

How to identify early-repolarization patients at risk?

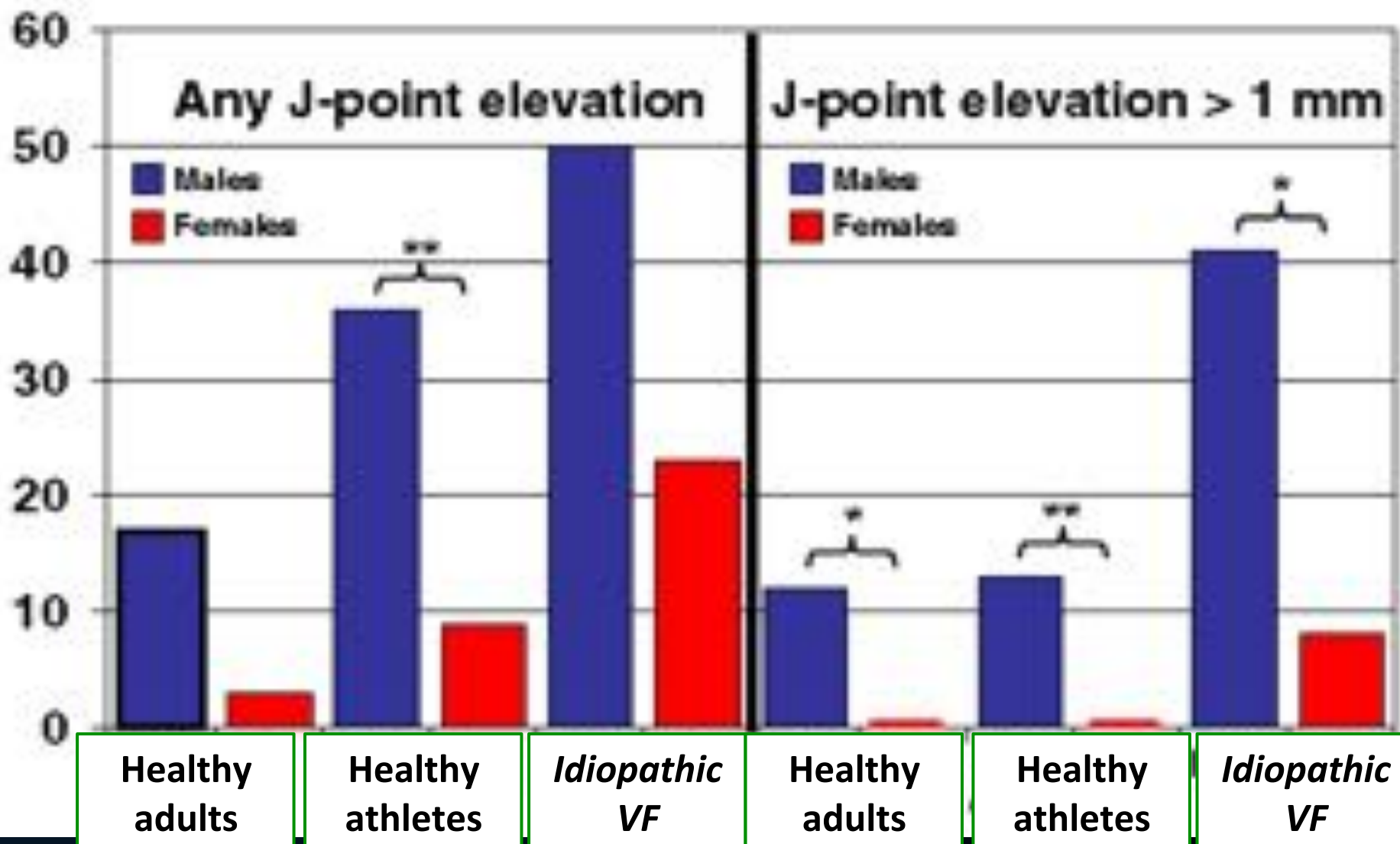
Sami Viskin.

Tel Aviv Medical Center, Israel



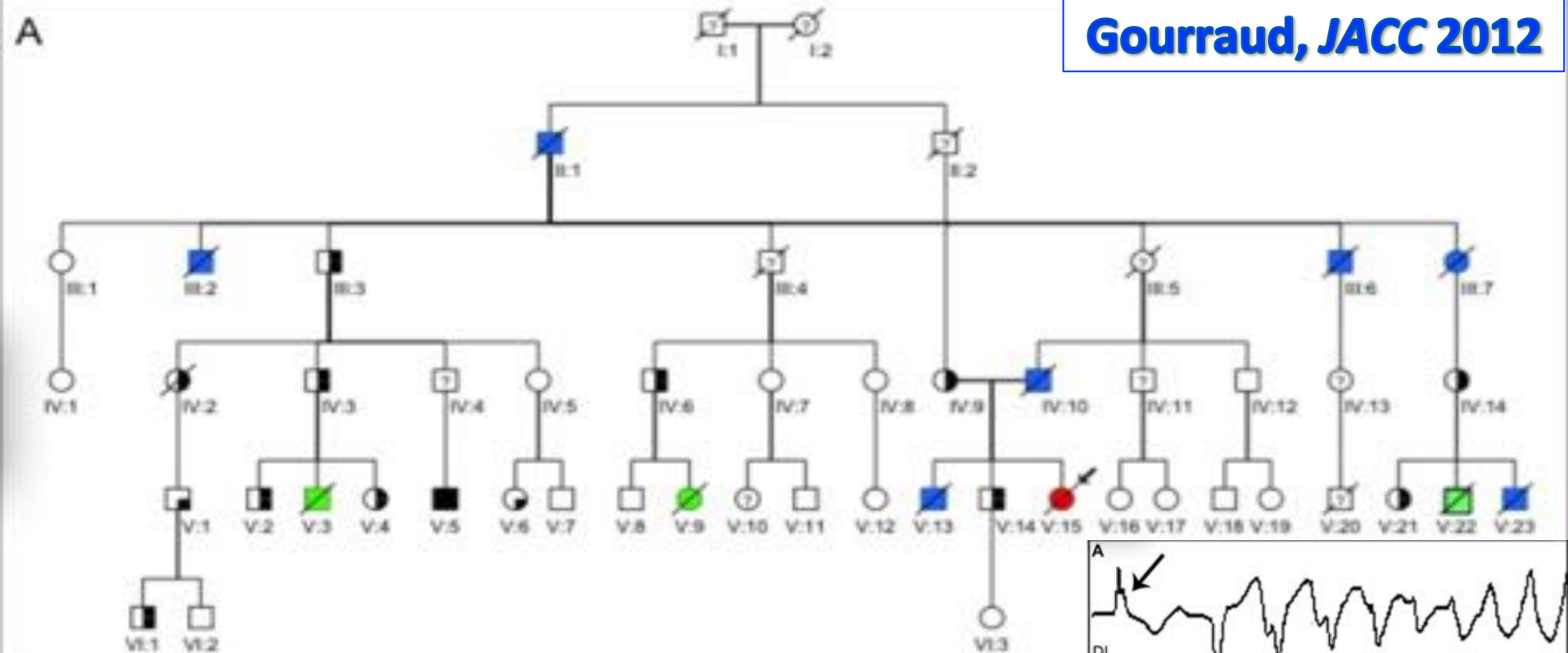
You are not the only one with a difficult Job

Influence of Gender on the Incidence of J-Point Elevation in the Different Patient Groups

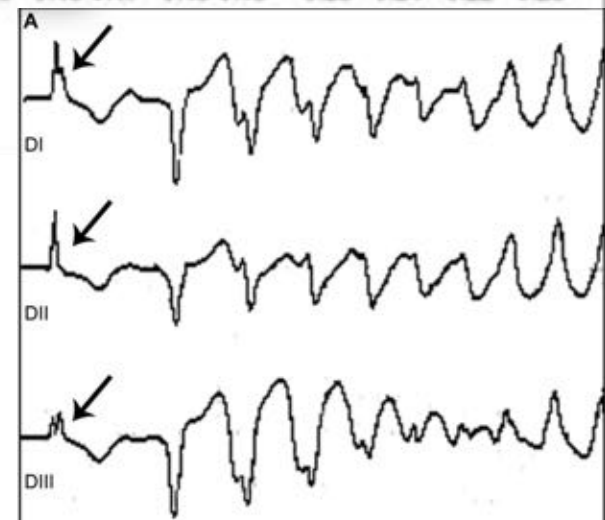


Identification of large families with early repolarization syndrome.

Gourraud, *JACC* 2012



- | | |
|--|--|
| ■ ER syndrome | ■ Major ER pattern (>2 mm) |
| ■ Negative autopsy | ■ Minor ER pattern (1-2 mm) |
| ■ Unexplained sudden death | ? Unavailable ECG |
| □ Normal ECG | ■ Probably normal ECG |



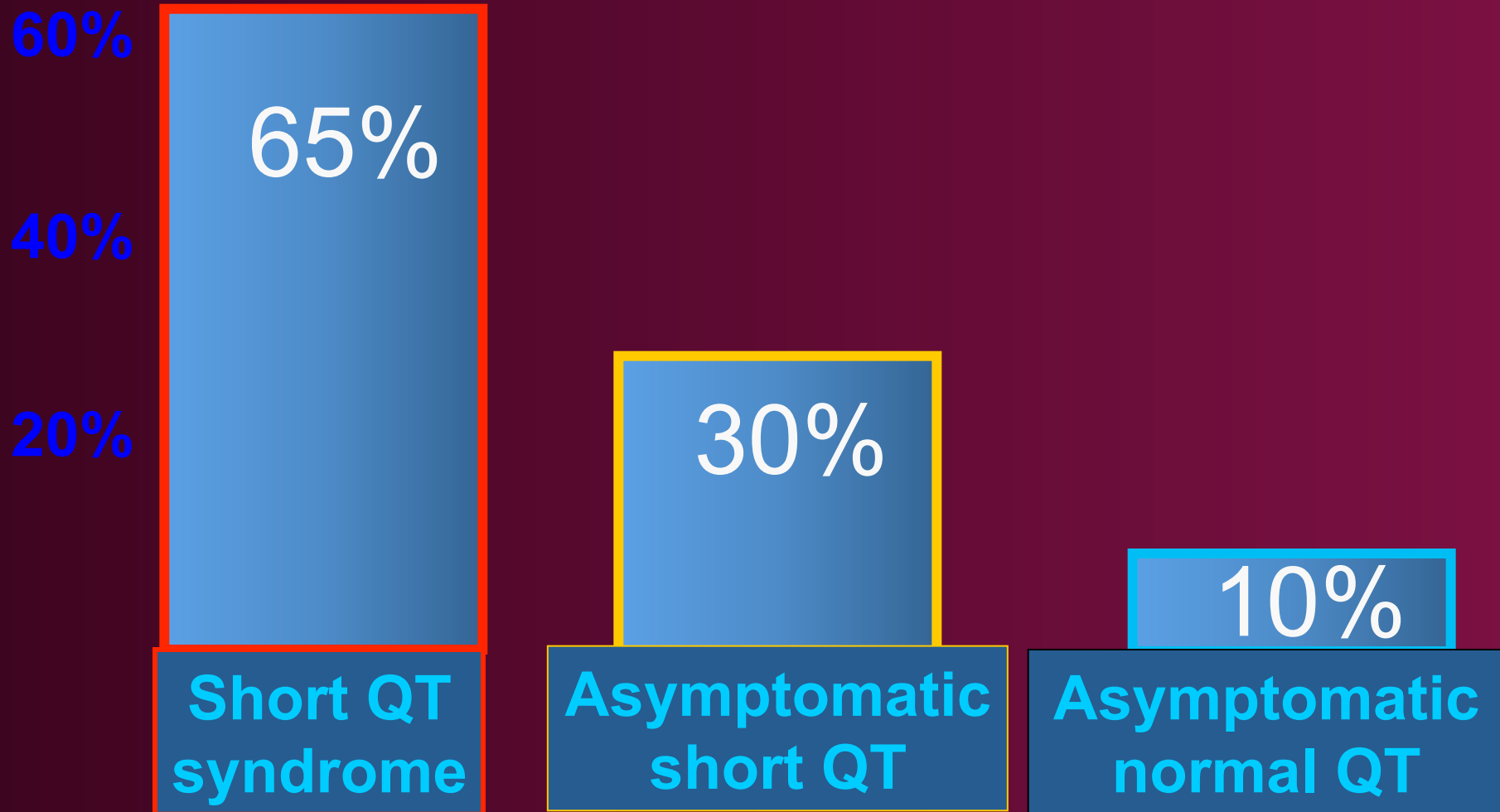
The Early Repolarization Pattern in the General Population

Clinical Correlates and Heritability

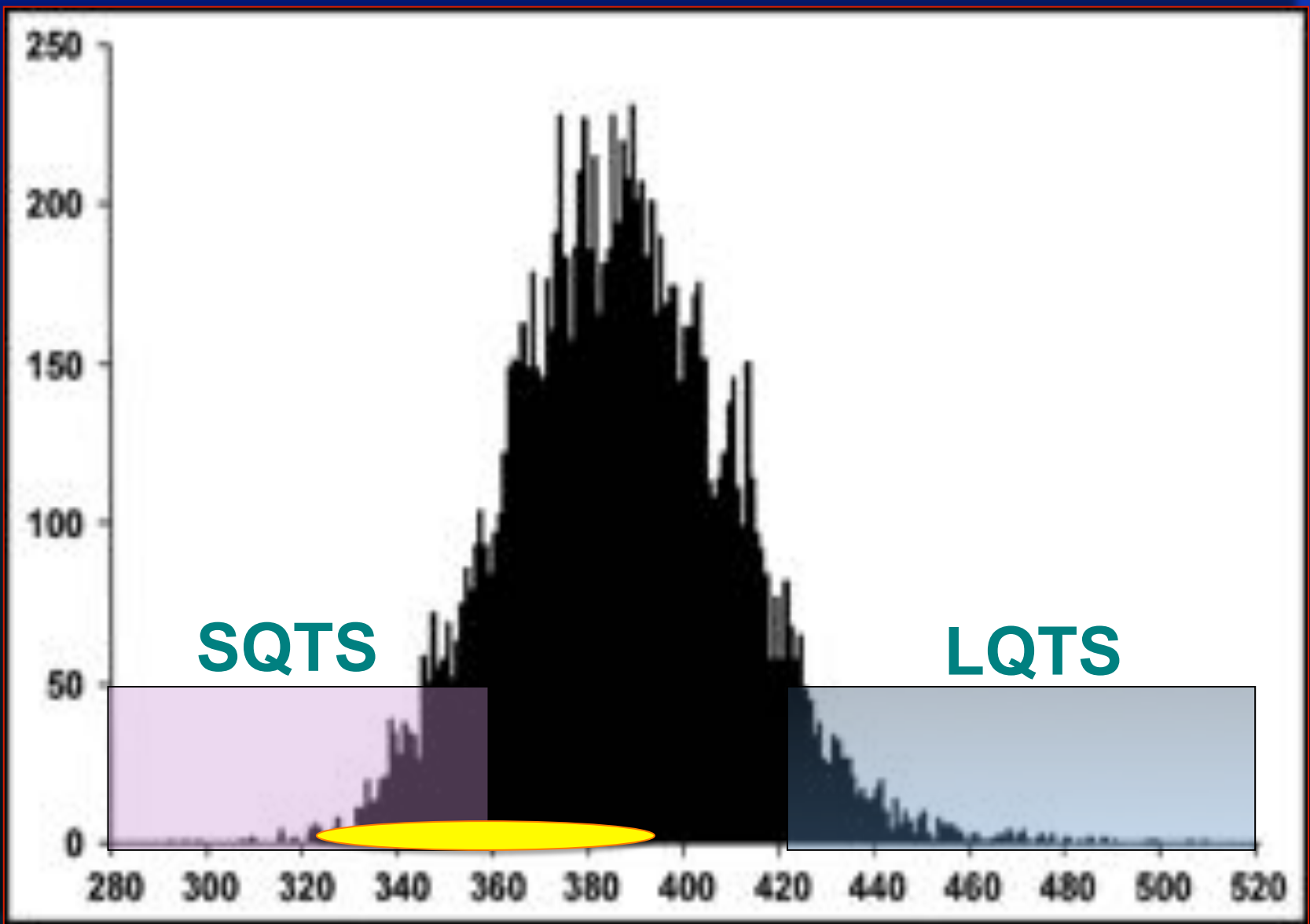
Peter A. Noseworthy, MD,[†] Jani T. Tikkanen, MB,[‡] Kirrano Porthan, MD,[§]
Lasse Oikarinen, MD, PhD,[§] Aaro Pietilä, MSc,[¶] Kenneth Harjula, MSc,[¶] Gina M. Peloso, MA,[‡]
Faisal M. Merchant, MD,^{*} Anni Jula, MD, PhD,[¶] Heikki Väänänen, Lic. Sc.,[§]
Shih-Jen Hwang, PhD,^{¶††} Christopher J. O'Donnell, MD, MPH,^{¶††} Veikko Salonen, MD, PhD,[¶]
Christopher Newton-Cheh, MD, MPH,^{†‡} Heikki V. Huikuri, MD[‡]
*Boston, Cambridge, and Framingham, Massachusetts; Oulu, Helsinki, and Turku, Finland;
and Bethesda, Maryland*

- Third generation Framingham Heart Study.**
- **Total: 9,444.**
 - **5% of ALL had early repolarization.**
 - **12% of siblings of individuals with ER also had ER [Odds ratio 2.2 (1.0 -4.9)]**

Early repolarization pattern in patients with SQTS, controls with short QT and controls with normal QT.

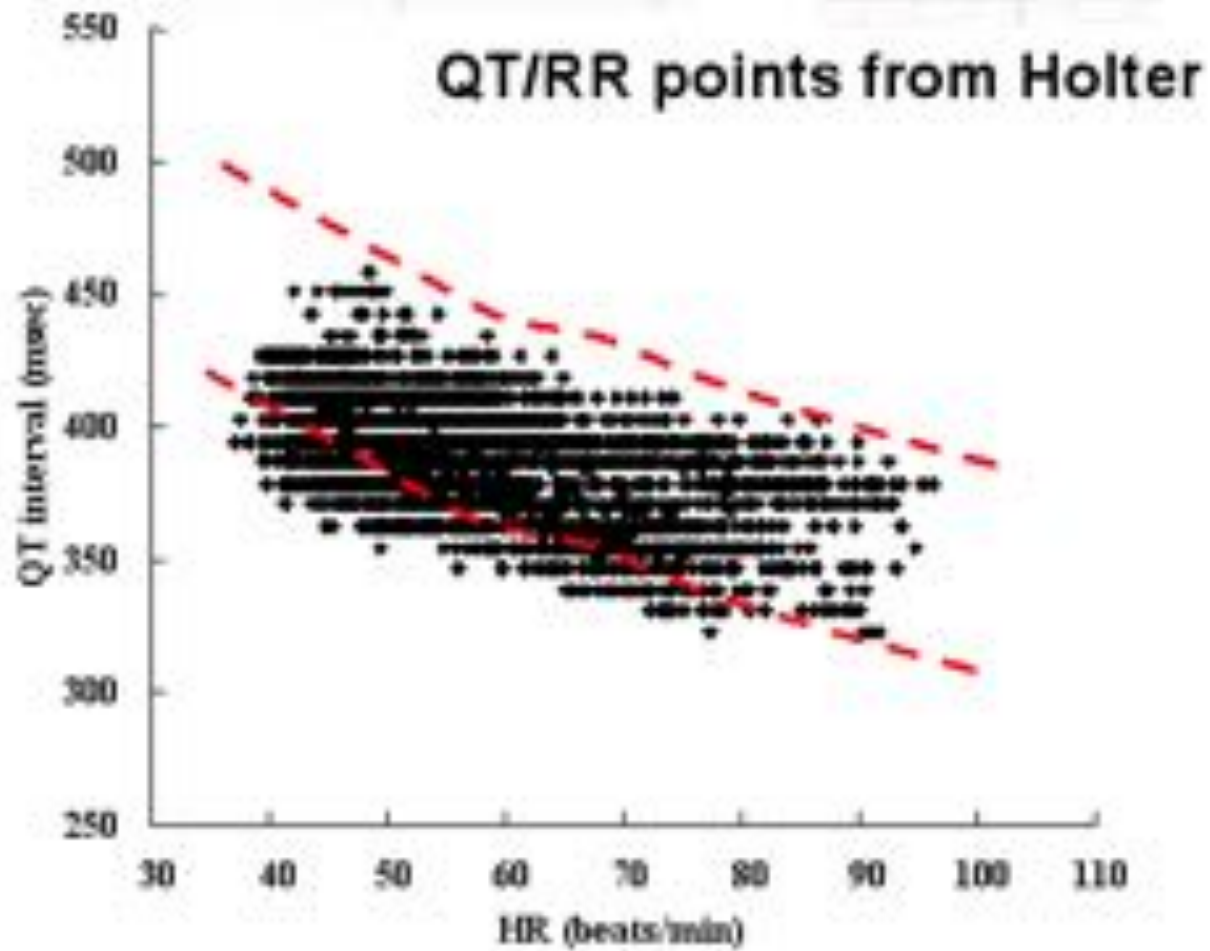


Watanabe (Shimizu), *HeartRhythm* 2010



Our Idiopathic VF patients
Viskin, *HeartRhythm* 2004.

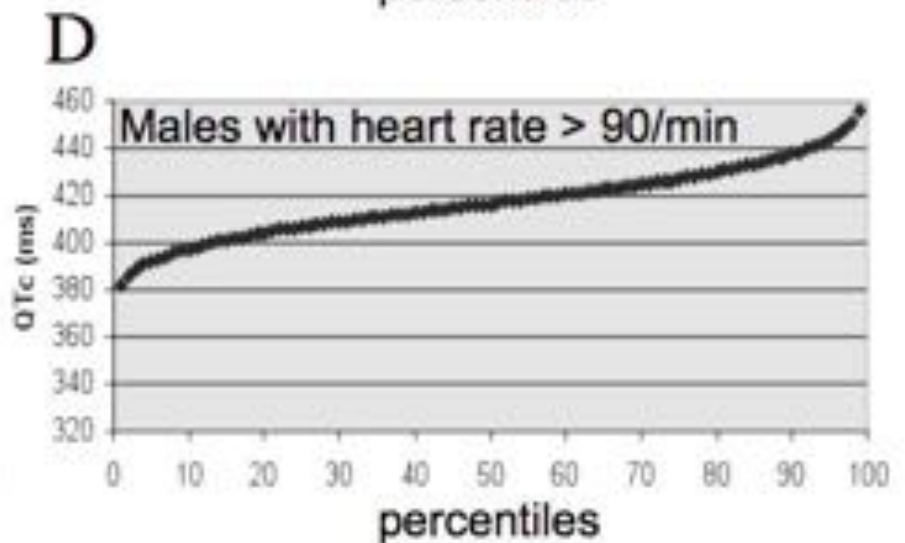
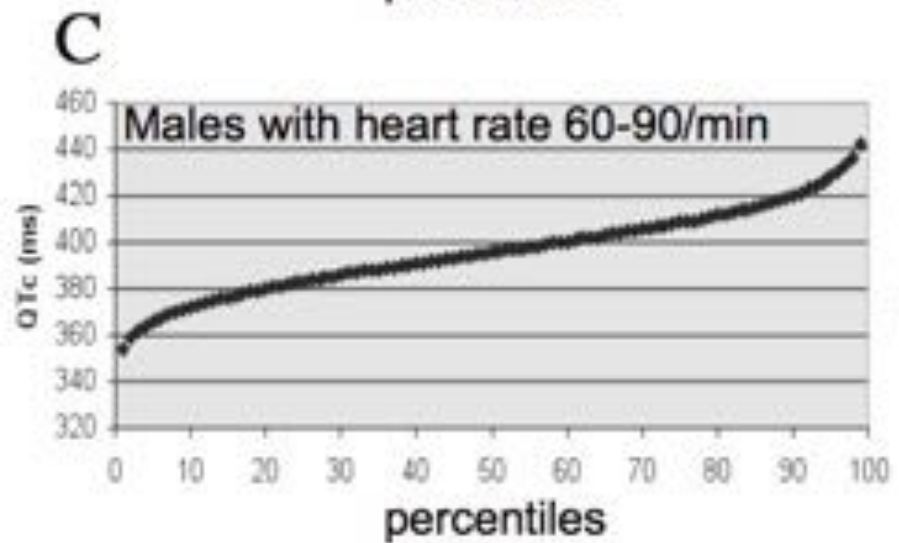
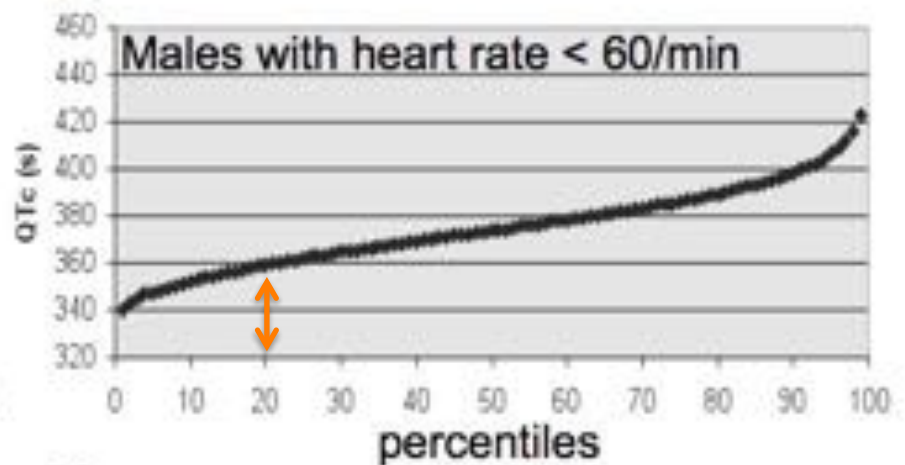
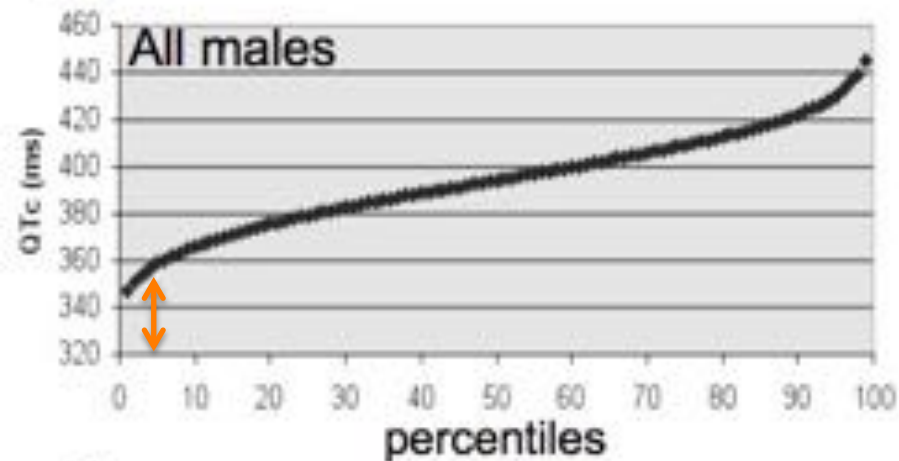
Male, 33 years old.
Idiopathic VF



Akira Fujiki, personal communication, 2005.

Distribution of QTc of 41,000 Swiss conscripts.

QTc shown as percentiles.

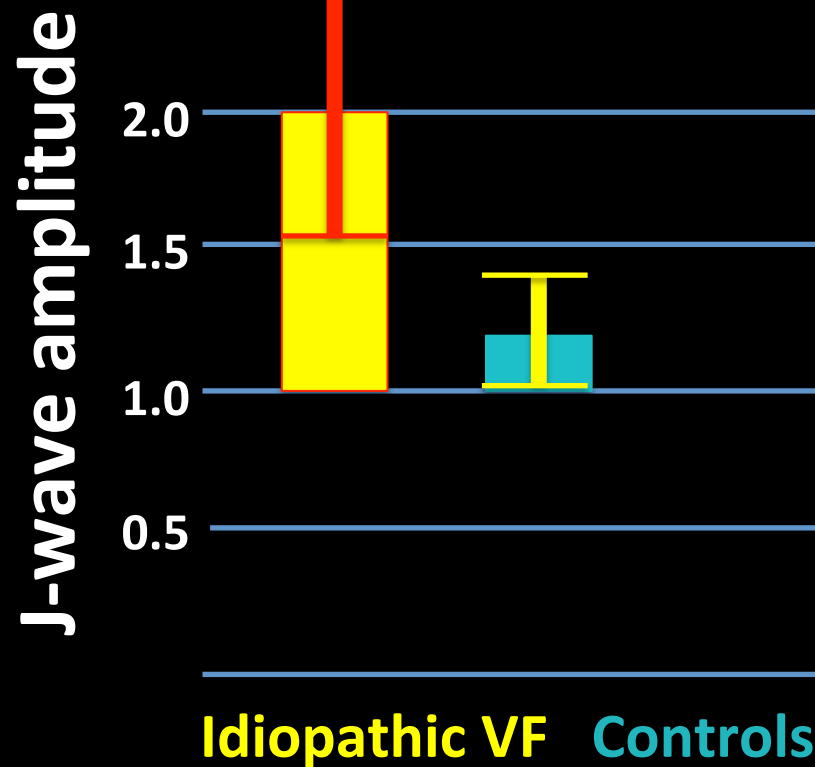
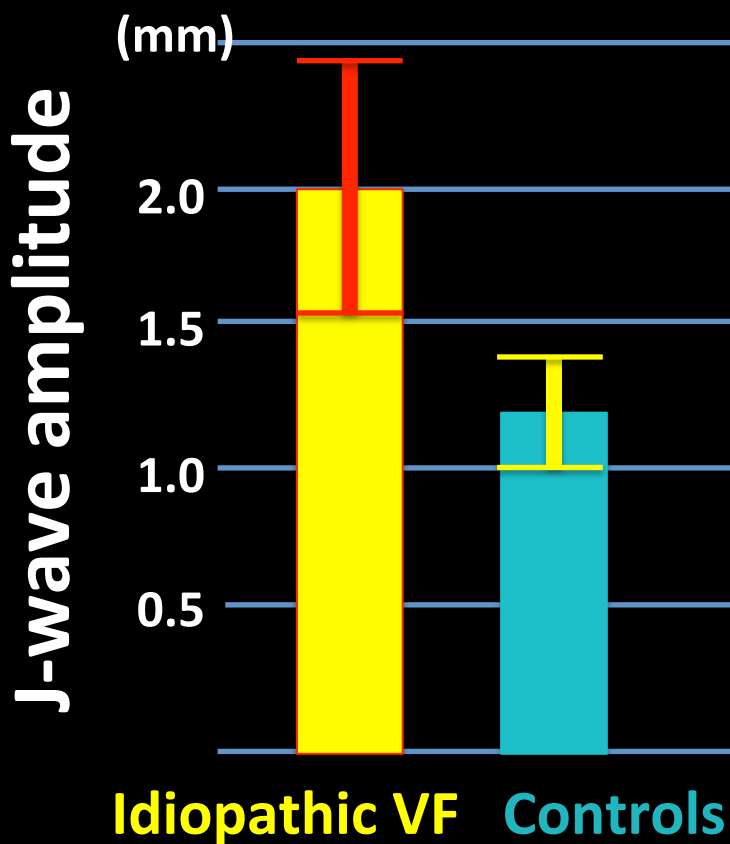


**Electrocardiographic
features to distinguish
“good” for “evil” early
repolarization?**

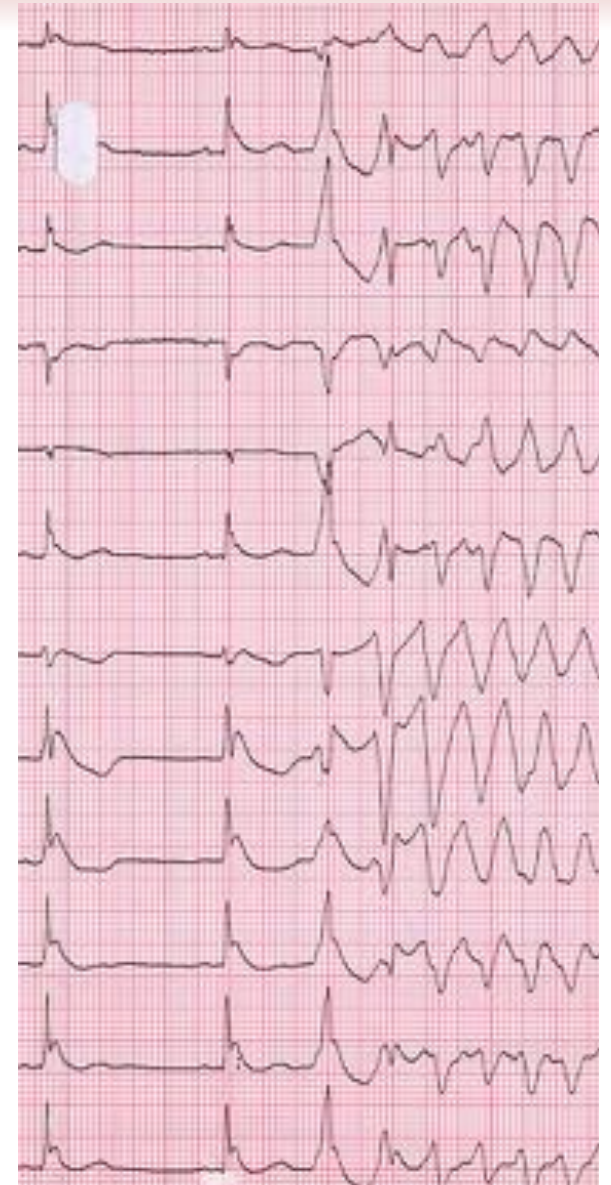
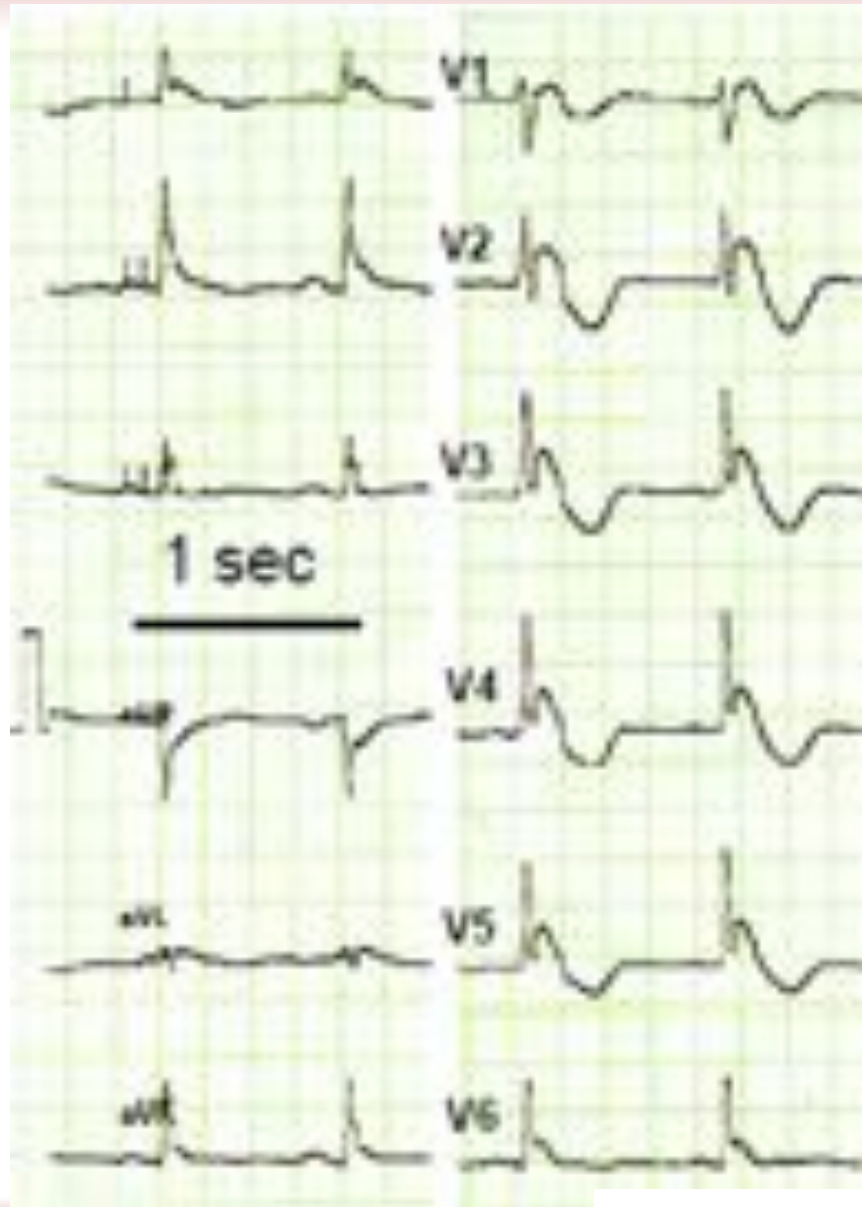


Size matters... but up to a limit

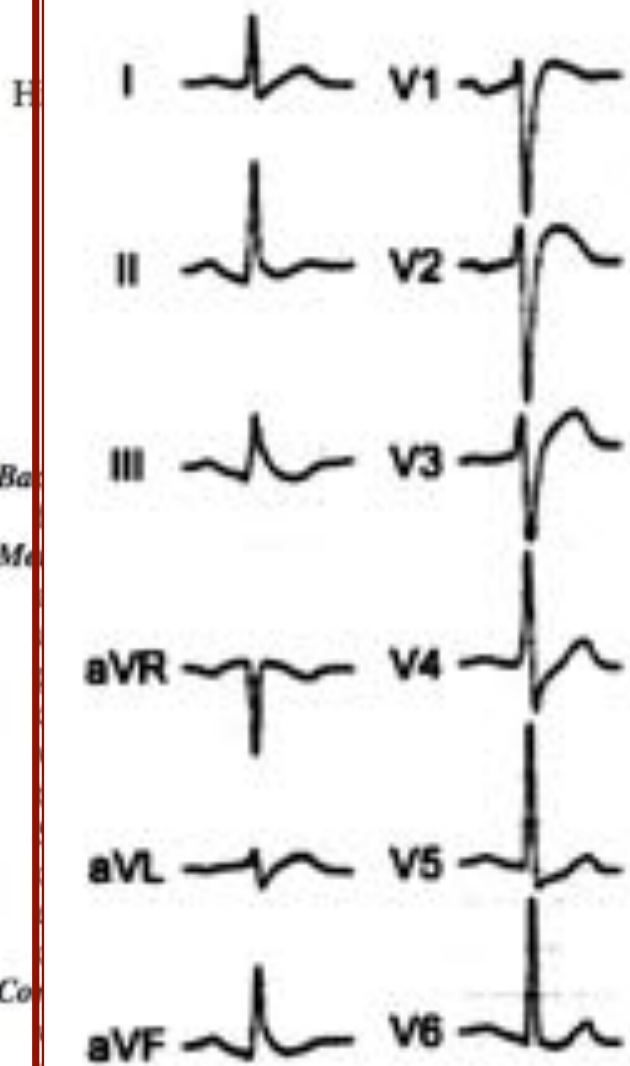
ORIGINAL ARTICLE



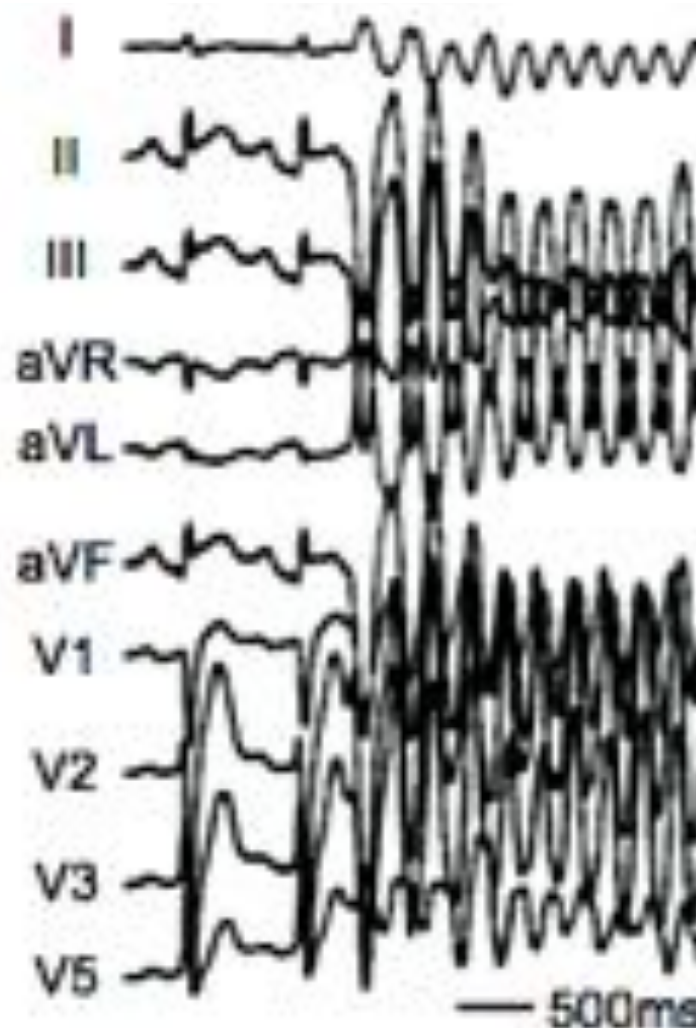
Monstrous J-waves



Electrocardiographic Characteristics and *SCN5A* Mutations in Idiopathic Ventricular Fibrillation Associated With Early Repolarization

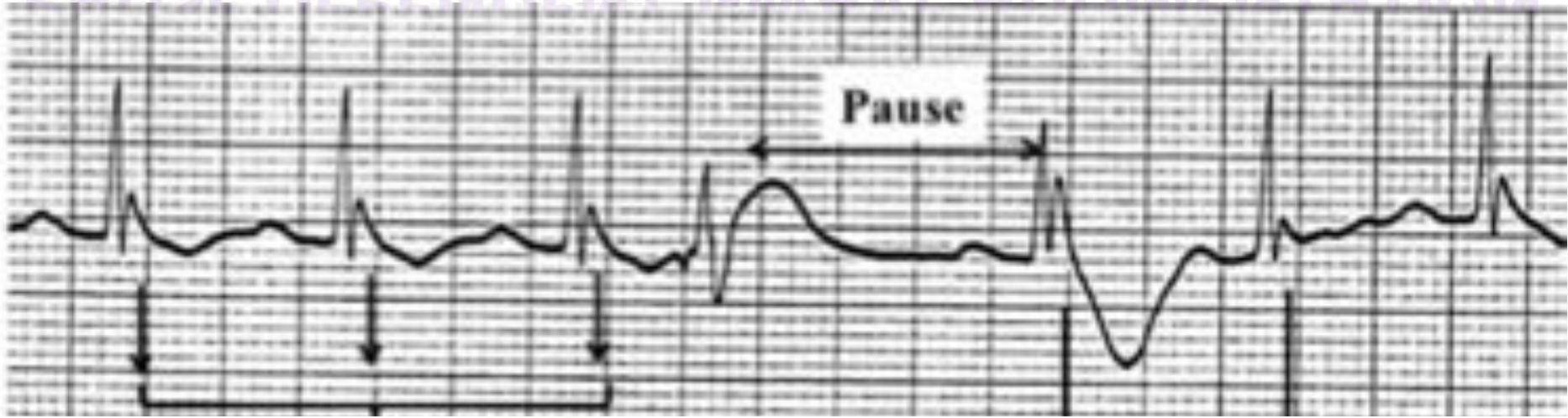


Pilsicainide

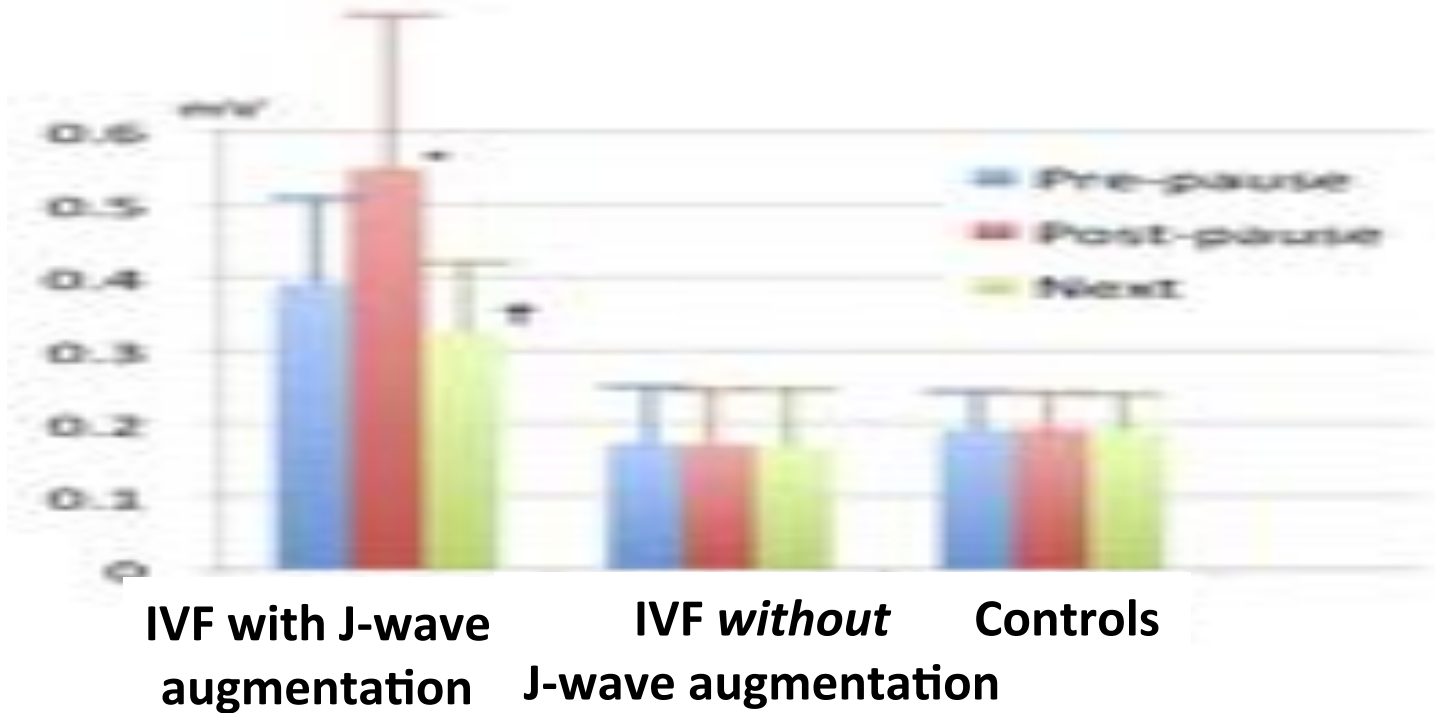


MD;
PhD;
S;
ventricular
fibrillation
perceived
terrible by
and QRS
monymous
residues
arrying an
velopment
etiological
rufficking
in patients
decreased
(81.)

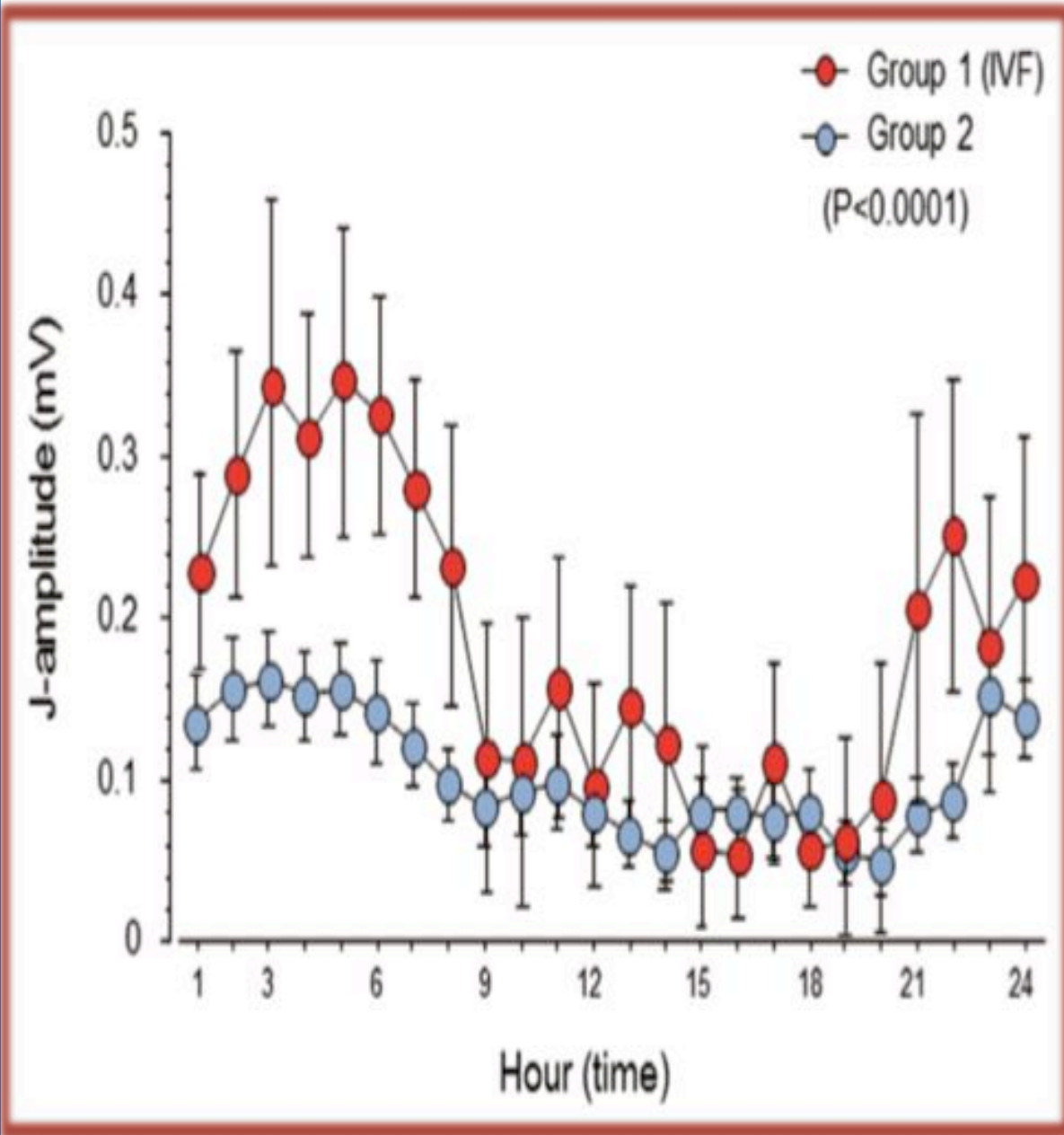
PAUSE DEPENDENT J-WAVE AUGMENTATION



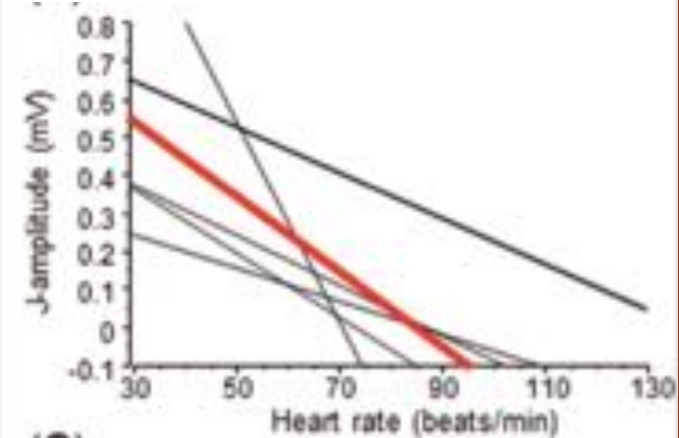
J-wave amplitude



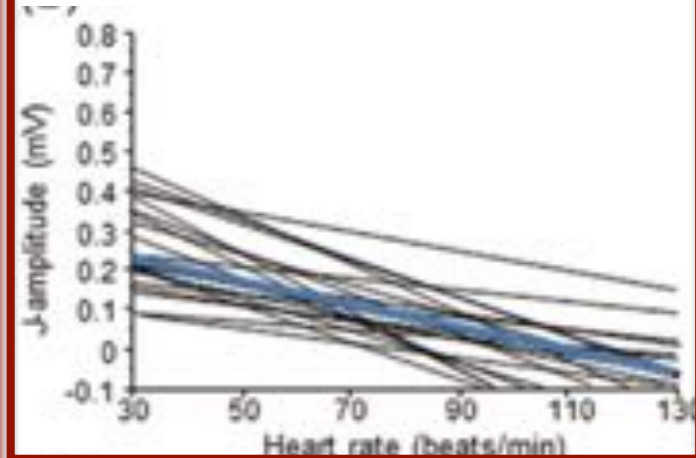
Steeper slope of J-wave to heart rate relationship.



Idiopathic VF



Healthy controls



Miyazaki, *Circ J* 2013

Bradycardia-dependent J-wave augmentation.

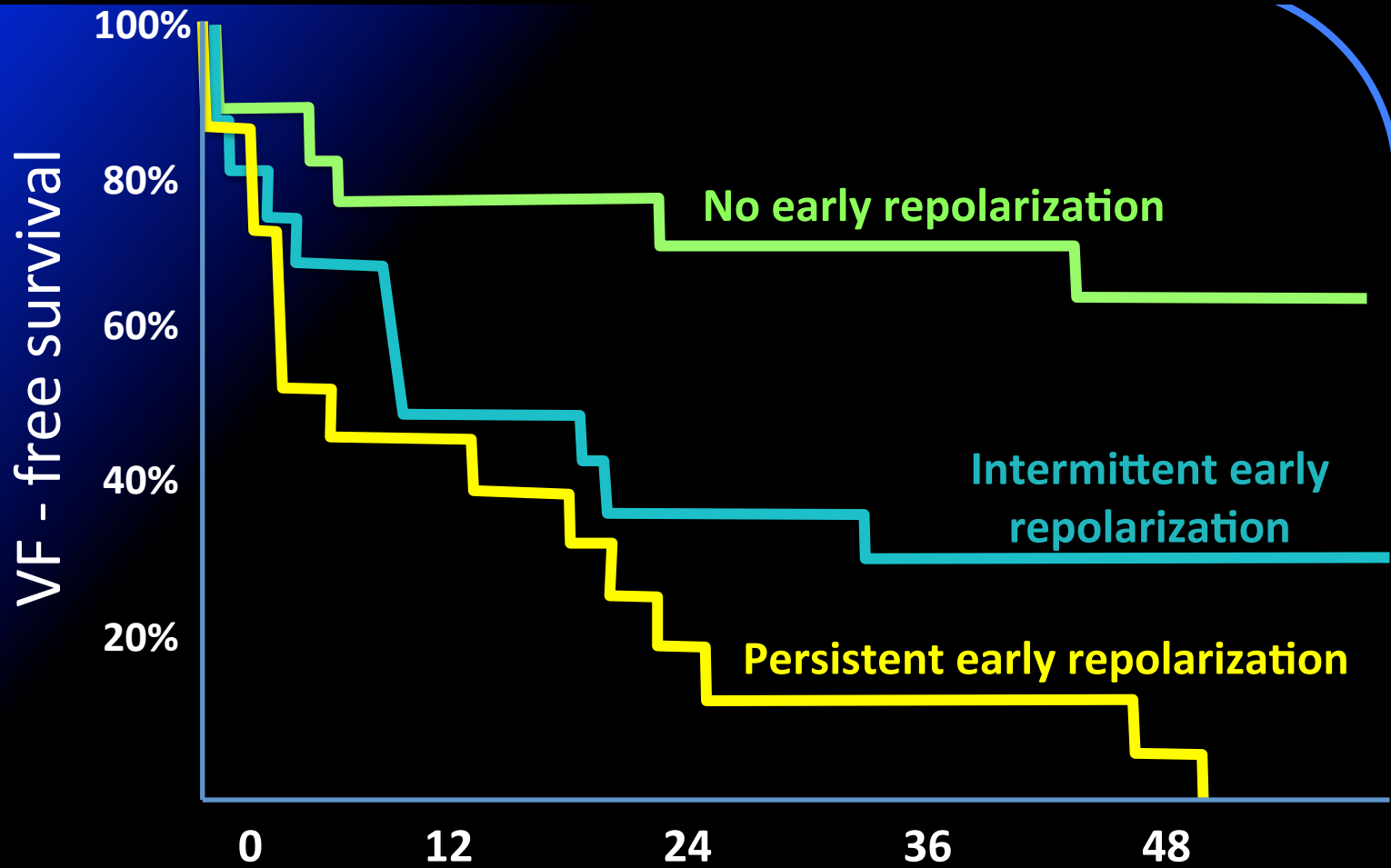


The Brugada-ER connection



VF recurrence in Brugada syndrome.

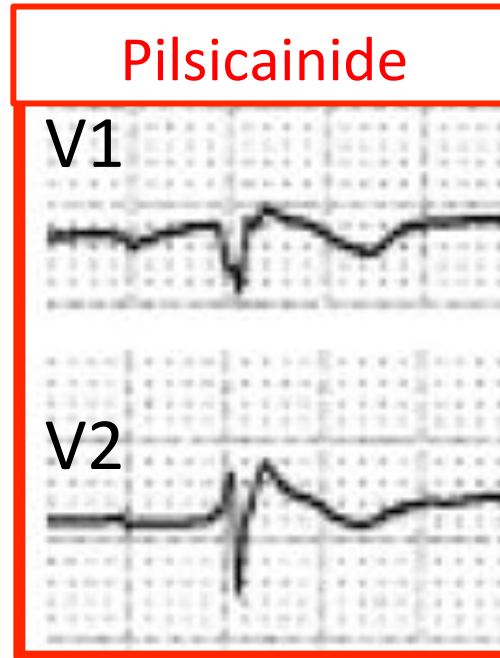
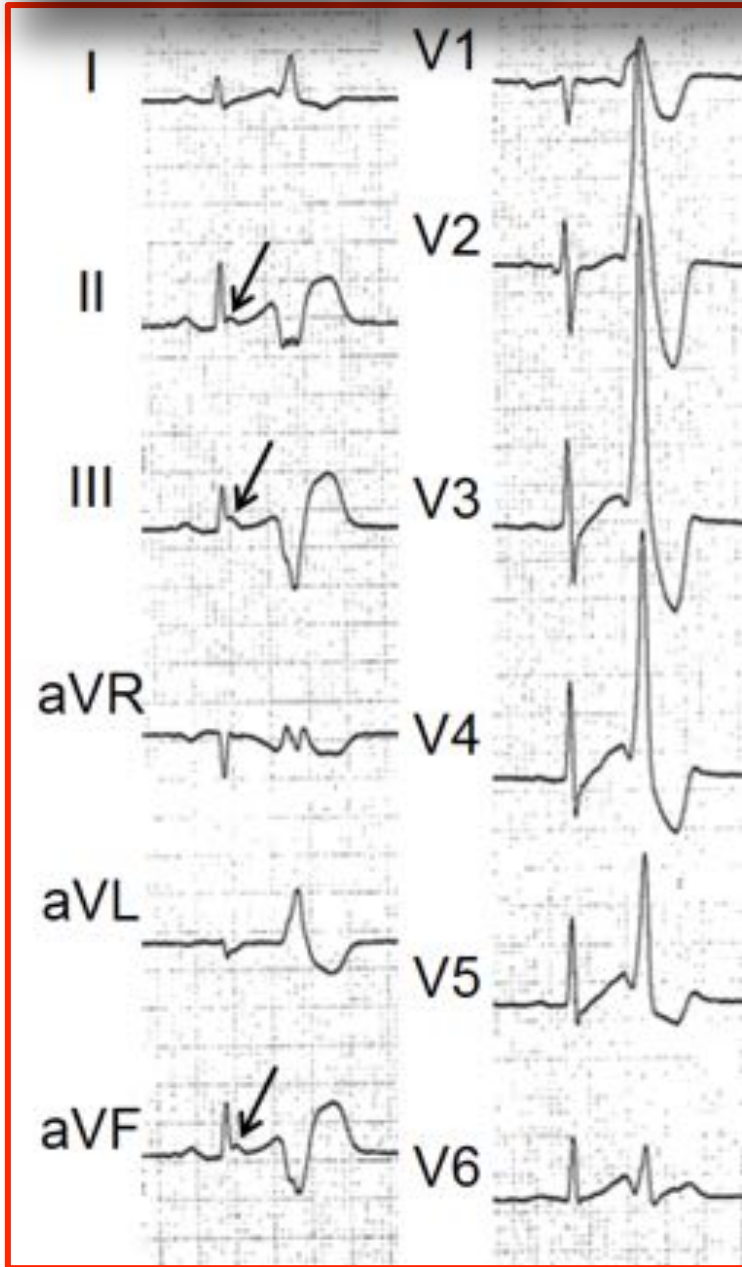
Kawata, HeartRhythm 2013



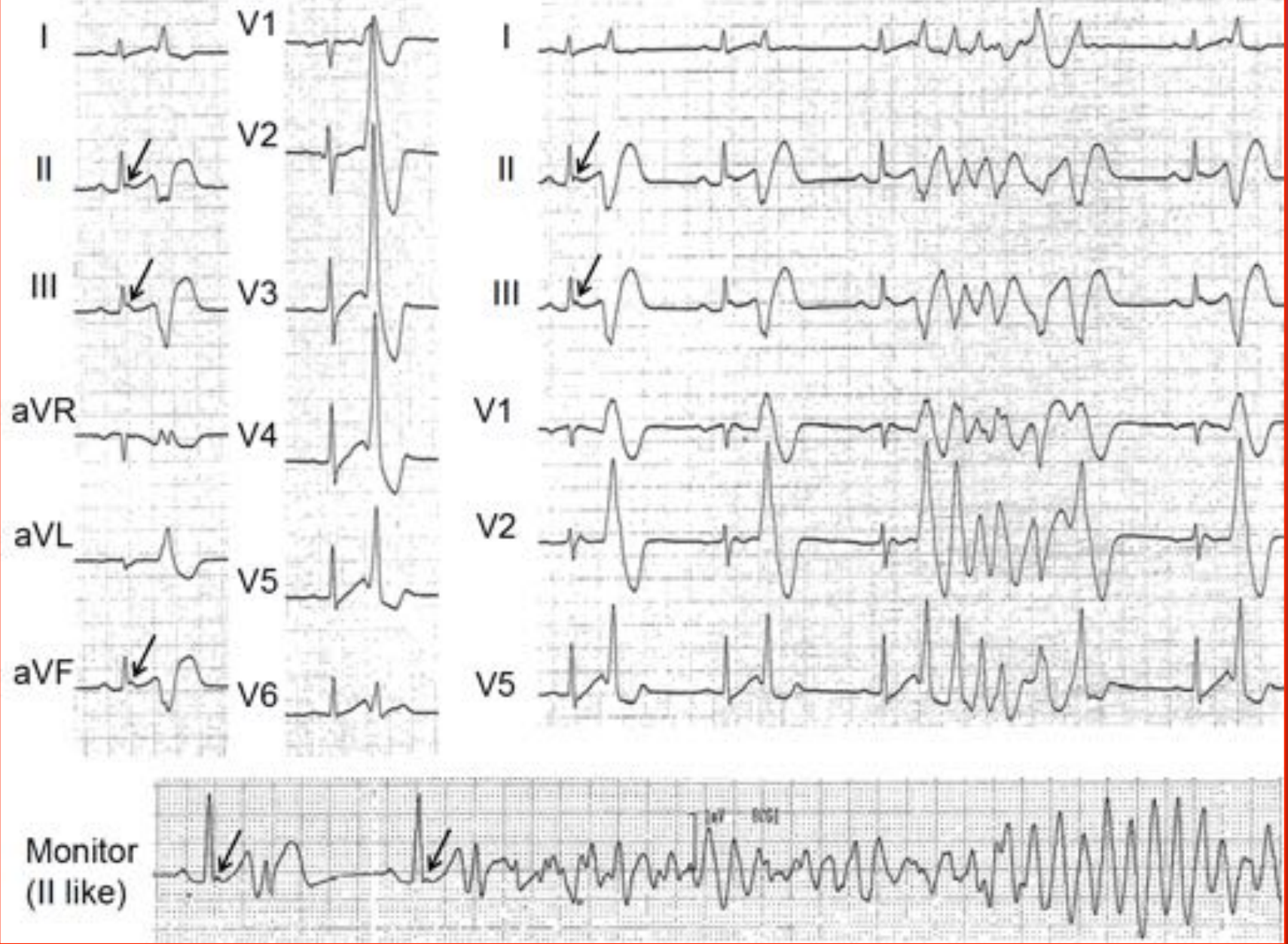
Patients at risk:

No ER	18	14	13	12	11
Intermittent ER	16	9	7	6	5
Persistent ER	15	8	4	3	2

Best figure of 2013: Kawata, HeartRhythm 2013



To be continued....



Best figure of 2013

Kawata, HeartRhythm 2013

**Don't measure J-waves:
look at them**



Experimental Hypothermia: Respiratory and Blood pH Changes in Relation to Cardiac Function

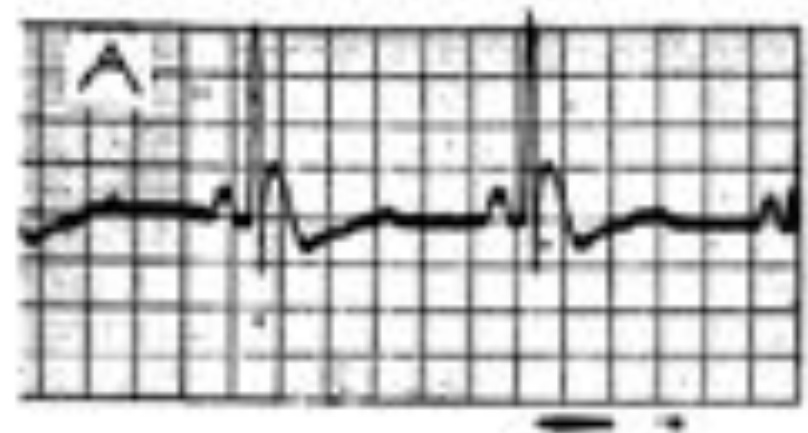
JOHN J. OSBORN¹

From the Department of Pediatrics, New York University College of Medicine, New York City

TEMPORARY whole-body hypothermia in theory offers an ideal way of greatly reducing metabolism, and seems to hold great promise in clinical surgery. Yet, although the reptile or the hibernating mammal can withstand very low body temperatures without distress, body temperatures much below 28°C produce severe and often fatal physiological stress in the non-hibernating mammal.

In the course of a series of studies of the physiology of experimental hypothermia in the dog, we have observed profound changes in the auto-regulation of respiration and of blood pH. These changes appear to be im-

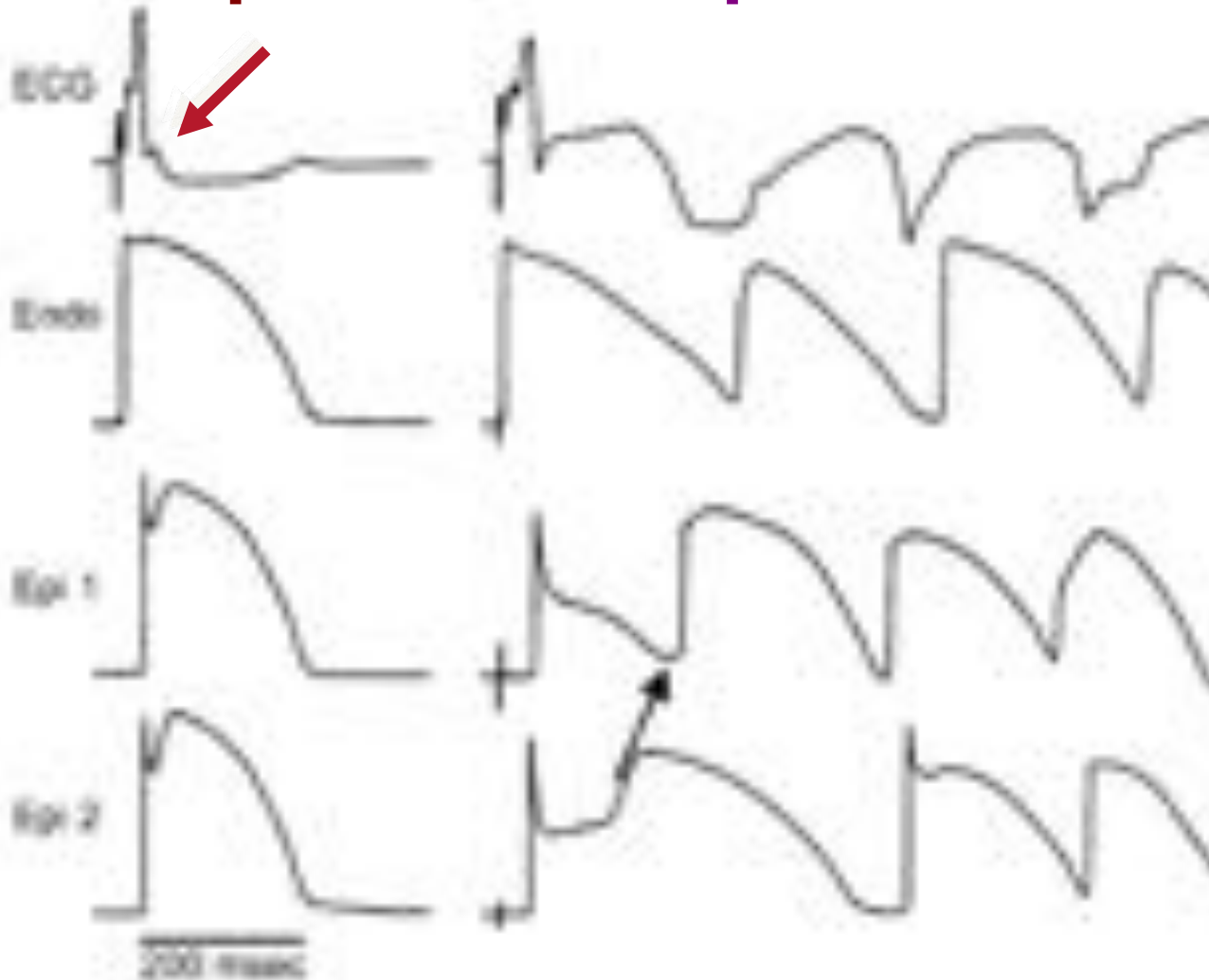
volume was measured directly in several ways, eventu-



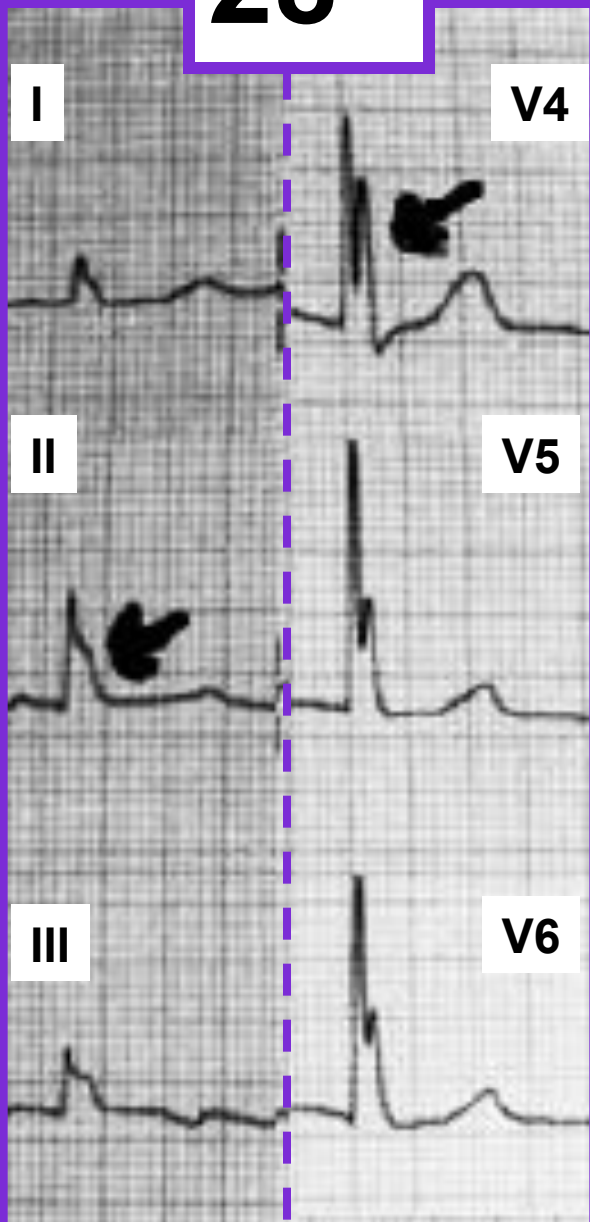
Am J Physiol 1953

Phase 2 reentry by cooling

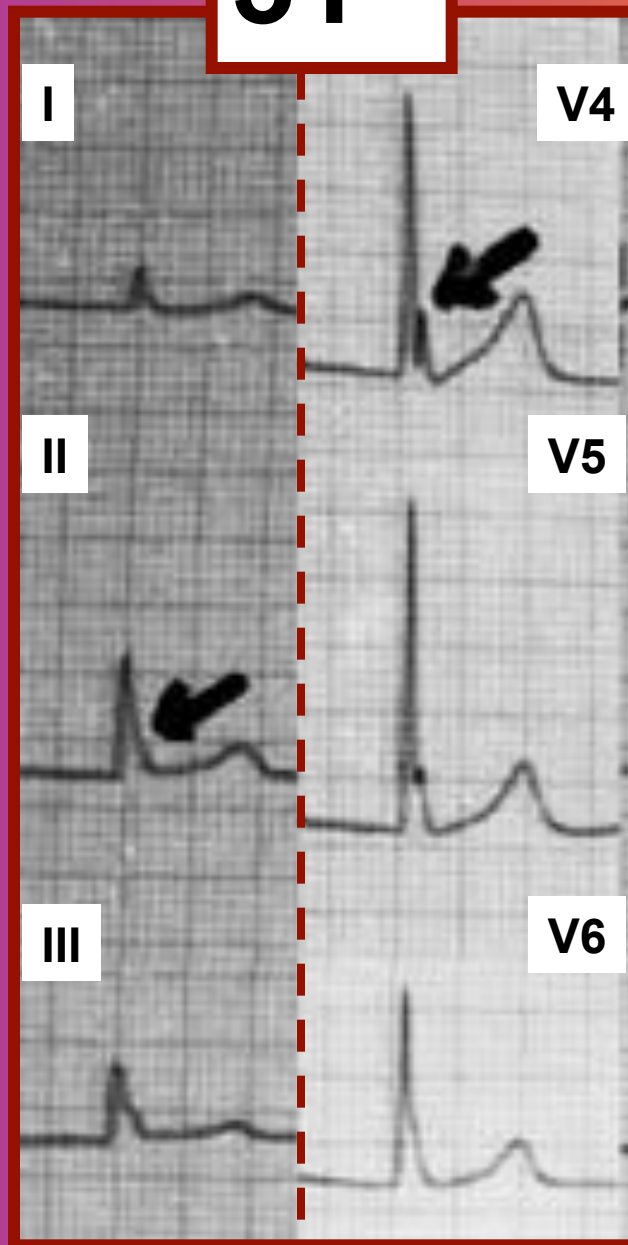
Temp = 37° Temp = 29°



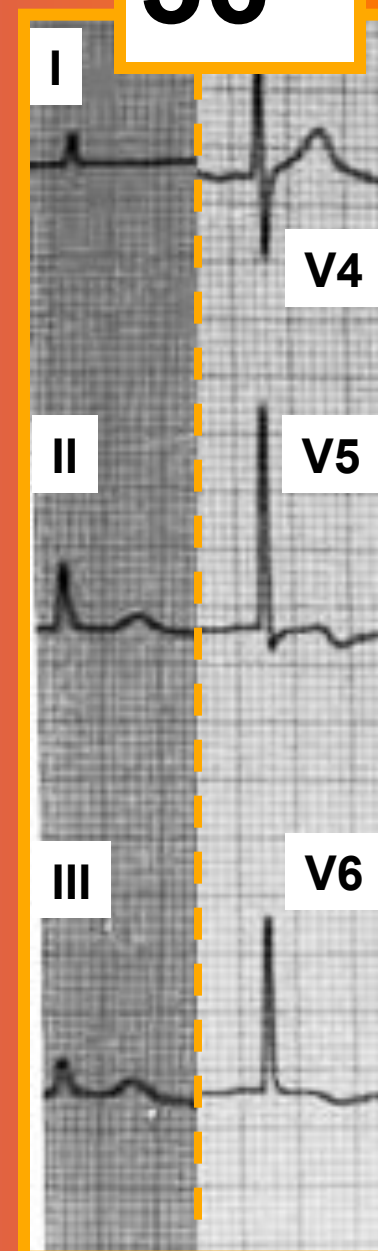
28°



31°



36°



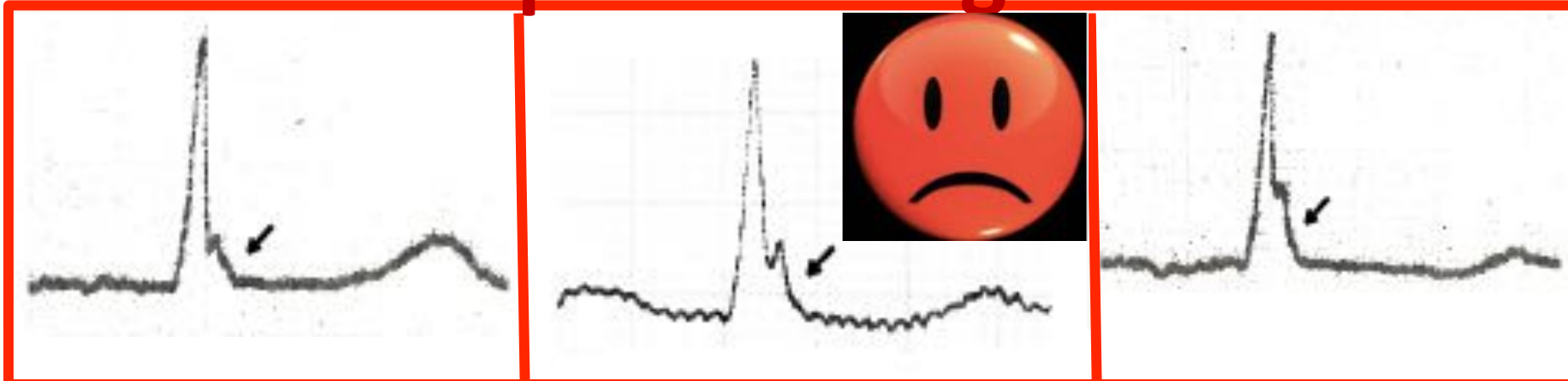
Early Repolarization: Electrocardiographic Phenotypes Associated with Favorable Long-Term Outcome

Jani T Tikkanen, Juhani M Junttila, Olli Anttonen, Aapo L Aro, Samuli Luttinen, Tuomas Kerola, Solomon J Sager, Harri A Rissanen, Robert J Myerburg, Antti Reunanen, and Heikki V Huikuri
CIRCULATIONAHA/2010/014068 [R1]

J-wave with ascending ST-segment



J-wave with plain ST-segment



Original Articles

J Wave, QRS Slurring, and ST Elevation in Athletes With Cardiac Arrest in the Absence of Heart Disease

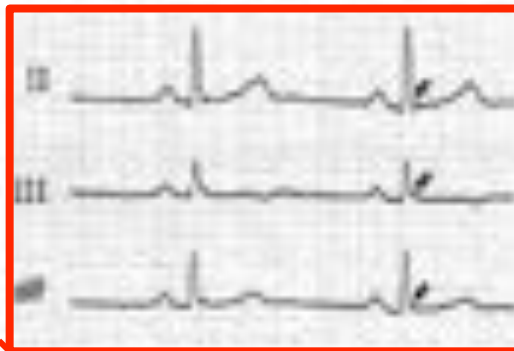
Cardiac arrest



Healthy athlete



...
slurring of
Complexes
than in co-
alignant



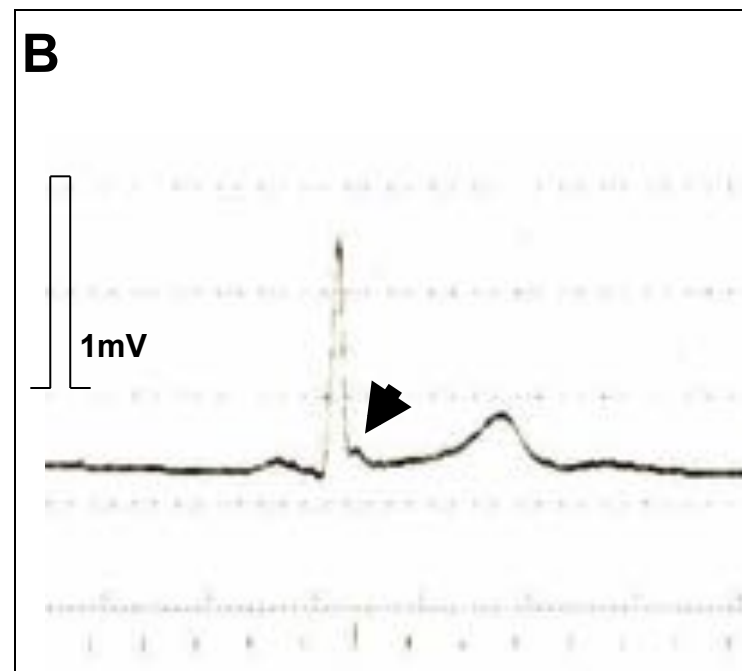
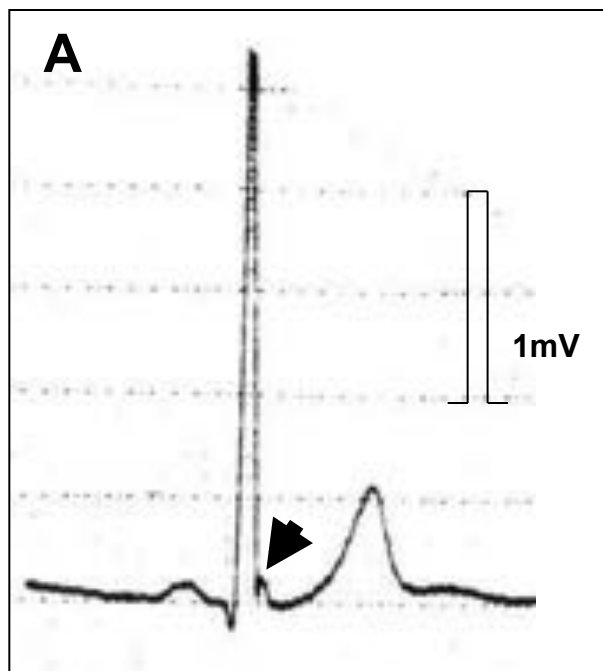
...
sudden death
& for recurrent



J-Point Elevation in Survivors of Primary Ventricular Fibrillation and Matched Control Subjects

Incidence and Clinical Significance

Distinguishing “benign” from “malignant early repolarization:”
The value of ST-segment morphology.

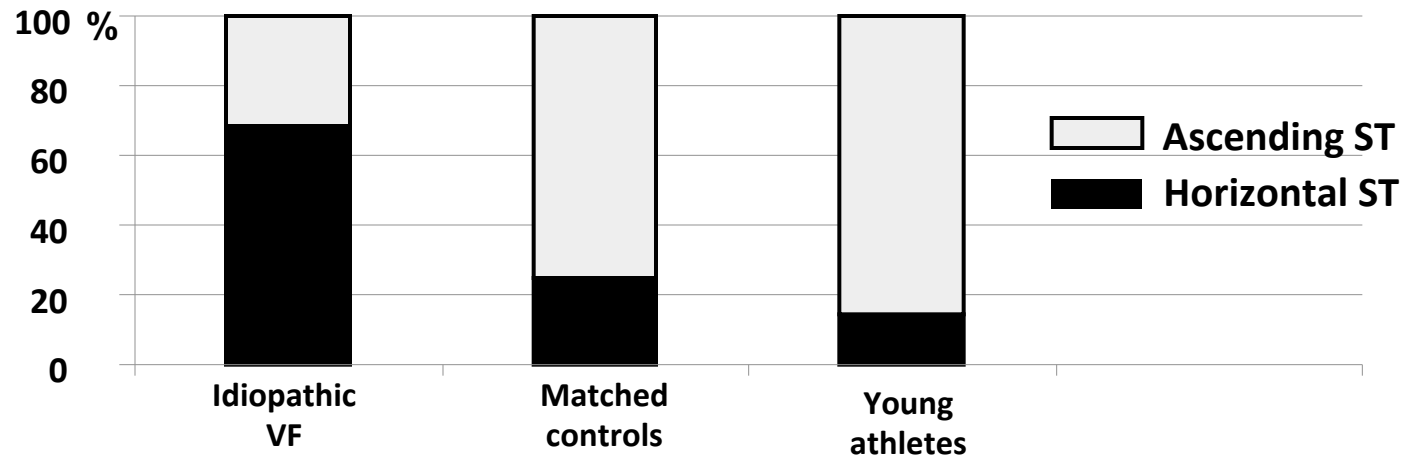


Rosso, (Viskin) *HeartRhythm* 2012

A

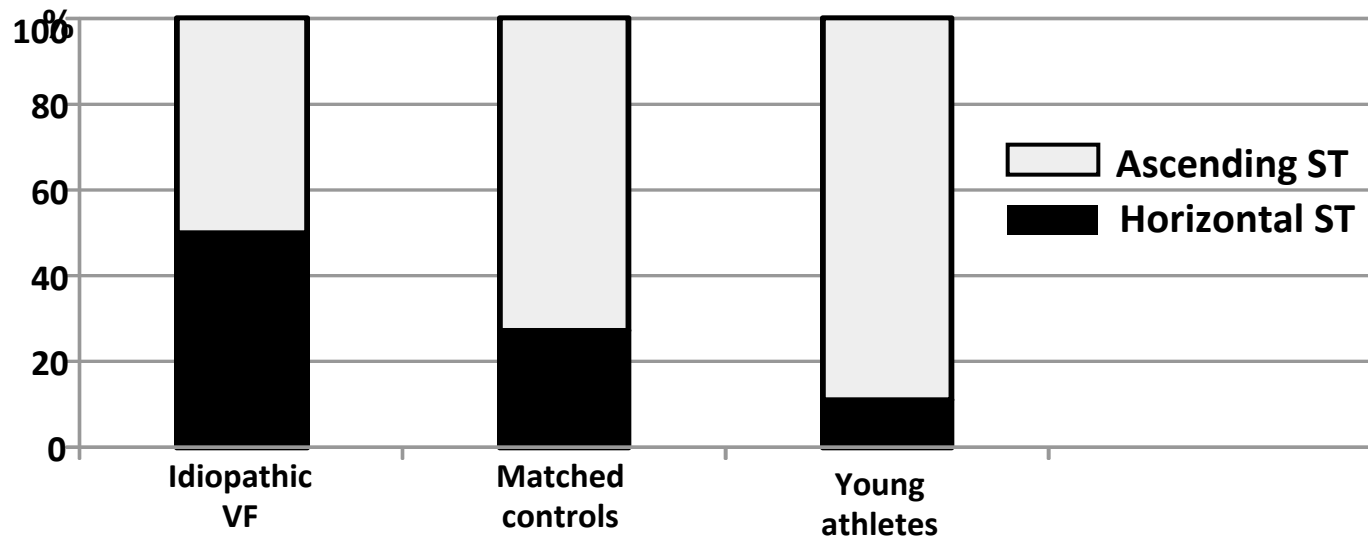
Distribution of ascending vs. horizontal ST elevation among patients with J-waves

Patients with J-point elevation or slurred-R-wave.

**B**

Distribution of ascending vs. horizontal ST elevation among patients with J-waves

Patients with J-point elevation



What Do We Know About the “Malignant Form” of Early Repolarization?

Arnon Adler, MD, Raphael Rosso, MD, Dana Viskin, Amir Halkin, MD, Sami Viskin, MD
Tel Aviv, Israel

There is an urgent need to identify electrocardiographic characteristics that differentiate the “benign early repolarization pattern” from “malignant early repolarization.” In a previous paper, we considered the different electrocardiographic elements of the early repolarization pattern and analyzed how they confer important prognostic information. In the present article, we review more recent information regarding the importance of the contour of the ST segment, with special emphasis on the currently termed malignant form and its value for risk stratification in early repolarization. (J Am Coll Cardiol 2013;62:863-8) © 2013 by the American College of Cardiology Foundation

There is an urgent need to identify electrocardiogram (ECG) characteristics that differentiate the “benign early repolarization” (ER) pattern from “malignant early repolarization” (1,2). Whereas the former ECG pattern is frequently observed in healthy persons—particularly young, male (3-5), athletic (6,7), and of African-American origin (4,8)—the latter is clearly associated with idiopathic ventricular fibrillation (VF) in case-control studies (9,10), and with increased mortality (presumably from myocardial ischemia-related arrhythmias) in population-based studies (11-13).

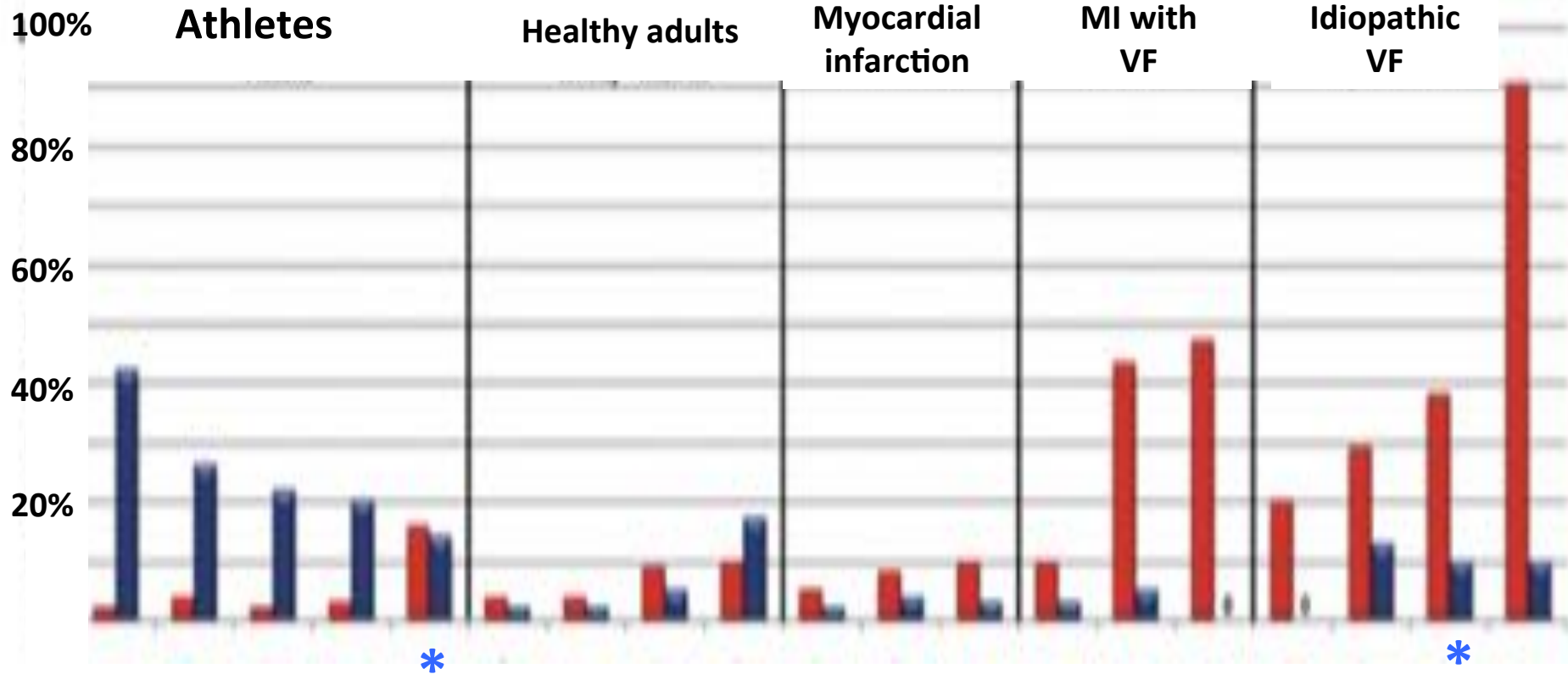
In previous papers, we considered the ongoing debates between basic scientists and clinical cardiologists regarding the actual pathophysiology of early repolarization (14,15), and we analyzed in detail the different ECG elements of the ER pattern and discussed how they are likely to confer prognostic information (16). In this review, we focus on

Historical Aspects: Evolution of Concept of Malignant (Horizontal) Versus Benign (Rapidly Ascending) ST-Segment Morphology

Tikkaenen et al. (6) were the first to focus on the contour of the ST-segment in ER. To define a benign form, Tikkaenen et al. (6) initially studied 2 populations of healthy athletes, knowing that ER is particularly frequent in this group who generally enjoys an excellent prognosis. He found that the vast majority of healthy athletes with ER (85% in 1 series and 96% in the other) had a “rapidly ascending” ST-segment blending with the T-wave (Fig. 1A). They naturally assumed this rapidly ascending form to be benign. The remaining minority of athletes with ER features an ST-segment that remains flat, horizontal, or even descends toward the T-wave (Fig. 1B). This “horizontal/descending” pattern drew Tikkaenen’s suspicion to a “potentially malig-

Distribution of early repolarization patterns in different populations.

 Horizontal/descending ER  Rapidly ascending ER

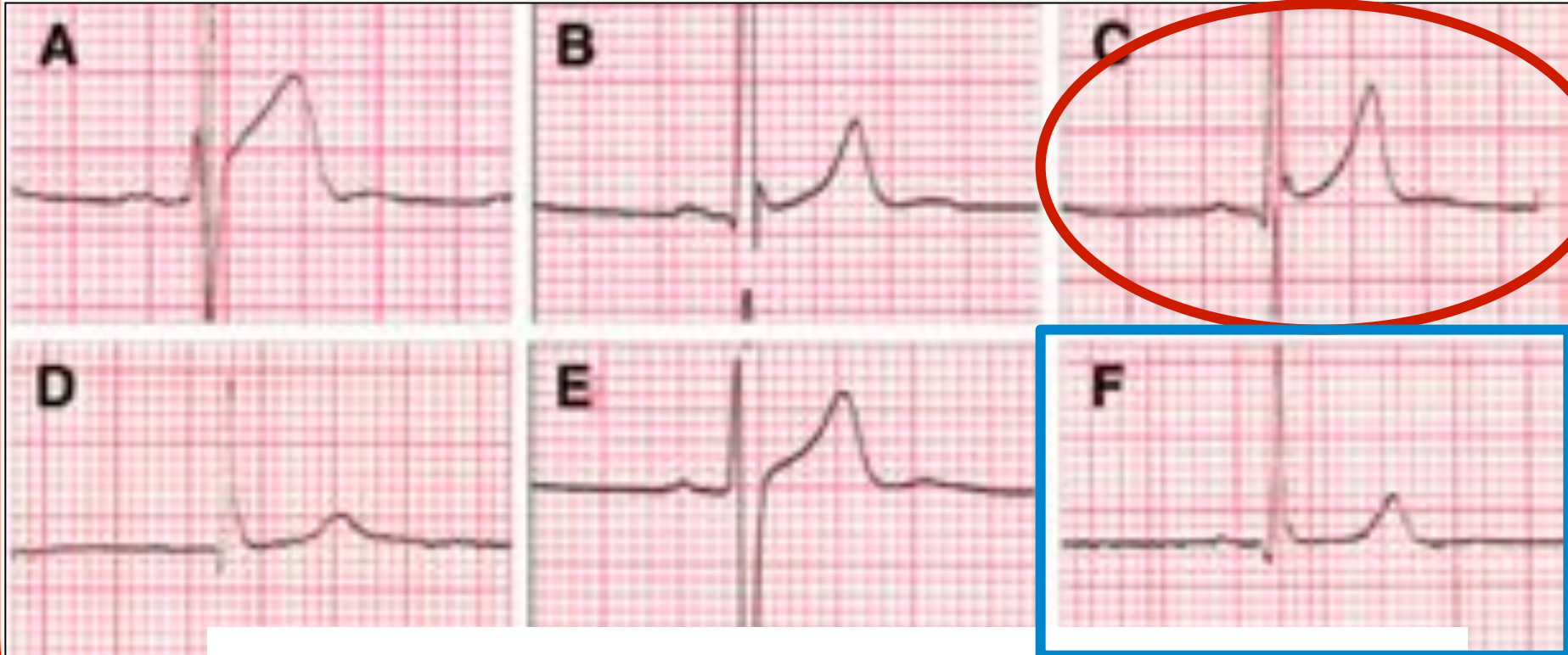


Early Repolarization Pattern in Competitive Athletes

Clinical Correlates and the Effects of Exercise Training

Peter A. Noseworthy, MD; Rory Weiner, MD; Jonathan Kim, MD; Varsha Keelara;
Francis Wang, MD; Brant Berkstresser, MS, ATC; Malissa J. Wood, MD;
Thomas J. Wang, MD; Michael H. Picard, MD; Adolph M. Hutter, Jr, MD;

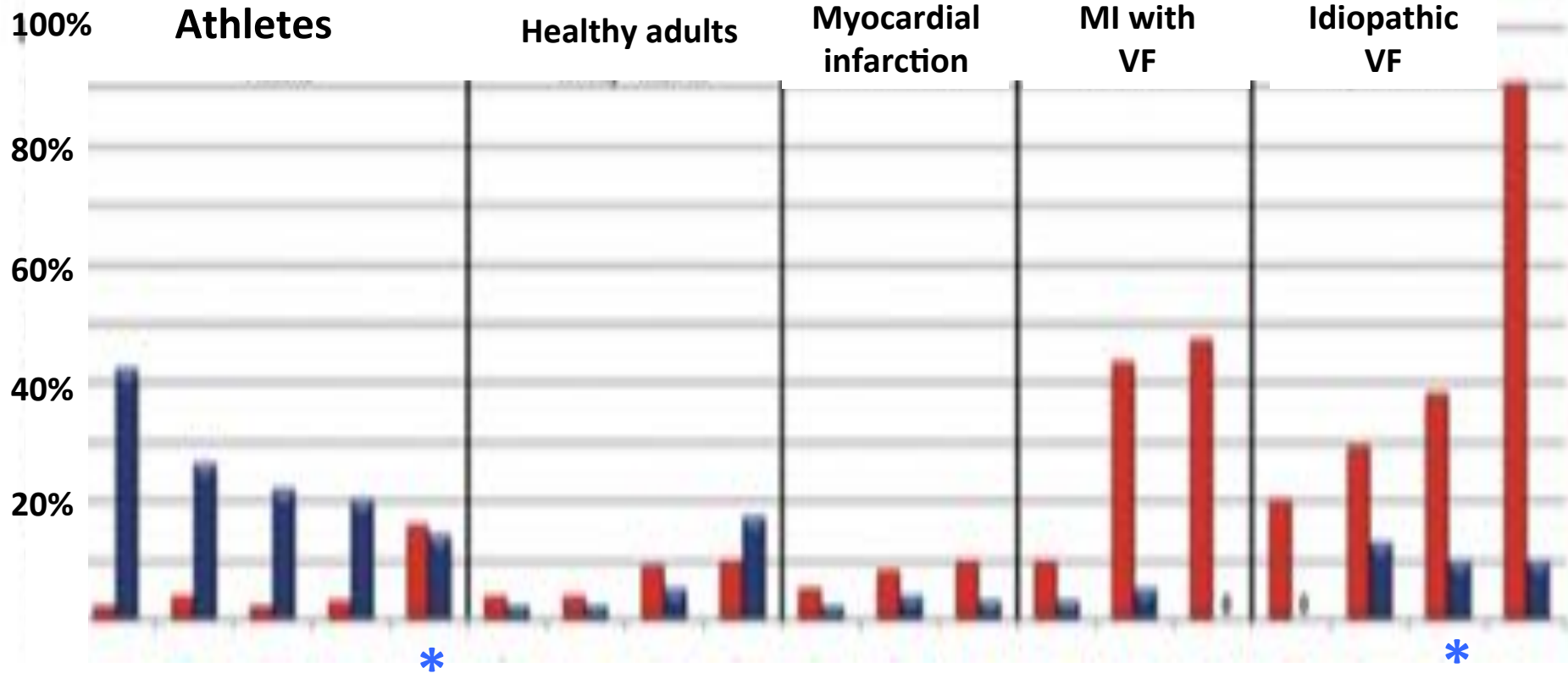
Ascending ST-segment = 99%



Horizontal ST-segment = 1%

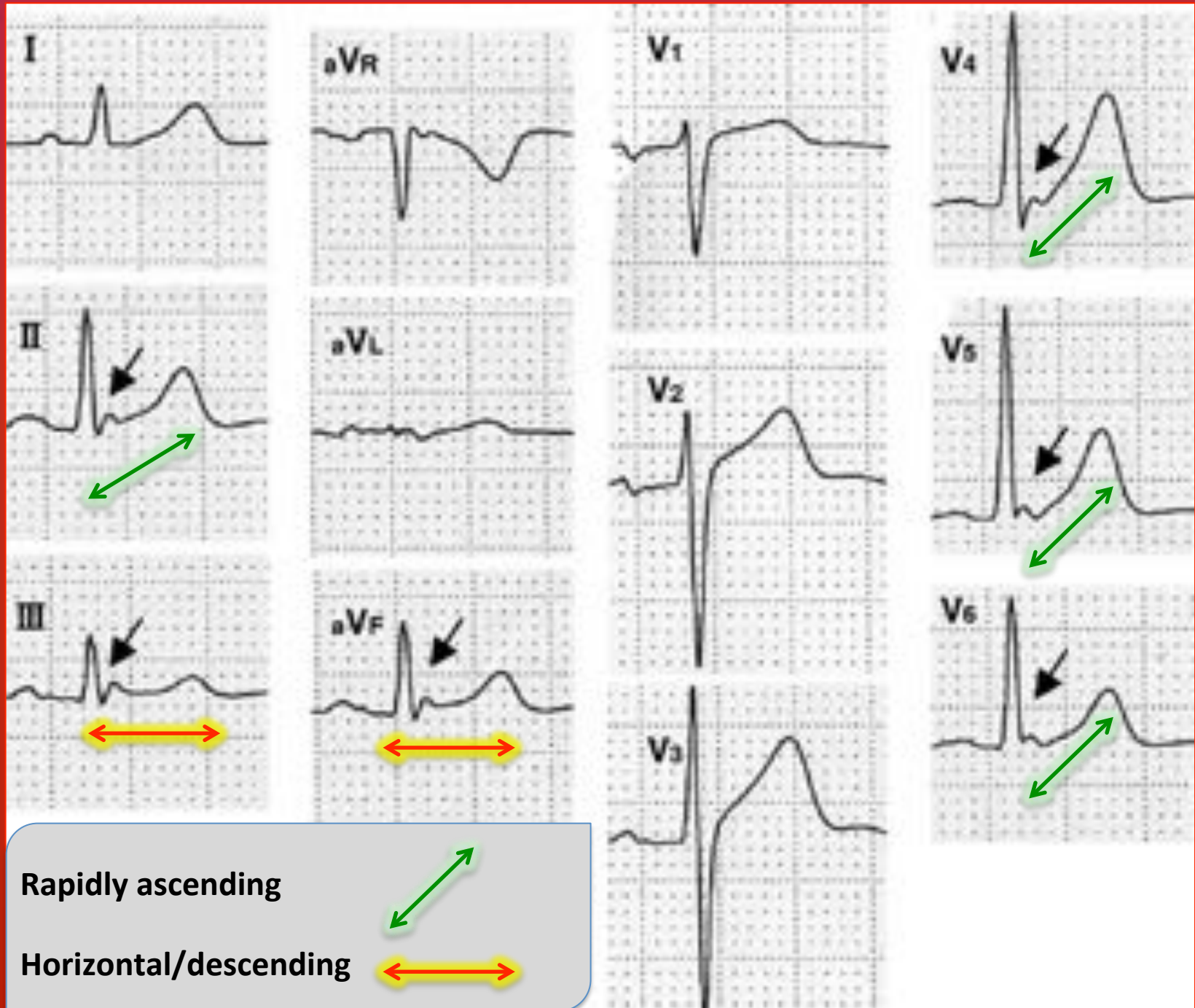
Distribution of early repolarization patterns in different populations.

 Horizontal/descending ER  Rapidly ascending ER



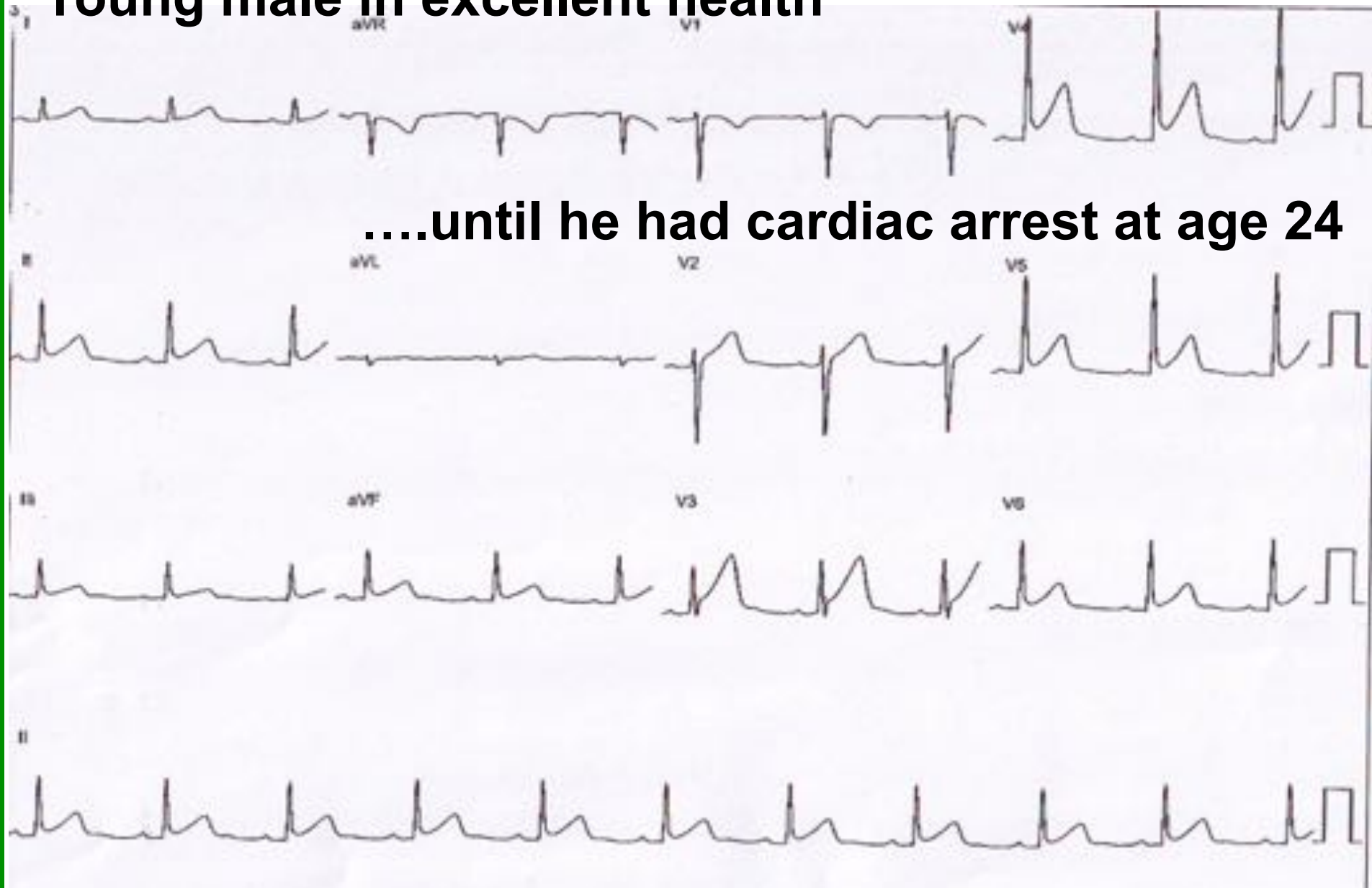


“malignant”



Young male in excellent health

....until he had cardiac arrest at age 24

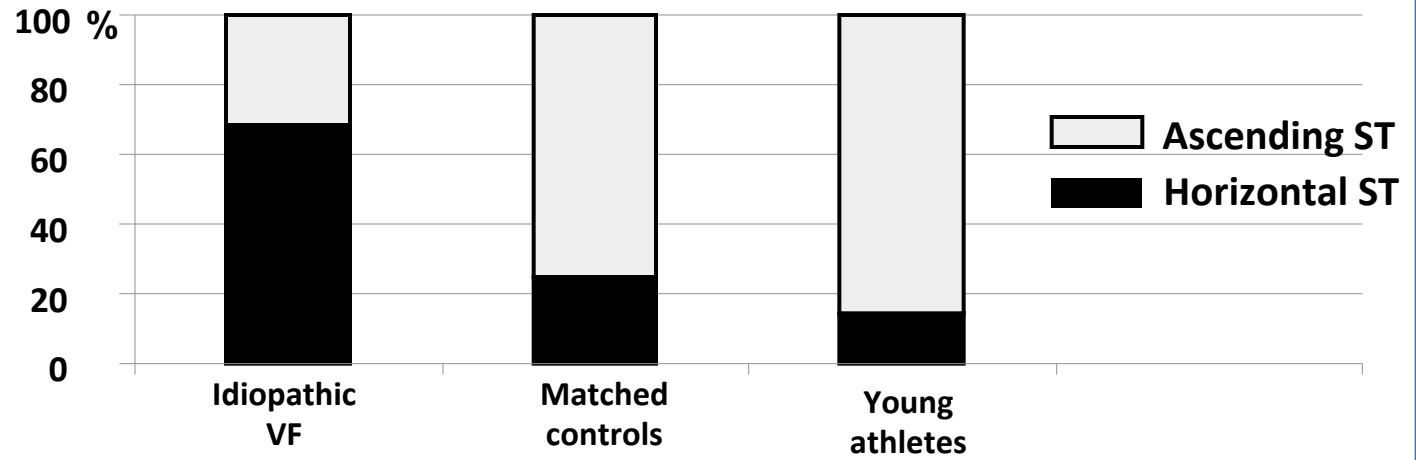


Slide stolen (with permission) from M. Haissaguerre.

A

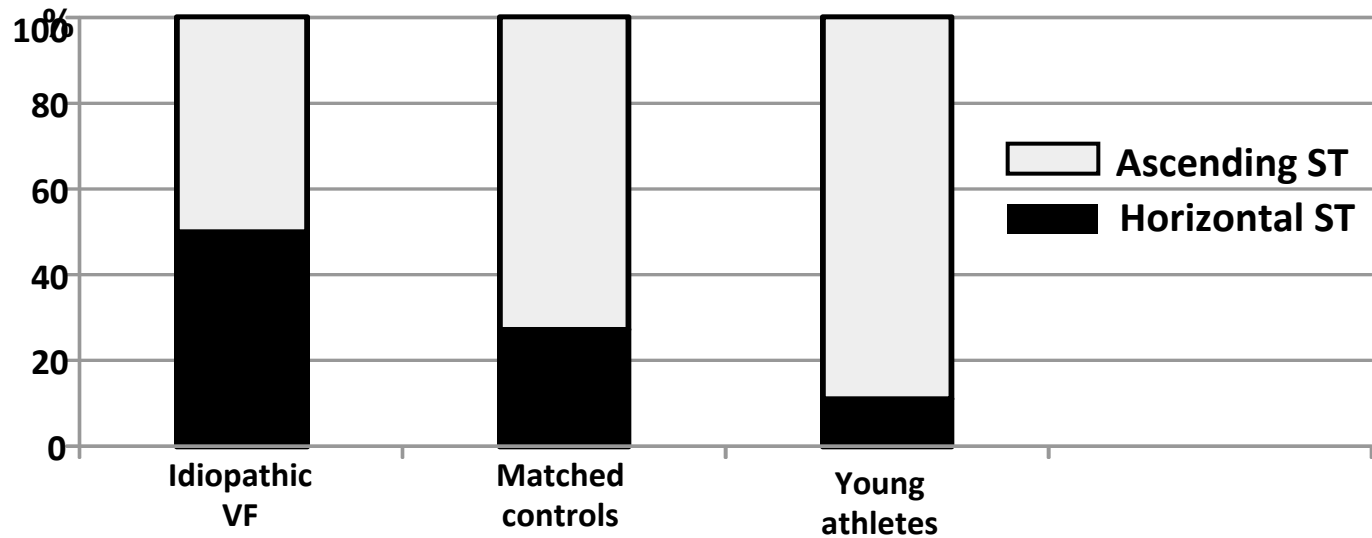
Patients with J-point elevation or slurred-R-wave.

Distribution of ascending vs. horizontal ST elevation among patients with J-waves

**B**

Patients with J-point elevation

Distribution of ascending vs. horizontal ST elevation among patients with J-waves



Risk of dropping dead (asymptomatic young individuals).

Someone
like me

With
J-Waves

With J-waves and
malignant ST

3 : 100,000

11 : 100,000

1 : 3,000

X4

X14

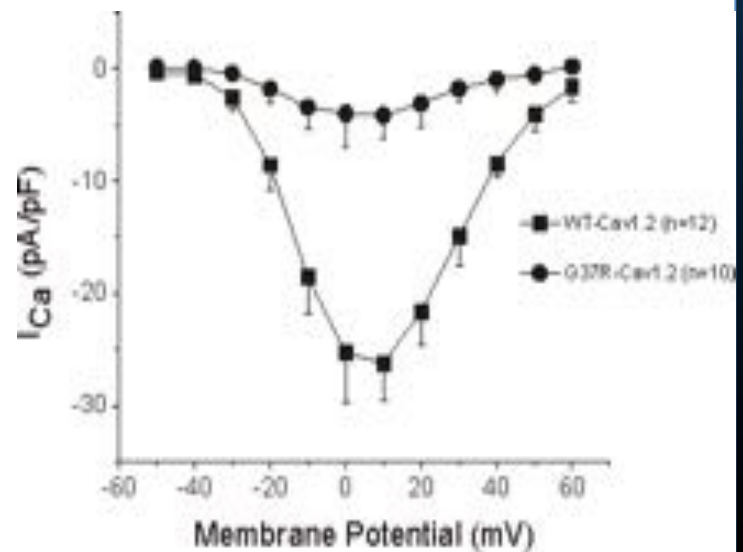
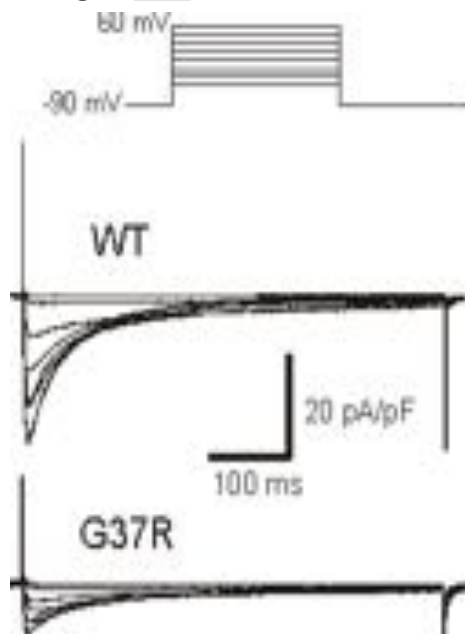
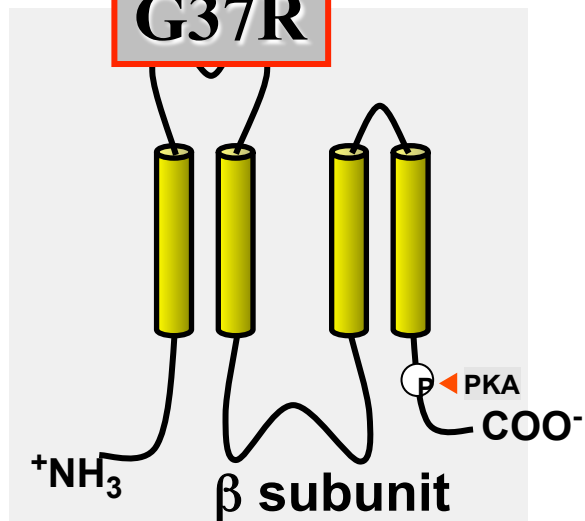
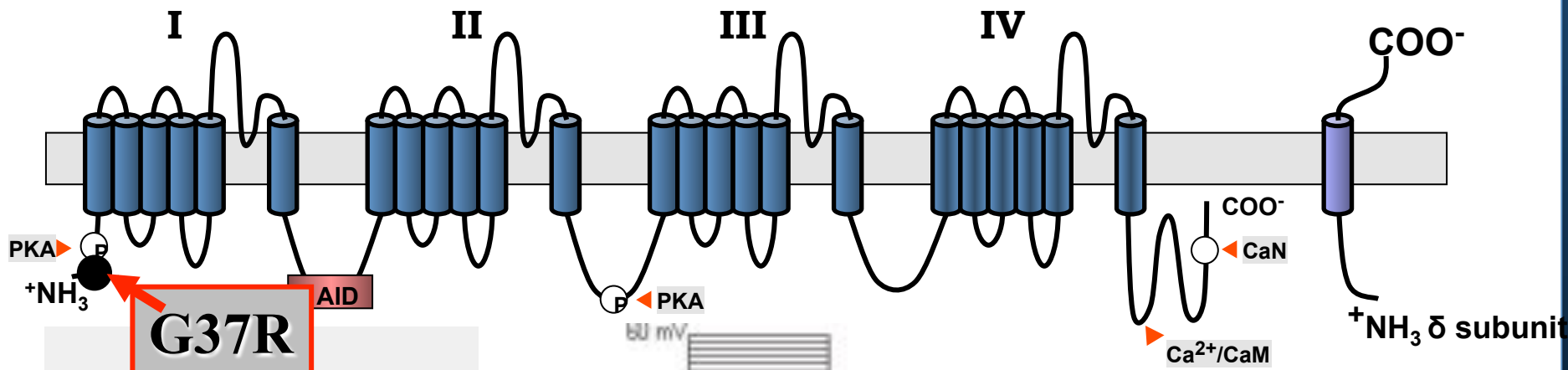
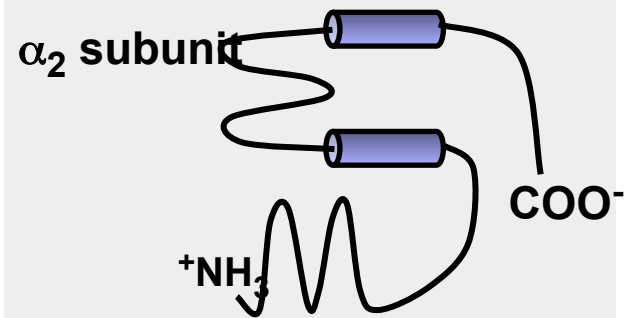


Asymptomatic 23 year old male

Referred after the sudden death of his younger brother



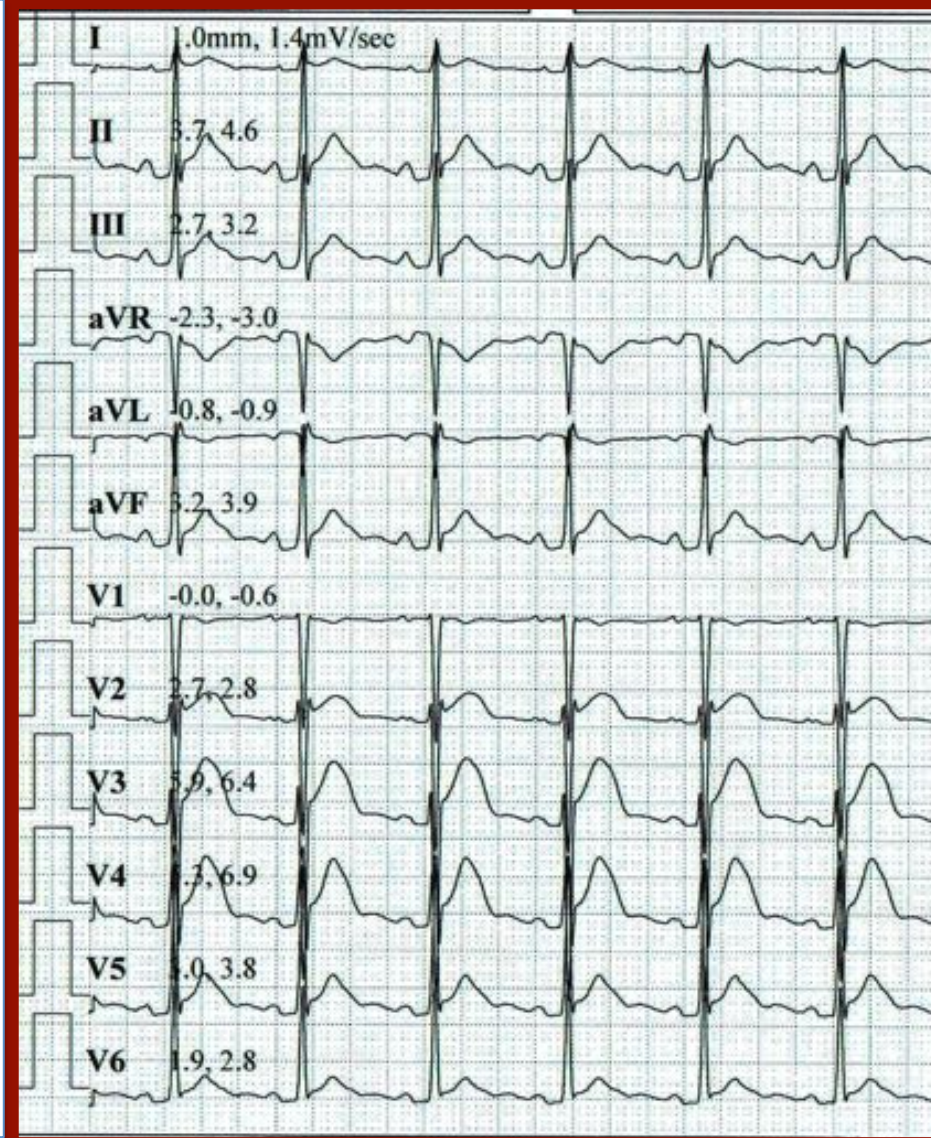
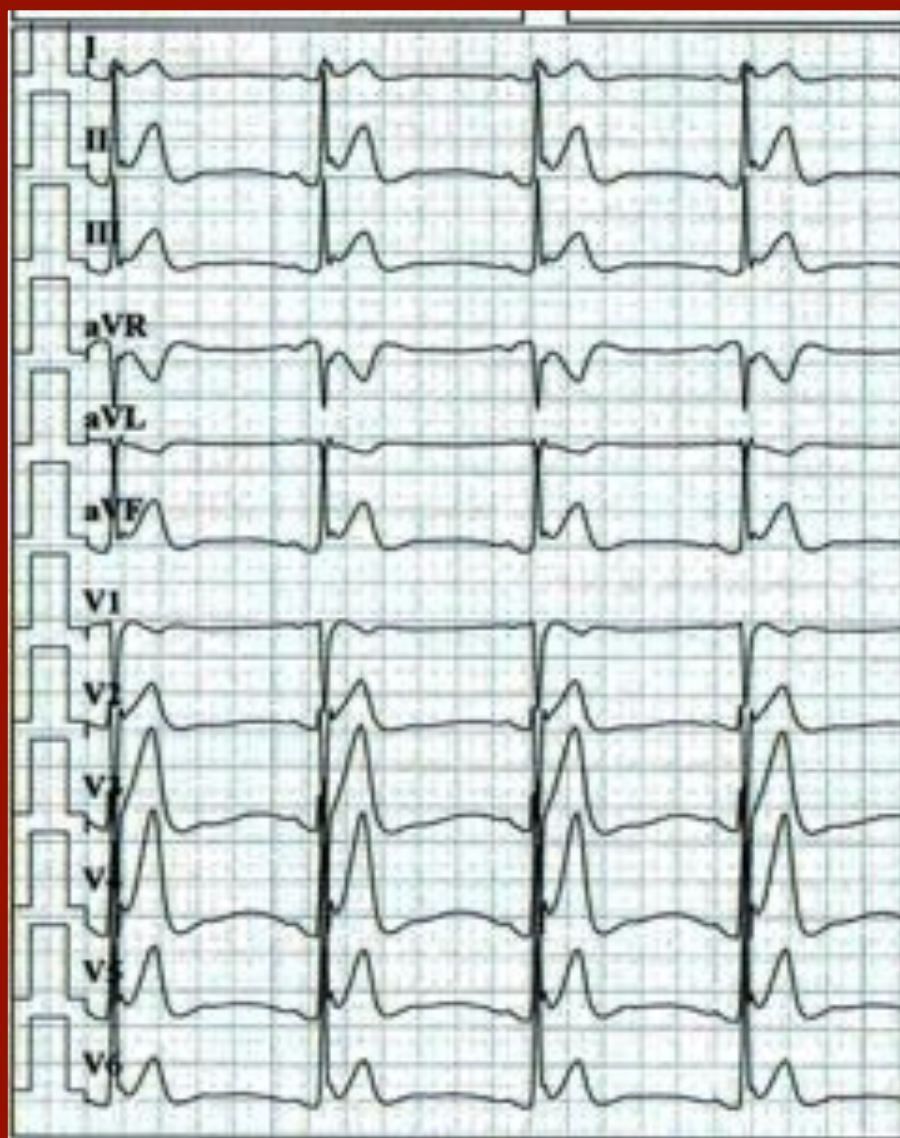
CaCNA1C (α_{1c} subunit)



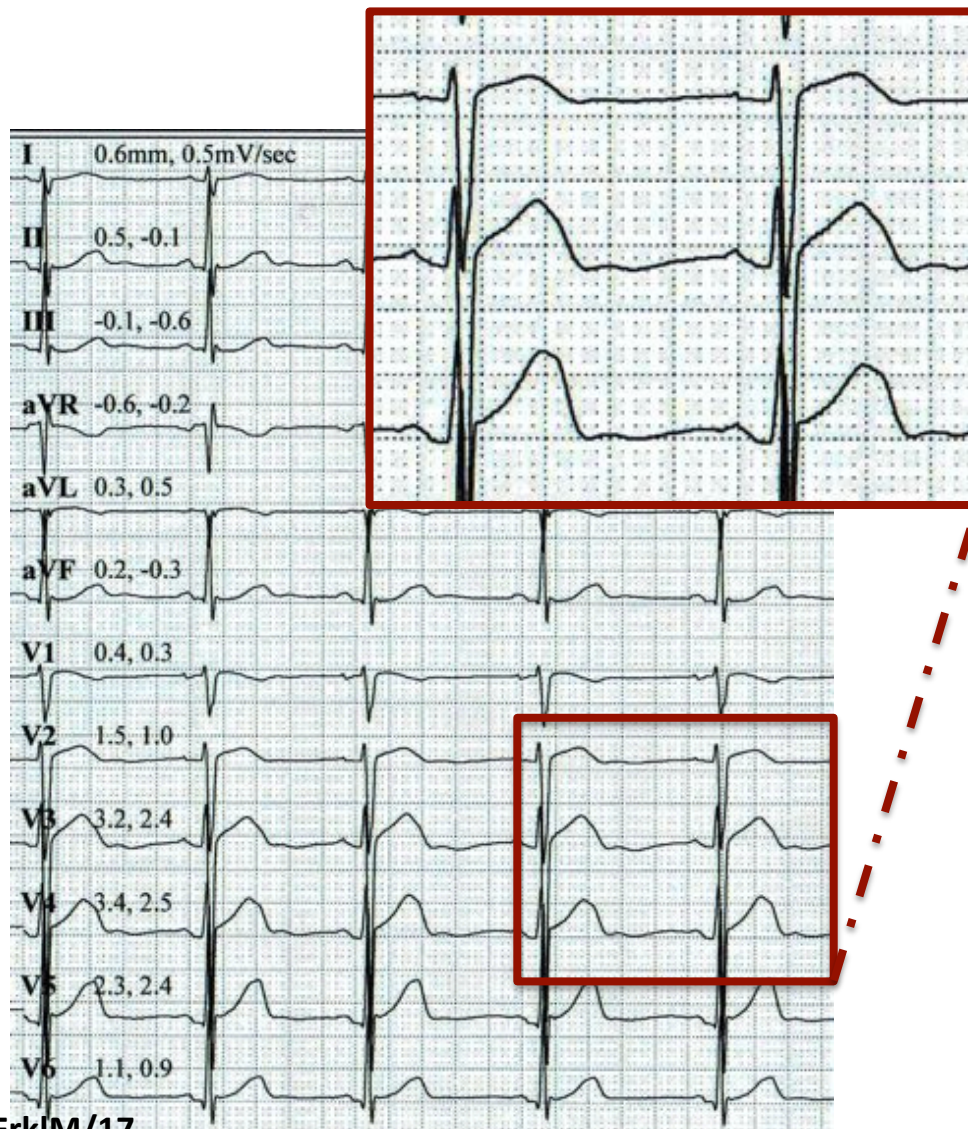
Barajas-Martinez H, Hu D, Antzelevitch C, 2014.

Before quinidine

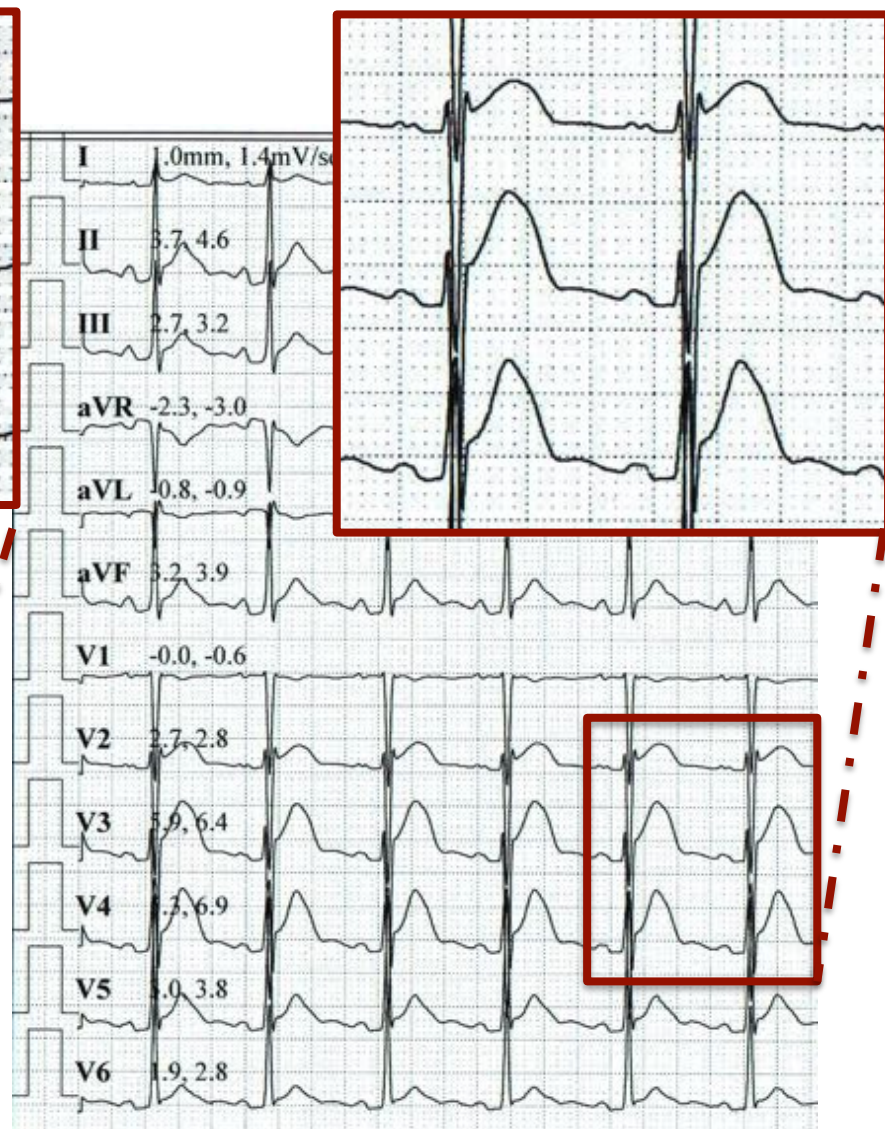
After quinidine



Male/17. Long QT syndrome (LQT2). Treated with β -blockers



Male/23. Early repolarization. Treated with quinidine



M/36, Typical vagal syncope. Heart rate 60/min, QTc 360 ms.



Risk stratification of early repolarization

History of symptoms: syncope?

Vagal syncope



ECG with E-R



Leave him alone
despite ER +

Malignant syncope



ECG without E-R



Investigate despite
absence of ER

**Trust me, the ECG always
looks worse.....
..... once the patient is dead !**

Sami Viskin, 2010