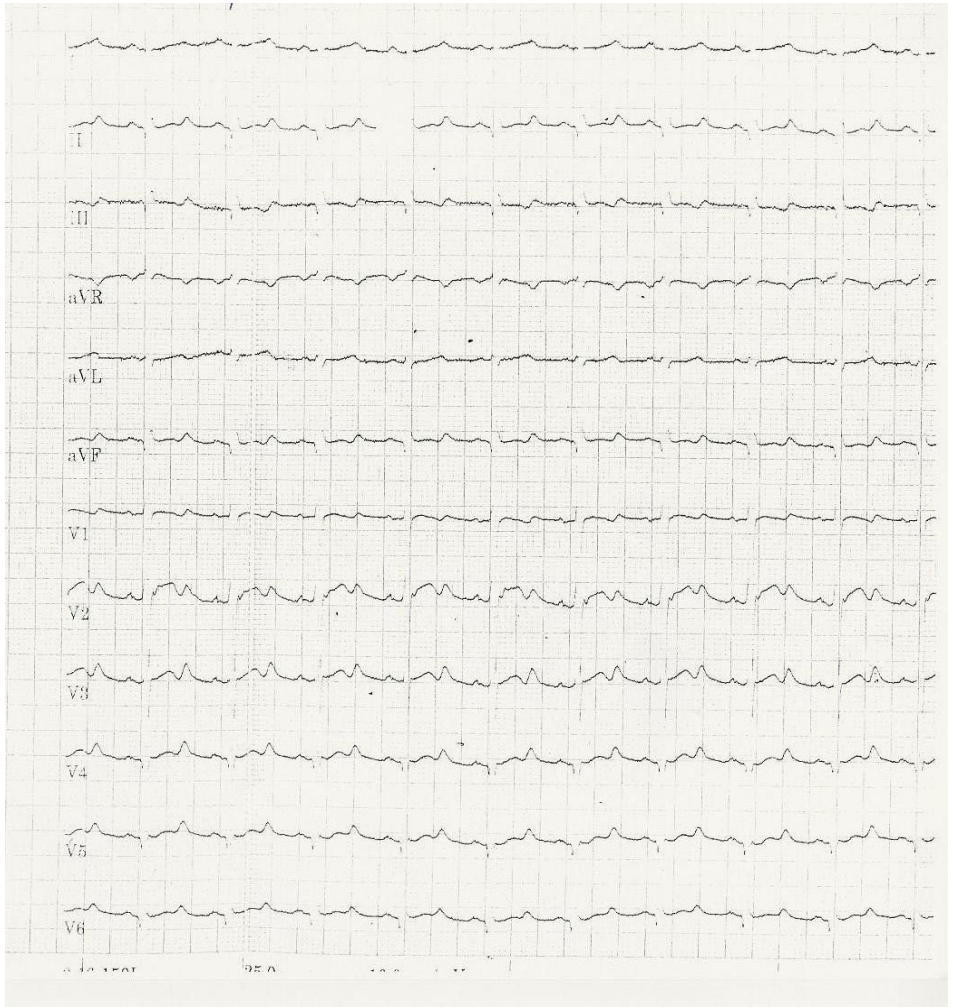
ECG debout : QTc 470ms



QT LONG

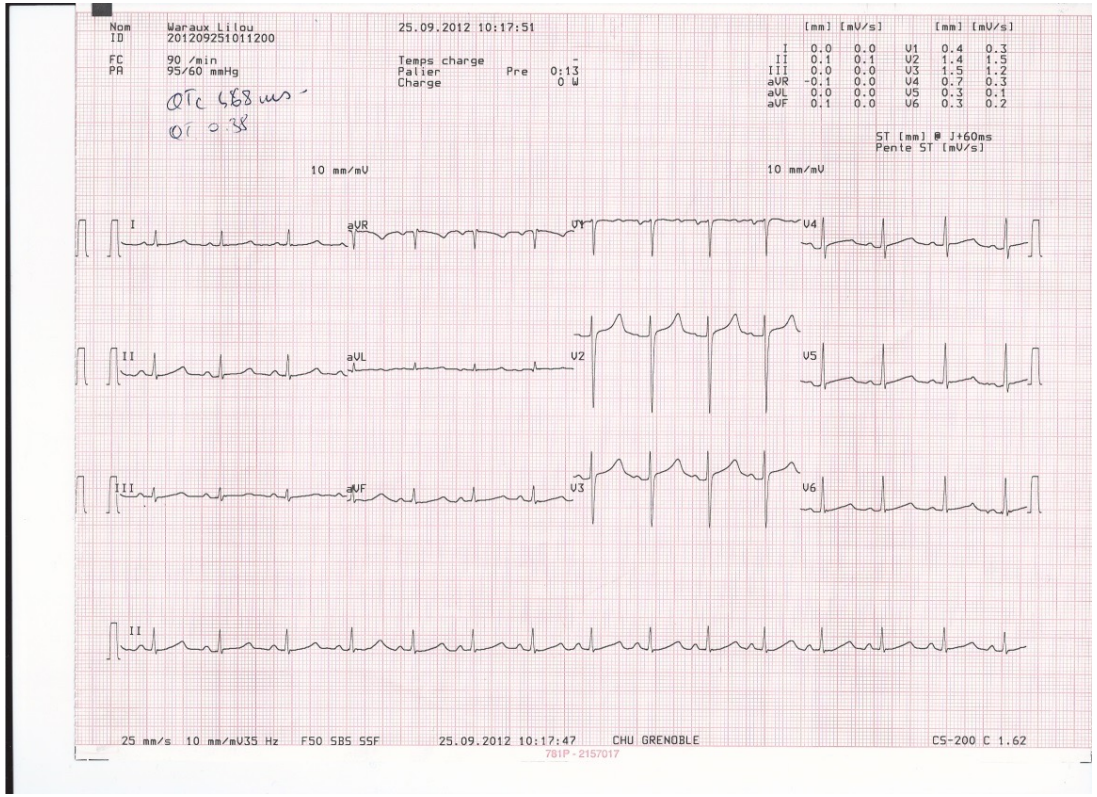


ECG de repos : QTc 450 ms

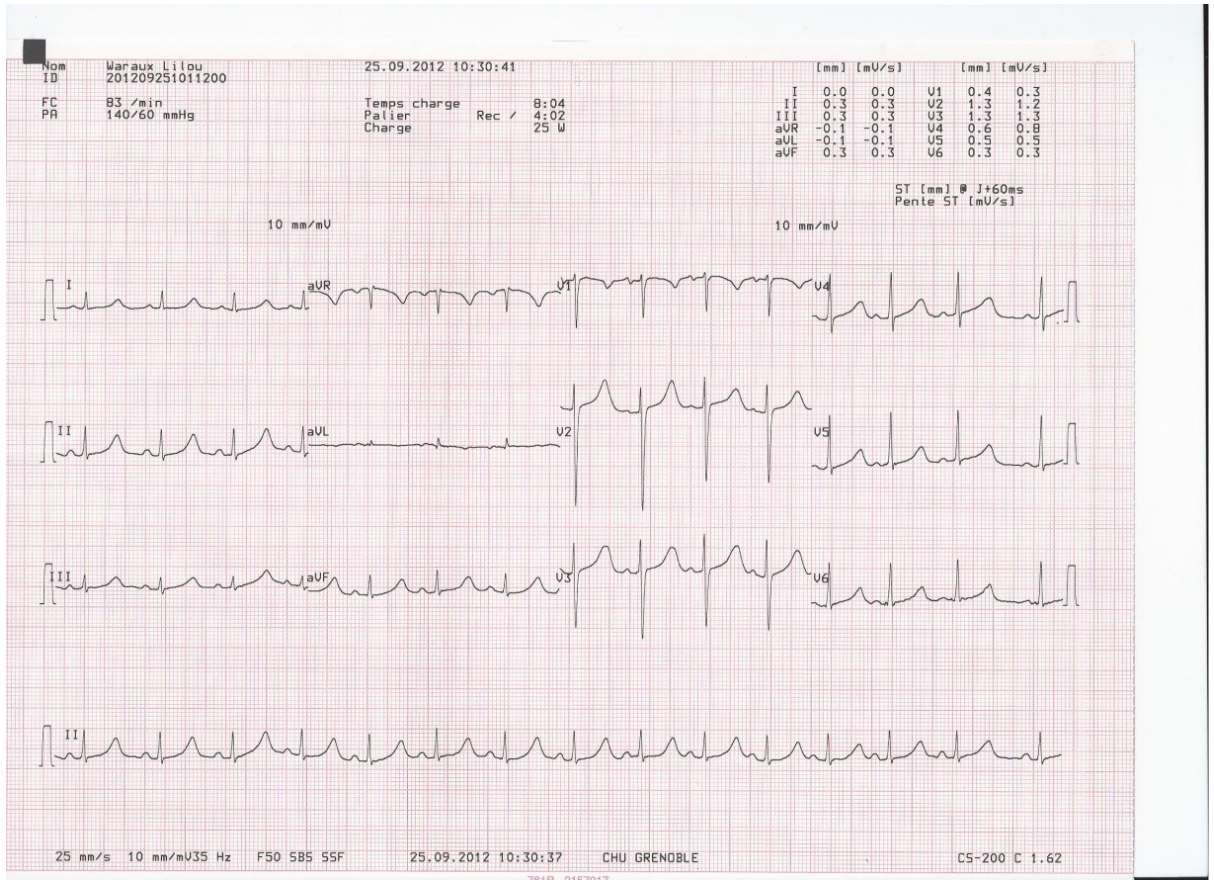


Test adrénaline : QTc 530 ms

QT LONG



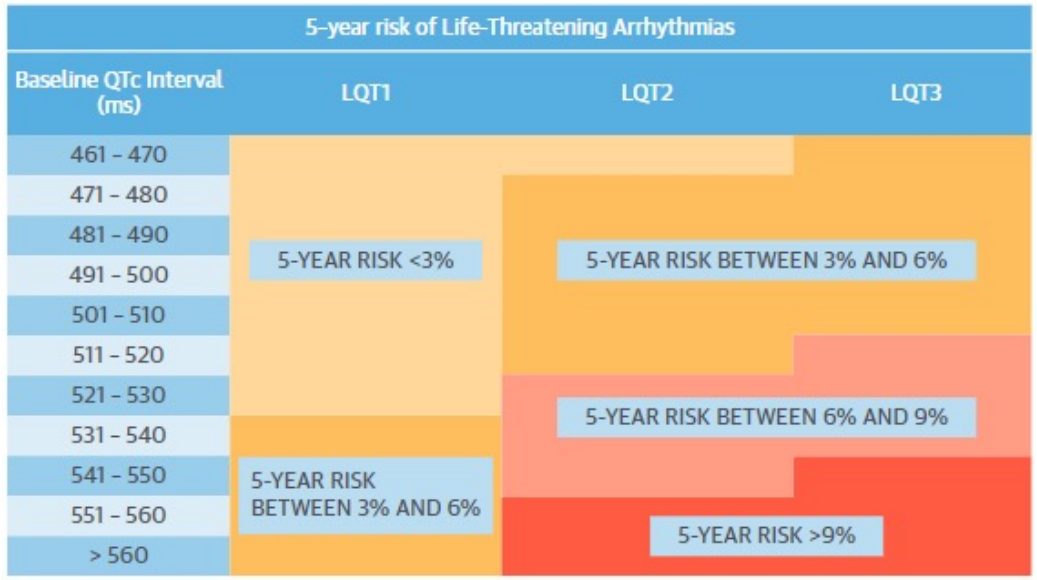
ECG de base



4ème mn de récupération

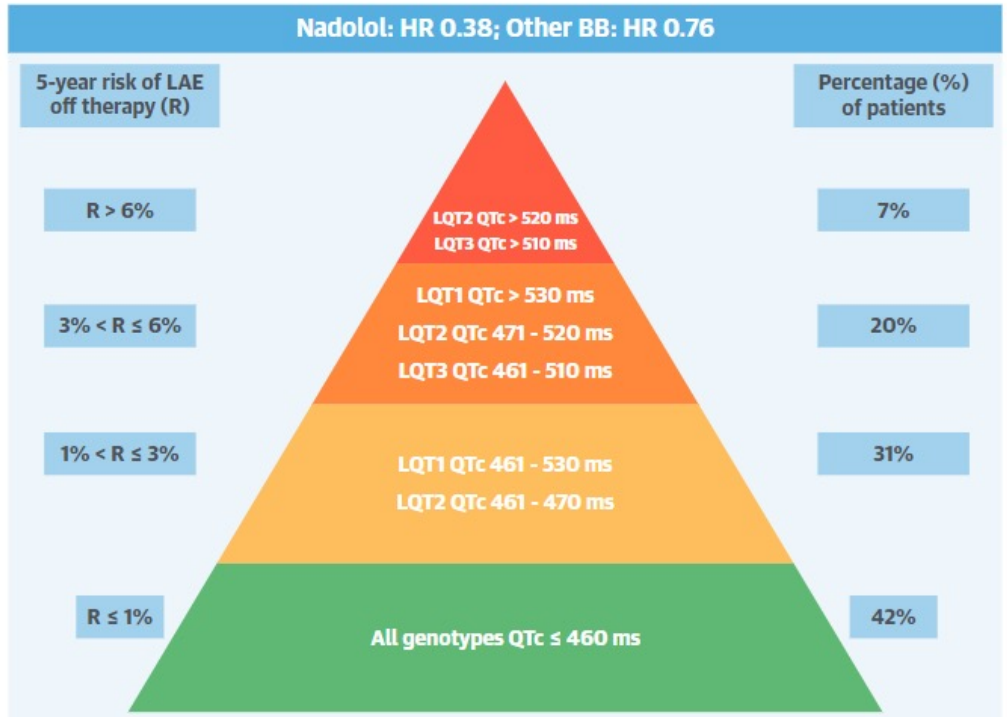
QT LONG

FIGURE 2 5-Year Risk of Life-Threatening Arrhythmic Events by Genotype for Each 10-ms Increment of QTc Duration for Patients Who Are Not Receiving Beta-Blockers



Visualization of the 5-year relative risk for patients with each genotype and for each QTc duration. The 4 colors group patients within the same 5-year risk of life-threatening arrhythmic events. This scheme can be used to personalize the risk estimate of patients at diagnosis in the absence of beta-blocker therapy and to estimate the risk of life-threatening arrhythmic events in patients who are not compliant with treatment. QTc = corrected QT interval.

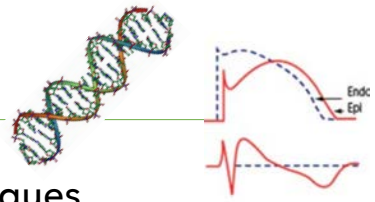
CENTRAL ILLUSTRATION 5-Year Risk of LAEs by Genotype and QTc Interval Before Therapy and Effect of BBs



Mazzanti et al. JACC 2018

BRUGADA

PHYSIOPATH



Anomalie canaux sodiques
Prévalence 20 / 100 000
Mutation 20% (SCN5A ++, CACN1Ac)
Autosomique dominant
Pénétrance variable, H >> F

PRONOSTIC

Taux mort subite annuel
- 1% si type 1 spontané
- 3% si syncope
- 10% si ACR

Type 1 induit de meilleur pronostic

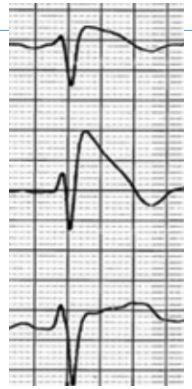
DAI PREVENTION Iaire

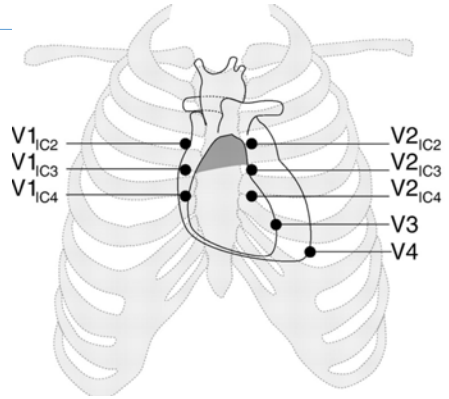
ESC European Society of Cardiology
ESC GUIDELINES

TV soutenue
Syncope rythmique

DIAGNOSTIC

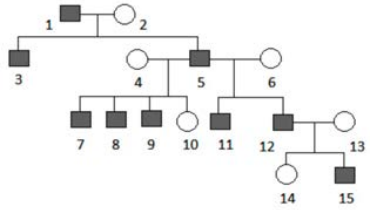
Type 1 ≥ 2 mm dans 1 dérivation
V1 ou V2 + dérivations hautes (2-3 EIC)
+/- ajmaline (1 mg/kg IV 5-10 min)





PRISE EN CHARGE

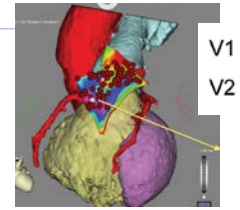
Médicaments contre indiqués
Traitement précoce fièvre
Eviter repas copieux ou alcool excessif
Restriction sportive
Dépistage familial
Orage rythmique: isuprel +/- quinidine

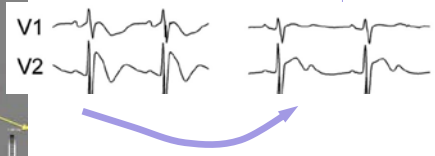


BrugadaDrugs.org
Safe drug use and the Brugada syndrome

PERSPECTIVES

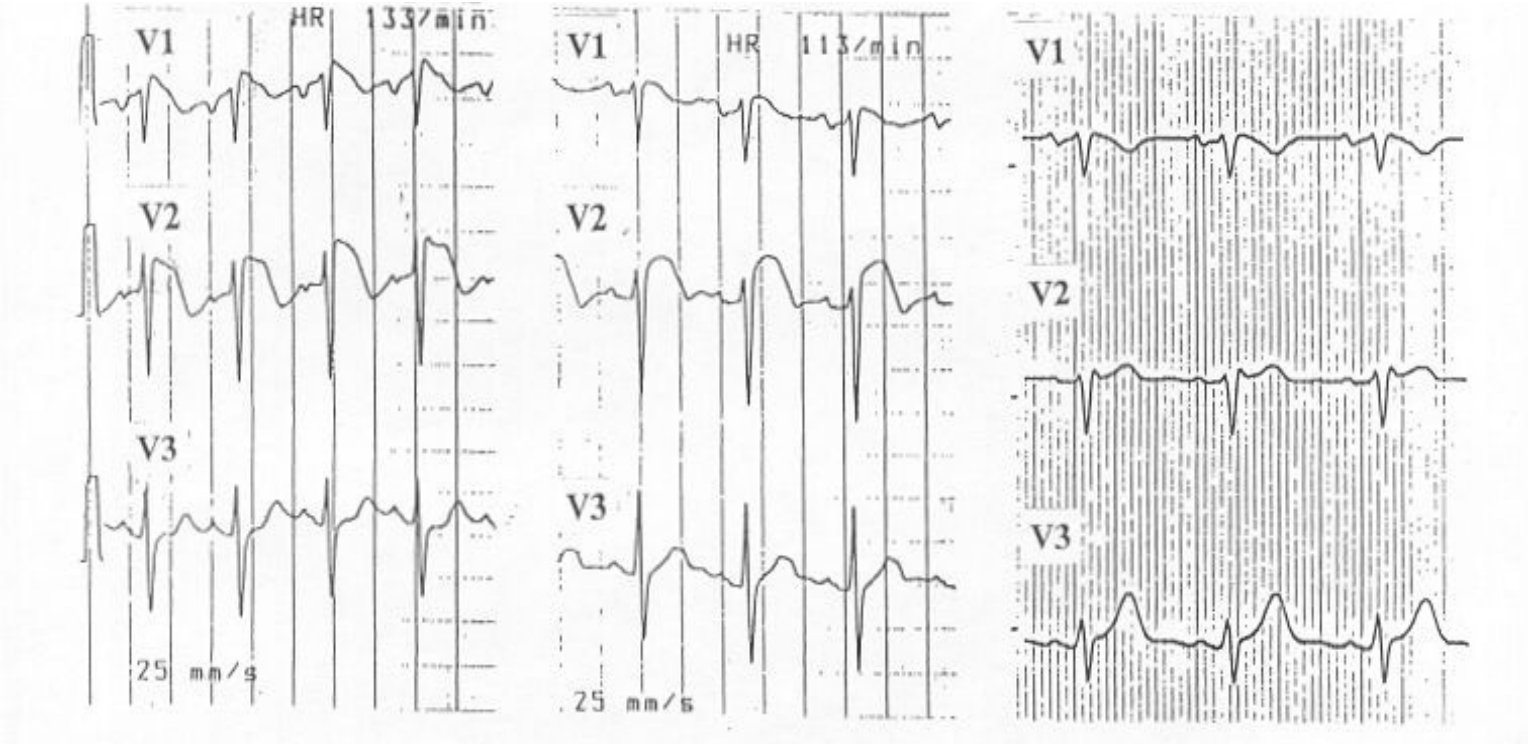
SVP controversée
Place de la quinidine
Indications élargies S-ICD ?
Ablations ?
(substrat épicardique VD)

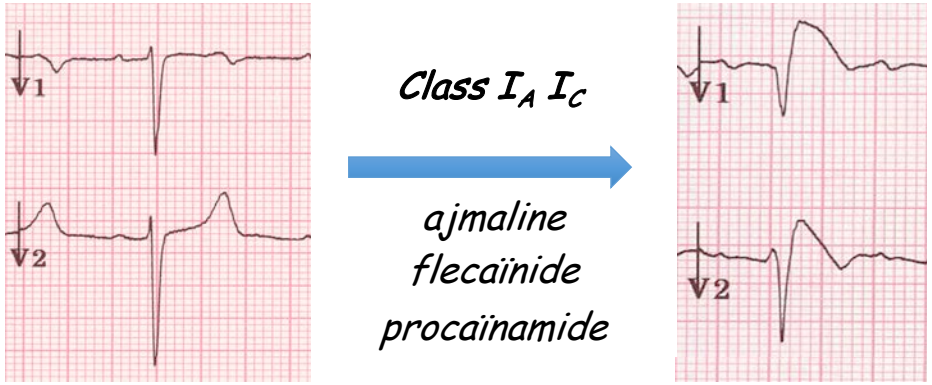




BRUGADA

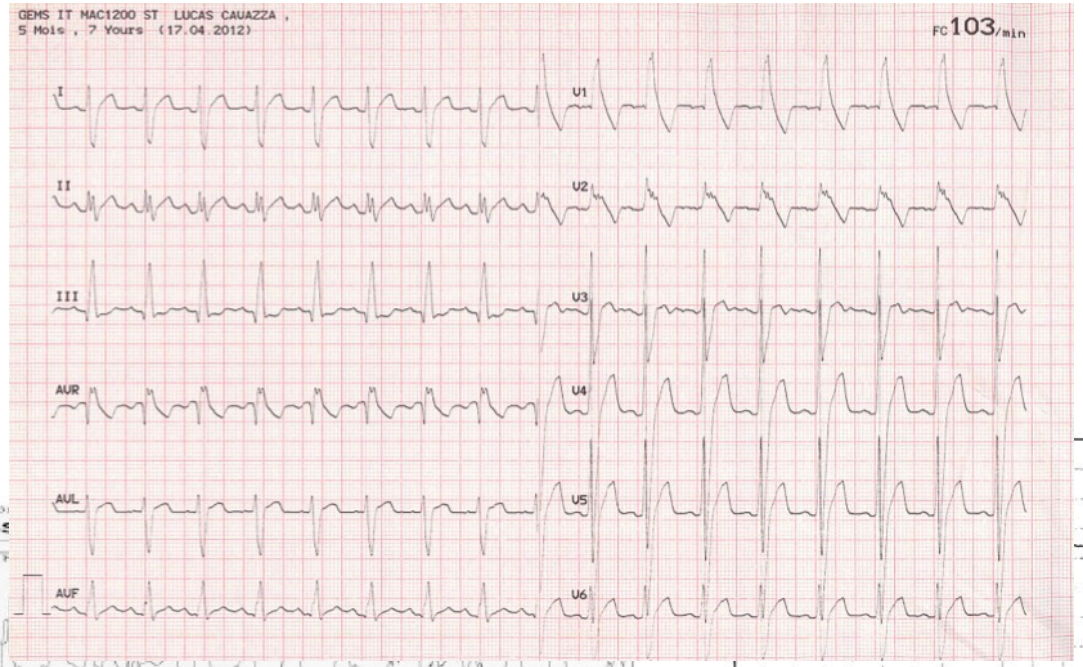
Temp. 41°C **Temp. 39°C** **Temp. 37°C**

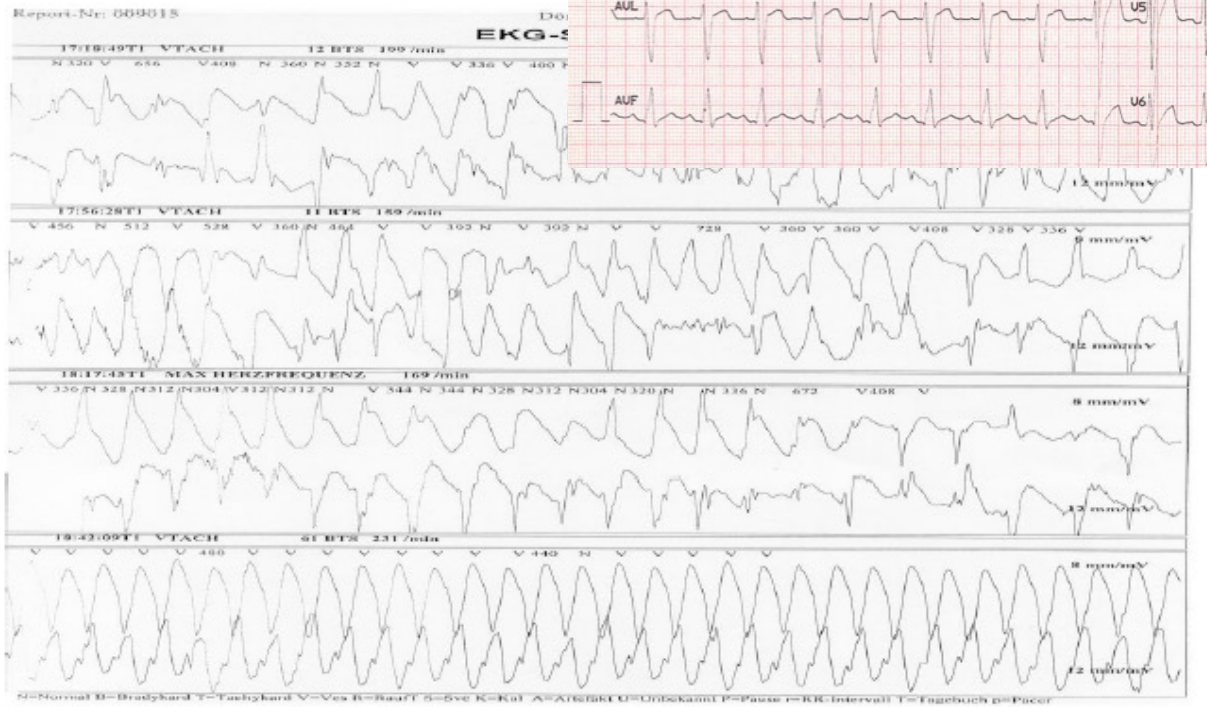


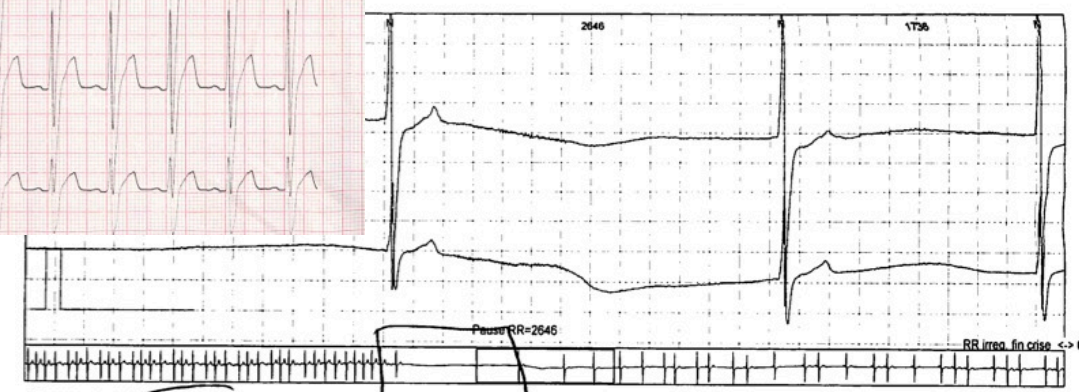


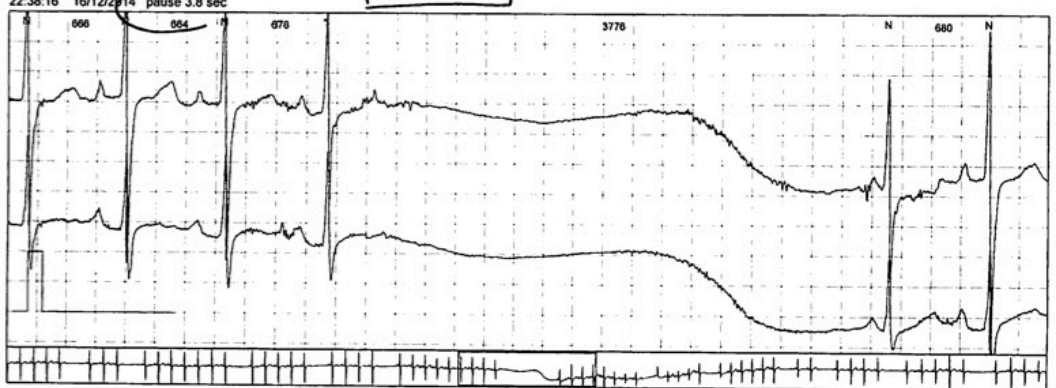
Test pharmaco après 15 ans ++
ou si morts subites pédiatriques

BRUGADA

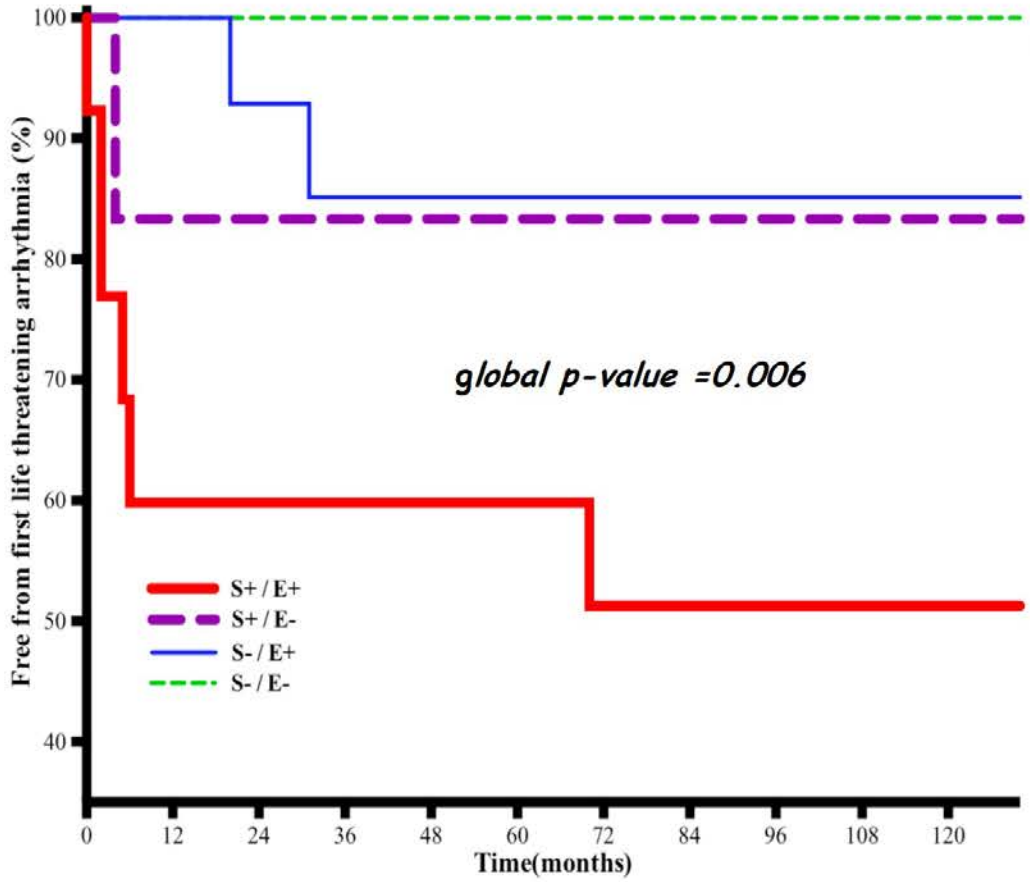

GEMS IT MAC1200 ST LUCAS CAUAZZA ,
5 Mois , 7 Yours (17.04.2012)
FC 103 /min
I
II
III
AUR
AUL
AUF
U1
U2
U3
U4
U5
U6


EKG-S
17:18:49TI VTACH 12 BTS 199 /min
17:56:28TI VTACH 11 BTS 189 /min
18:17:48TI MAX HERZFREQUENZ 169 /min
18:42:09TI VTACH 61 BTS 231 /min


2646
1736
Pause RR=2646
RR irreg. fin crise <-> 00:01:37


22:38:16 16/12/2014 pause 3.8 sec
666
664
676
3776
680

BRUGADA



n=106 months	0	12	24	60	96	120
S+/E+ = Sympto. & Spont. Type 1	14	6	6	6	3	2
S+/E- = Sympto. & Drug induced	7	5	5	4	3	2
S-/E+ = Asympto. & Spont. Type 1	22	22	13	11	6	3
S-/E- = Asympto. & Drug induced	63	63	63	63	63	63

Asymptomatic AND drug-induced type 1 ECG pattern → LOW RISK

Others clinical situations

→ Intermediate risk ?

Symptoms AND Spontaneous type 1 ECG pattern → HIGH RISK

Andorin et al. Heart Rhythm 2016

BRUGADA

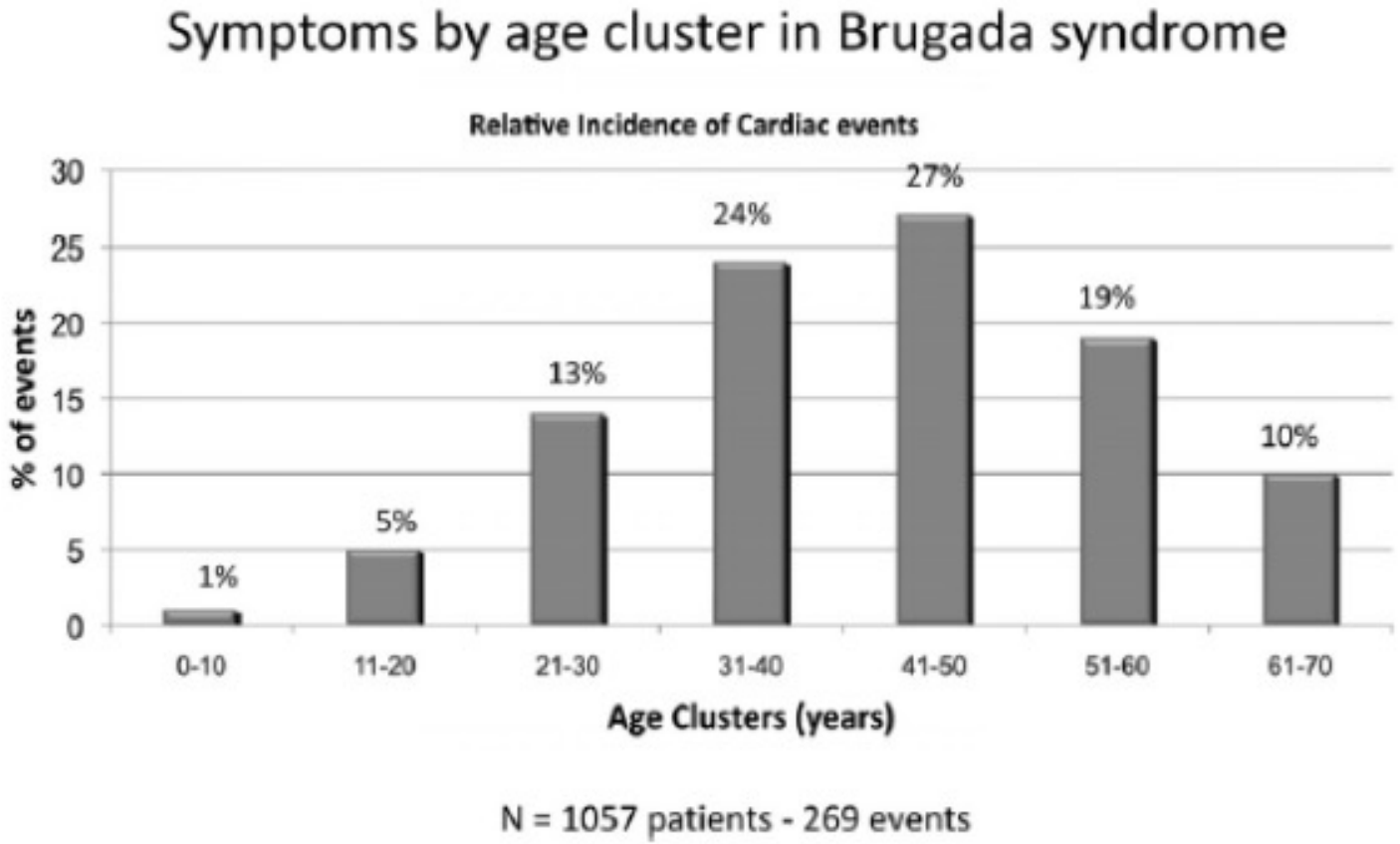
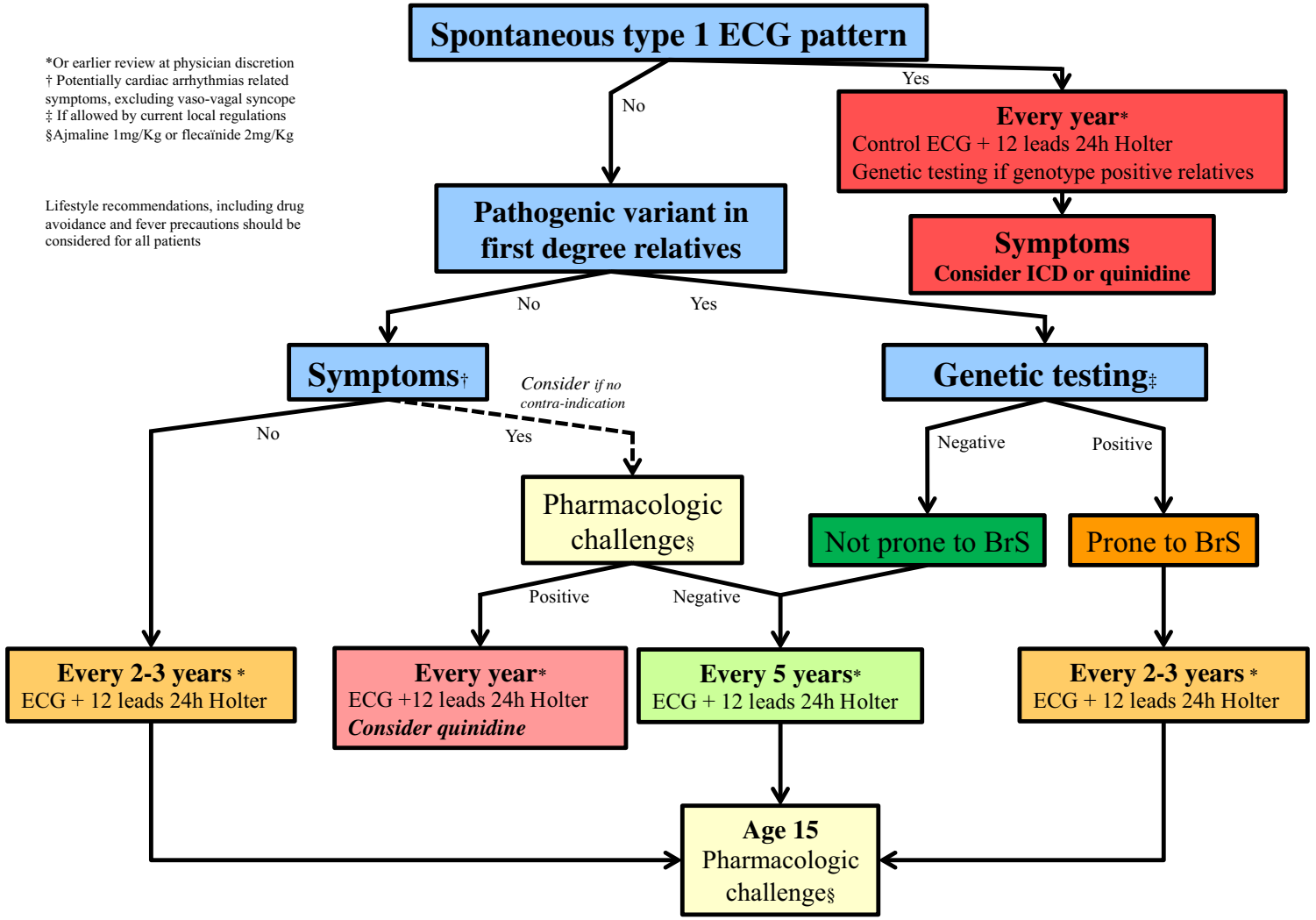


Figure 4. Relative percentage of symptomatic Brugada syndrome patients by age clusters showing a peak of incidence in the third and fourth decades of life (data from the Pavia Brugada syndrome registry).

BRUGADA



*Or earlier review at physician discretion
† Potentially cardiac arrhythmias related symptoms, excluding vaso-vagal syncope
‡ If allowed by current local regulations
§Ajmaline 1mg/Kg or flecaïnide 2mg/Kg

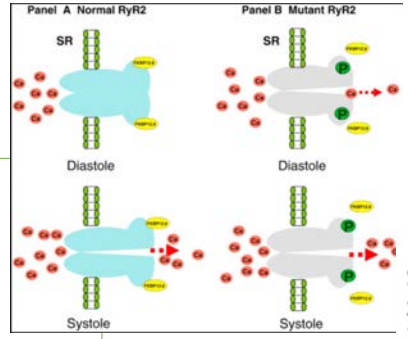
Lifestyle recommendations, including drug avoidance and fever precautions should be considered for all patients

Management of the Young with a known BrS in the Family

CPVT

PHYSIOPATH

RyR2 ++ AD
CASQ2 AR
Mutation ~ 60%
Trigger effot/émotion ++



PRONOSTIC

1ères manifestations 10-20 ans

Mort subite à 8 ans → 11% sous B-bloquants
25% sans traitement

DAI PREVENTION Iaire

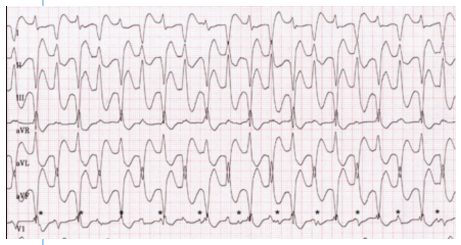
ESC European Society of Cardiology
ESC GUIDELINES

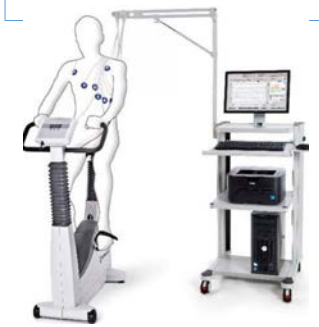
TV ou syncope sous B-bloquants

Programmation DAI → zones hautes
longue détection
Choc = stim Σ

DIAGNOSTIC

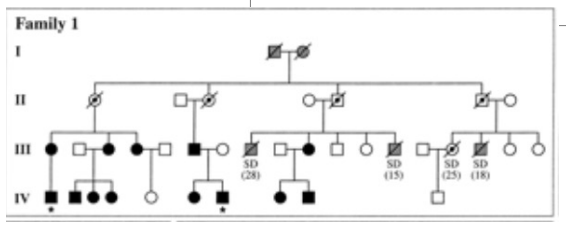
TV polymorphes
TV bidirectionnelles
Bilan morpho normal
Epreuve d'effort ++
Holter
Génétique





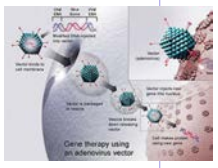
PRISE EN CHARGE

B-bloquants ++ (IIa pour porteur sain)
+/- Flecaine
Restriction sportive
Dépistage familial

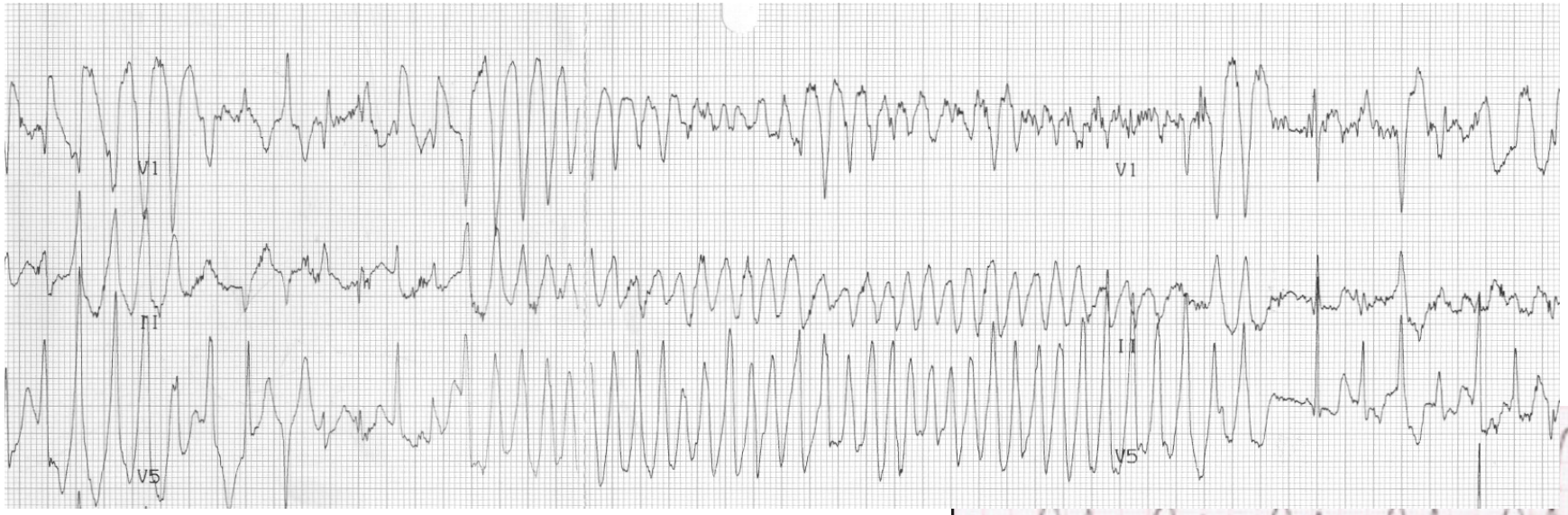


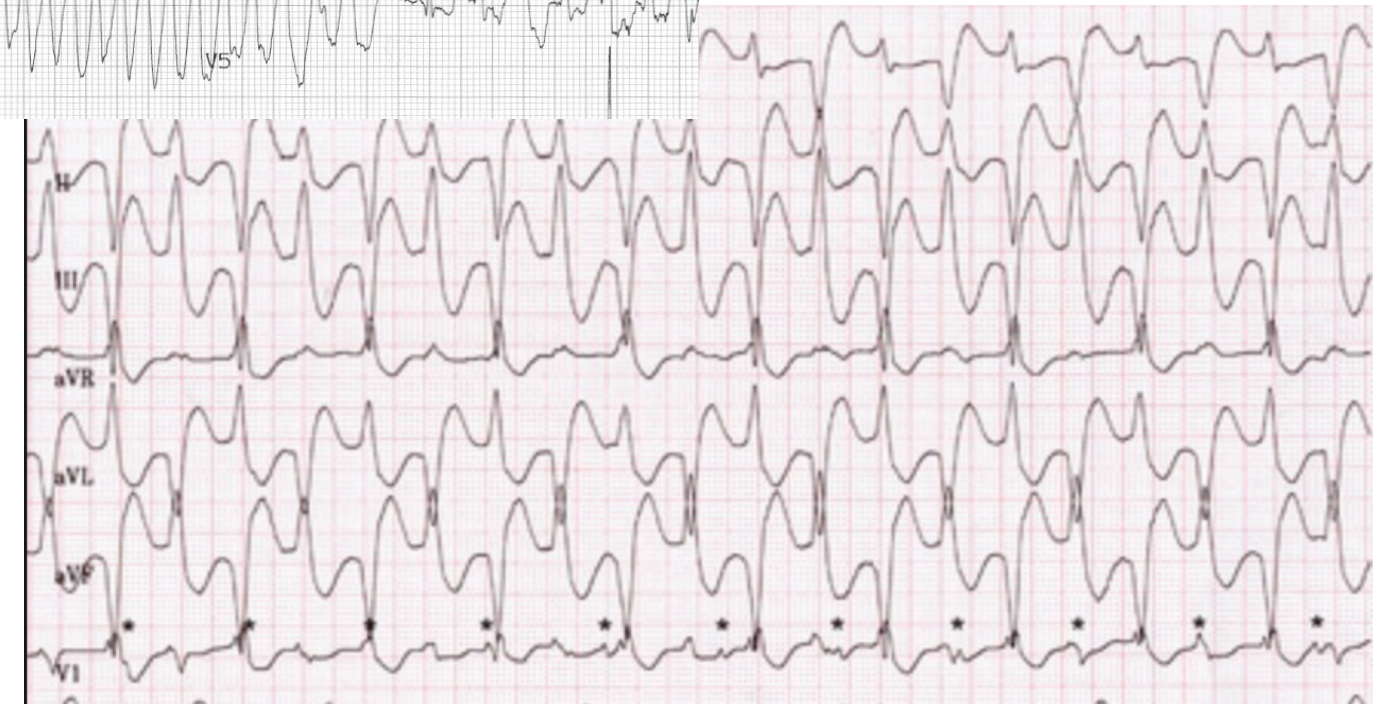
PERSPECTIVES

Dénervation
Verapamil
Test adrenaline
Ablation
Thérapie génique



CPVT

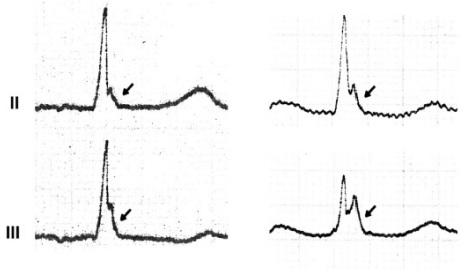




REPOLARISATON PRECOCE

PHYSIOPATH

??? H>F
Influence vagale
Génétique mal élucidée
Overlap Brugada
Pattern = 5% popu générale !



DIAGNOSTIC

Sus dec point J ≥1 mm dans 2 dérivations contiguës en inférieur ou latéral
+
TV polymorphe ou FV

PRISE EN CHARGE

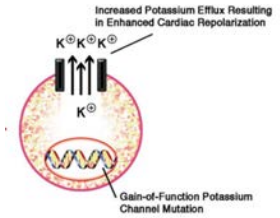
Isuprel orage rythmique
+/- Quinidine prévention IIaire

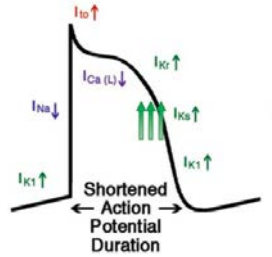
DAI PREVENTION Iaire

A priori pas d'indication
A discuter ++ centre expert (IIb)
(histoire familiale, syncope, pattern à risque)

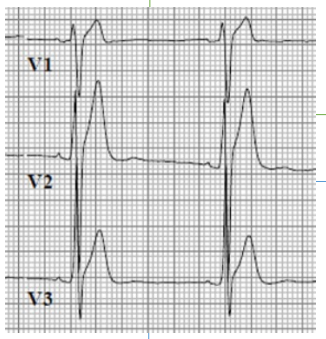
>2mm
ST horizontal ou descendant

QT COURT



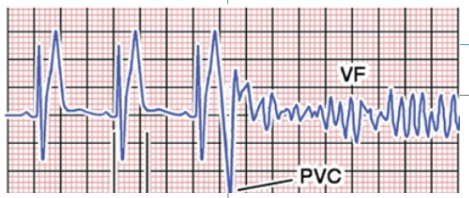


5 gènes mais mutation 20%
Overlap gènes LQTS et Brugada
40% de mort subite à 40 ans



QTc ≤ 340
QTC ≤ 360 +:
Mutation
Histoire famille SQTS ou SCD < 40 ans
TV/FV idiopathique

ESC European Society of Cardiology
ESC GUIDELINES



Quidine ? Sotalol ?
Si refus ou CI de DAI ou mort subite familiale (IIb)

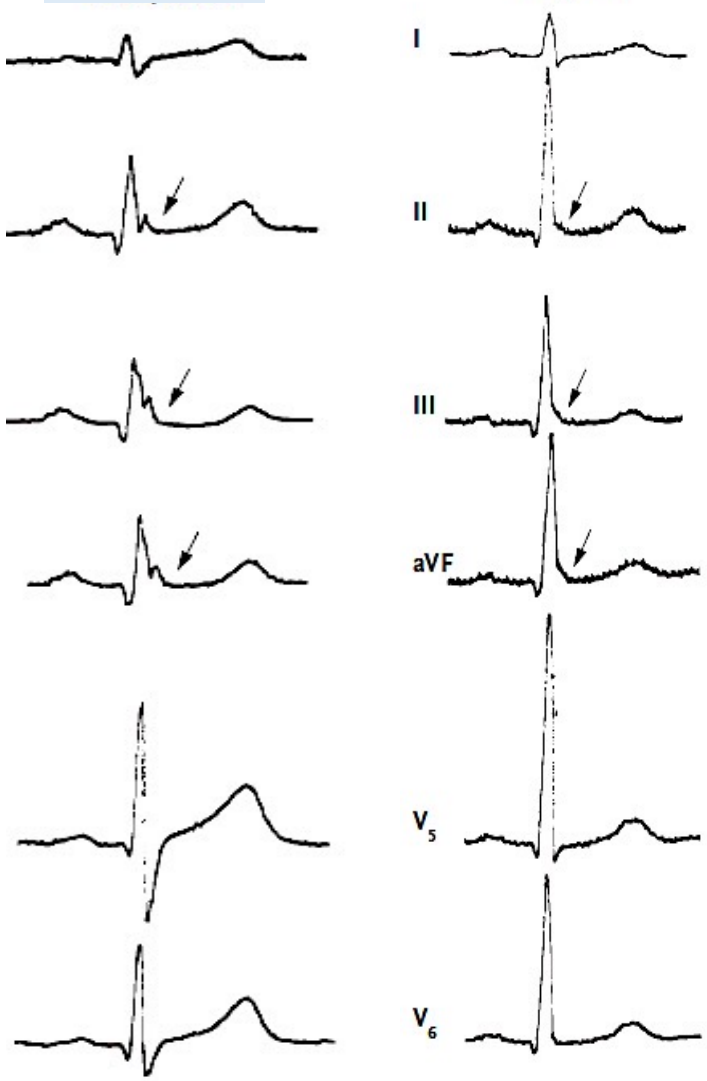
TV soutenue
Histoire familiale SCD ? (IIb)

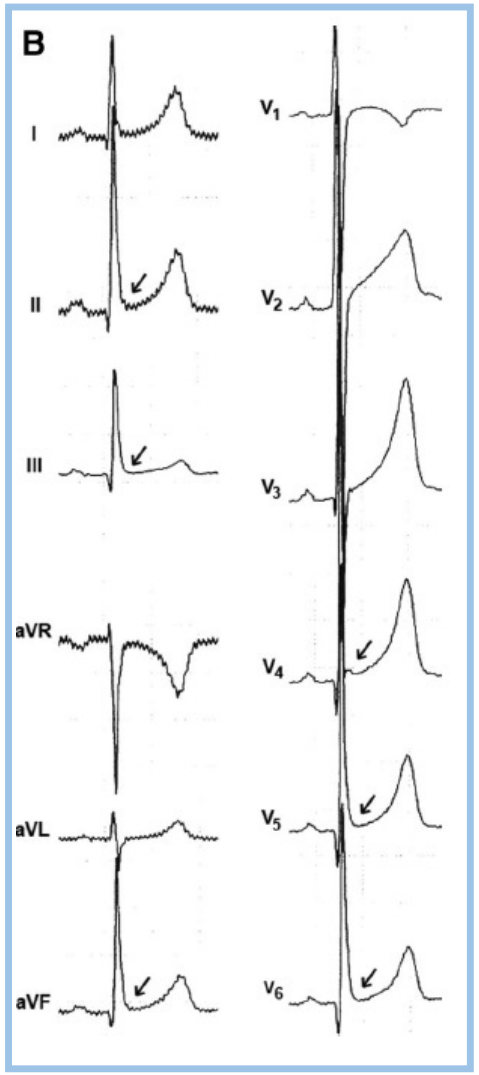
Eliminer cause 2aire:
hyperCa, hyperK, acidose, tachycardie, catécholamines…

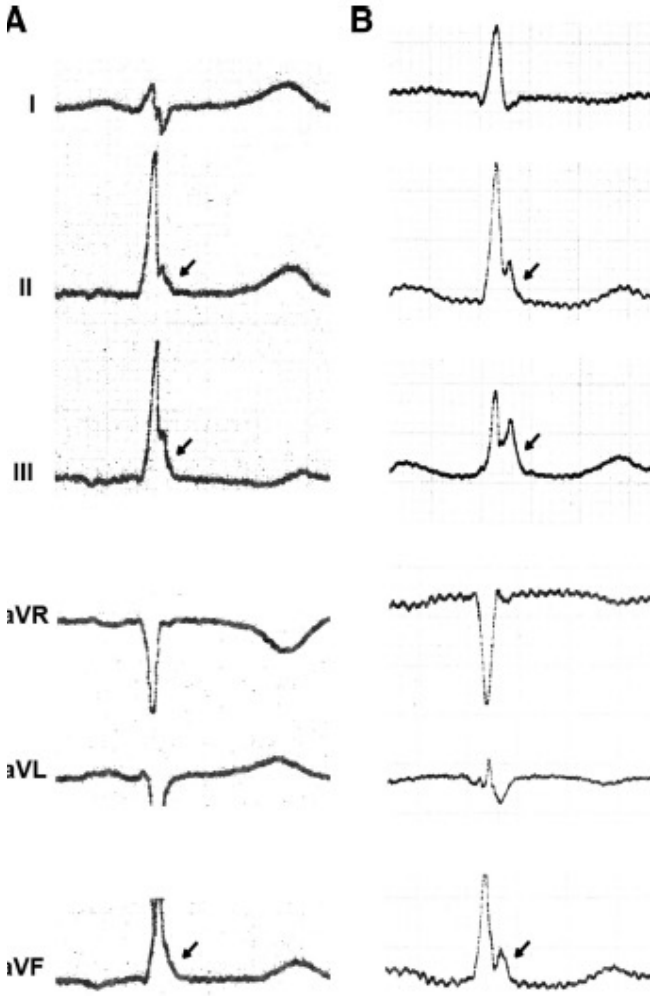
REPOLARISATON PRECOCE

Notching

Slurring



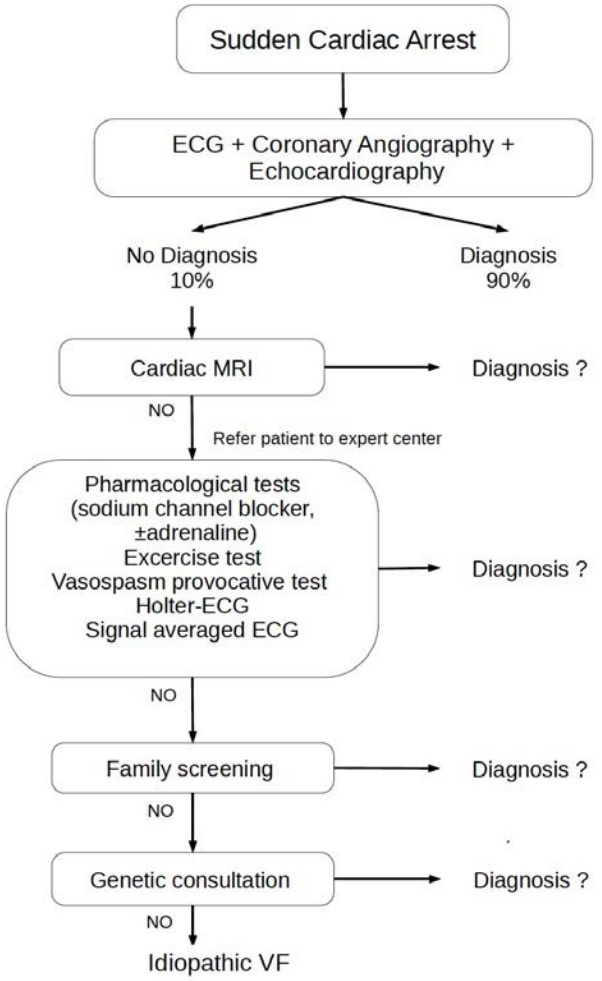




ST horizontal ou descendant = mauvais pronostic

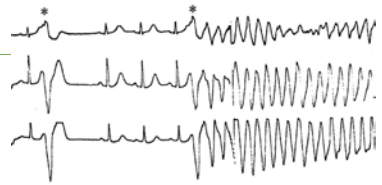
FV IDIOPATHIQUE

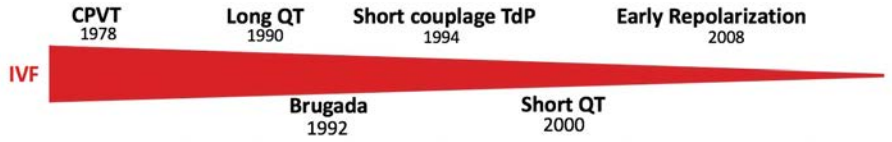
DIAGNOSTIC



PHYSIOPATH

???
ESV du Purkinje
5% ACR





PRONOSTIC

Risque de récidive significatif
20% à 4 ans registre francilien

ESC European Society of Cardiology
European Heart Journal (2018) 00, 1–9
doi:10.1093/eurheartj/ehy098
CLINICAL RESEARCH
Arrhythmia/electrophysiology

Characteristics and clinical assessment of unexplained sudden cardiac arrest in the real-world setting: focus on idiopathic ventricular fibrillation

PRISE EN CHARGE

Bilan étiologique exhaustif ++
Prise en charge psychologique
DAI en prévention II^{aire}
Enquête familiale:

Approach	Action*
History taking and physical examination	• Personal clinical history • Family history focused on cardiac diseases or sudden deaths
ECG	• Baseline 12-lead ECG with standard and high precordial leads • 24-hour ambulatory ECG • Exercise stress test • Signal-averaged ECG • Provocative test with ajmaline/flecainide (when Brugada syndrome is suspected)
Cardiac imaging	• Two-dimensional echocardiography and/or CMR (with or without contrast)
Genetic testing	• Targeted molecular testing and genetic counselling if there is the clinical suspicion of a specific disease • Referral to a tertiary centre specialized in evaluation of the genetics of arrhythmias

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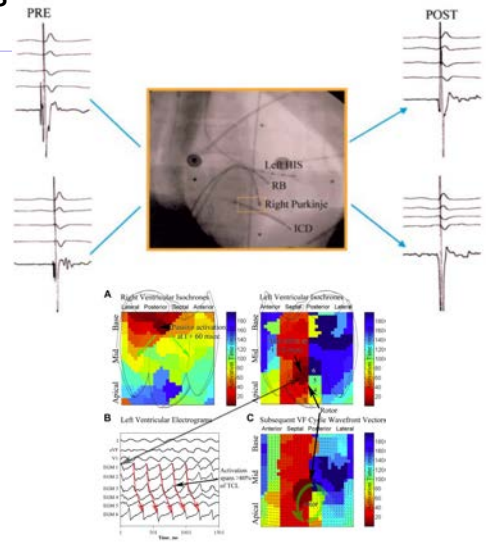
ESC GUIDELINES

PERSPECTIVES

Nouveaux phénotypes ?
Ablation ESV initiatrice
Rotors



FV IDIOPATHIQUE

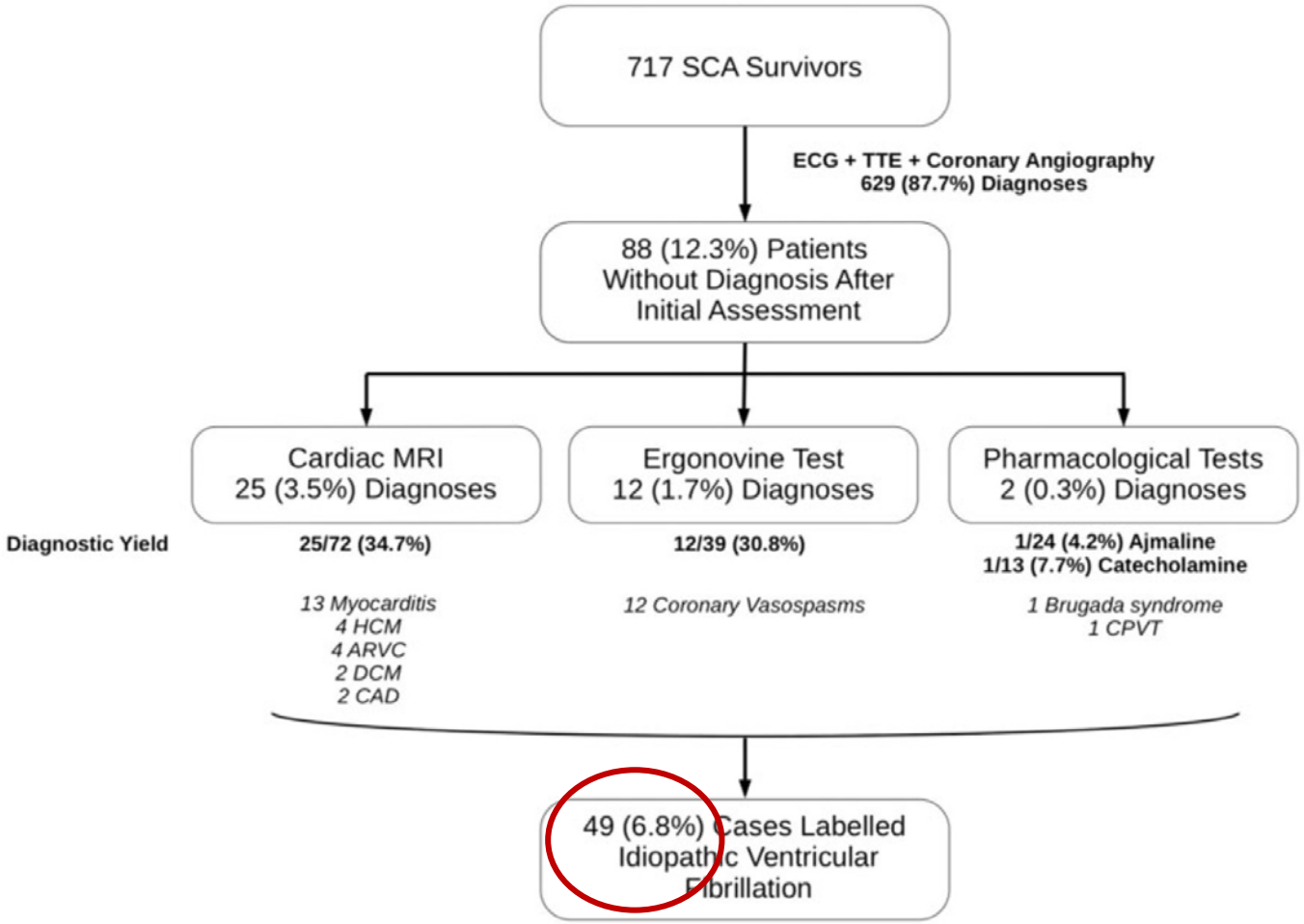


Table 2 **Medical investigations of cases labelled idiopathic ventricular fibrillation (performed during the index hospitalization following the sudden cardiac arrest or planned subsequently after discharge)**

	IVFs (n = 49), n (%)
Coronary angiography	47 (95.9)
Cardiac MRI	40 (81.6)
Provocative testing	
Ergonovine	19 (38.8)
Ajmaline	21 (42.9)
Isoprenaline	10 (20.4)
Adenosine	2 (4.1)
Adrenaline	0 (0)
Electrophysiological study	12 (24.5)
Genetic testing	9 (18.4)
Holter-ECG	6 (12.2)
Right ventricular angiography	5 (10.2)
Exercise testing	4 (8.2)
Signal averaged ECG	2 (4.1)
Coronary CT	1 (2.0)
Cardiac scintigraphy (for ARVC)	1 (2.0)
Cardiac biopsy	0 (0)

Waldmann et al. European Heart Journal 2018

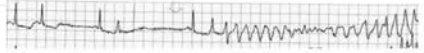
QT LONG

PHYSIOPATH

17 gènes connus – 1/2500
Mutation identifiée dans 75%:
LQTS1 KCNQ1 (effort ++, natation)
LQTS2 KNCH2 (émotion ou bruit)
LQTS3 SCN5A (repos ou sommeil)
Autosomique dominant (95%)

PRONOSTIC

Taux mort subite annuel 0.3-0.9%
5% par an si antécédent de syncope
LQT3 et QTc > 500 ms à haut risque



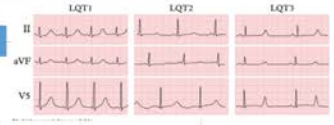
« Short-long-short »

DAI PREVENTION Iaire

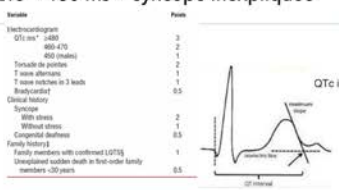
ESC GUIDELINES

TV malgré B-bloquants
Syncope

DIAGNOSTIC



QTc ≥ 480 ms
Score > 3
Mutation positive
QTc > 460 ms + syncope inexpliquée



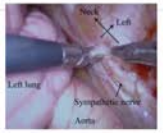
Bazett

$$QTc\ interval = \frac{QT\ interval}{\sqrt{RR\ interval}}$$

D2 ++ ou V5

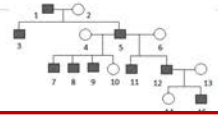
PERSPECTIVES

Dénervation
Flecaine ou mexiletine LQTS3
Stratification guidée par génétique



PRISE EN CHARGE

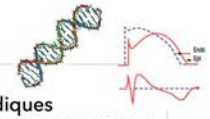
Médicaments contre indiqués
B-bloquants ++ (IIa pour porteur sain)
Restriction sportive
Dépistage familial
Orage rythmique: isuprel +/- SEES



CREDIBLEMEDS®
https://crediblemeds.org/

BRUGADA

PHYSIOPATH



Anomalie canaux sodiques
Mutation 20% (SCN5A ++, CACN1Ac)
Autosomique dominant
Pénétrance variable, H >> F

PRONOSTIC

Taux mort subite annuel
- 1% si type 1 spontané
- 3% si syncope
- 10% si ACR

Type 1 induit de meilleur pronostic

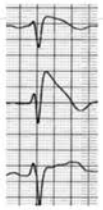
DAI PREVENTION Iaire

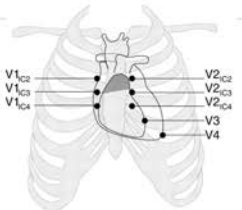
ESC GUIDELINES

TV soutenue
Syncope rythmique

DIAGNOSTIC

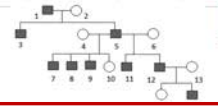
Type 1 ≥ 2 mm dans 1 dérivation
V1 ou V2 + dérivations hautes (2-3 EIC)
+/- ajmaline (1 mg/kg IV 5-10 min)





PRISE EN CHARGE

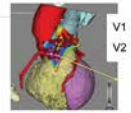
Médicaments contre indiqués
Traitement précoce fièvre
Eviter repas copieux ou alcool excessif
Restriction sportive
Dépistage familial
Orage rythmique: isuprel +/- quinidine



BrugadaDrugs.org

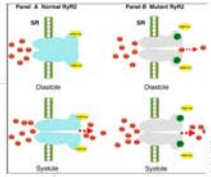
PERSPECTIVES

SVP controversée
Place de la quinidine
Indications élargies S-ICD ?
Ablations ?
(substrat épicardique VD)

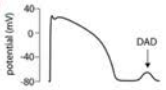


CPVT

PHYSIOPATH



RyR2 ++ AD
CASQ2 AR
Mutation ~ 60%
Trigger effot/émotion ++



PRONOSTIC

1ères manifestations 10-20 ans

Mort subite à 8 ans
- 11% sous B-bloquants
- 25% sans traitement

DAI PREVENTION Iaire

ESC GUIDELINES

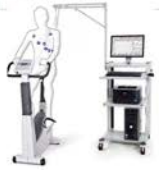
TV ou syncope sous B-bloquants

Programmation DAI
- zones hautes
- longue détection

Choc = stim Σ

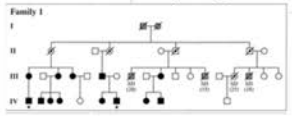
DIAGNOSTIC

TV polymorphes
TV bidirectionnelles
Bilan morpho normal
Epreuve d'effort ++
Holter
Génétique



PRISE EN CHARGE

B-bloquants ++ (IIa pour porteur sain)
+/- Flecaine
Restriction sportive
Dépistage familial



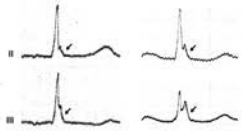
PERSPECTIVES

Dénervation
Verapamil
Test adrenaline
Ablation
Thérapie génique

REPOLARISATON PRECOCE

PHYSIOPATH

??? H>F
Influence vagale
Génétique mal élucidée
Overlap Brugada
Pattern = 5% popu générale !



DIAGNOSTIC

Sus dec point J ≥1 mm dans 2 dérivations contiguës en inférieur ou latéral
+
TV polymorphe ou FV

PRISE EN CHARGE

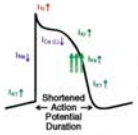
Isuprel orage rythmique
+/- Quinidine prévention IIaire

DAI PREVENTION Iaire

A priori pas d'indication
A discuter ++ centre expert (IIb)
(histoire familiale, syncope, pattern à risque)

>2mm
ST horizontal ou descendant

QT COURT



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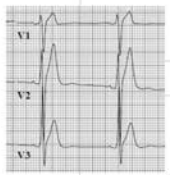

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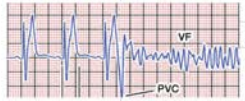
ESC GUIDELINES



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Si refus ou CI de DAI ou mort subite familiale (IIb)

TV soutenue
Histoire familiale SCD ? (IIb)

Eliminer cause 2aire:
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Merci pour votre attention !

Victor WALDMANN

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