VENICE 2015 ARRHYTHMIAS

AV-block and Torsade de Pointes: Who is at Risk?

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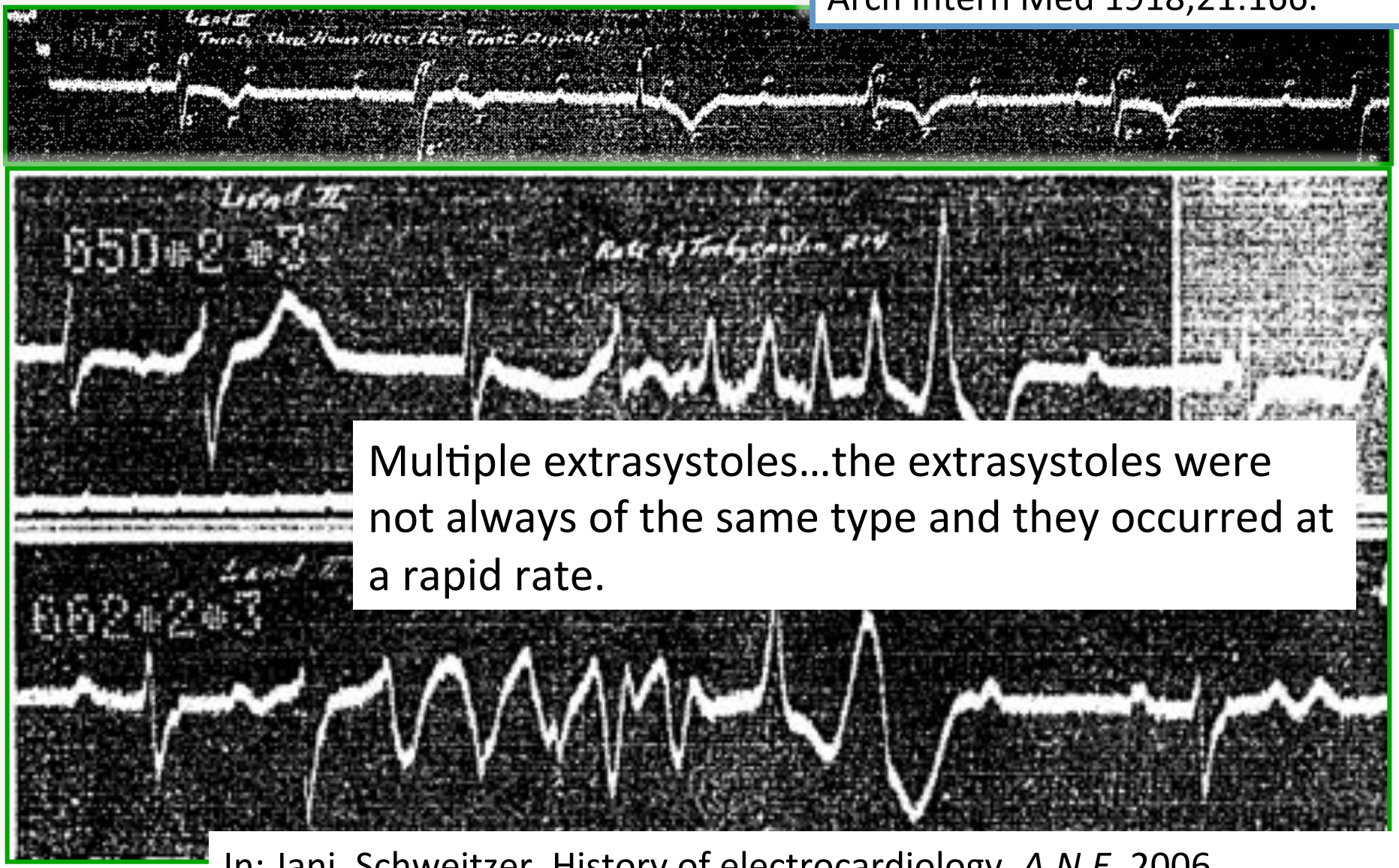
Tel Aviv Medical Center, Israel

No Disclosures

AV-block The most common (and least studied) form of torsade de pointes.

Two cases of complete heart block showing “unusual features.”

Wilson F, Robinson C.
Arch Intern Med 1918;21:166.



Multiple extrasystoles…the extrasystoles were not always of the same type and they occurred at a rapid rate.

In: Jani, Schweitzer, History of electrocardiology. *A.N.E.* 2006

TRANSIENT VENTRICULAR FIBRILLATION. V.

The Effects of the Oral Administration of Quinidine Sulphate on Patients with Transient Ventricular Fibrillation During Established Atrioventricular Dissociation.

Sidney P. Schwartz, M.D., M. Price Margolies, M.D., and Anthony Firenze, M.D.

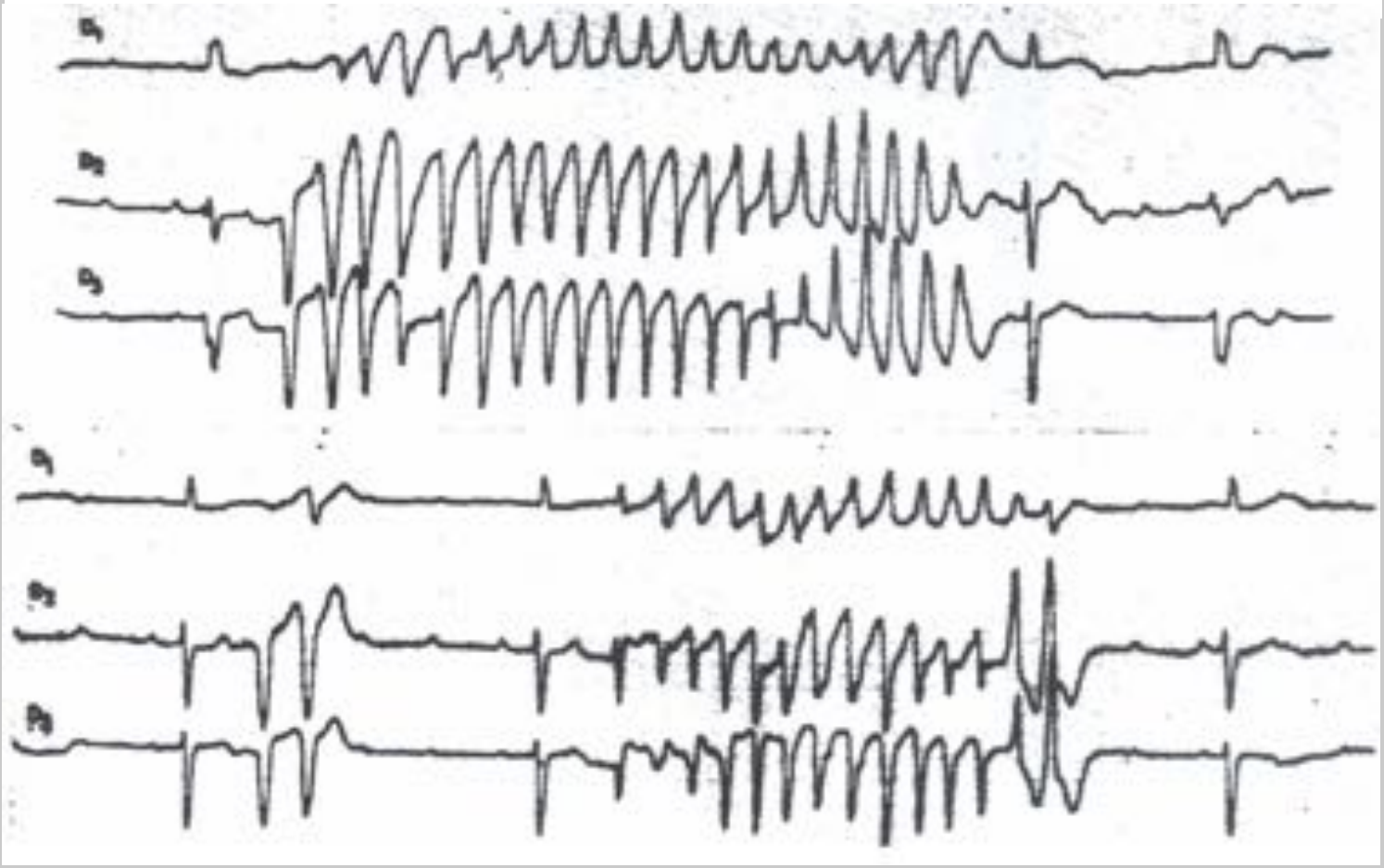
New York, N. Y.

Am Heart J 1953;45:404-415

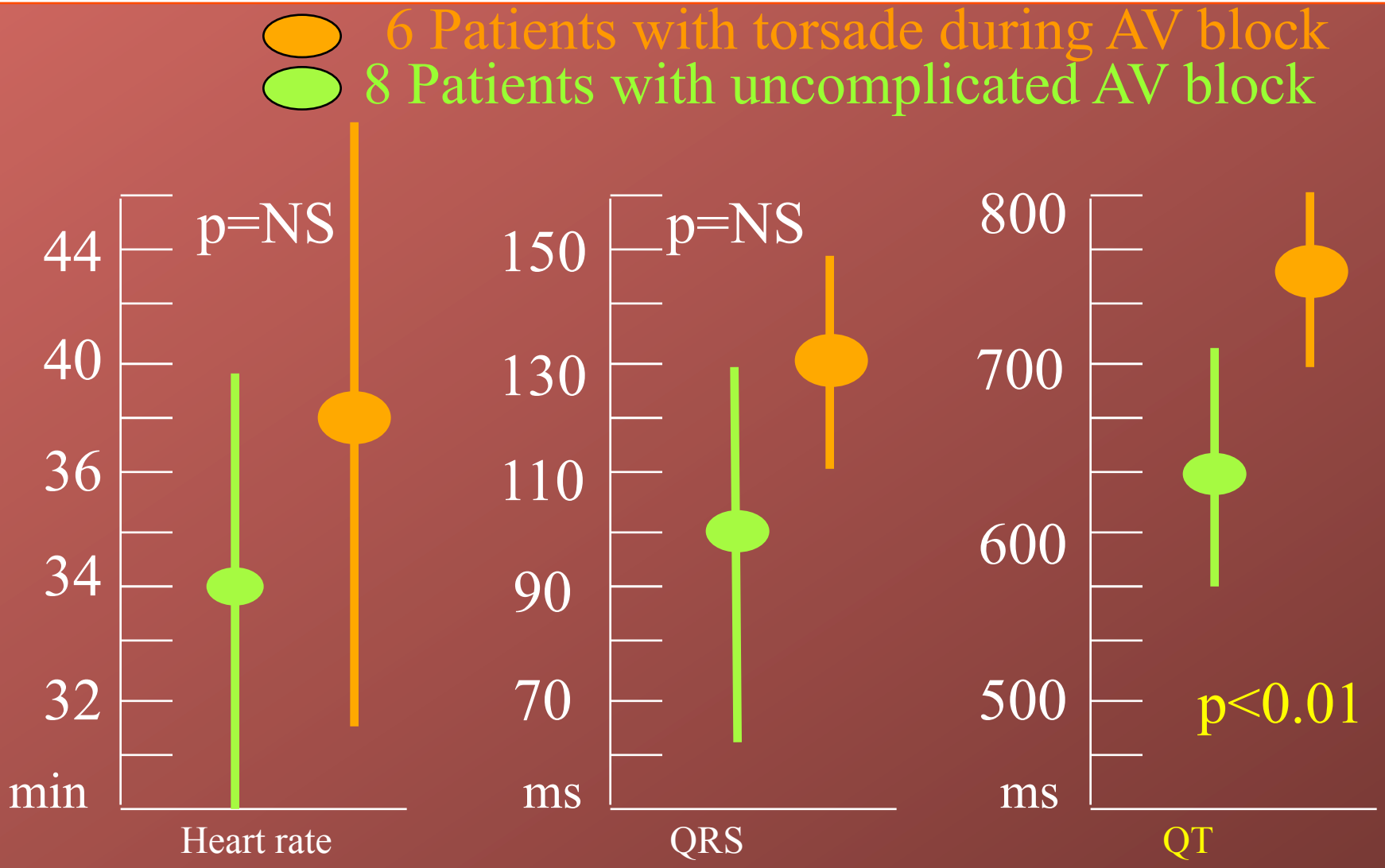
La tachycardie ventriculaire a deux foyers opposes variables.

F. Dessertenne.

Arch Mal Coeur Vaiss 1966;59:263.

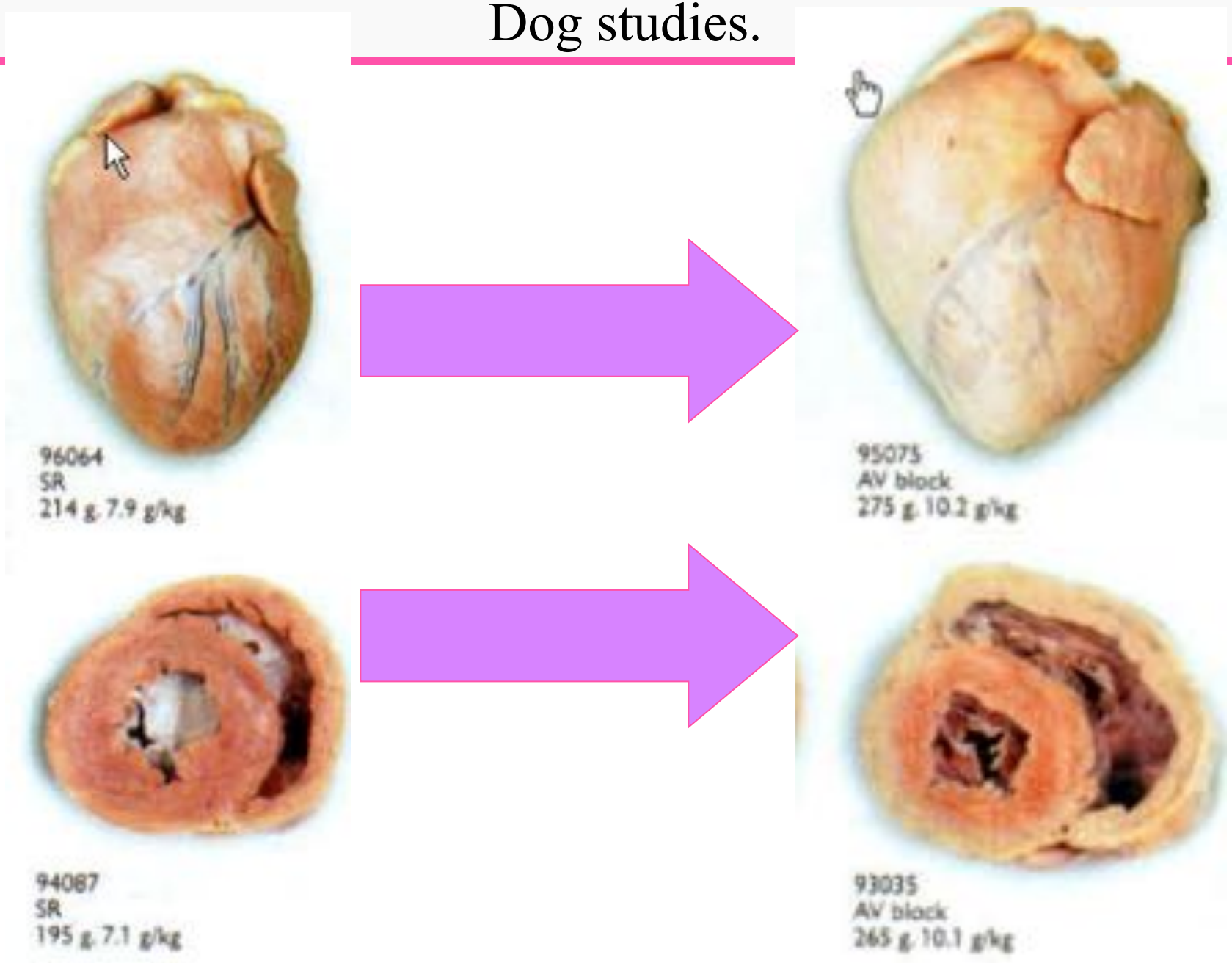


Complete AV-block with/without torsade.



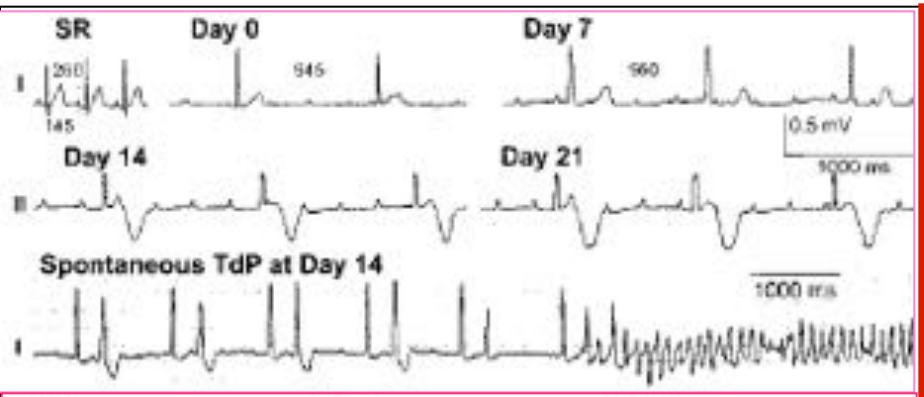
Kurita, *Am J Cardiol* 1992

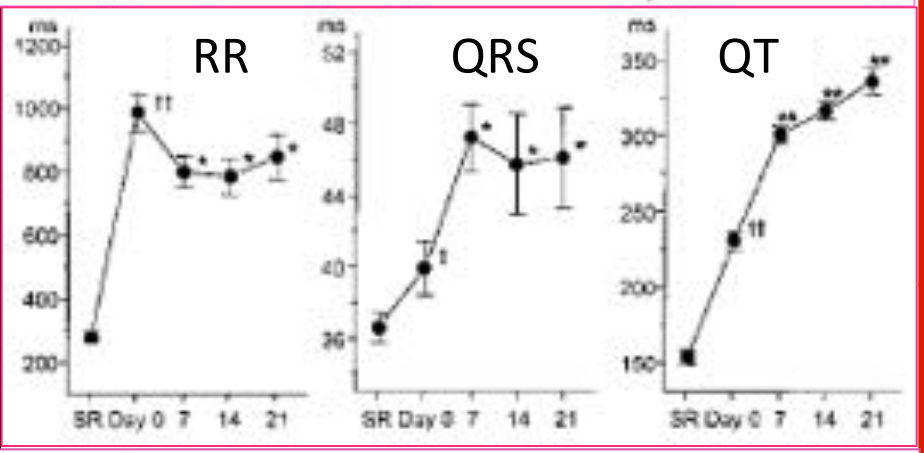
Biventricular hypertrophy and dilatation after AV block. Dog studies.

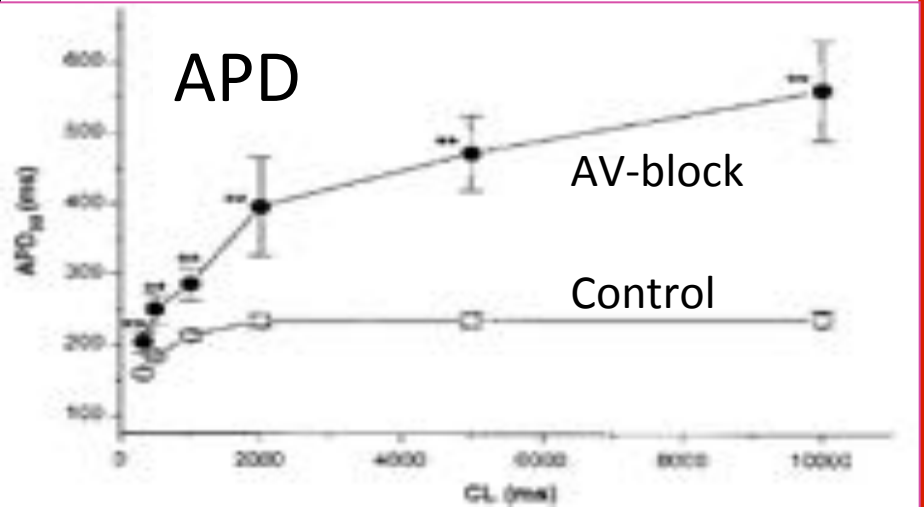


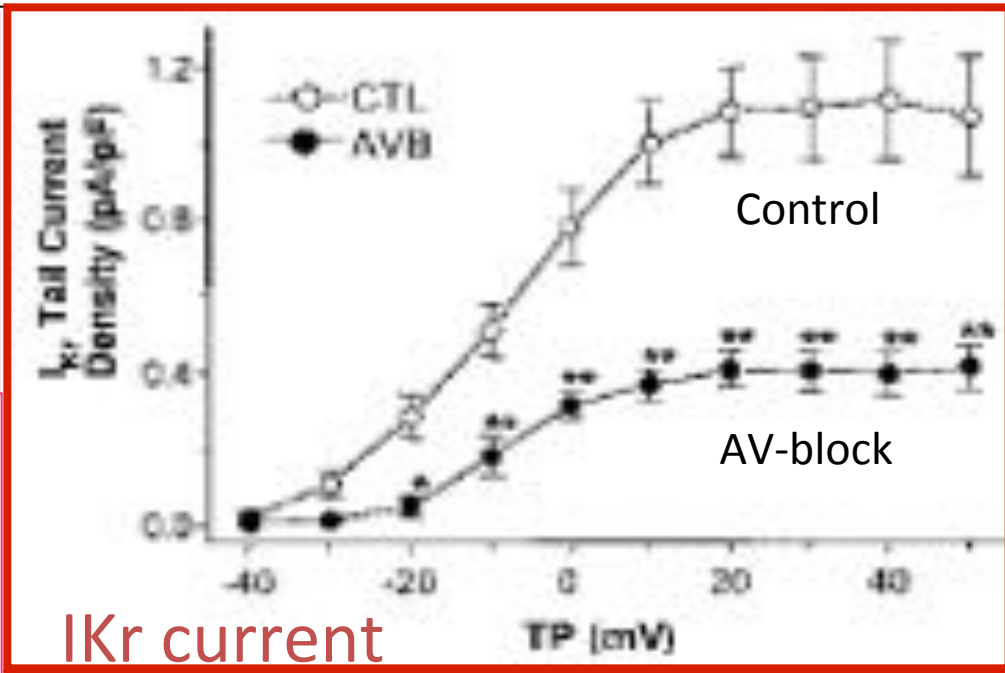
Vos, *Circulation* 1998.

LQTS in AV block: The rabbit model [Tsuji, *Circulation* 2002]

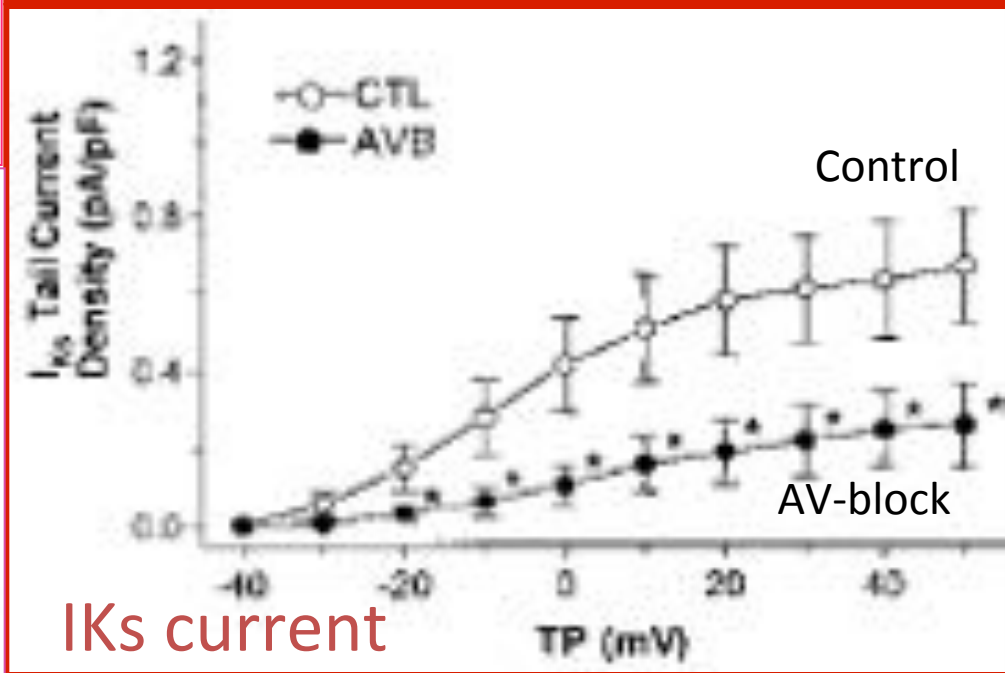








IKr current



IKs current

Torsades de pointes complicating atrioventricular block: Evidence for a genetic predisposition

Philippe Chevalier, MD, PhD,* Chloé Bellocq, PhD,† Gilles Millat, PhD,* Eric Piqueras, MD,* Franck Potet, PhD†, Jean-Jacques Schott, PhD†, Isabelle Baró, PhD†, Hervé Lemarec, MD, PhD†, Jacques Barhanin, PhD‡, Robert Rousson, MD, PhD,* Claire Rodriguez-Lafrasse, PhD*

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BACKGROUND The prevalence of genetic risk factors has not been systematically evaluated in the setting of complete atriventricular (AV) block complicated by long QT syndrome (LQTS).

OBJECTIVE This study was performed to determine to what extent acquired LQTS in the context of AV block has a genetic substrate.

METHODS Among 420 recipients of pacemakers implanted over a 3-year period, we identified retrospectively 29 patients with complete AV block and a QT interval >600 ms in duration. A second study group included 22 randomly selected patients who had AV block and a QT interval <600 ms. Normal controls were 100 consecutive individuals without medical history. Genetic studies screening for HERG, KCNQ1 KCNE1, KCNE2, and SCN5A mutations were performed.

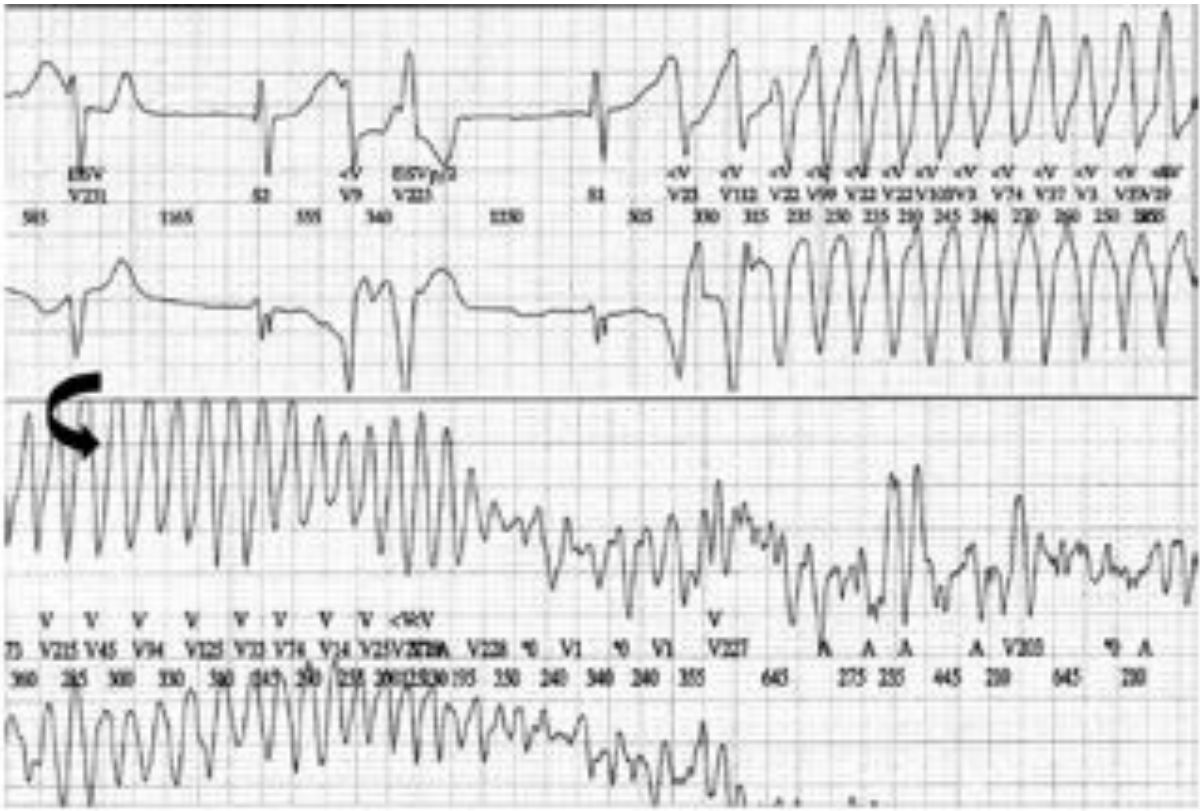
RESULTS We identified four mutations on genes encoding potassium channels in five patients with AV block and acquired LQTS. These mutations were not found among patients with AV block and a QT interval <600 ms in duration or in healthy volunteers. Functional expression of three HERG mutations (R328C, R696C, and R1047L) had a dominant negative effect on wild-type I_{Kr}. One KCNE2 mutation (R77W) identified in a patient treated with flecainide did not alter I_{Kr}.

CONCLUSIONS This study showed that complete AV block complicated by LQTS was associated with HERG mutations in 17% of cases. Further studies are needed to identify factors, genetic or environmental, which may be implicated in bradycardia-related abnormalities of ventricular repolarization.

KEYWORDS Atrioventricular block; Long QT interval; Torsades de pointes; HERG mutation

(Heart Rhythm 2007;4:170–174) © 2007 Heart Rhythm Society. All rights reserved.

	Group 1, AVB with long QT syndrome (n = 24)	Group 2, AVB without long QT syndrome (n = 22)	Group 3, AVB with long QT syndrome and genetic variant (n = 5)
Age (mean ± SD)	69 ± 17	70 ± 12	71 ± 12
Females	12 (50)	13 (59)	1 (20)
History of atrial fibrillation	7 (29)	6 (27)	1 (20)
Cardiomyopathy	10 (42)	7 (27)	1 (20)
Left ventricular ejection fraction (<50)	1 (4)	1 (4.5)	1 (20)
Hypokalemia (<3.50 mmol/L)	5 (20)	1 (4.5)	1 (20)
Treatment with a QT-prolonging drug	7 (29)	0	1 (20)
Family history of sudden cardiac death before 35 years of age	0	0	4 (80)
Long QTc interval in previous electrocardiogram without AVB	0[a]	0[b]	1[c]
QTc during AVB (mean ± SD)	744 ± 69	529 ± 51	768 ± 59



The Morphology of the QT Interval Predicts Torsade de Pointes During Acquired Bradyarrhythmias

Ian Topilski, MD, Ori Rogowski, MD, Rafael Rosso, MD, Dan Justo, MD, Yitschak Copperman, MD, Michael Glikson, MD, FACC, Bernard Belhassen, MD, Marek Hochenberg, MD, Sami Viskin, MD

Tel Aviv, Israel

JACC 2007

Objectives The purpose of this study was to define the electrocardiographic (ECG) predictors of torsade de pointes (TdP) during acquired bradyarrhythmias.

Background Complete atrioventricular block (CAVB) might lead to downregulation of potassium channels, QT interval prolongation, and TdP. Because potassium-channel malfunction causes characteristic T-wave abnormalities in the congenital long QT syndrome (LQTS), we reasoned that T-wave abnormalities like those described in the congenital LQTS would identify patients at risk for TdP during acquired bradyarrhythmias.

Methods In a case-control study, we compared 30 cases of bradyarrhythmias complicated by TdP with 113 cases of uncomplicated bradyarrhythmias. On the basis of the criteria used for the congenital LQTS, T waves were defined as LQT1-like (long QT interval with broad T waves), LQT2-like (notched T waves), and LQT3-like (small and late) T waves.

Results Neither the ventricular rate nor the QRS width at the time of worst bradyarrhythmia predicted the risk of TdP. However, the QT, corrected QT (QTc), and T_{peak}–T_{end} intervals correlated with the risk of TdP. The best single discriminator was a T_{peak}–T_{end} of 117 ms. LQT1-like and LQT3-like morphologies were rare during bradyarrhythmias. In contrast, LQT2-like "notched T waves" were observed in 55% of patients with TdP but in only 3% of patients with uncomplicated bradyarrhythmias ($p < 0.001$). A 2-step model based on QT duration and the presence of LQT2-like T waves identified patients at risk for TdP with a positive predictive value of 84%.

Conclusions Prolonged QT interval, QTc interval, and T_{peak}–T_{end} correlate with increased risk for TdP during acquired bradyarrhythmias, particularly when accompanied by LQT2-like notched T waves. (J Am Coll Cardiol 2007;49:320–8)
© 2007 by the American College of Cardiology Foundation

Comparison of patients with AV block complicated by torsade de pointes to patients with uncomplicated AV block

	AV-block with Torsade de pointes	Uncomplicated AV-block	P-Value
Age	72 ± 16	76 ± 11	NS
Female	77%	40%	<0.001
CAVB	78%	37%	<0.001
R-R	1490 ± 480	1540 ± 300	NS
QT	684 ± 100	494 ± 68	<0.001
QTc	571 ± 73	402 ± 53	<0.001

Topilski (Viskin) *J Am Coll Cardiol* 2007

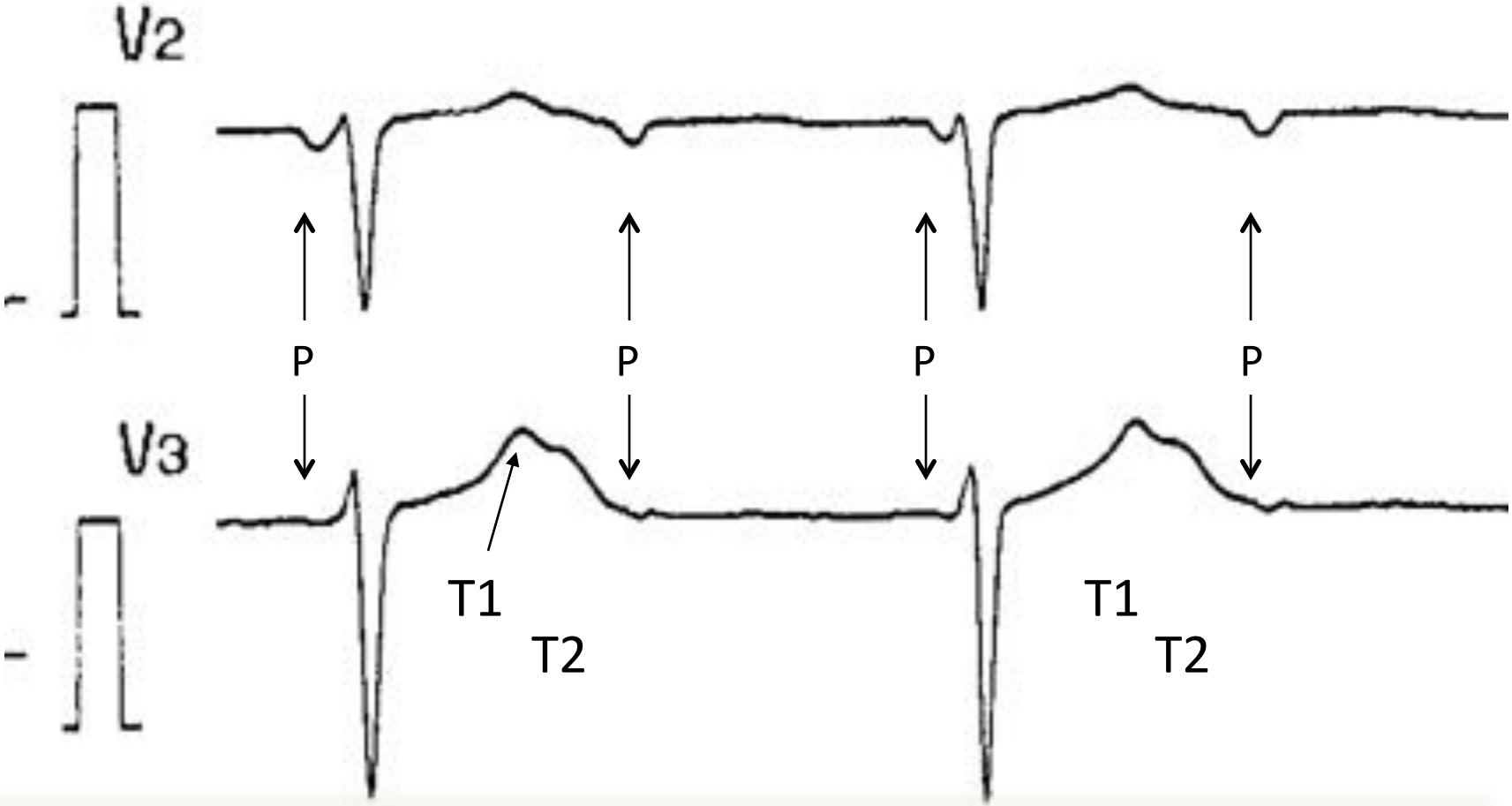
T-wave morphology defined according to data from the *CONGENITAL* LQTS.

LQT1 (I_{Ks})

LQT2 (I_{Kr})

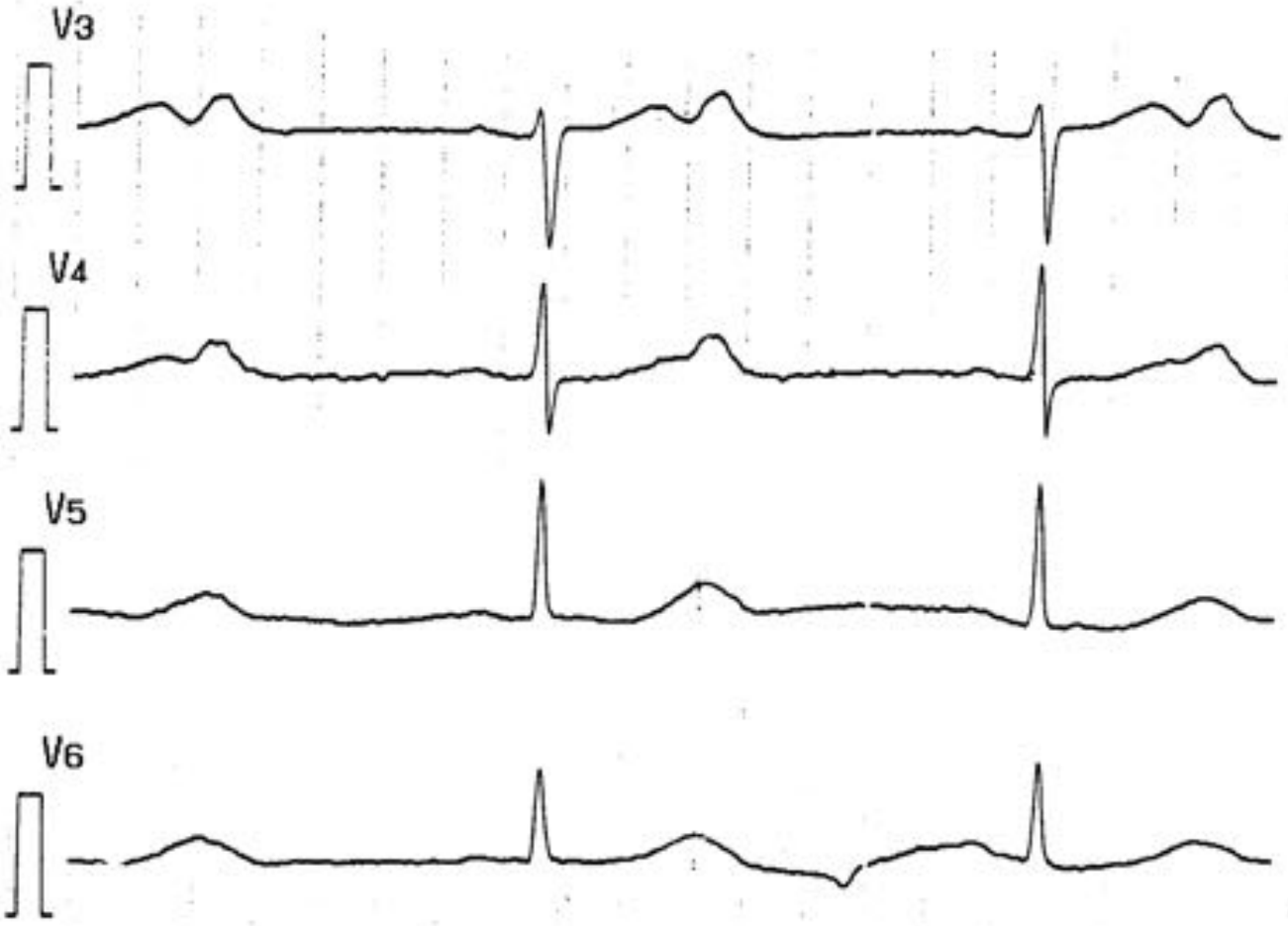
LQT3 (I_{Na})

LQT2-like morphology during AV block.



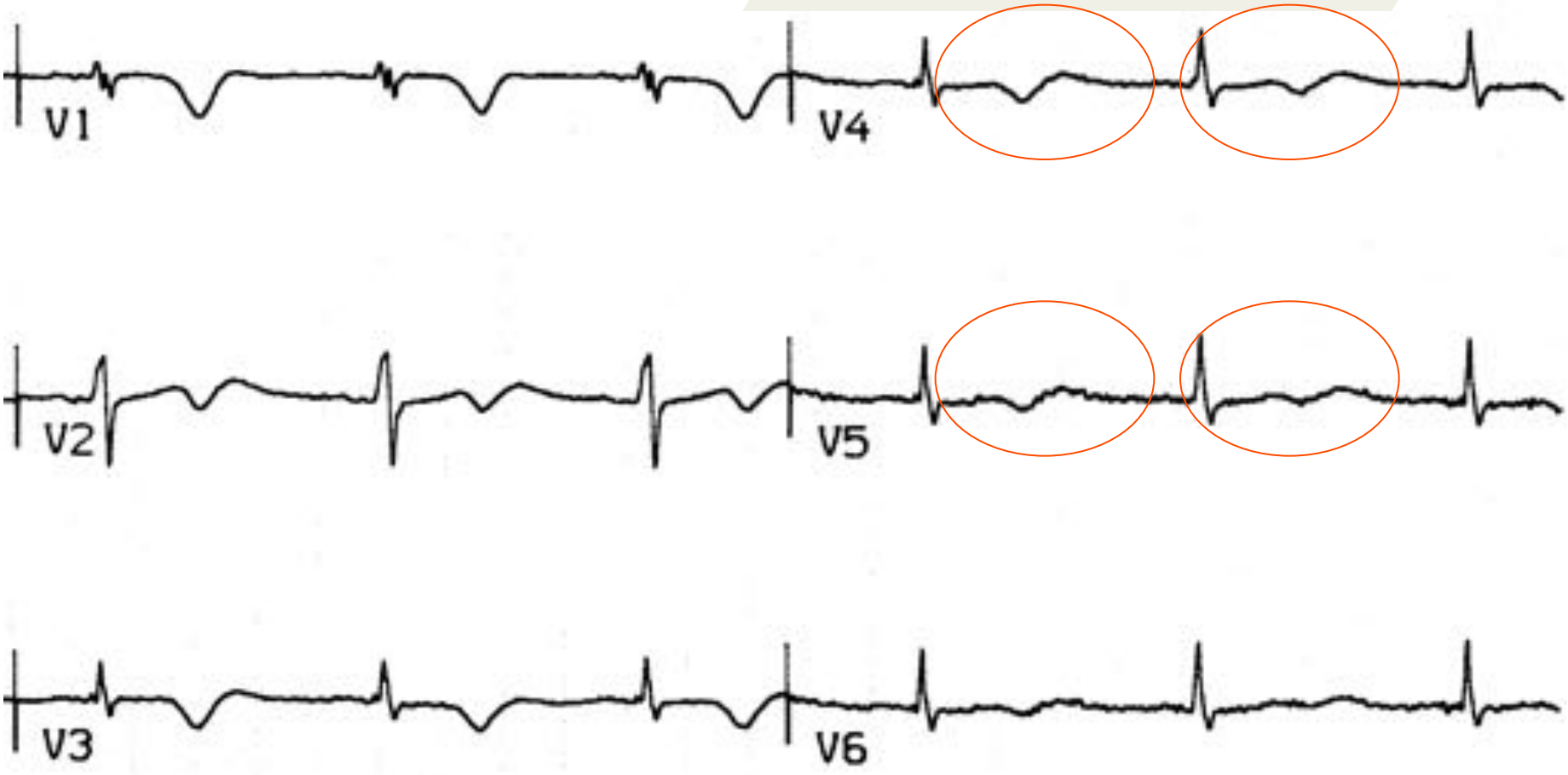
TdP	54%	
No TdP	3%	*p*=0.001

LQT2-like morphology..

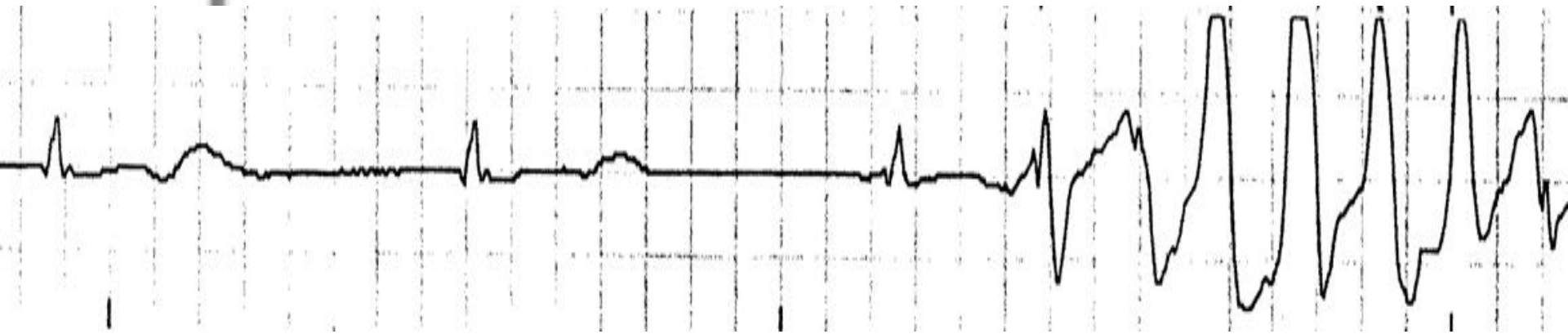


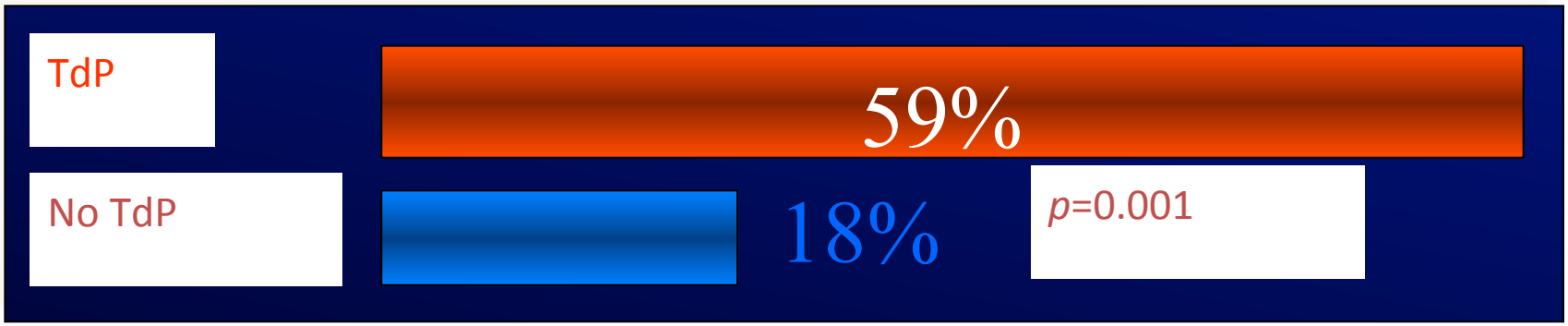
Sinus node dysfunction

"Bumps-ahead"

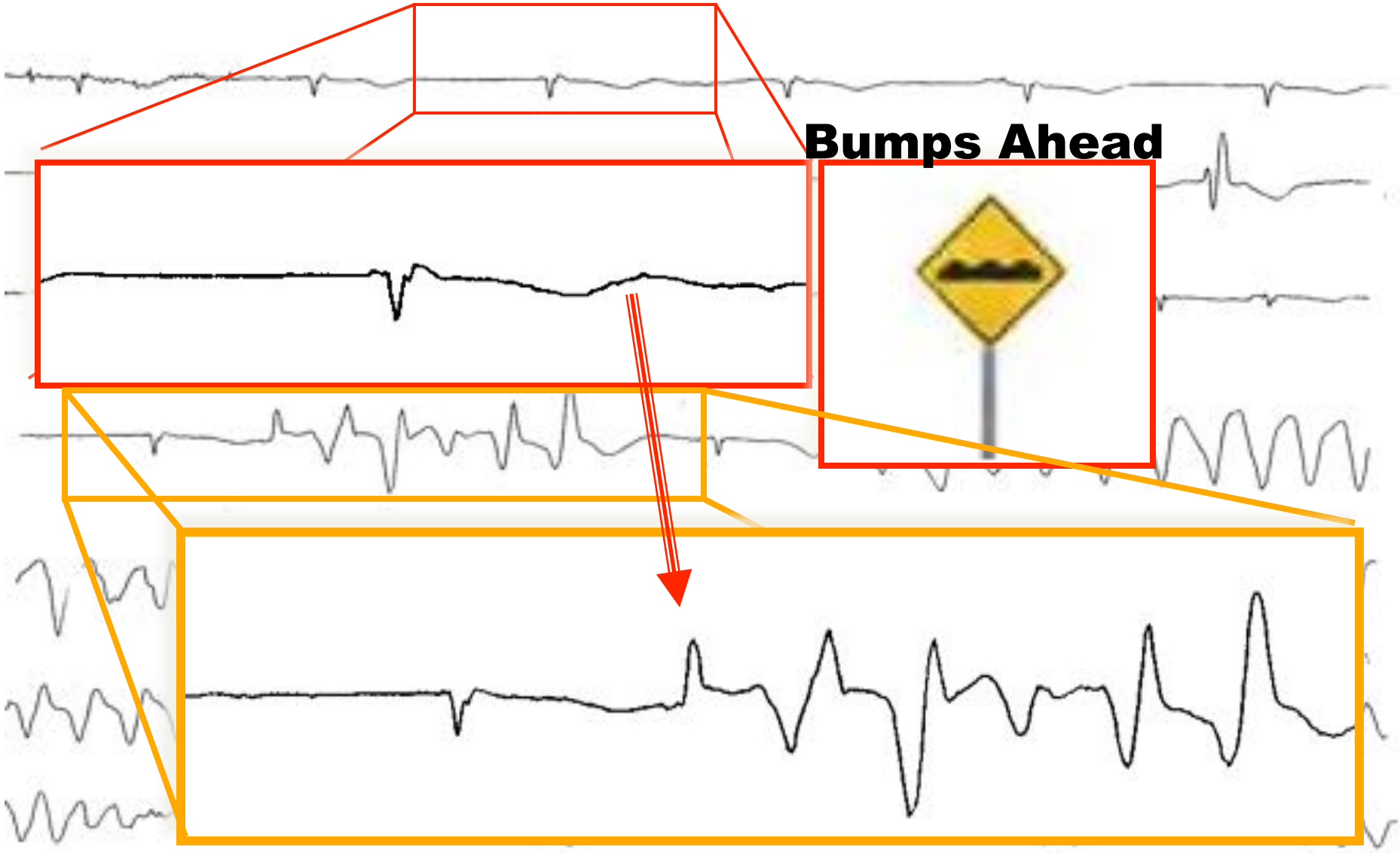


"Bump sign"



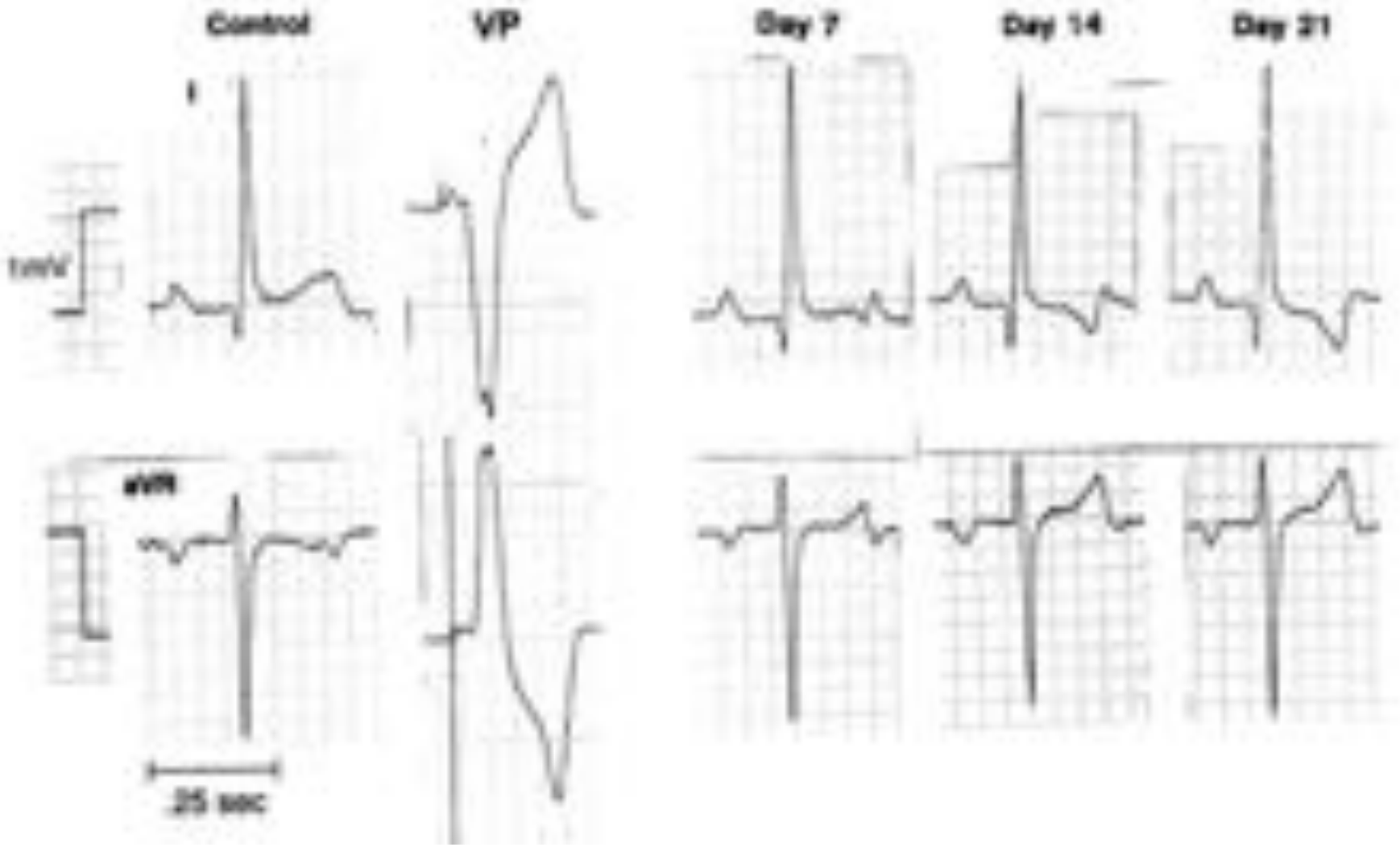


Atrial fibrillation with average ventricular rate of 42/min



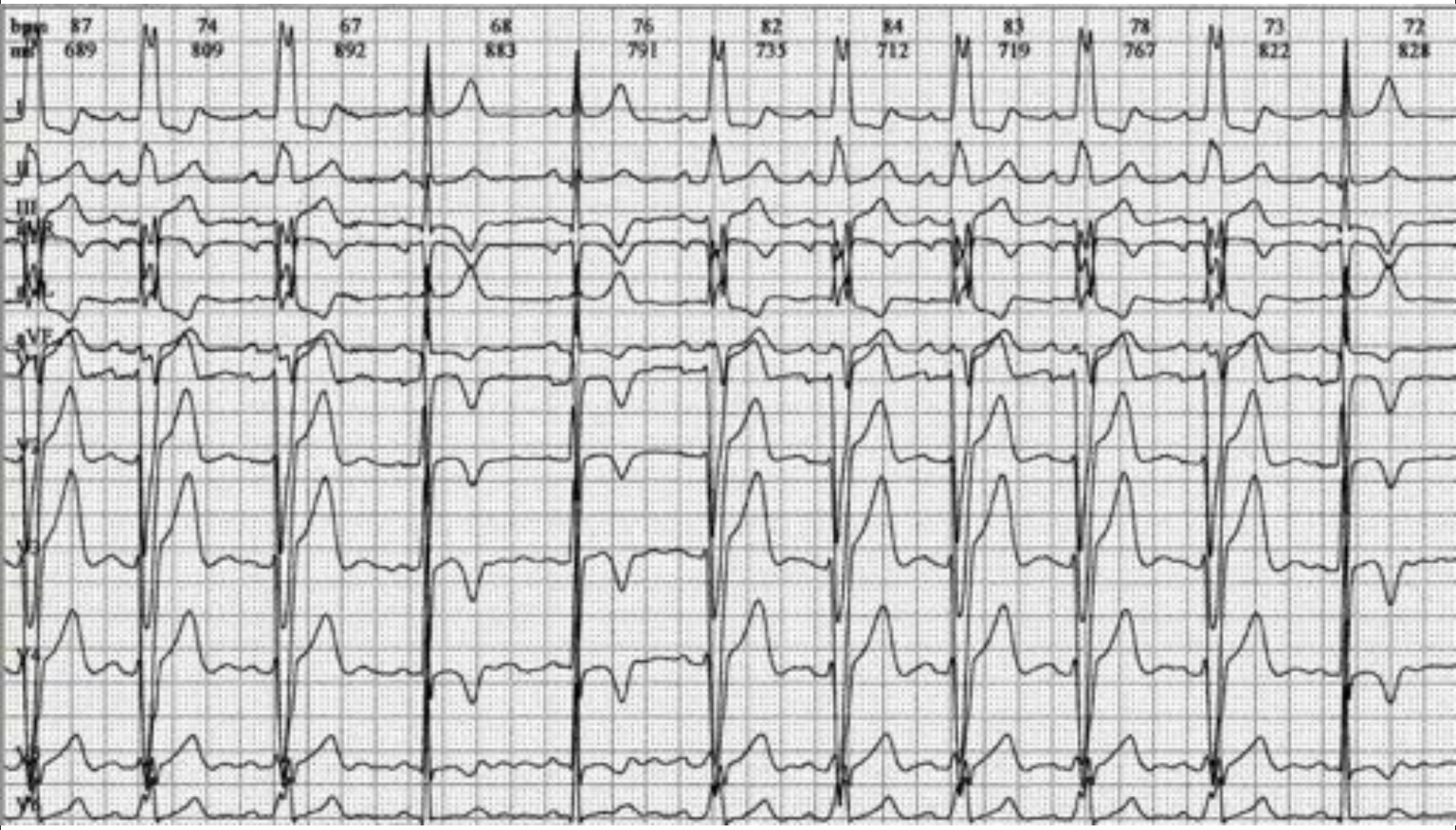
From the first extrasystole to VF in only 15 seconds !

Cardiac memory induced by pacing.



Shvilkin (Rosen), *Circulation* 1998.

Cardiac memory from transient LBBB



Original Article

Long QT Syndrome Complicating Atrioventricular Block

Arrhythmogenic Effects of Cardiac Memory

Raphael Rosso, MD*; Arnon Adler, MD*; Boris Strasberg, MD; Milton E. Guevara-Valdivia, MD; Riyaz Somani, MD; Adrian Baranchuk, MD; Amir Halkin, MD; Manlio F. Márquez, MD; Melvin Scheinman, MD; Arie Steinvil, MD; Bernard Belhassen, MD; Mark Kazatsker, MD; Amos Katz, MD; Sami Viskin, MD

Background—The magnitude of QT prolongation in response to bradycardia, rather than the bradycardia per se, determines the risk for torsade de pointes during atrioventricular block (AVB). However, we do not know why some patients develop more QT prolongation than others, despite similar bradycardia. We hypothesized that in patients who develop significant QRS vector changes during AVB, the effects of cardiac memory lead to excessive QT prolongation.

Methods and Results—We studied 91 patients who presented with AVB and who also had an ECG predating the bradyarrhythmia for comparison. We correlated changes in QRS morphology and axis taking place during AVB with the bradycardia-induced QT prolongation. Patients with and without QRS morphology changes at the time of AVB were of similar age and sex. Moreover, despite similar R-R interval during AVB, cases with a QRS morphology change had significantly longer QT (648±84 versus 561±84; $P<0.001$) than those without. Patients who developed a change in QRS morphology at the time of AVB had a 7-fold higher risk of developing long QT. This risk nearly doubled when the change in QRS morphology was accompanied by a change in QRS axis.

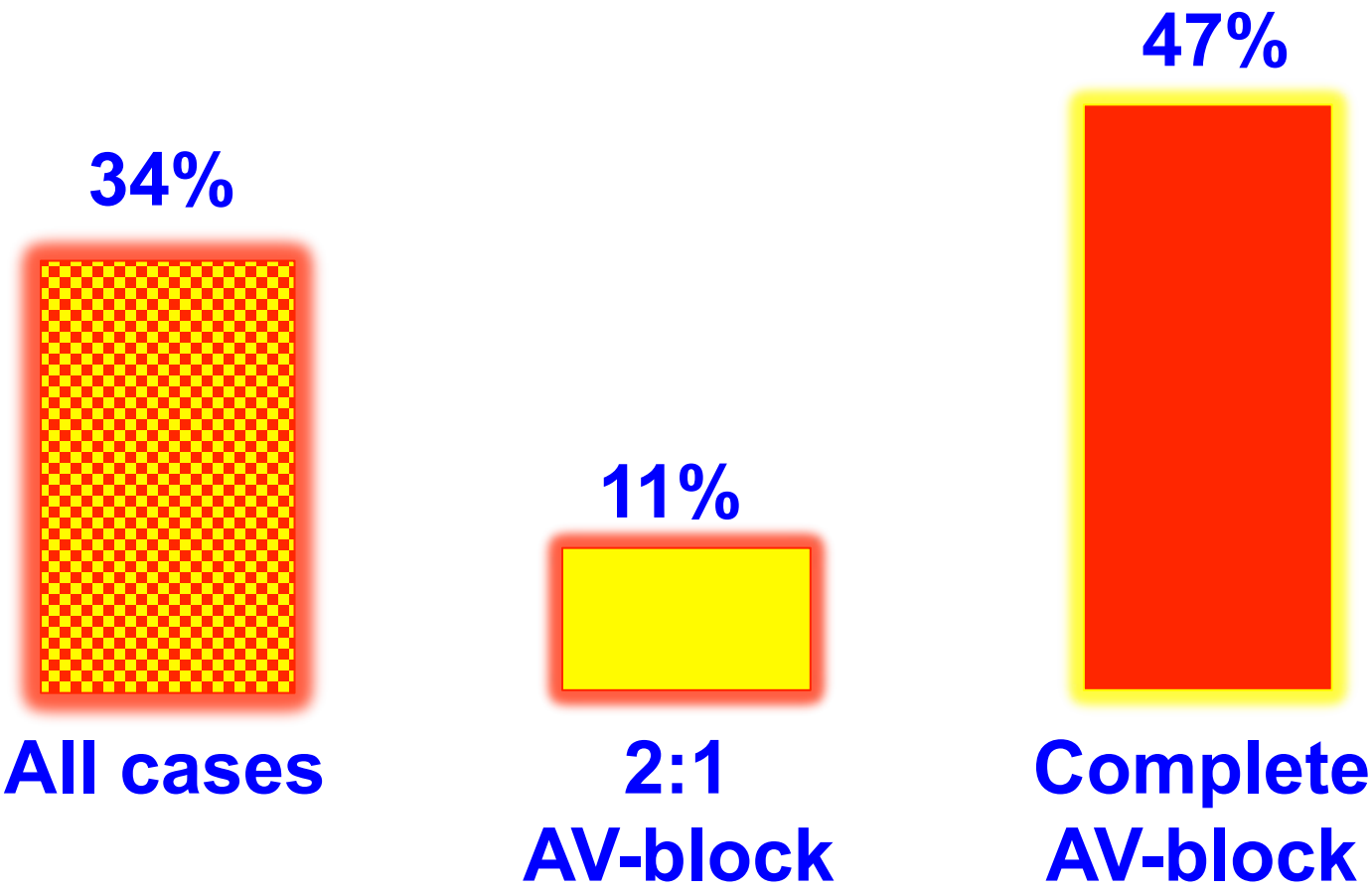
Conclusions—Cardiac memory resulting from a change in QRS morphology during AVB is independently associated with QT prolongation and may be arrhythmogenic during AVB. (***Circ Arrhythm Electrophysiol.* 2014;7:1129-1135.)**

Key Words: atrioventricular block ■ long QT syndrome ■ torsade de pointes

Long QT syndrome complicating AV-block:
The proarrhythmic role of cardiac memory.

	2:1 AVB	CAVB	
Heart rate beats/min	44 ± 5	37 ± 8	*p=NS*
QT msec	532 ± 107	602 ± 87	*p=0.004*
QTc msec	452 ± 92	465 ± 75	*p=NS*

Changes in QRS-morphology or QRS-axis at the time of AV block (in comparison to baseline)



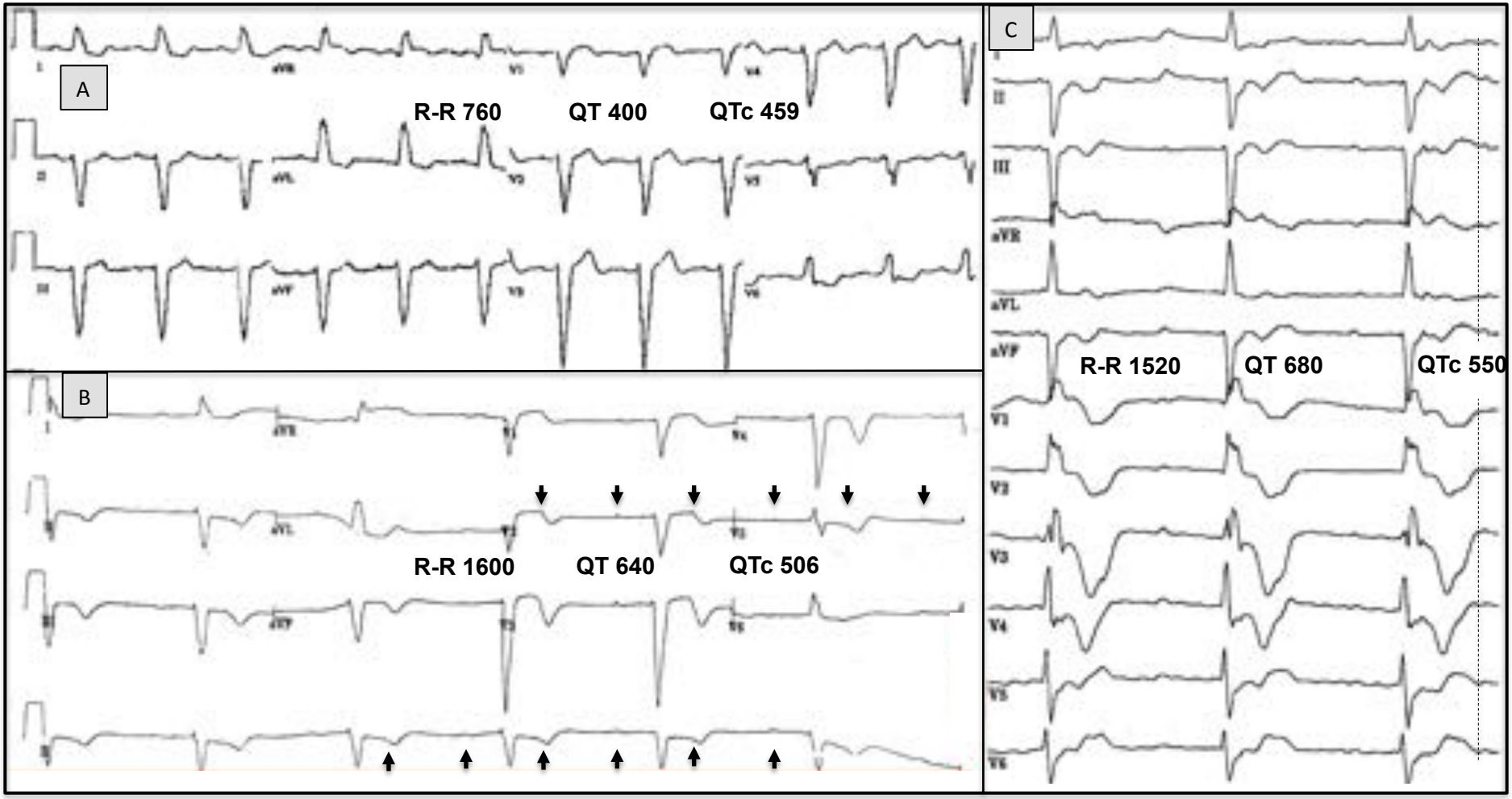
Comparison of patients with *and without* changes in QRS morphology at the time of AV block

	Change in QRS pattern	No change	P-Value
Age	78 ± 110	76 ± 14	NS
Female	45%	58%	NS
R-R	1690 ± 390	1670 ±470	NS
QT	684 ± 84	561 ± 84	<0.001
QTc	505 ± 76	440 ± 70	<0.001
ΔQTc	46 ± 80	6 ± 74	0.001

Effects of changes in QRS morphology during AV block.

50-year-old male.

Baseline

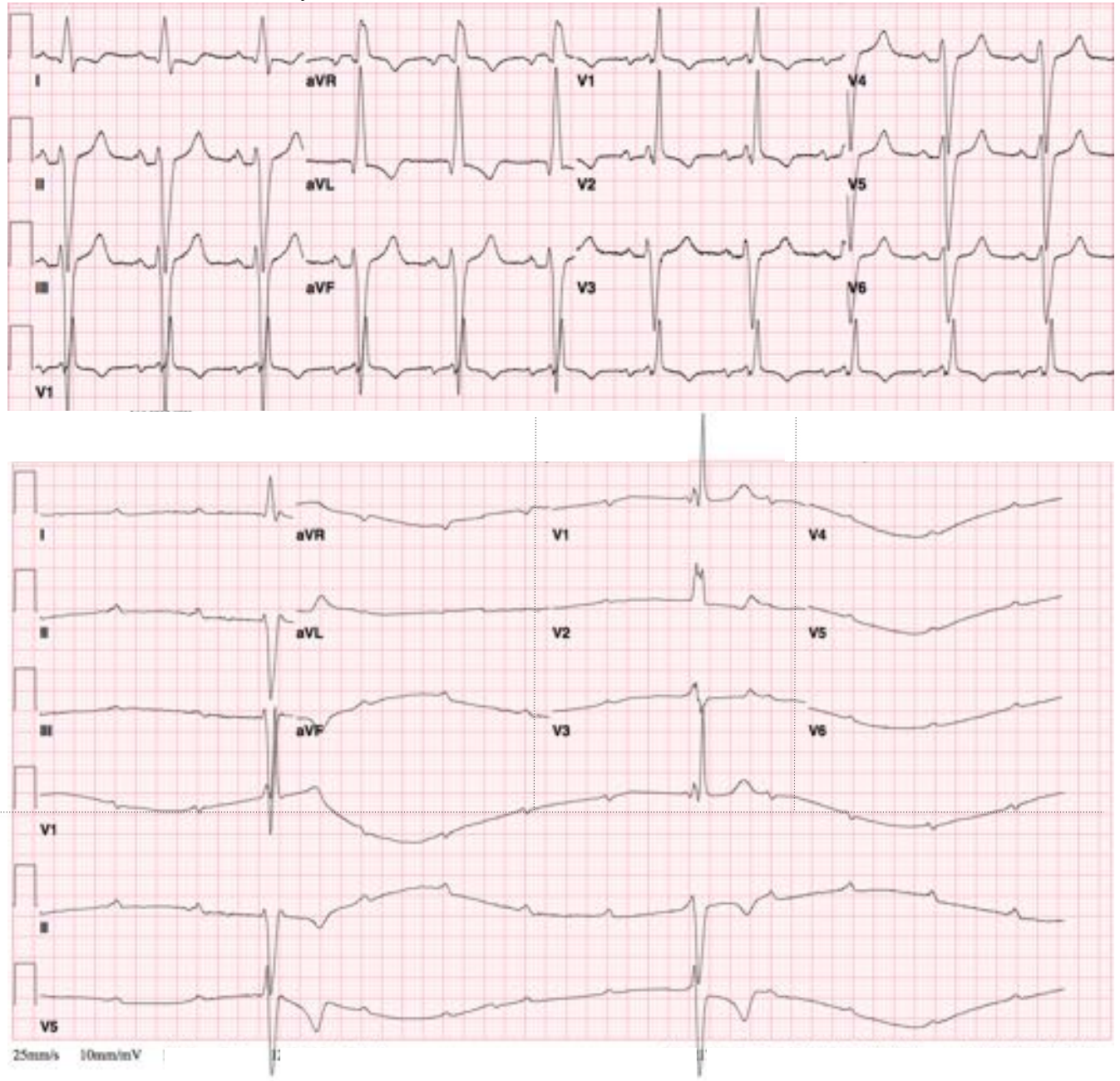


2:1 AV block:
no change in QRS morphology

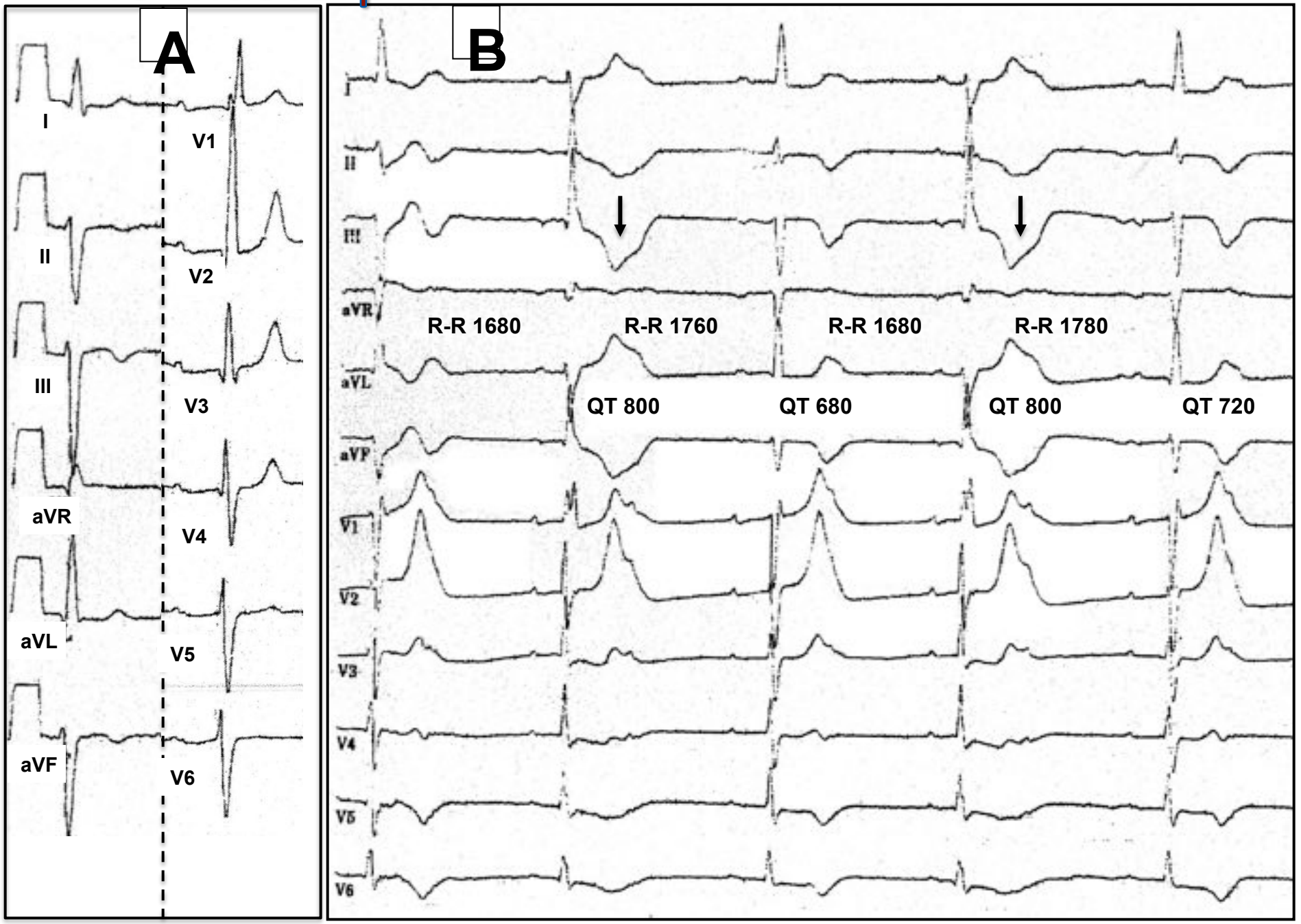
Complete AV block:
QRS change: LBBB➔RBBB

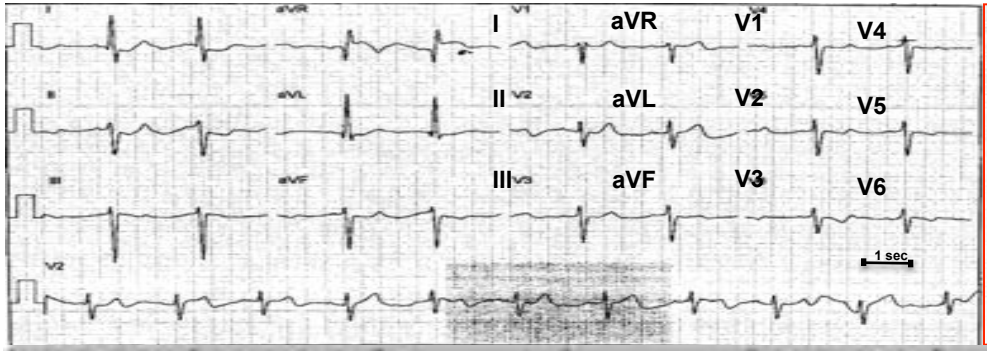
Absence of QT prolongation despite extreme bradycardia

60-year old male. Ventricular rate 28 betas/min



The masterpiece




I
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aVL
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III
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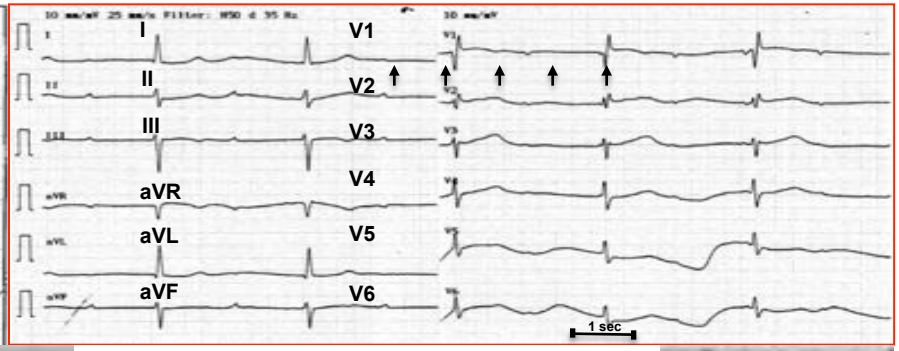
V3
V6
1 sec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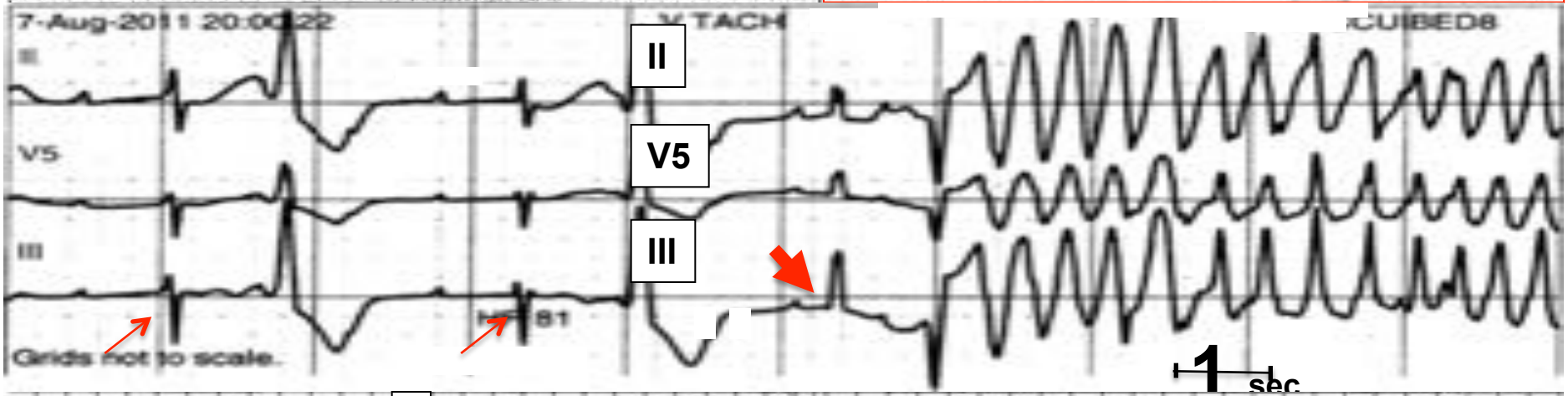
II
V5
III
Grids not to scale.
1 sec


I
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aVR
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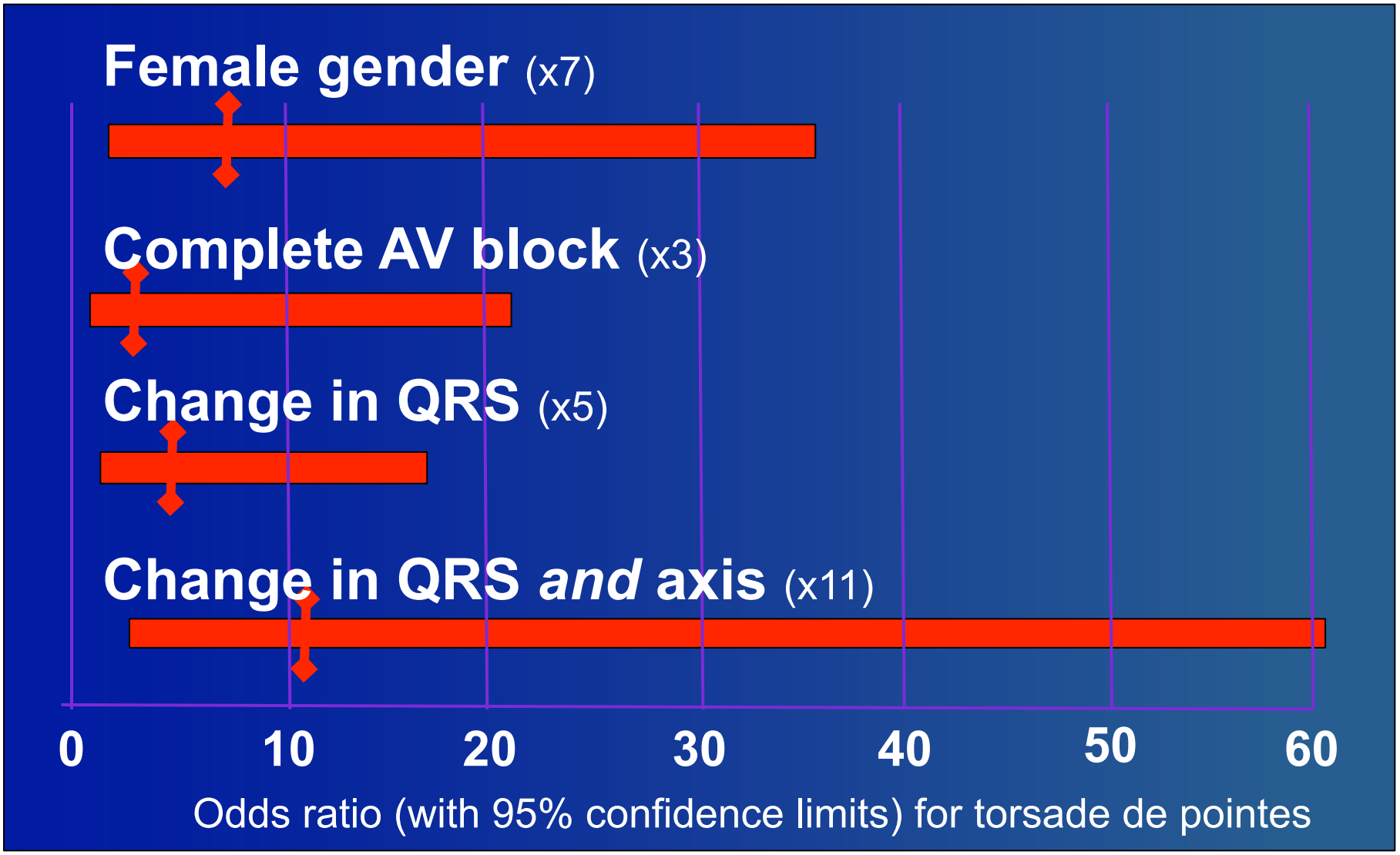
Predictors of torsade de pointes during AV block



Electrocardiographic predictors of bradycardia-induced torsades de pointes in patients with acquired atrioventricular block

Min Soo Cho, MD,* Gi-Byoung Nam, MD, PhD,* Yong-Guin Kim, MD,* Ki-Won Hwang, MD,* Yoo Ri Kim, MD,* HyungOh Choi, MD,* Sung-Hwan Kim, MD,* Kyoung-Suk Rhee, MD, PhD,† Nam-Joon Kim, MD,‡ June Soo Kim, MD, PhD,‡ Jun Kim, MD, PhD,* Kee-Joon Choi, MD, PhD,* You-Ho Kim, MD, PhD, FHRS*

*From the *Heart Institute, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, †Division of Cardiology, Department of Internal Medicine, Chonbuk National University Hospital, Chonbuk National University, Chonju, Korea, and ‡Department of Cardiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.*

BACKGROUND Predictors of torsades de pointes (TdP) in bradyarrhythmia-induced acquired long QT syndrome are not well defined.

OBJECTIVE The purpose of this study was to search for electrocardiographic (ECG) TdP predictors in patients with acquired atrioventricular block (AVB) and QT prolongation.

METHODS We analyzed 12-lead ECGs from 20 patients (15 females, age 65.9 ± 15.6 years) with TdP episodes from among 898 AVB patients (2.2%) in 3 tertiary hospitals. The ECG repolarization parameters in TdP patients were compared with those of 80 age- and sex-matched control AVB patients with no TdP episodes.

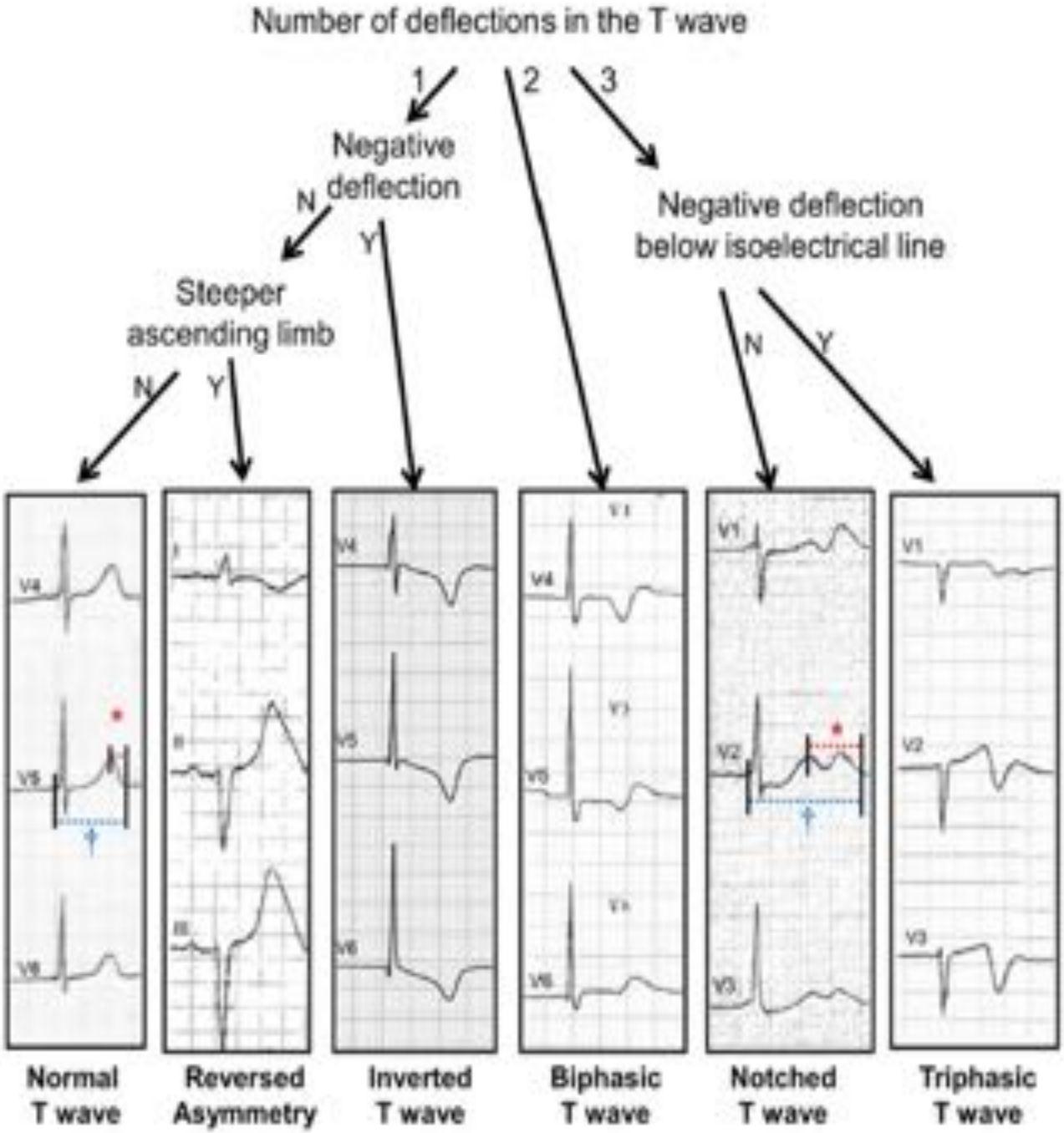
RESULTS TdP was initiated by premature ventricular complexes with a long–short sequence of activation. The average cycle length of the long sequence was 1289.9 ± 228.9 ms and was 2.3 ± 0.6 times longer than the cycle length of the short sequence. TdP patients had a significantly longer mean QT interval (716.4 ± 98.9 ms vs 523.2 ± 91.3 ms, $P = .001$), mean T peak to end interval (334.2 ± 59.1 ms vs 144.0 ± 73.7 ms, $P = .001$) and a higher T peak to end interval/QT ratio (0.49 ± 0.09 vs 0.27 ± 0.11, $P = .001$) compared with non-TdP controls. TdP patients showed a higher prevalence of notched T waves in which T_2 was at least 3 mm taller than T_1 (45.0% vs 1.3%, $P = .001$), triphasic T waves (30.0% vs 1.3%, $P = .001$), reversed asymmetry (20.0% vs 0%, $P = .001$), and T-wave alternans (35.0% vs 0%, $P = .001$). An algorithm combining these morphologic parameters was able to differentiate TdP patients from non-TdP patients with high sensitivity (85.0%) and specificity (97.5%).

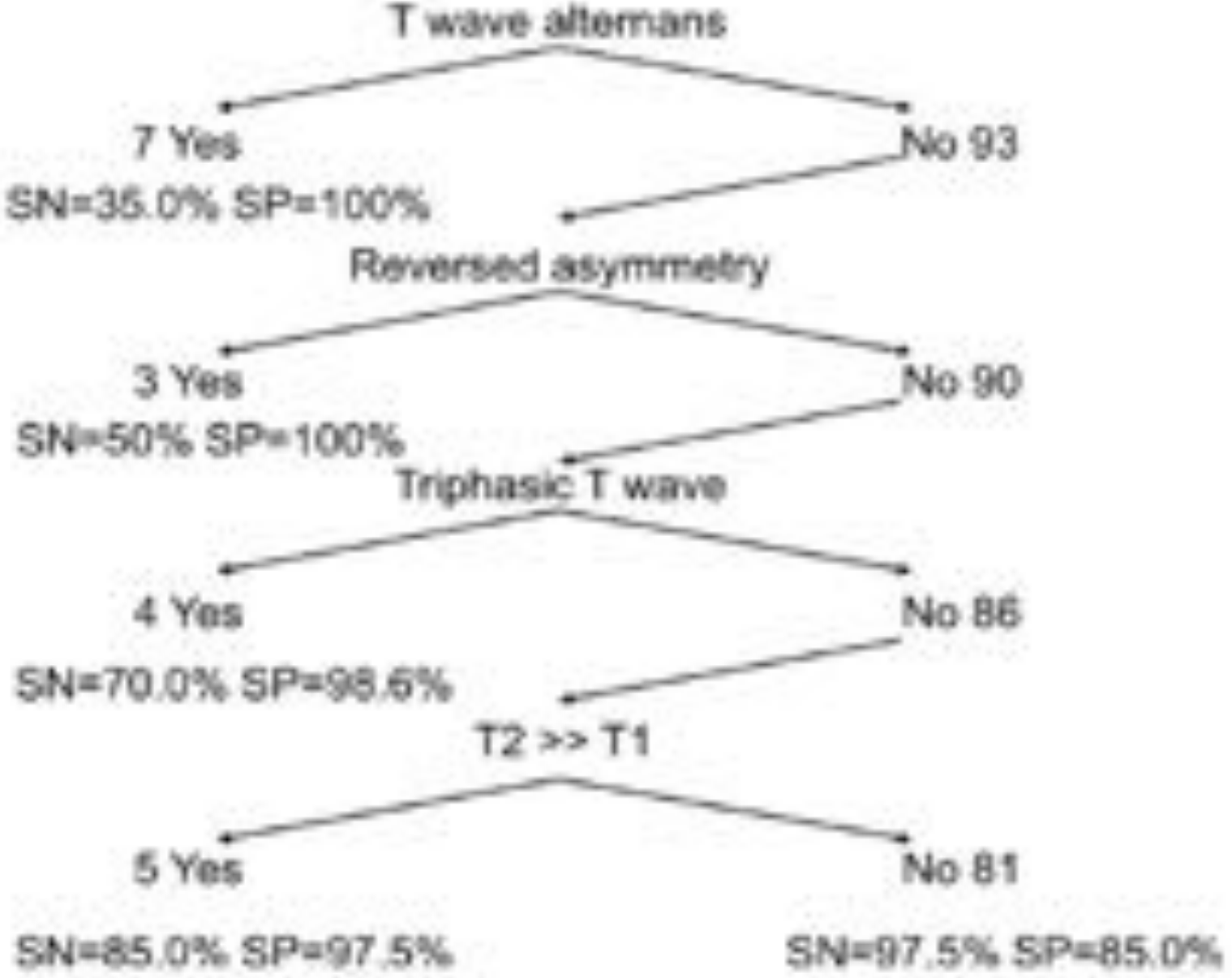
CONCLUSION An algorithm combining specific T-wave morphologies was useful for identifying patients with AVB who are at risk for developing TdP.

KEYWORDS Atrioventricular block; Bradycardia; Torsades de pointes; T waves; Long QT syndrome

ABBREVIATIONS **AUC** = area under the curve; **AVB** = atrioventricular block; **CI** = confidence interval; **ECG** = electrocardiography; **IQR** = interquartile range; **LQTS** = long QT syndrome; **ROC** = receiver operating characteristic; **TdP** = torsades de pointes; **Tpe** = T peak to end interval; **TWA** = T-wave alternans

(Heart Rhythm 2015;12:498–505) © 2015 Heart Rhythm Society. All rights reserved.


Number of deflections in the T wave
1
2
3
Negative deflection
N
Y
Steeper ascending limb
N
Y
Negative deflection below isoelectrical line
N
Y
Normal T wave
Reversed Asymmetry
Inverted T wave
Biphasic T wave
Notched T wave
Triphasic T wave


T wave alternans
7 Yes
SN=35.0% SP=100%
No 93
Reversed asymmetry
3 Yes
SN=50% SP=100%
No 90
Triphasic T wave
4 Yes
SN=70.0% SP=98.6%
No 86
T2 >> T1
5 Yes
SN=85.0% SP=97.5%
No 81
SN=97.5% SP=85.0%

So… how to predict torsade? Who should get an temporary pacemaker?

Conclusions: Torsade de pointes during acquired bradyarrhythmias.

Step 1.

Select patients with QT >510 msec.

Sensitivity 100%, PPV=41%.

2.

Heart rate and QRS are not predictors.

QT, QTc, Tpeak-Tend are predictors

3.

T wave morphology is important