CARDIAC ARREST EPISODE DURING STRONG EMOTION IN YOUNG COMPETITIVE SOCCER PLAYER

EPISODIO DE PARADA CARDIORESPIRATORIA DURANTE FUERTE EMOCIÓN EN JUGADOR DE FUTBOL PROFESIONAL

EPISÓDIO DE PARADA CARDÍACA DURANTE FORTE EMOÇÃO EM JOVEM JOGADOR DE FUTEBOL COMPETITIVO

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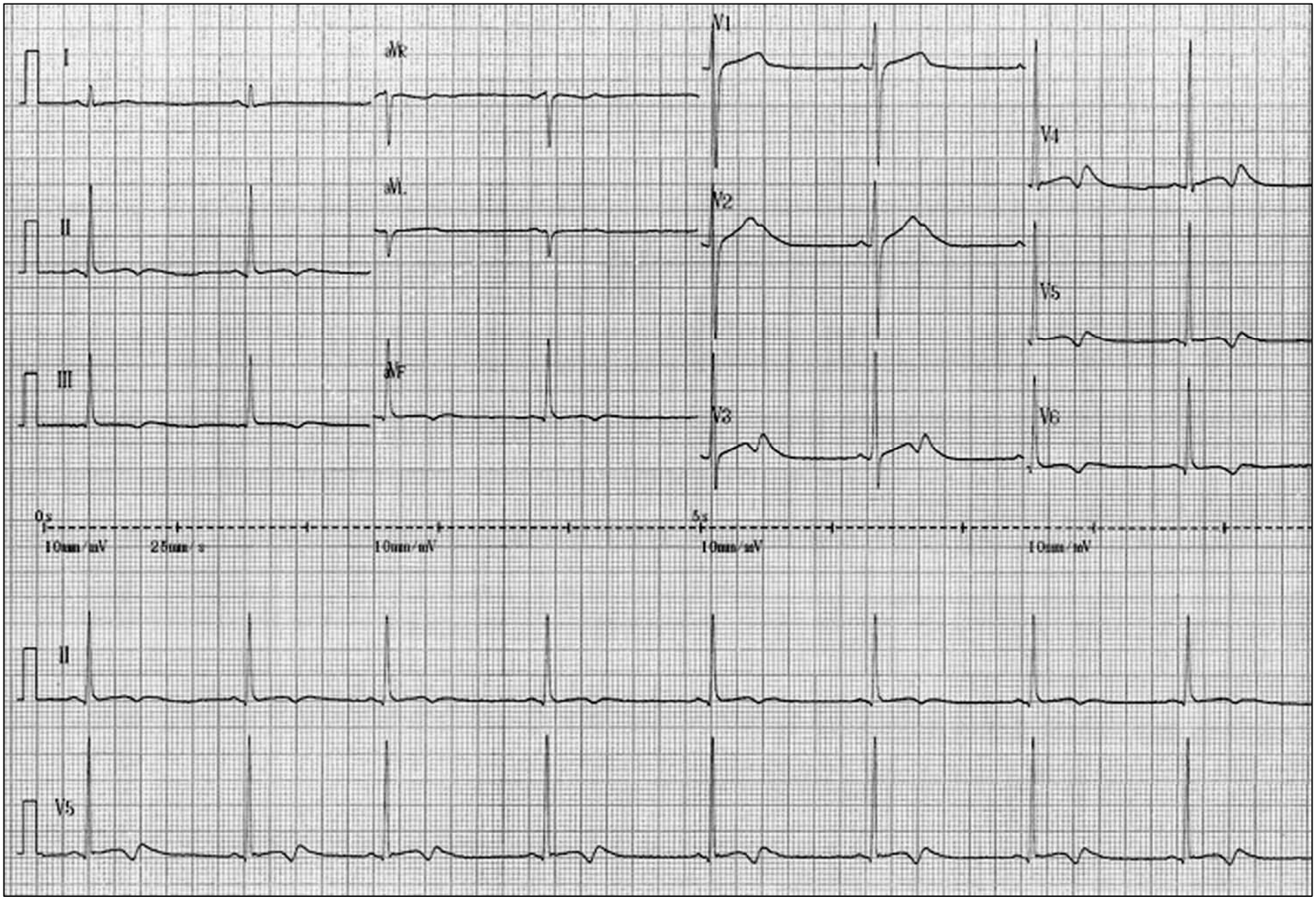
Comments
Dr Sami Viskin (Tel Aviv).Israel
Dr Andrés Ricardo Pérez-Riera from São Paulo Brazil

Estimados colegas.
Pongo a consideración del foro el siguiente reciente caso.
Joven sano de 17 años de edad, jugador competitivo de futbol, entrenamientos diarios. Nunca presentó sintomatología alguna, hasta que en un momento de una fuerte discusión con un hermano colapsa, siendo reanimado exitosamente. Fibrilación ventricular fue documentada. Días después se le realiza: ecocardiograma= normal, ergometría= sin arritmia alguna, cinecoronariografia= sin anomalías coronarias.
Adjunto ECG basal y en fase de strain-relajación de Valsalva realizado 3 semanas post evento.
Esperando vuestras opiniones, les saludo cordialmente
José Luis Serra

Dear colleagues.
I put to the forum the following recent case.
Young healthy 17-year-old competitive soccer player, daily workouts. Never presented any symptoms, until in a moment of heated discussion with a brother collapses, being resuscitated successfully. Ventricular fibrillation was documented. Days later he was done: = normal echocardiogram, normal exercise stress testing = no arrhythmia any, normal coronary angiography. no coronary anomalies. Deputy baseline ECG and strain-relaxation phase of Valsalva performed 3 weeks after the event. Waiting for your opinions,

I greet you cordially
Jose Luis Serra M.D.


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
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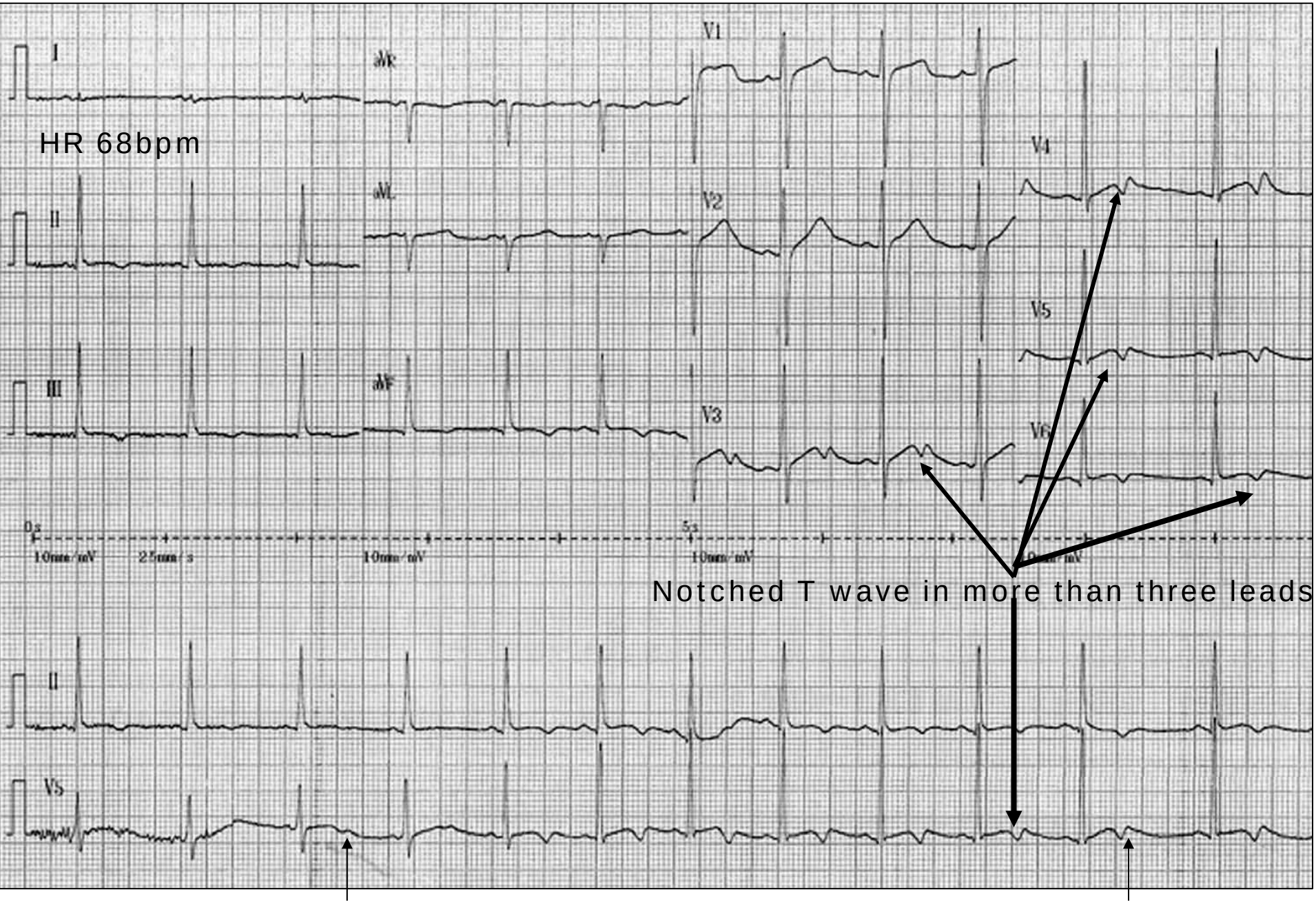

I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
HR 68bpm
Notched T wave in more than three leads
II
V5
Spontaneous dynamic changes of repolarization second T2-wave will become taller

There is very high suspicion for long QT syndrome of the LQT2 type.
Only God knows where the QT ends in lead II but I think that in lead V2 you can get a reliable measurement of QT 520 and QTc of 475 msec. I would do the following:

1. Holter recordings (preferably with multiple leads) to see how the QT looks at night (during bradycardia) and after pauses. My guess is that the bizarre second T-wave will become taller.
2. Our standing test (1) and now in press: (2). I think the standing test will very useful in this patient.
3. If you are still insecure, adenosine test and exercise test.
4. Genetic tests (for LQT2 if you have limited funding or for all the LQTS genes if you have unlimited funding).

Hope this helps

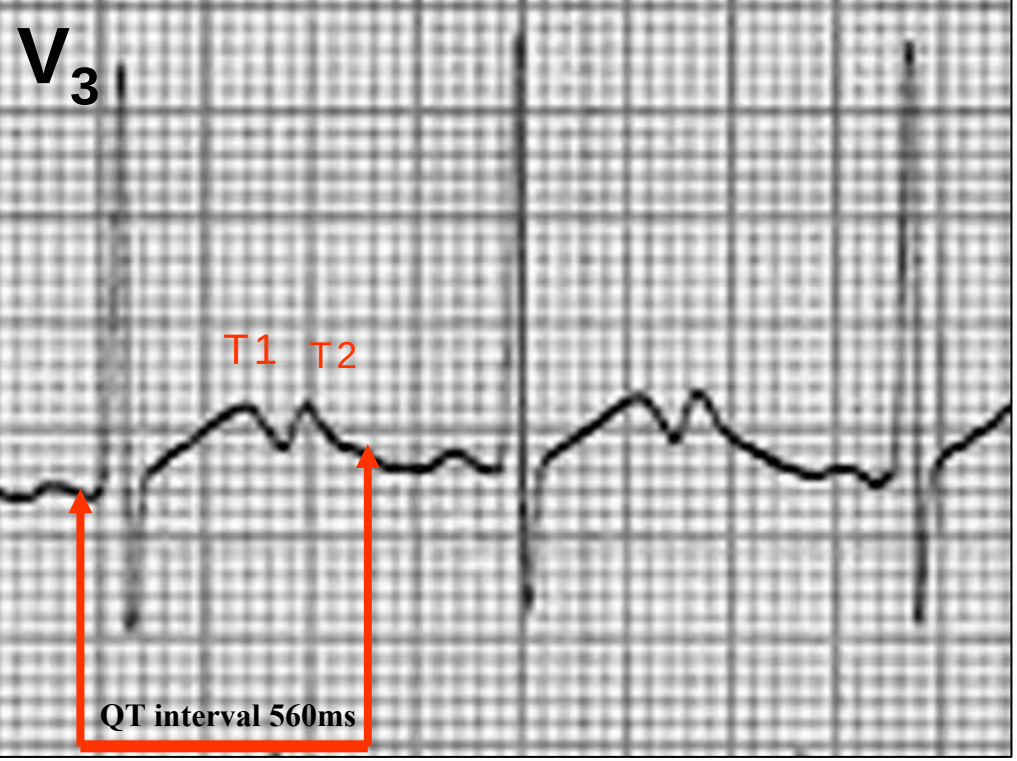
References

1. **Viskin S, Postema PG, Bhuiyan ZA, Rosso R, Kalman JM, Vohra JK, Guevara-Valdivia ME, Marquez MF, Kogan E, Belhassen B, Glikson M, Strasberg B, Antzelevitch C, Wilde AA. The response of the QT interval to the brief tachycardia provoked by standing: A bedside test for diagnosing long QT syndrome. J Am Coll Cardiol. 2010; 55: 1955-1961.**
2. **Adler A, van der Werf C, Postema P, Rosso R, Bhuiyan ZA, Kalman JM, Vohra JK, Guevara-Valdivia ME, Marquez MF, Halkin A, Antzelevitch C, Wilde AA, Viskin S. The phenomenon of "QT-stunning": The abnormal QT prolongation provoked by standing, in patients with long QT syndrome, persists even as the heart rate returns to normal. Heart Rhythm. 2012 (on line)**.

Sami Viskin (Tel Aviv).

Replica: dear Sami, recently Mauriello et al(1) concluded that routine Holter monitoring appears to be of minimal clinical utility from a diagnostic and prognostic perspective in evaluating LQTS, and may not be cost effective. Whether Holter monitoring aids in therapeutic decisions such as dosing or whether ambulatory QTc measurements, provided by some newer devices, might help in the diagnostic evaluation warrants further scrutiny. Holters where classified as positive if prestent an episode of NS-VT, supraventricular tachycardia, ≥4 couplets/day, ≥10 PVCs/hour, or >5-second sinus pause. Any comments? Thank in advance. Andrés.

1. **Mauriello DA, Johnson JN, Ackerman MJ. Holter monitoring in the evaluation of congenital long QT syndrome.Pacing Clin Electrophysiol. 2011 Sep;34:1100-4.**



HR= 79bpm QT interval: 560ms
Mean predicted QT values at RR cycle length
QT for Men in seconds
RR seconds 0.75. Mean value 0.345
Lower Limit 0.301
Upper limit.389

The normal maximal value that is accepted for the QT interval in males is 446 ms and in females 447 ms $\pm$ 15. If it exceeds 450 ms in males and 470 ms in females, the QT interval should be considered as prolonged. Values above 500 ms may cause a tendency to TdP.

The LQT2 type is the second most common gene location that is affected in long QT syndrome, making up about 25 to 30 percent of all cases. This form of long QT syndrome most likely involves mutations of the *human ether-a-go-go related gene* (hERG) on chromosome 7.

The hERG gene (also known as KCNH2) is part of the rapid component of the potassium rectifying current (I_{Kr}). (The I_{Kr} current is mainly responsible for the termination of the cardiac action potential, and therefore the length of the QT interval. The normally functioning hERG gene allows protection against early after depolarizations (EADs).

Most drugs that cause long QT syndrome do so by blocking the I_{Kr} current via the hERG gene. These include erythromycin, terfenadine, and ketoconazole.

The hERG channel is very sensitive to unintended drug binding due to two aromatic amino acids, the tyrosine at position 652 and the phenylalanine at position 656. These amino acid residues are poised so that a drug binding to them will block the channel from conducting current. Other potassium channels do not have these residues in these positions and are, therefore, not as prone to blockage.

The diagnosis of LQTS is not easy since 2.5% of the healthy population have prolonged QT interval, and 10–15% of LQTS patients have a normal QT interval.(1)
A commonly used criterion to diagnose LQTS is the LQTS "diagnostic score".(2) The score is calculated by assigning different points to various criteria. With four or more points, the probability is high for LQTS; with one point or less, the probability is low. A score of two or three points indicates intermediate probability.

Torsades de pointes ventricular tachycardia - 2 points
T wave alternans- 1 point
Notched T wave in at least 3 leads - 1 point
Low heart rate for age (children) - 0.5 points
Syncope (one cannot receive points both for syncope and torsades de pointes)
Congenital deafness - 0.5 points
Family history (the same family member cannot be counted for LQTS and sudden death)

In the present case we have completed the Schwartz diagnosis score because 2 points of documented arrhythmia (history) + 1 point of notched T wave in at least 3 leads

1. **Moric-Janiszewska E, Markiewicz-Łoskot G, Łoskot M, Weglarz L, Hollek A, Szydłowski L. Challenges of diagnosis of long-QT syndrome in children. Pacing Clin Electrophysiol. 2007 Sep;30:1168-1170.**
2. **Schwartz PJ, Moss AJ, Vincent GM, Crampton RS. Diagnostic criteria for the long QT syndrome. An update. Circulation. 1993 Aug; 88:782-784**.

Another diagnostic option is the Treadmill Exercise Test. Chattha et al (1) studied the characterization genotype-specific QT responses during recovery from exercise.
Seventy-five patients were age and sex matched into three groups (n = 25):
• LQT1
• LQT2
• Unaffected controls based on Schwartz score and genetic testing results.
Each group underwent upright burst and gradual bicycle exercise testing while being monitored by 12-lead ECG.

LQT1 patients had significantly longer corrected QT (QTc) than LQT2 intervals during early recovery. LQT1 patients began the recovery period at a QTc of 492 +/- 11 ms, after which the QTc decreased by 33 +/- 11 ms during recovery.

The LQT2 patients began recovery at its lowest mean QTc of 420 +/- 10 ms, which increased by 40 +/- 16 ms. At the end of recovery.

Control subjects showed little variation in QTc throughout the recovery period, maintaining a QTc within normal limits.

A QTc cut-off value of 445 ms distinguished 92% of LQTS patients from unaffected controls, while a start-of-recovery QTc cut-off of 460 ms correctly identified genotype in 80% of LQT1 and 92% of LQT2 patients. The authors concluded that genotype-specific differences exist in QT recovery after exercise. These differences can help to identify LQTS patients and distinguish LQT1 from LQT2 genotypes.

1. **Chattha IS, Sy RW, Yee R, et al. Utility of the recovery electrocardiogram after exercise: a novel indicator for the diagnosis and genotyping of long QT syndrome? Heart Rhythm. 2010 Jul;7: 906-911.**

PHASE 3, FINAL RAPID REPOLARIZATION

It corresponds in surface ECG, to T wave, and it responds to K^+ outflow by delayed opening of voltage-dependent delayed rectifier K^+ channels, made up by the following components:

I) A slow activation channel (I_{Ks}), that in fact activates from the end of phase 2;

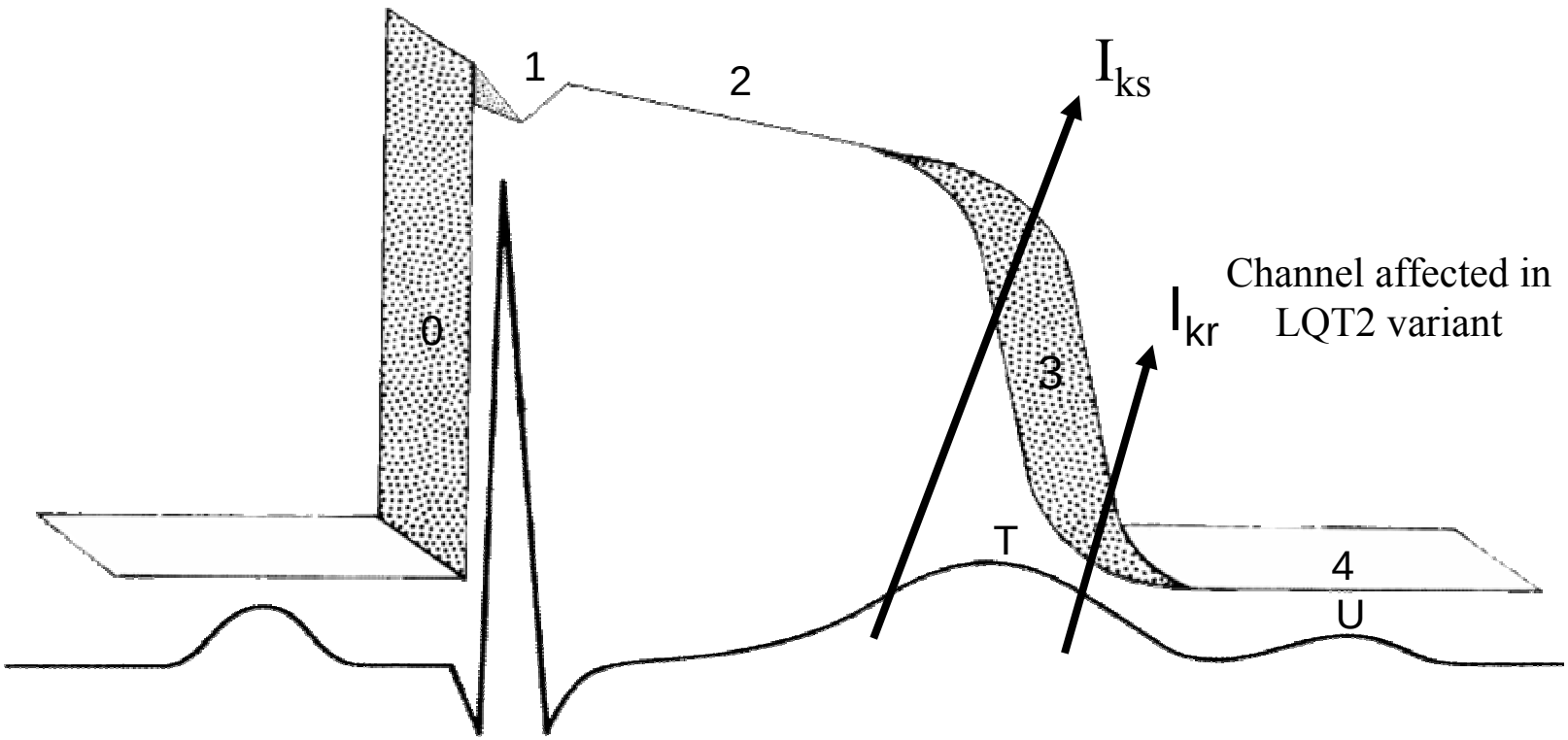
II) A rapid activation channel (I_{Kr});

III) An ultra-rapid activation channel (I_{Kur});

Additionally, during phase 3, inactivation of the slow L-$Ca^{2+}_{Ca\text{-}L}$ channel occurs;

Increase of the Na^+/K^+_{ATPase} pump activity, with increase of intracellular Na^+ concentration;

K^+ channel activation, I_{K1} (continued background inward steady-state K^+ current), which will remain activated during phase 4. In the final part of this phase additional K^+ outflow may occur through the so-called I_{K1} channel.



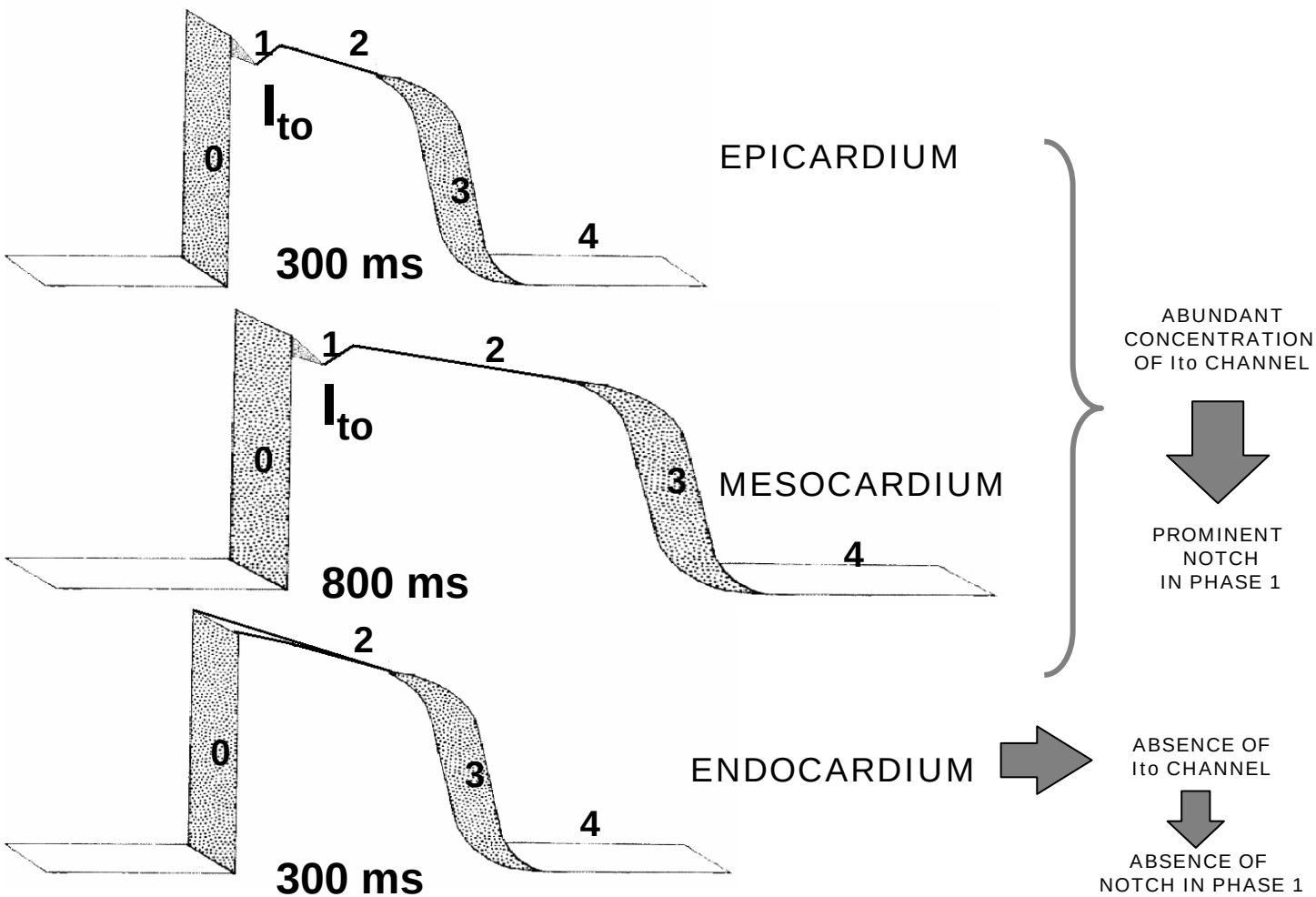
CONCEPT OF CONGENITAL OR INHERITED LONG QT SYNDROME

Rare syndrome, heredo-familial and autosomal (there are isolated nonfamilial sporadic cases), genetically heterogeneous, caused by mutations in the genes encoding potassium or sodium sarcolemmal channels (channelopathies), causing their dysfunction and thus, prolonging ventricular repolarization, which in turn predisposes the appearance of a special modality of polymorphic or atypical malignant ventricular tachycardia, known as Torsade de Pointes (TdP) that may cause syncope and possibly, degenerate into VF and sudden cardiac death (SCD)[1].

1) Ackerman MJ. The long QT syndrome: ion channel diseases of the heart. Mayo Clin Proc. 1998;73:250-69.

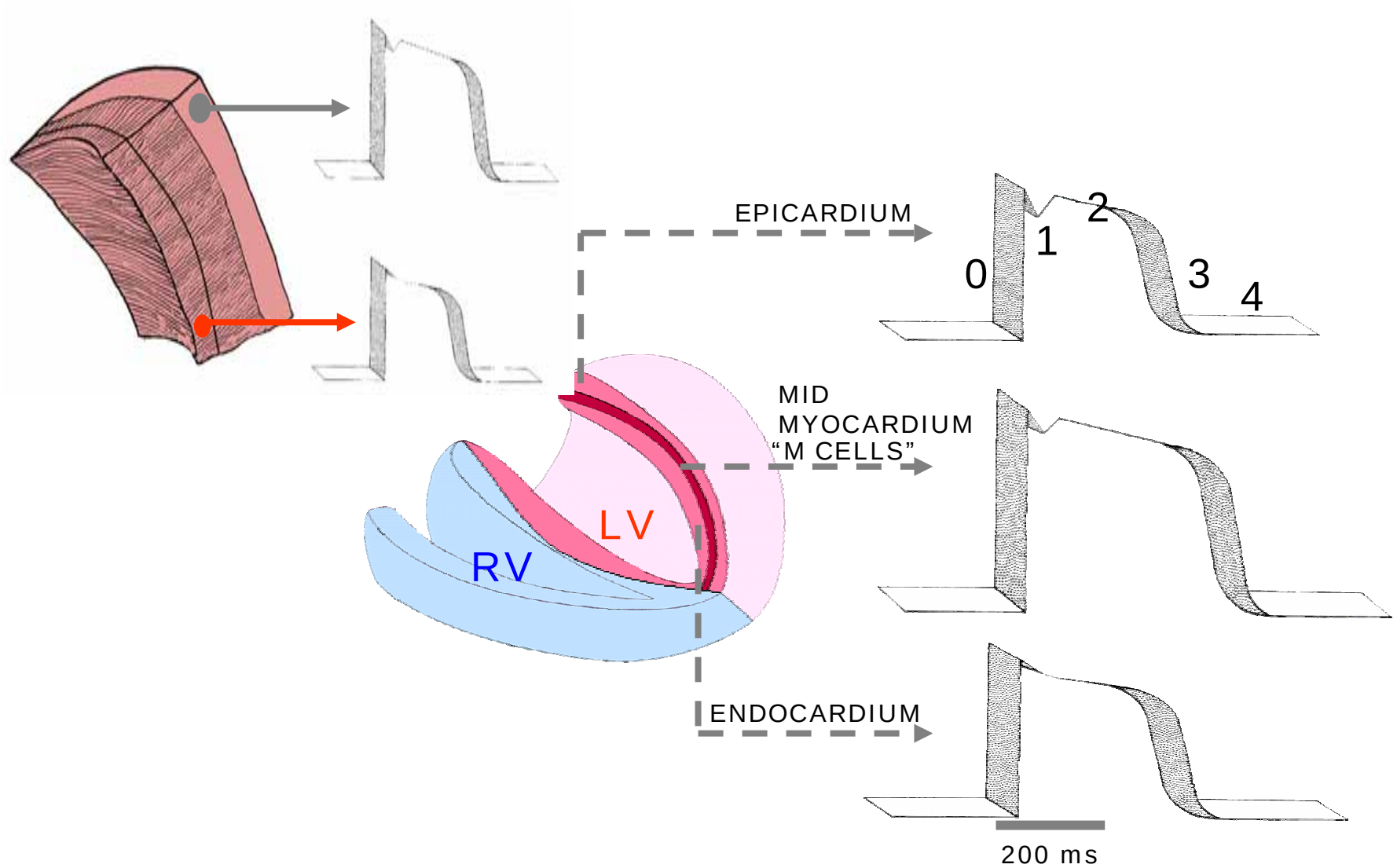
Concept of congenital or heredo-familial long QT syndrome.

EPI, MESO AND ENDOCARDIUM: HETEROGENEITY IN VENTRICULAR WALL THICKNESS



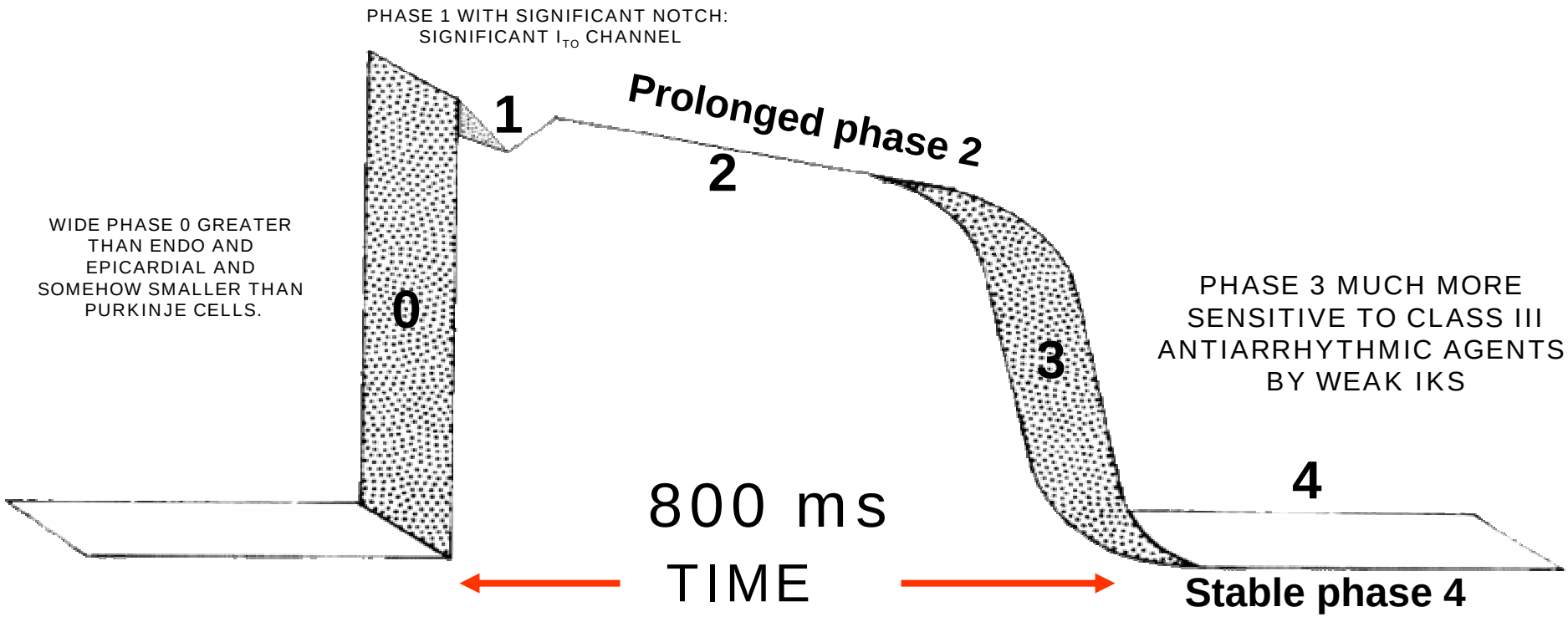
Outline of action potential in ventricular wall thickness. Differences in epi, meso and endocardium action potential profile and duration. The heterogeneous character of action potential is clearly observed in the 3 areas.

ACTION POTENTIAL OF VENTRICULAR CONTRACTILE CELLS IN WALL THICKNESS: EPI, MESO AND ENDOCARDIUM: HETEROGENEITY.



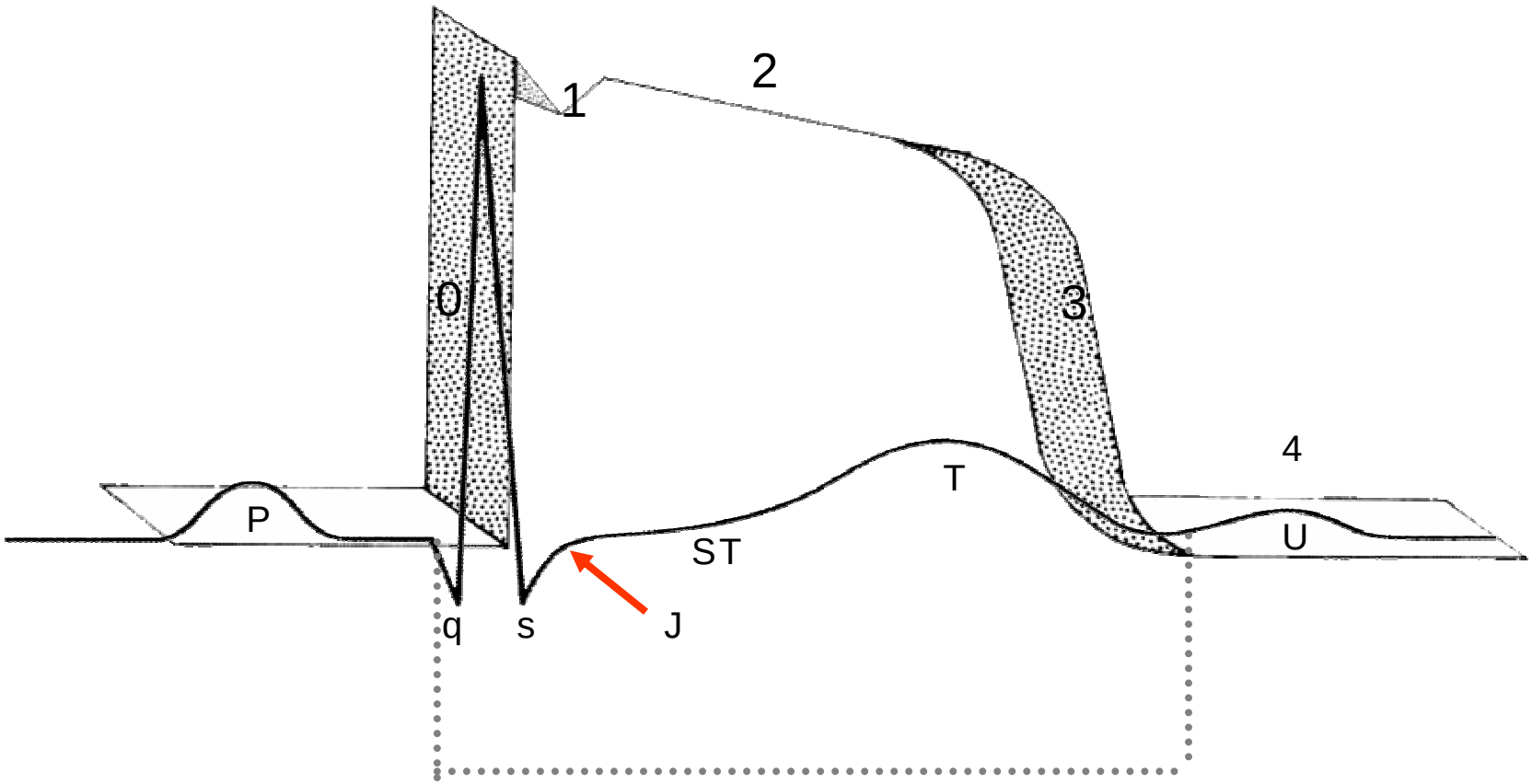
Outline of action potential in ventricular wall thickness. Differences in epi, meso and endocardium action potential profile and duration. The heterogeneous character of action potential is clearly observed in the 3 areas.

CHARACTERISTICS OF ACTION POTENTIAL OF "M" CELLS OF THE VENTRICULAR MID-MYOCARDIUM



Features of M cells action potential, essential in electrogenesis of long QT syndromes.

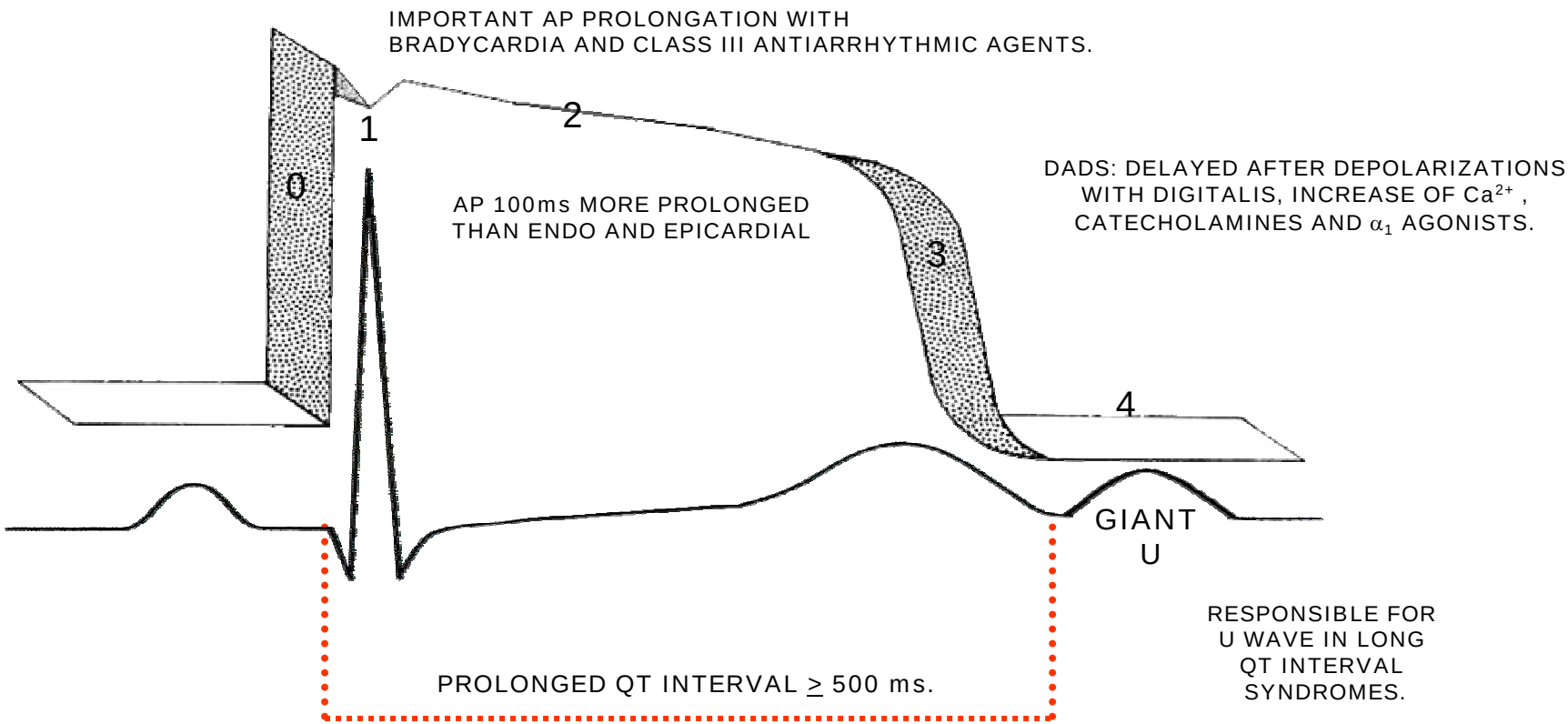
CORRELATION BETWEEN NORMAL ACTION POTENTIAL AND ECG WITH NORMAL QT INTERVAL



Correlation between normal action potential and ECG with normal QT interval.

“M” CELL ACTION POTENTIAL AND ECG WITH LONG QT INTERVAL

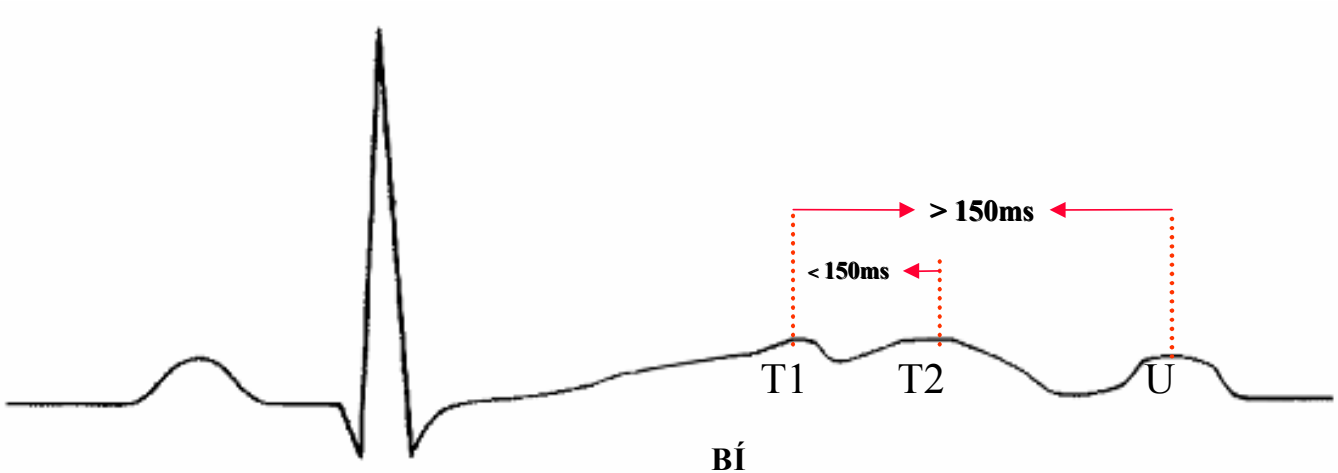
EADS: EARLY AFTER DEPOLARIZATIONS WITH CLASS III ANTIARRHYTHMICS AGENTS.



M cells action potential and ECG with long QT interval.

DIFFERENTIATION OF BIMODAL OR NOTCHED T1-T2 WAVES WITH T-U INTERVAL

Bimodal T1-T2 or notched T waves may be distinguished from the T-U interval: the second apex of bimodal T wave (T2) is at a distance from the first one (T1) < 150 ms; the T1-U interval is > 150 ms ([1-2]).



The second apex of bimodal T wave (T2) is at a distance < 150 ms from the first module (T1): The T1-U interval is always > 150 ms.

1) Lepeschkin E.: Physiologic basic of the U wave. In Advances in Electrocardiography. Edited by Schlant RC, and Hurst JW. New York, Grune & Stratton 1972;pp 431-447.
2) Lepeschkin, E.:The U wave of the electrocardiogram. Mod Concepts Cardiovasc Dis 1969;38:39.

Differentiation between bimodal or notched T waves in T-U interval.

SUDDEN CARDIAC DEATH

Cardiovascular diseases account for 40% of all deaths in the West. Sudden cardiac death (SCD) is a major health problem affecting over 300,000 patients annually in the United States alone.(1) Despite more than 30 years of research, survival rates remain extremely low. Only 5% of the victims survive.

The causes of SCD may include:

a) With structural heart disease

b) Without apparent structural heart disease: Genetic channelopathies or primary electrical diseases

Long QT syndrome
Short QT syndrome
Brugada syndrome
Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)
Overlapping syndromes
Short-coupled TdP, a normal QTc interval and without demonstrable structural heart disease.(2;3)

Recognizing risk factors may help in the identification of patients with predisposition to SCD.

1. **Aziz EF, Javed F, Pratap B, Herzog E.Strategies for the prevention and treatment of sudden cardiac death. Open Access Emerg Med. 2010 Dec;2010:99-114.**
2. **Van den Branden B, Wever E, Boersma L. Torsade de pointes with short coupling interval. Acta Cardiol. 2010 Jun;65:345-346.**
3. **Leenhardt A, Glaser E, Burguera M, Nürnberg M, Maison-Blanche P, Coumel P. Short-coupled variant of torsade de pointes. A new electrocardiographic entity in the spectrum of idiopathic ventricular tachyarrhythmias. Circulation. 1994 Jan;89:206-215.**

ENTITIES WITH RISK OF SCD IN CHILDREN ADOLESCENTS AND ADULT YOUNGER THAN 35 YEARS OLD

- Hypertrophic Cardiomyopathy (HCM) it is the most common cause of SD in childhood and adolescence.
- Arrhythmogenic Right Ventricular Cardiomyopathy/ Dysplasia (ARVC/D)
- Congenital anomalous origin of coronary arteries
- Myocarditis
- Wolff-Parkinson-White syndrome
- Congenital heart diseases before and after surgical correction
- Commotio Cordis or cardiac concussion.

Sudden cardiac death is devastating at any age, but it is especially among children adolescents and young adults.

Cardiac channelopathies associated with structurally normal hearts or primary electrical disorders

1. Long QT syndrome (LQTS).
2. Short QT syndrome (SQTS).
3. Brugada syndrome/ "Pokkuri Death Syndrome" (PDS) (Japan), "Lai Tai" (Thailand), "Bangungut" (Philippines), "Dream Disease" (Hawaii), and "Sudden Unexpected Nocturnal Death Syndrome" among South Asian immigrants in the USA.
4. Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)
5. Idiopathic Ventricular Fibrillation (IVT)
6. Progressive Cardiac Conduction Disease (PCCD) (Lenégre disease)
7. Sick Sinus Syndrome (SSS)
8. Familial Atrial Fibrillation (FAF)
9. Sudden Unexpected Infant Death The acronym SUID is being increasingly used by investigators of infant deaths. SUID is an intentionally broad category used for any sudden infant death when the cause of death is unapparent or multifactorial. Sudden Infant Death Syndrome (SIDS) is a subset of SUID, which in addition to SIDS includes sudden unexpected infant deaths of any cause.
10. Overlapping entities.

Short-coupled TdP, with normal QTc interval and without demonstrable structural heart disease

The evaluation should continue after the funeral: Molecular autopsy!!

LONG QT SYNDROME

Genetic entity potentially lethal cardiac channelopathy that affects one in 2,000 persons
Long QTc in ECG.
Hallmark of arrhythmia: TdP
The most common symptom is: unexplained syncope.
Syncope during exercise in pediatric patients should be considered malignant until the contrary is proved.
SCD in children or young adults.
Family history of dizziness or deafness.

CAUSES OF ARRHYTHMIC SYNCOPE

1) Very fast VT or TdP with hypotension
2) AF or atrial flutter with high rate of ventricular response in WPW
3) AV block
4) Sinus arrest.

SYMPTOMS IN CONGENITAL LQTS

Syncope
Dizziness
Palpitations or chest pain.
Cardiac arrest, and sudden death

HOW SHOULD WE PROCEED TO READ THE ECG IN SUSPICION OF LQTS?

Do not perform the measurement of intervals and waves by the computerized method.
Conduct an independent review of ECG.
The measurement of the QT interval should be made by an experienced cardiologist.
The general cardiologist, before the suspicion of congenital LQTS, should refer the patient to a colleague familiar with this for cardiological evaluation.

DIAGNOSTIC CRITERIA OF LQTS

ECG: long QTc interval, TdP, T wave with notches, low HR for the age;
HISTORY: dizziness, syncope, aborted SCD;
FAMILY BACKGROUND: early sudden death in first degree family members. Unexplained early sudden death.

SYNCOPE EVENTS TRIGGERS

Exercise, especially swimming in LQT1 variant;
Emotion or stress and noises: LQT2 (the present case)
Events during sleep or at rest: LQT3.

LONG QT SYNDROMES CLASSIFICATION

A) HEREDOFAMILIAL, CONGENITAL, "IDIOPATHIC" OR ADRENERGICO-DEPENDENT:

1. Rare syndrome (sensorineural deafness) of recessive autosomal Jervell-Lange-Nielsen. 0.25% to 1%

Of deaf and mute individuals. One each 300,000 individuals.

2. Common Romano-Ward syndrome, without deafness, dominant autosomal.
3. Nonfamilial, acquired, sporadic.

B) ACQUIRED LONG QT SYNDROMES

By severe bradyarrhythmias;
By electrolytic alterations;
By effect of different drugs;
By toxins e.g.: organophosphorate compounds;
By cocaine;
By subarachnoid hemorrhage and effusions;
By liquid protein diets;
By myocardial ischemia;
By autonomic neuropathy;
By mitral valve prolapse;
By hypothyroidism;
By Beri-Beri;
By HIV.

ROMANO-WARD SYNDROME GENETIC BASIS

TYPE OF LQT	CHROMOSOMAL LOCUS	GENETIC MUTATION	AFFECTED ION CHANNEL
LQT1	11p15.5	*KVLQT1* (*KCNQ1*) (heterozygote)	Slow outward potassium rectifier channel (I_{Ks})
LQT2	7q35-36	*HERG*	Rapid outward potassium rectifier channel (I_{Kr})
LQT3	3p21-24	*SCN5A*	Rapid sodium channel (INa^{+})
LQT4	4q25-27	?	?
LQT5	21q22.1-22.2	*KCNE1* (heterozygote) Jervell and Lange-Nielsen syndrome.	Slow outward potassium rectifier channel (I_{Ks})
LQT6	21q22.1-22.2	*MiRP1*	Rapid outward potassium rectifier channel (I_{Kr})
LQT7	17	KCNJ2	Associated to Andersen-Tawil syndrome (ATS1) (I_{K1})

ROMANO-WARD SYNDROME GENETIC BASIS

TYPE OF LQT	CHROMOSOMAL LOCUS	GENETIC MUTATION	AFFECTED ION CHANNEL
LQT8 Timothy's Syndrome	12p13.3	CACNA1C Cav1.2	LTCC: L-type Calcium Channel
LQT9	3p25	CAV3	Late inward Na^+ current in phase 2
LQT10	11q23	SCN4B	Prolonged Na+ influx
LQT11	7q21-q22	AKAP9	I_{ks}
LQT12	22q11.2	SNTA1	I_{Na+}
LQT13	11q24	KCNJ5	I_{kACTH} I_{K1}

Genetic basis of Romano-Ward syndrome: types, chromosomal locus, mutation, and affected ion channel.

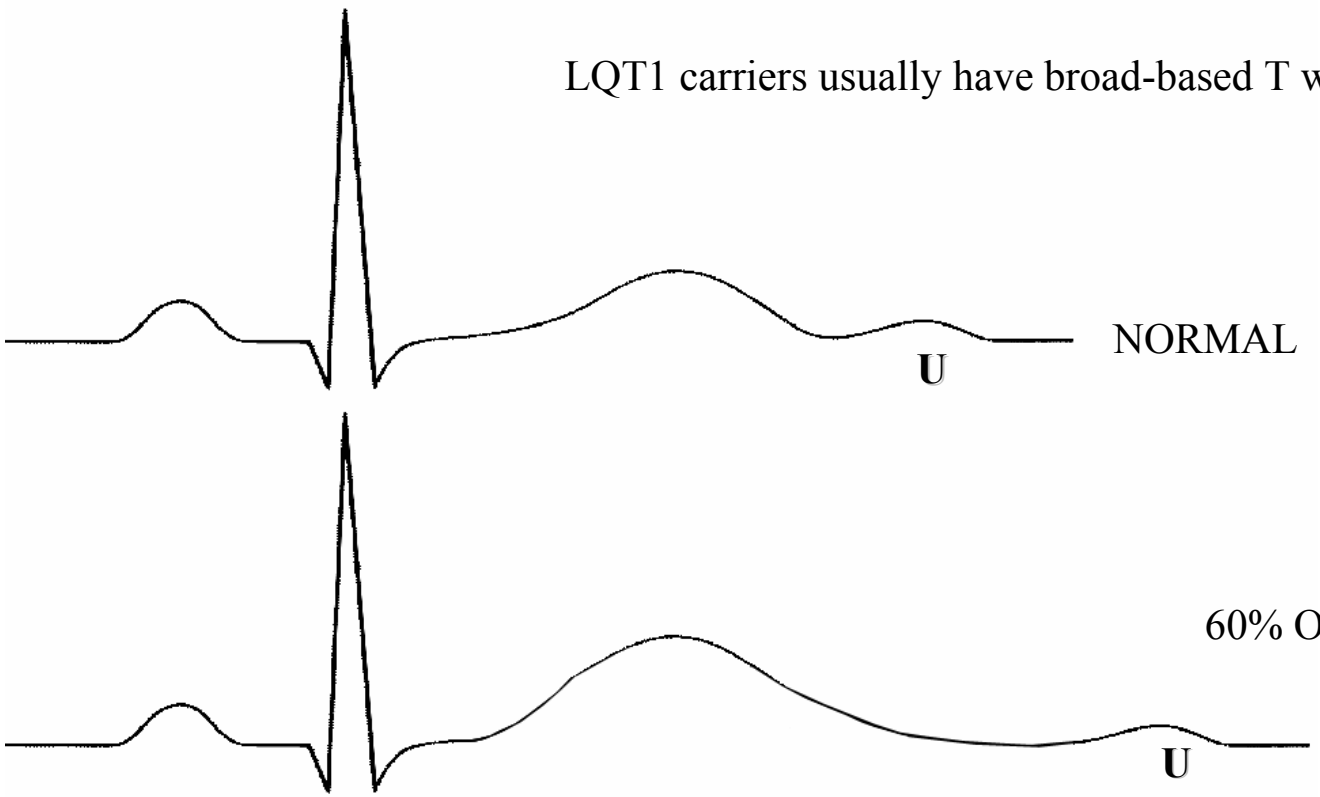
JERVELL AND LANGE-NIELSEN SYNDROME
GENETIC BASIS

TYPE OF LQT	CHROMOSOMAL LOCUS	GENETIC MUTATION	AFFECTED ION CHANNEL
JLN1	11p15.5	*KVLQT1* (*KCNQ1*) (homozygote)	Slow outward potassium rectifier channel (I_{Ks})
JLN2	21q22.1-22.2	*KCNE1* (homozygote)	Slow outward potassium rectifier channel (I_{Ks})

Prevalence of Jervell and Lange-Nielsen syndrome in children aged 4 to 15 years in England, Wales, and Ireland is between 1.6 and 6 per million.

Genetic basis for Jervell and Lange-Nielsen syndrome: types, chromosomal locus, mutation, and affected ion channel.

CHARACTERISTICS OF LQT1 VARIANT OR kvLQT1 DEFECT



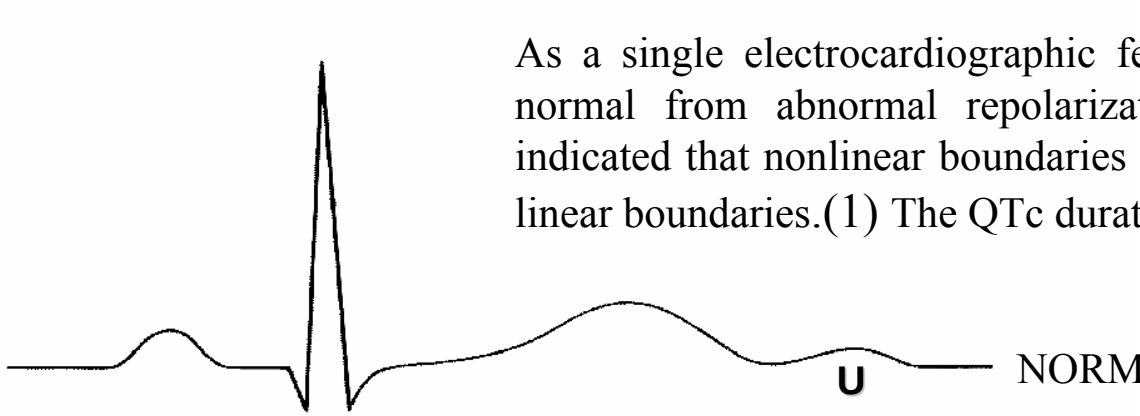
- Broad-based prolonged T waves.
- Moderate HR dependence of QT interval.
- Short arm of chromosome 11.

ECG Characteristics of LQT1 variant.

- Mutation: 11p15.5.
- Affected channel in TAP: I_{ks} delayed rectifier potassium current.
- Single variant with high % of events during exercise or swimming.

1. **Zareba W. Genotype-specific ECG patterns in long QT syndrome. J Electrocardiol. 2006 Oct; 39(4 Suppl):S101-106.**

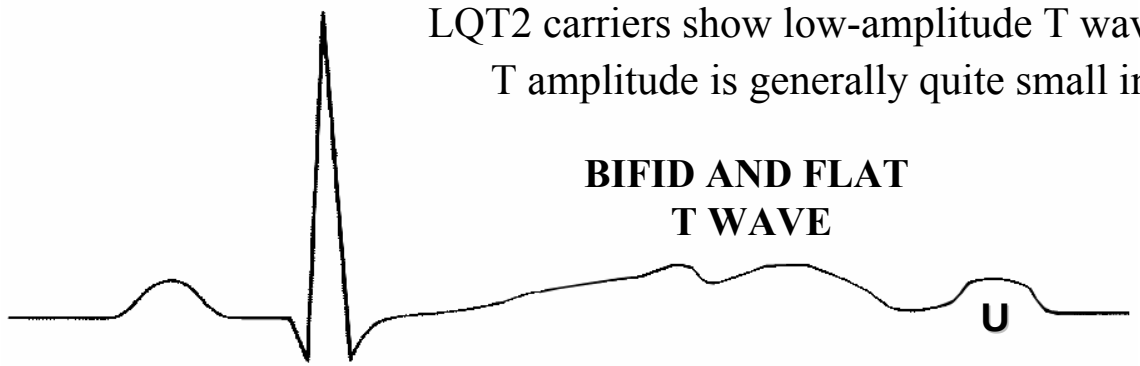
ECG CHARACTERISTICS OF LQT 2 VARIANT (HERG DEFECT)



As a single electrocardiographic feature, T-wave morphology separates normal from abnormal repolarization better than QTc. It is further indicated that nonlinear boundaries can provide stronger classifiers than a linear boundaries.(1) The QTc duration does not differentiate LQTS types.

NORMAL

LQT2 carriers show low-amplitude T waves with high incidence of notches.
T amplitude is generally quite small in the chromosome 7 genotype.



BIFID AND FLAT T WAVE

35% OF TOTAL

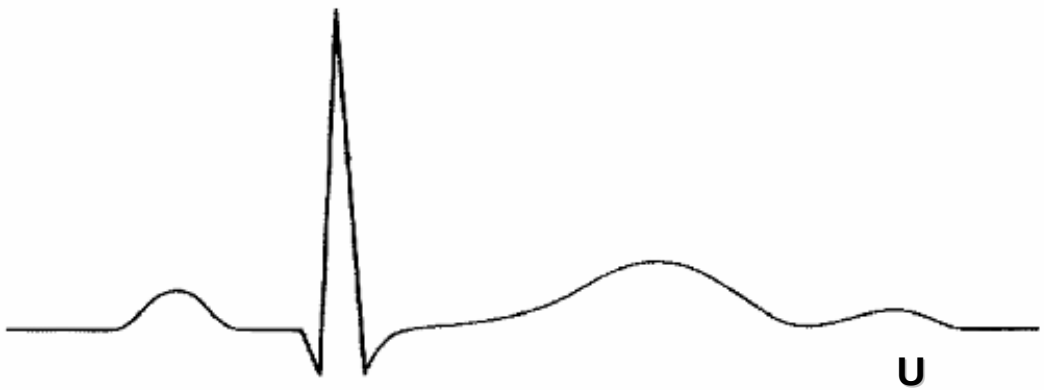
LQT2

T wave with low amplitude and a notched appearance; QT interval with moderate dependence on HR. KCNH2 in L413P and L559H mutations are associated to bifid T wave in ECG.

ECG characteristics of HERG LQT2 variant.

1. **Shakibfar S, Graff C, Ehlers LH, Toft E, Kanters JK, Struijk JJ. Assessing common classification methods for the identification of abnormal repolarization using indicators of T-wave morphology and QT interval. Comput Biol Med. 2012 Feb 3. [Epub ahead of print]**

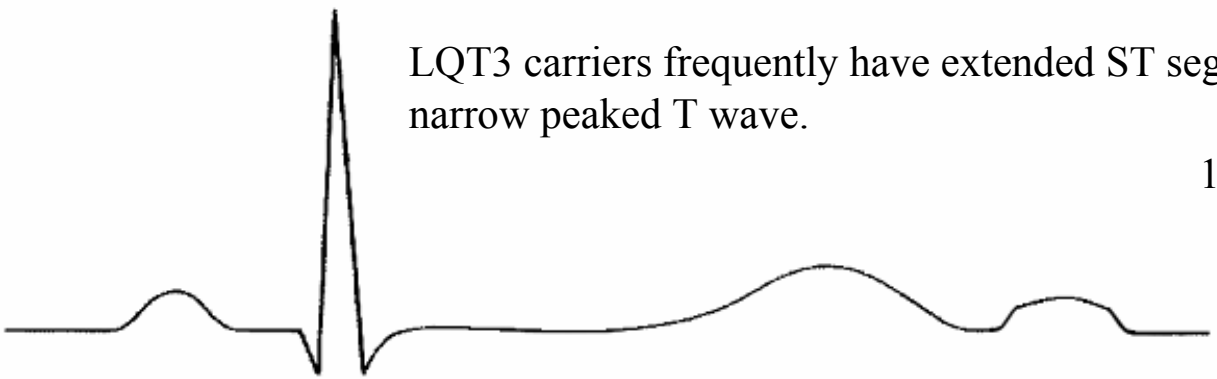
ECG CHARACTERISTICS OF LQT 3 VARIANT



NORMAL

LQT3 carriers frequently have extended ST segment with relatively narrow peaked T wave.

1% OF TOTAL



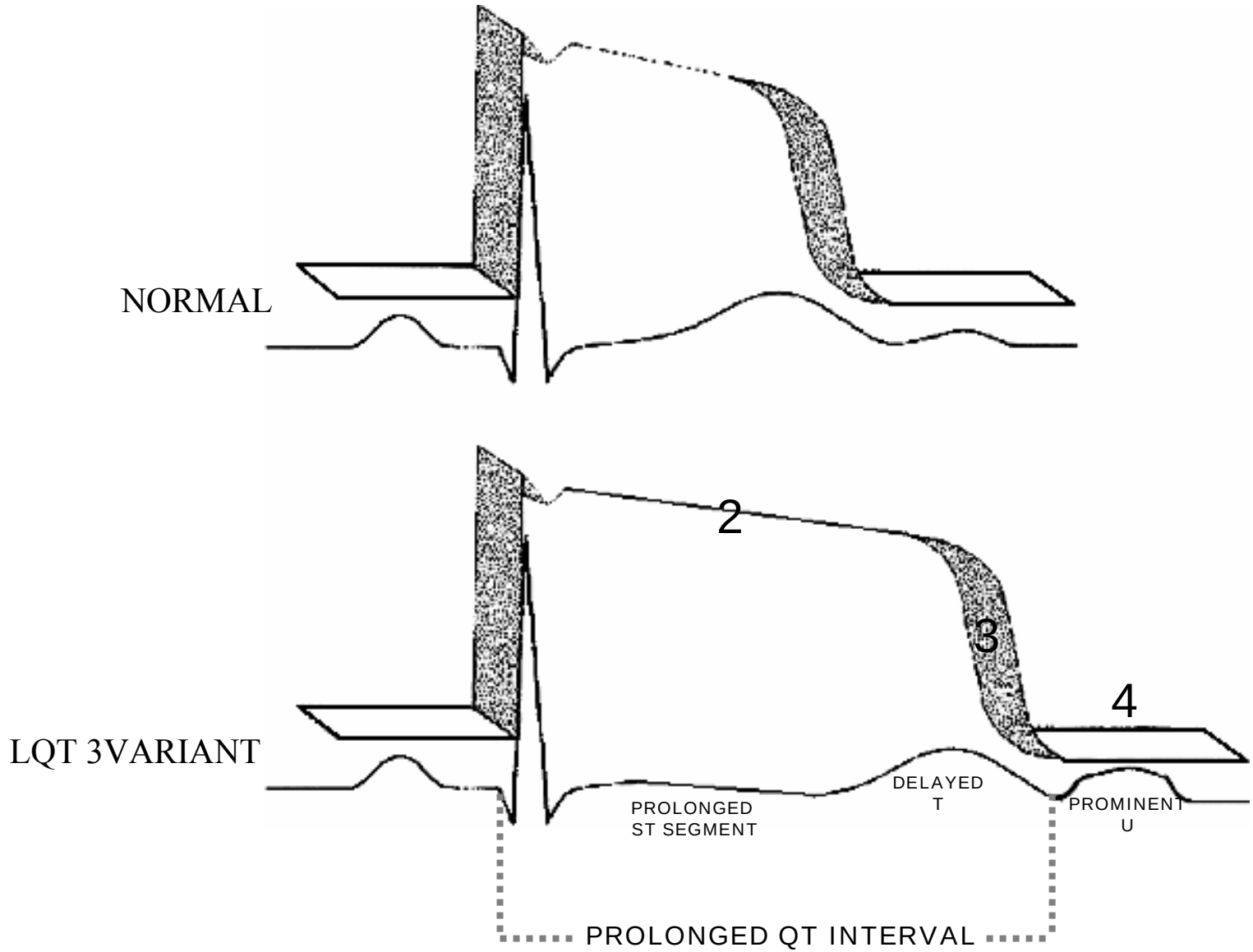
LQT3

Long QT interval by ST segment prolongation.
Delayed appearance of T wave, significant dependence on heart rate of QT interval, affected gene: SCN5A, p21-24 mutation in chromosome 3, TAP phase: plateau, dome or phase 2 by persistent sodium inflow.

ECG characteristics of LQT3 variant, SCN5A mutation.

1. **Moss AJ, Zareba W, Benhorin J, et al. ECG T-wave patterns in genetically distinct forms of the hereditary long QT syndrome.Circulation. 1995 Nov 15;92:2929-2934.**

NORMAL AND LQT3 VARIANT ACTION POTENTIAL/ECG RELATIONSHIP



Action potential and ECG characteristics of LQT3 variant, SCN5A mutation.