Electro-vectorcardiographic aspects of an Orphan Disease: Congenital Short QT syndrome

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Case report

Caucasian 44 asymptomatic man.

Reason for consultation: patient referred to a cardiologist for risk assessment of prostate biopsy under sedation. Asymptomatic.

Personal history: Minimal increase of serum prostate specific antigen (PSA test) in recent lab. Checkup. Digital rectal exam performed by urologist.

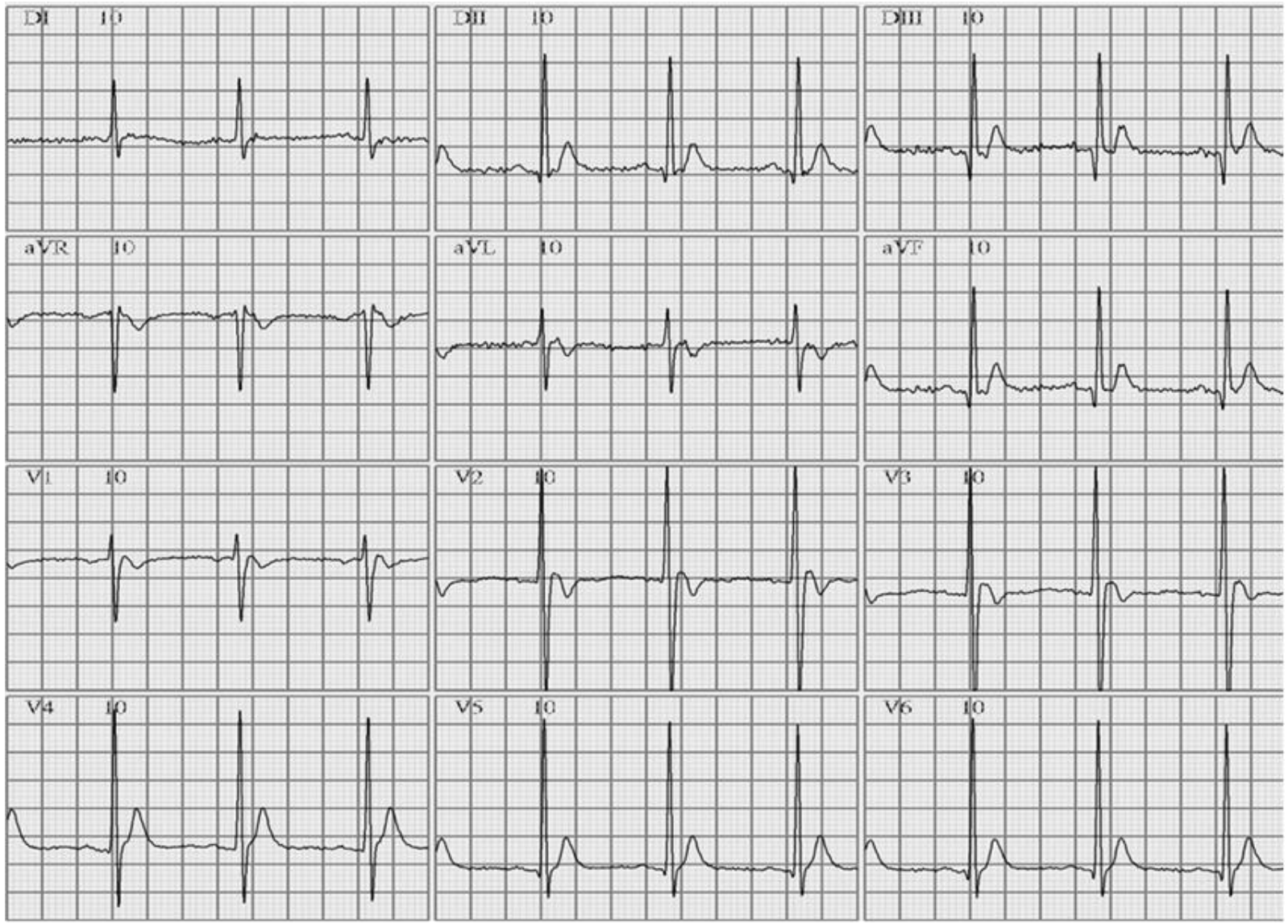
Family history: strong history of sudden death in first-degree relatives: Mother died suddenly aged 62, a sister aged 6 years and a brother 13 years. He has also two asymptomatic sisters with 36 and 41 years old.

Physical examination: Normal. Nothing to be noted.

Questions: Which is the ECG diagnosis of this family? And why? It is very important for us your meticulous ECG analysis.

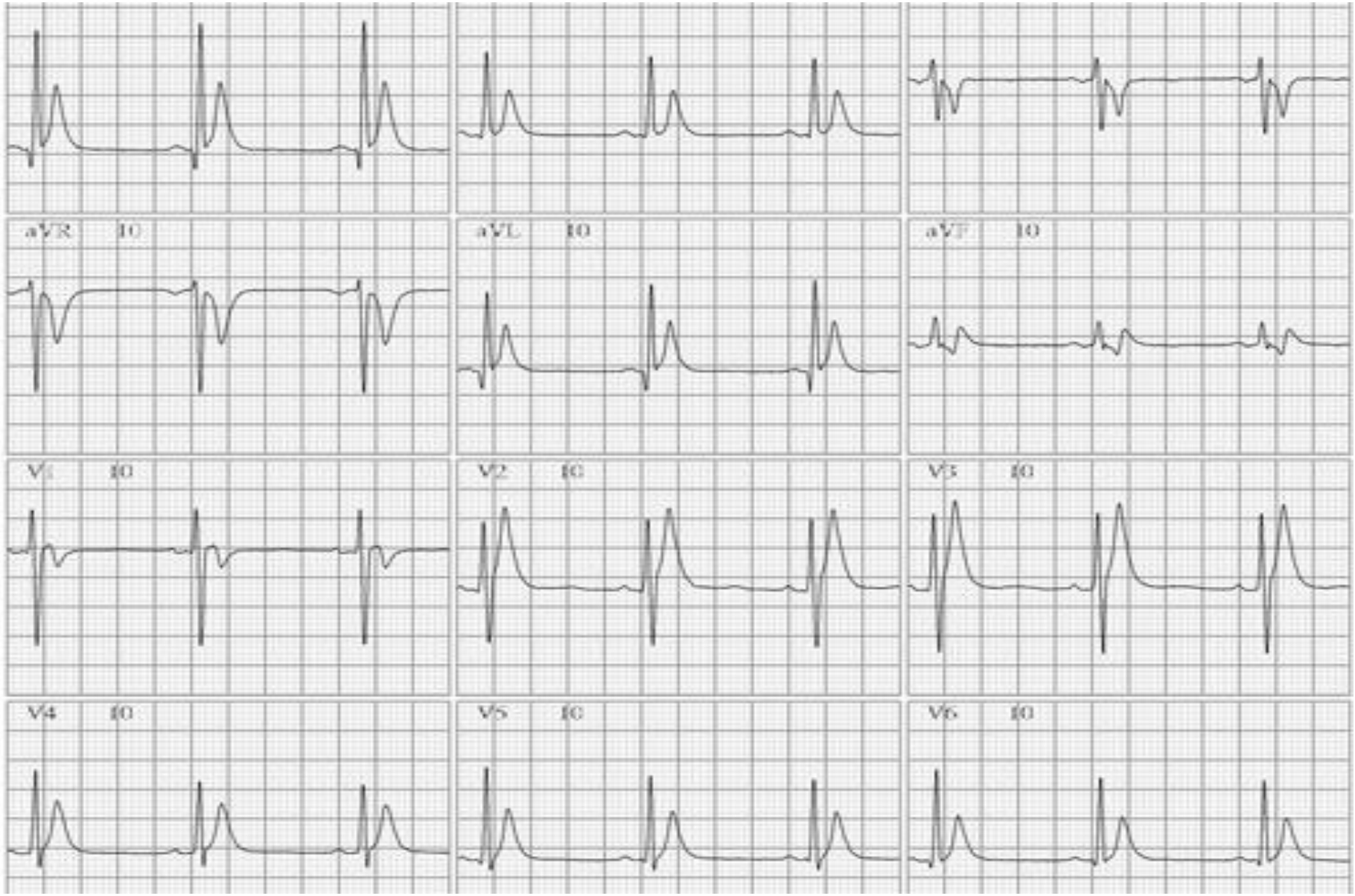
We are waiting for your valuable inputs.

Name: VTC. **Gender:** Masculine. **Ethnic group**: Caucasian. **Age:** 44 yo. (From Bahia/ Brazil in February 12/1968.). **Weight:** 84Kg. **Height:** 1.79 m**. Date:** April 19/2012. **Drugs in use:** None. This is the ECG of the proband, index case or propositus.



ECG diagnosis: sinus rhythm, heart rate (HR) = 83 bpm; SÂP + 60º, PR interval duration: 120ms, QRS duration: 60ms. SÂQRS: + 65º and to left, ST segment with minimal duration, SÂT + 63º and to back. QT = 220 ms; QTc = 353 ms (proband).
Conclusion: Extremely short QT interval.

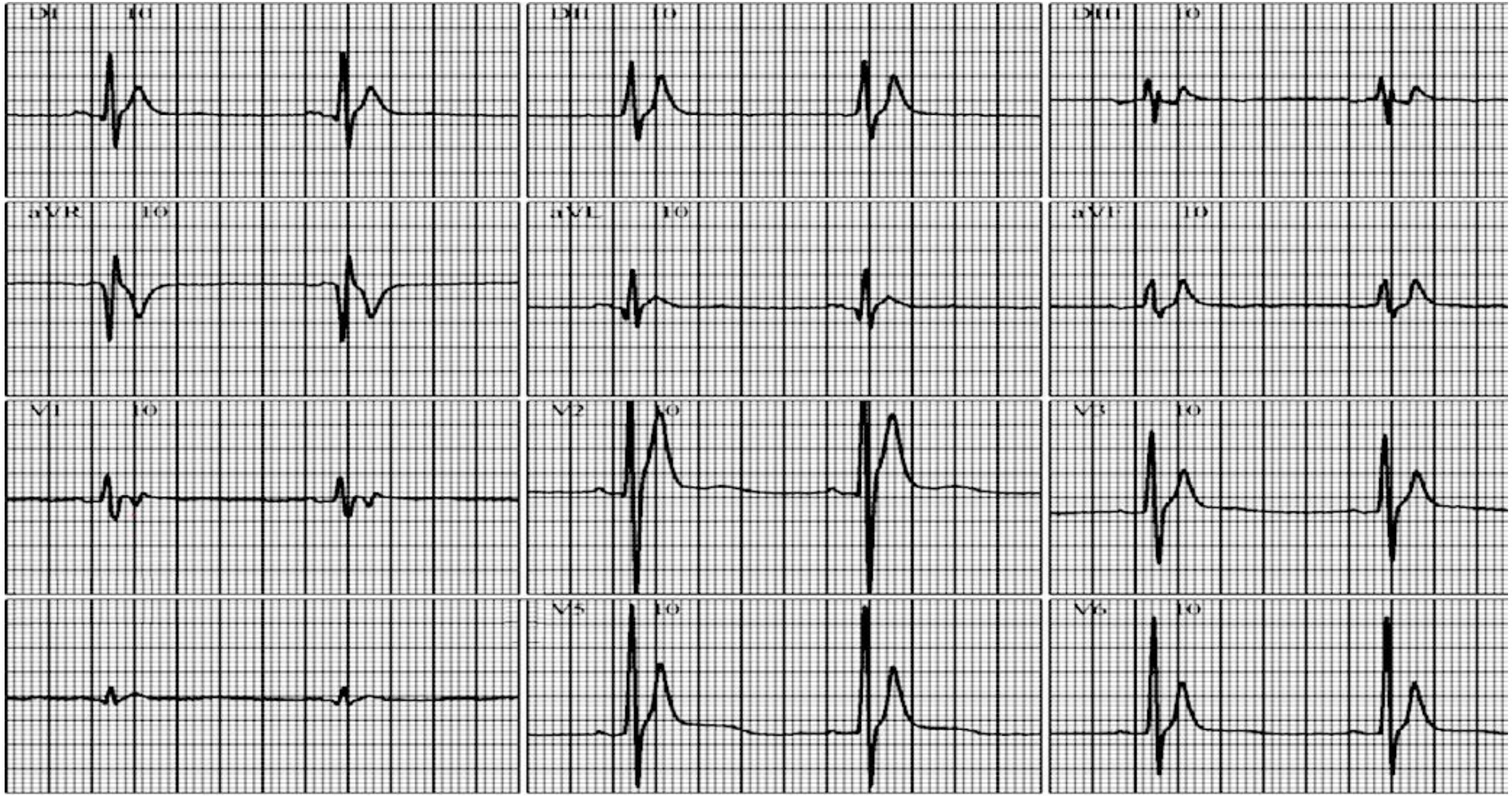
Name: MTC; **Sex**: F; **Age**: 54 y/o; **Date**: March 20, 2014; **Ethnic group**: Caucasian. ECG of one sister of the proband.



Clinical diagnosis: Congenital short QT syndrome with mutation in Caveolin-3 (SQT7). Unpublished yet.

ECG diagnosis: Sinus rhythm, HR = 68 bpm; P wave: ; SÂP + 32º, PR interval duration: 120ms, PR segment depression (> 0,5 mm) in II and V5, absence of ST segment, positive-negative T-wave or "minus-plus T wave sign" in aVF, and QT = 280 ms; QTc = 295 ms;

Name: WTC; **Gender:** Masculine.; **Ethnic group:** Caucasian.; **Age:** 23 yo. (From Bahia, Brazil in March 21, 1989.); Weight: 68 Kg.; Height: 172m.; Date: April 24/2012 Drugs in use: None. It belongs to 23 yo son of the proband.



ECG diagnosis: HR = 60 bpm; QT = 280 ms; QTc = 280 ms. We observe a very short QT interval and different the father (proband) additionally tall with narrow base T wave. Similar mild hyperkalemic tall T wave.

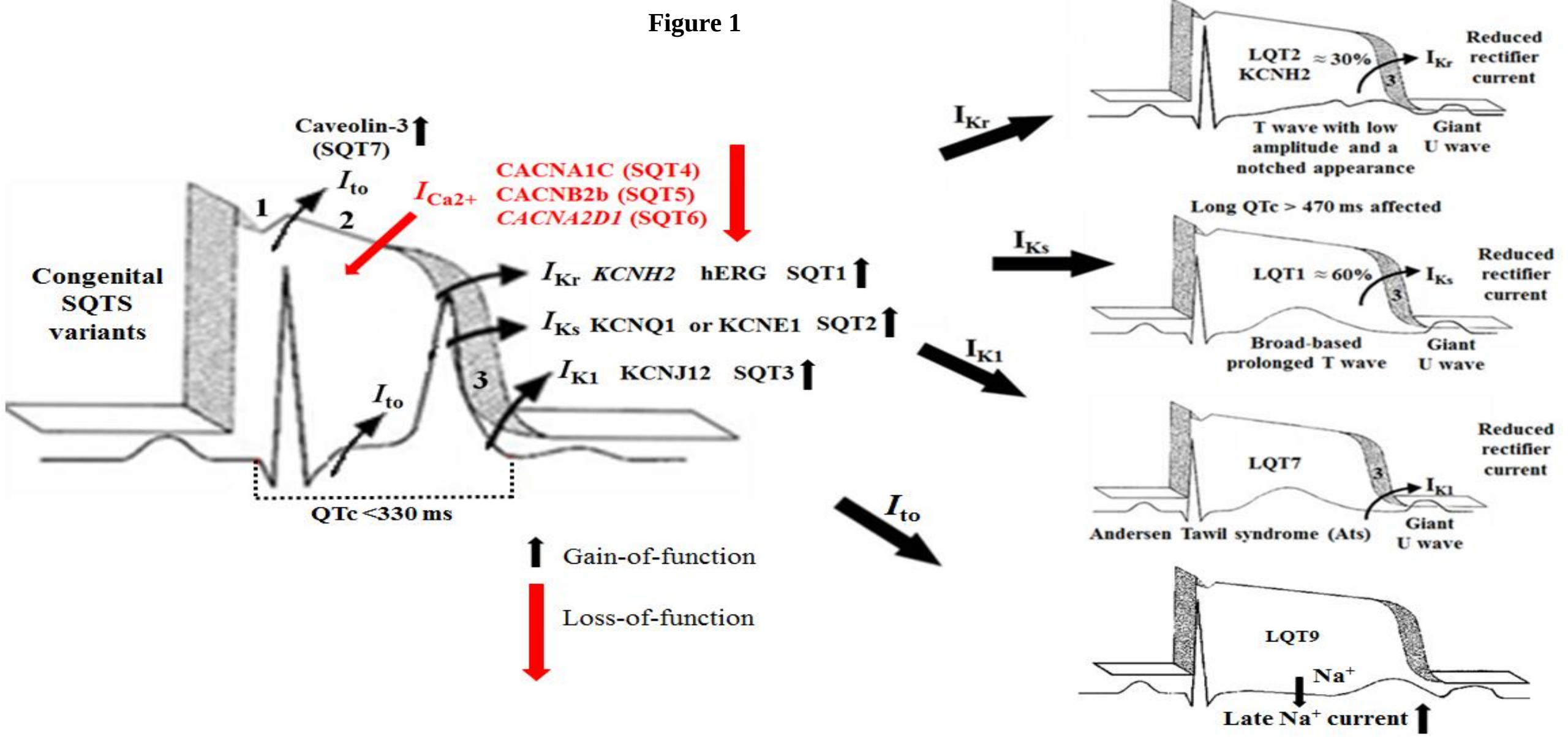
Introduction: Congenital Short QT syndrome (SQTS) is an hereditary, congenital, familial or sporadic orphan entity which is part of the so-called ion channel defects or channelopathies with dominant autosomal or sporadic and, genetically heterogeneous both from genotypic and phenotypic point of view, which affects the electric system of the heart, and where the hallmark of the disease is a very short QT/QTc interval on the electrocardiogram in potassium genetic forms and relatively short QT/QTc in calcium forms. A universally accepted diagnostic cut off value of a short QT interval has not been defined. (QTc interval ≤ 340–360 ms?) (1). Additionally, characteristically, the heart rate (HR) is not significantly modified with HR changes (2), and sometimes the T waves have great voltage, narrow base, which resemble T wave in "desert tent" of mild hyperkalemia **(**5.5 to 6.0 mEq/L**)**. The entity is clinically characterized by a large set of signs and symptoms, such as syncope, sudden cardiac death and palpitations dizziness and high tendency to appearance of episodes of paroxysmal runs of atrial fibrillation.

From the structural point of view, the heart is normal and electrophysiologically, there is significant shortening of refractory periods of atria and ventricles, being inducible (sustained VF) by programmed stimulation. A few families have been identified, with several types existing: To date mutations in seven genes has been reported to associate with SQTS: HERG or KCNH2 (**SQT1**), KCNQ1 (**SQT2**). KCNJ2 (**SQT3**), CACNA1C (**SQT4**), CACNB2b (**SQT5**) *CACNA2D1* (**SQT6**) and Caveolin-3 (**SQT7**),They have been labeled **SQT1-SQT7** based on the chronology of their discovery. Table 1.

Table 1

SQT Variant	QTc duration	Gene symbol and effect	Author
SQT 1	260-280 ms	*hERG* (human ether-ã-go-go-related gene *KCNH2* (I_{ks})	Brugada R et al. Circulation. 2004 Jan 6;109(1):30-5
SQT 2	302 ms	*KCNQ1*	Bellocq C, et al. Circulation. 2004;109:2394
SQT 3	315-320 ms	*KCNJ12* (Kir2.2) i	Priori SG et al. Circ Res. 2005 Apr 15;96(7):800-7.
SQT 4	331-370 ms	*CACNA1C*(I_{Ca}^{2+})	Antzelevitch C et al. Circulation 2007;115:442
SQT 5	346-360 ms	*CACNB2b* (ICa2+) loss-of-function	Antzelevitch C et al. Circulation 2007;115:442.
SQT 6	329 ms	*CACNA2D1* (I_{Ca}^{2+})	Templin C et al. Eur Heart J. 2011 May;32(9):1077-88.
SQT 7	320 ms	*caveolin-3*	Barajas-Martinez H. 2015. Umpublished yet. Brazilian family

Figure 1

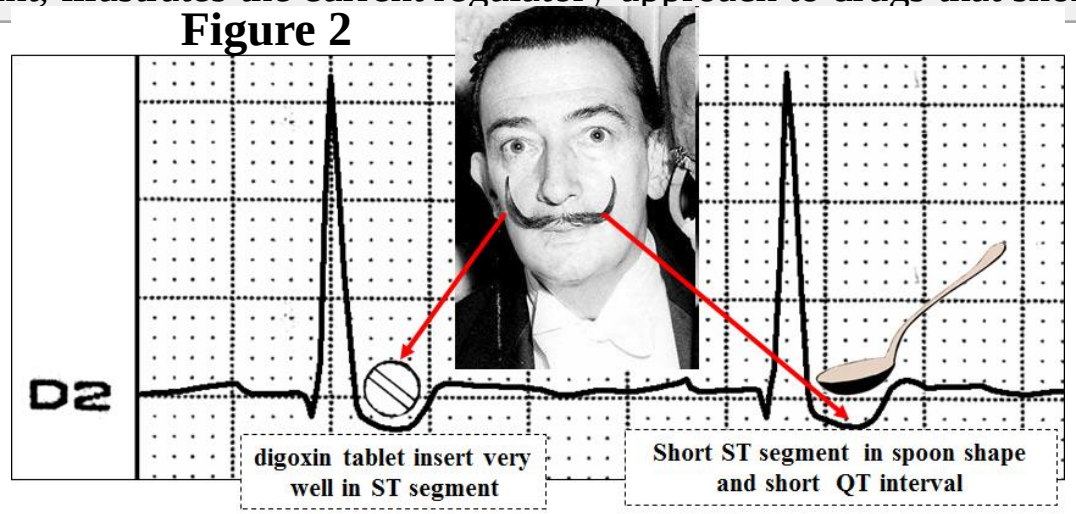


The figure 1 shows the representation of monophasic action potentials and ECGs of the four congenital SQTS potassium channels variants and their respective counterparts LQTS variants (mirror image): Congenital SQT1: I_{Kr}: LQT2; Congenital SQT2: I_{Ks}: LQT1; Congenital SQT3: I_{K1} LQT7 or Andersen-Tawil Syndrome; Congenital SQT7: I_{to} LQT9 Caviolin-3
And the three calcium channel variants: CACNA1C (SQT4), CACNB2b (SQT5), and *CACNA2D1* (SQT6).

Acquired and other genetic causes of short QT/QTc interval

Mild hyperkalemia serum potassium < 6.5 mEq/L: narrow-based, peaked T waves. T waves with short duration, approximately 150 to 250 msec,
Hypercalcemia
Hyperthermia
Acidosis
Effect of catecholamine
Toxicity and digitalis effect. PR prolongation is a commonly present. Additionally, characteristic sagging, “coved,” or “scooped” appearance of the asymmetric and downsloping ST depression, which resembles a reversed check mark (3; 4). Figure 2.
Autonomic tone alterations
in response to atropine
Dysautonomia of Chronic Fatigue Syndrome with QTc mean values of 371 a 384 ms (5).
Selective K^{+}_{ATP} channel activation* ATP-dependent potassium channel openers such as pinacidil and levcromakalim have long been known to shorten action potential duration and to be profibrillatory in non-clinical models
Activation of K_{Ach} caused by strong parasympathetic stimuli to the heart
Klinefelter syndrome (KS) Itis a sex chromosomal aneuploidy (47,XXY) affecting 1/660 males. QTc was shortest among testosterone treated males with KS, while untreated and thus hypogonadal KS had QTc interval comparable to controls (6).
Rufinamide, a recently approved anticonvulsant, illustrates the current regulatory approach to drugs that shorten QT interval (7).

Figure 2



Main features of congenital SQTS

1. Familial clinical-electrocardiographic entity
2. Autosomal dominant inheritance or sporadic, and genetically heterogeneous.
3. Considered an orphan disease: according to US criteria, a disease that affects fewer than 200,000 people or a prevalence rate lower than 5/10,000 inhabitants of the community population
4. Constant and uniform very short QT and QTc intervals (QTc interval $\leq$ 330 ms)
5. Positive family history for sudden cardiac death (SCD)
6. Manifested by syncope, sudden death, dizziness and high tendency to appearance of episodes of paroxysmal runs of atrial fibrillation (AF)
7. The response to exercise testing is a slight reduction of the QT interval during the increase in heart rate and decrease HR in recuperation phase.
8. Short refractory periods and tendency for inducible AF and VF were seen in electric physiological studies (EPSs).
9. Autopsy did not reveal any structural heart disease: The entity is among so-called autopsy-negative or sudden arrhythmic death syndrome (SADS)
10. Possible cause of SIDS (8). 1 point in Gollob's score (table 3).
11. Predominance in males (91%)

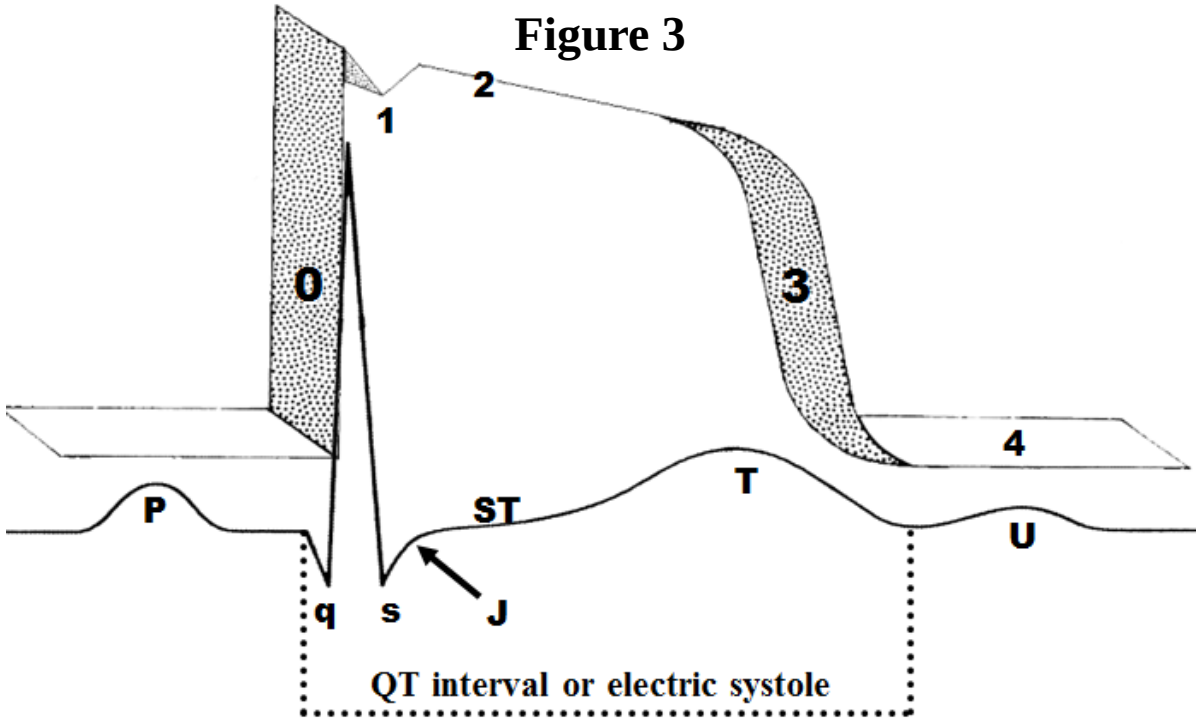
Electrocardiographic and electrophysiological features

The study of ECG abnormalities in channelopaties showed characteristic phenotypic traits, which in combination with information derived from molecular genetics, have allowed using the ECG as a prognostic tool as well as a diagnostic test. The assessment of genotype-phenotype correlations in inherited arrhythmogenic diseases has allowed to advance the idea of the ECG as an inheritable trait. Such heritable quantitative traits are potentially related to the risk of sudden death in the general population, which is known to have a familial predisposition (9).

Electrovectorcardiographic features in congenital short QT syndrome

1. Very short QT/QTc interval
2. Bad HR adaptation of QT interval during increasing (QT interval shortens with exercise) and decreasing heart rates (recovery phase)
3. PR or PQ segment depression level
4. Absent or minimal ST segment
5. Short J point-T peak interval (<120 ms)
6. Short Q-aT interval
7. Short Q-oT interval
8. Tall and narrow base T waves
9. Short JT interval: used only in cases of broad QRS duration (≥ 120 ms)
10. Prolongation of T peak/Tend interval (Tpe)
11. Alteration on T(p-e)/QT ratio
12. High prevalence of early repolarization pattern
13. Eventual presence of negative-positive-T wave sign or “minus-plus” T-wave sign
14. Eventual presence of prominent U waves
15. Very frequent paroxismal atrial fibrillation
16. Eventual presence and characteristics of premature ventricular contractions with very short coupled period
17. Polymorphic ventricular tachycardia
18. Ventricular fibrillation.

Figure 3



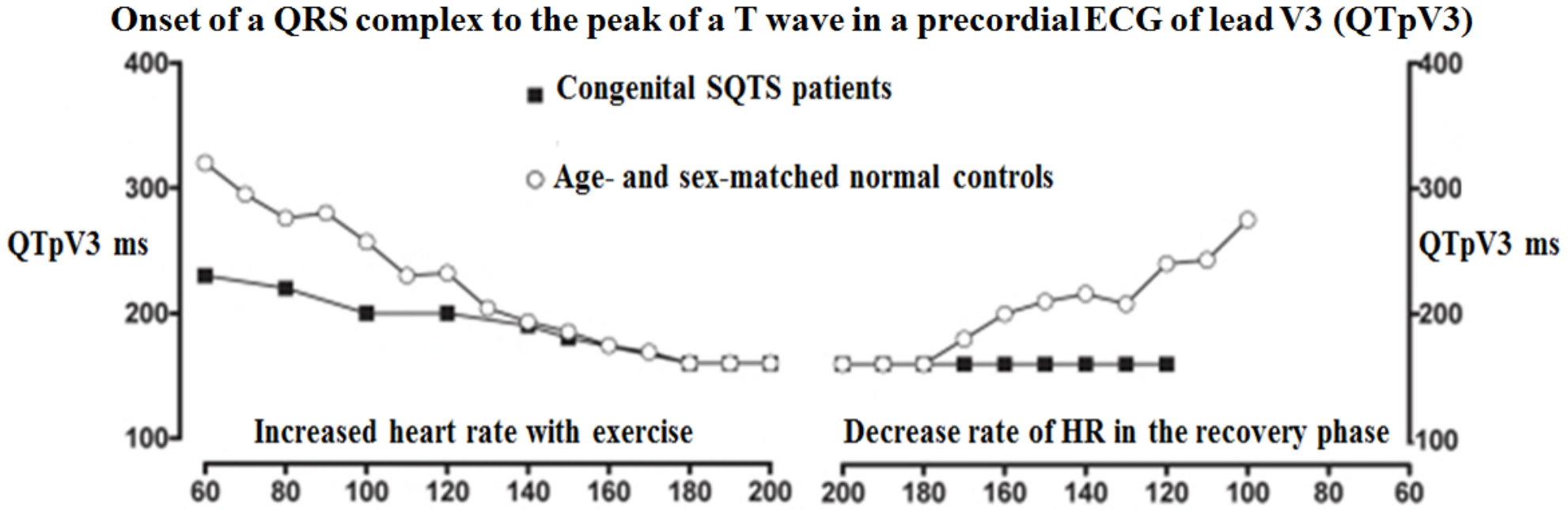
Representation of minimal and maximal normal values of QTc interval and its correlation with monophasic action potential. QTc values < 330 ms are considered short QT interval. Values of QTc > 450 ms are considered long QT intervals. Normal values of QTc are between 350 to 440 ms or 446 + - 15%. QTc intervals are considered very long with values of QTc ≥ 470 ms for men and ≥ 480 ms for females. LQTS even if asymptomatic.

Table 2

	Men	Females
Very long QTc	≥ 470 ms	≥ 480 ms
Long QT interval	450 ms to 470ms	460 to 480 ms
Normal QT interval	360ms to 390 ms	370ms to 400ms
Congenital SQTS	< 330 ms	< 340ms

Reduced heart rate-adaptation of QT interval during increasing and decelerated heart rates

Figure 4



The QT interval, an index of ventricular repolarization, is heart rate (HR) dependent, in other words the QT interval shortens with exercise. Some of this shortening is due to an increase in HR, and some is due to other effects of exercise, probably mostly neuroendocrine effects. In normal hearts, two-thirds of exercise-induced QT interval shortening are due to an increase in HR, and one-third to other effects. Changes in plasma catecholamine levels on exercise are not closely related to changes in the QT interval on exercise (10).

Both exaggerated or lesser rate dependence of repolarization is arrhythmogenic. Adaptation of the QT-interval to changes in HR reflects on the body-surface ECG the adaptation of action potential duration (APD) at the cellular level. The initial fast phase of APD adaptation has been shown to modulate the arrhythmia substrate. Whether the slow phase is potentially, proarrhythmic remains unclear.

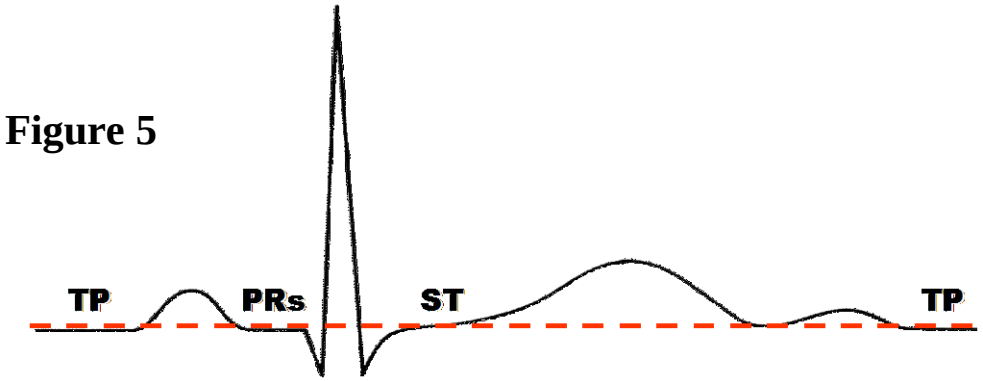
Patients with congenital SQTS have less variation of the QT interval in relation to the change in HR. Treadmill testing show a lack of adaptation of the QT interval, in congenital SQTS. Relative lack of adaptation of the QT interval (onset of a QRS complex to the peak of a T wave in a precordial ECG of lead V3 (QTpV3) to accelerated HR during exercise and lack of adaptation of the QT interval during decelerated HR in the recovery phase when compared with age- and sex-matched normal controls. Figure 4.

Quinidine restores the relationship toward control values. *QRpV3 denotes the interval form the beginning of QRS complex to the peak of T wave, measured in lead V3.* The QT-RR relationship lack of rate dependence Therefore, QTc corrected by any formula will fail to reflect the true QTc. At rapid rates, QTc will falsely approximate normal values leading to a false-negative diagnosis. This is particularly important for the diagnosis of SQTS in pediatric populations, where resting HR is >100 bpm. *Sometimes, Holter monitoring shows impaired adjustment of QT interval with change in HR.* Long-term ECG monitoring becomes necessary in such cases to make the correct diagnosis. The range of HRs is increased at baseline by using ambulatory electrocardiogram recordings in addition to those collected under semisupine, resting conditions (11).

Quinidine is a Class IA antiarrhythmic drug –isomer of quinine found in the bark of the cinchona tree. The drug affects depolarization and repolarization by blocking Na^+ and K^+ channels respectively. Quinidine blocks the fast Na^+ current; I_{to1} channel or transient outward current, inward rectifier I_{K1}, delayed rectifier: I_{Ks}, I_{Kr} and I_{Kur}, I K_{ATP} or adenosine triphosphate ATP sensitive potassium channel, IK_{-Ach}, alpha 1 and alpha 2 adrenergic receptors: can cause orthostatic hypotension and reflex sinus tachycardia; M_2 muscarinic receptor. In short QT syndrome oral quinidine is effective in suppressing the gain of function in I_{Kr} responsible for SQT1 variant with a mutation in HERG and thus restoring normal HR dependence of the QT interval and rendering VT/VF noninducible. Additionally, quinidine prolongs the QT interval into the normal range, restored the HR dependence of the QT interval toward a range of adaptation reported for normal subjects (12).

PR or PQ segment depression (PQD)

Figure 5



Regarding the level of PRs, in normal conditions is at the same level as ST segment (isoelectric) and TP segment of precedent beat. Usually, PR segment (end of P wave up to QRS complex onset), ST segment (from J point or the end of QRS up to the beginning of the T wave) and TP segment (from the end of the T wave up to the P wave of the following cycle) are at the same level. The figure shows a normal ECG and a line of dots pointing out the level of the three segments: PR, ST and TP.

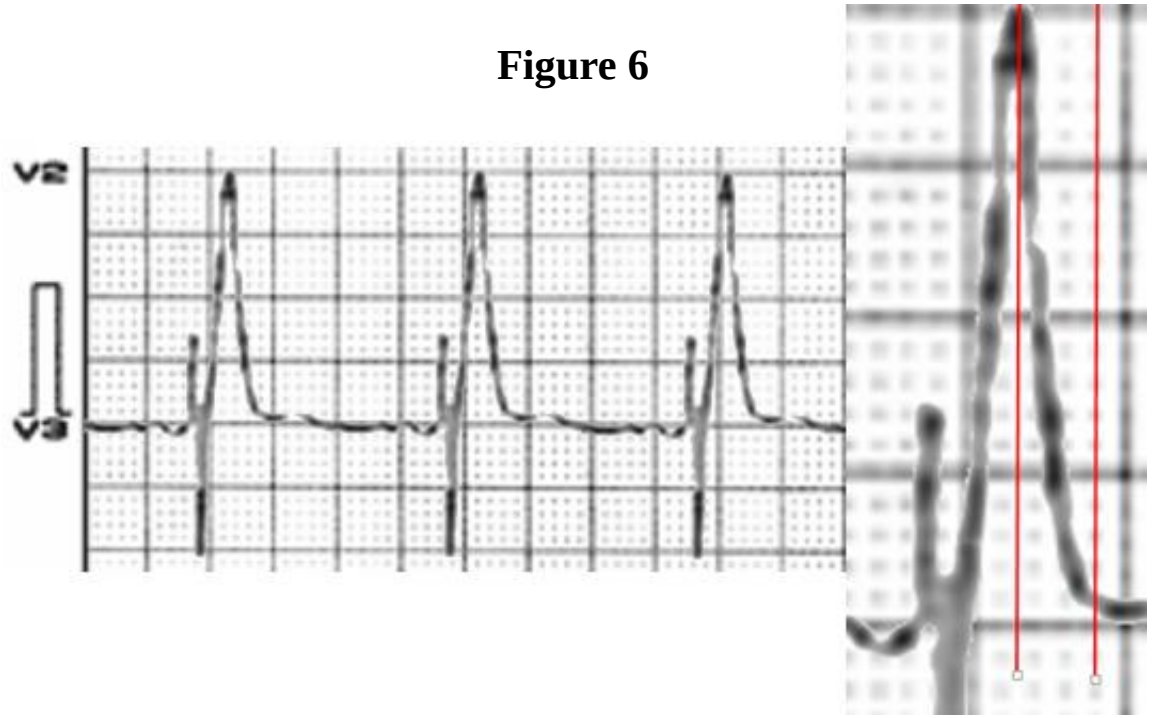
PR (PRs) or PQ segment: it stretches from the end of P wave to the onset of QRS complex. The PR segment is leveled when it is at the same level of the PR segment of the beat being studied. If the PR segment falls below the baseline (TP segment of precedent beat), then it is said to be depressed.

ST segment: it stretches from the from the J point (union of ST with the end of QRS complex) up to the onset of the T wave.

TP segment: it stretches from the end of T wave to the onset of the P wave of the next cycle. TP segment is between the end of the T wave and the beginning of the next P wave. It is the true isoelectric interval in the electrocardiogram. In other words the PR segment changes are relative to the baseline formed by the precedent TP segment of anterior beat.

Absent or minimal ST segment "hypercalcemic like phenotype"

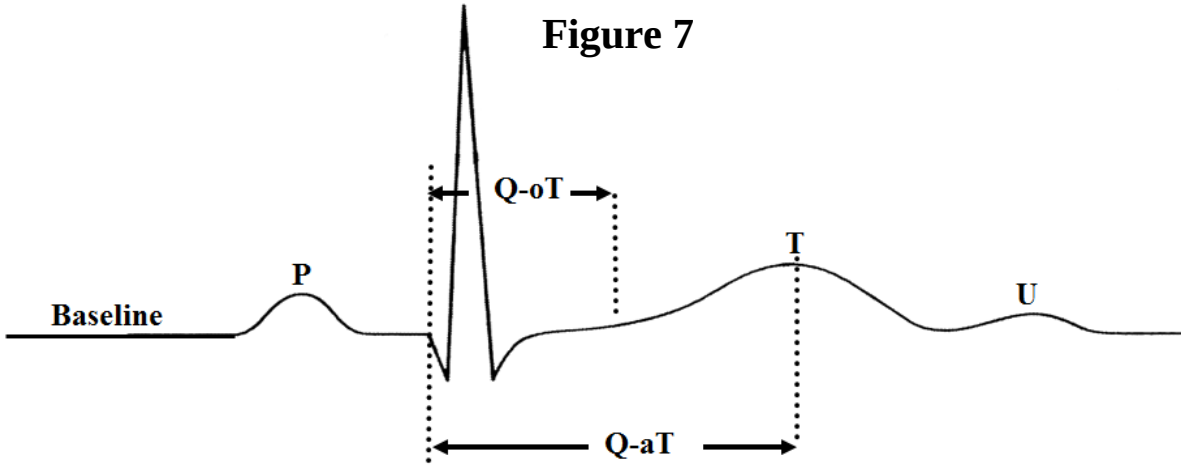
Figure 6



T-wave originates directly from QRS without identifiable ST segment. Additionally the distance between T-apex/T-end = 100 ms: transmural dispersion of repolarization.

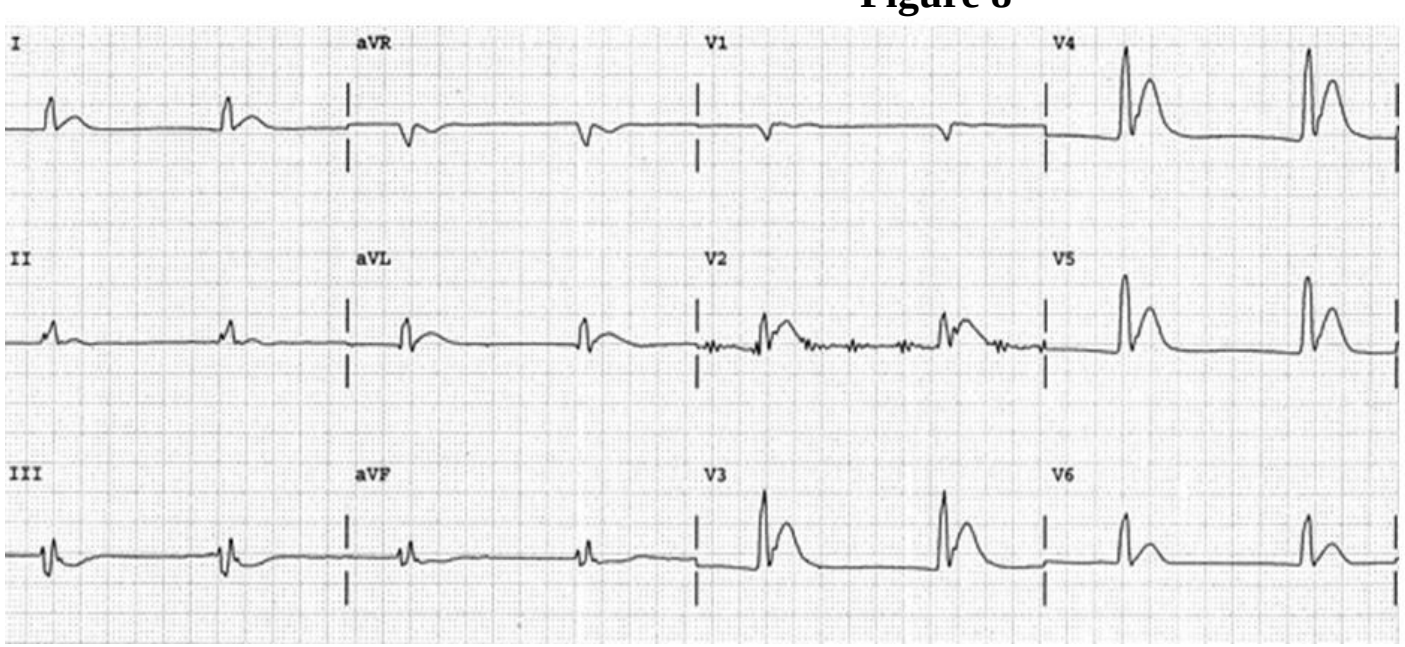
- Short Q-oTc interval: interval that extends from QRS onset up to T wave onset, corrected by heart rate.
- Short Q-aTc interval: interval that extends from QRS onset up to apex T wave corrected by heart rate.

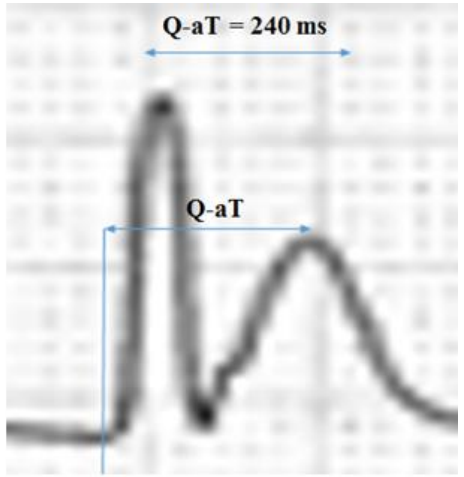
Figure 7



Q-oTc interval: interval that extends from QRS onset up to T wave onset, corrected by heart rate.
Q-aTc interval: interval that extends from QRS onset up to apex T wave corrected by heart rate.

Figure 8

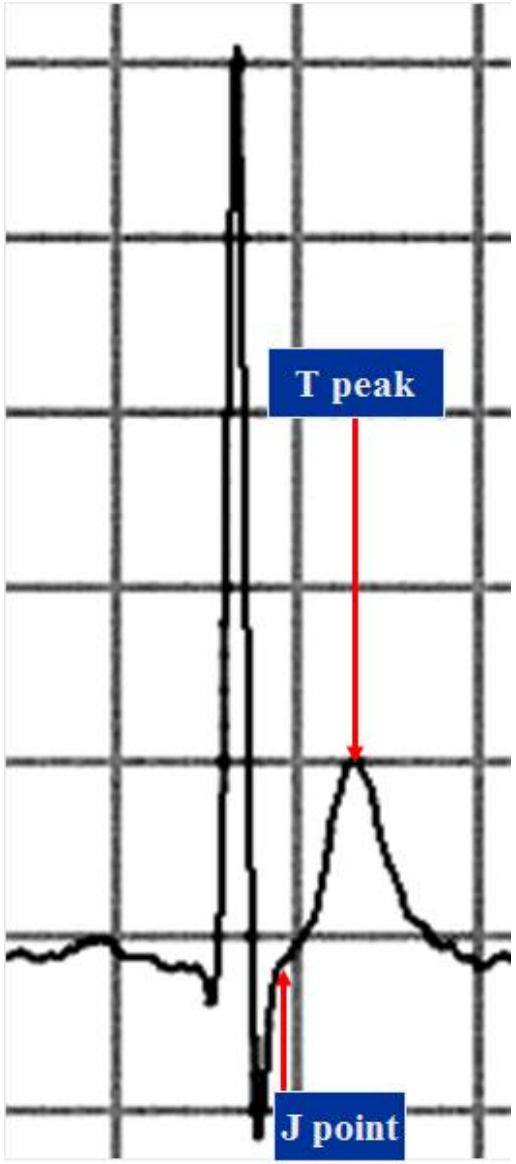




12-lead ECG of a patient with severe hypercalcemia showing marked shortening of the QT interval (QTc =260ms) and Q-aT values < 270 ms.

Short J point-T peak interval <120 ms

Figure 9



The J point-T peak interval is the distance from J point to T peak Values <120 ms have value for the diagnosis of the congenital SQTS (13).

Gollob's score

Table 3

QTc in miliseconds	Pontuation
< 370	1
< 350	2
< 330	3
J point – T peak interval	
< 120	1
Clinical history	
Sudden cardiac arrest	2
Polymorphic VT or VF	2
Unexplained syncope	1
Atrial fibrillation	1
Family history	
1st or 2nd degree relative with SQTS	2
1st or 2nd degree relative with sudden death	1
Sudden infant death syndrome	1
Genotype	
Genotype positive	2
Mutation of undetermined significance in a culprit gene	1

Interpretation: High-probability: ≥ 4 points; Intermediate probability: 3 points; Low probability: ≤ 2 points.

Difference of T waves morphologies in the potassium congenital SQTS variants

- **SQT1**: The T waves in the precordial leads, appear often tall, narrow and symmetrical, with a relatively prolonged Tpeak-Tend interval (14).

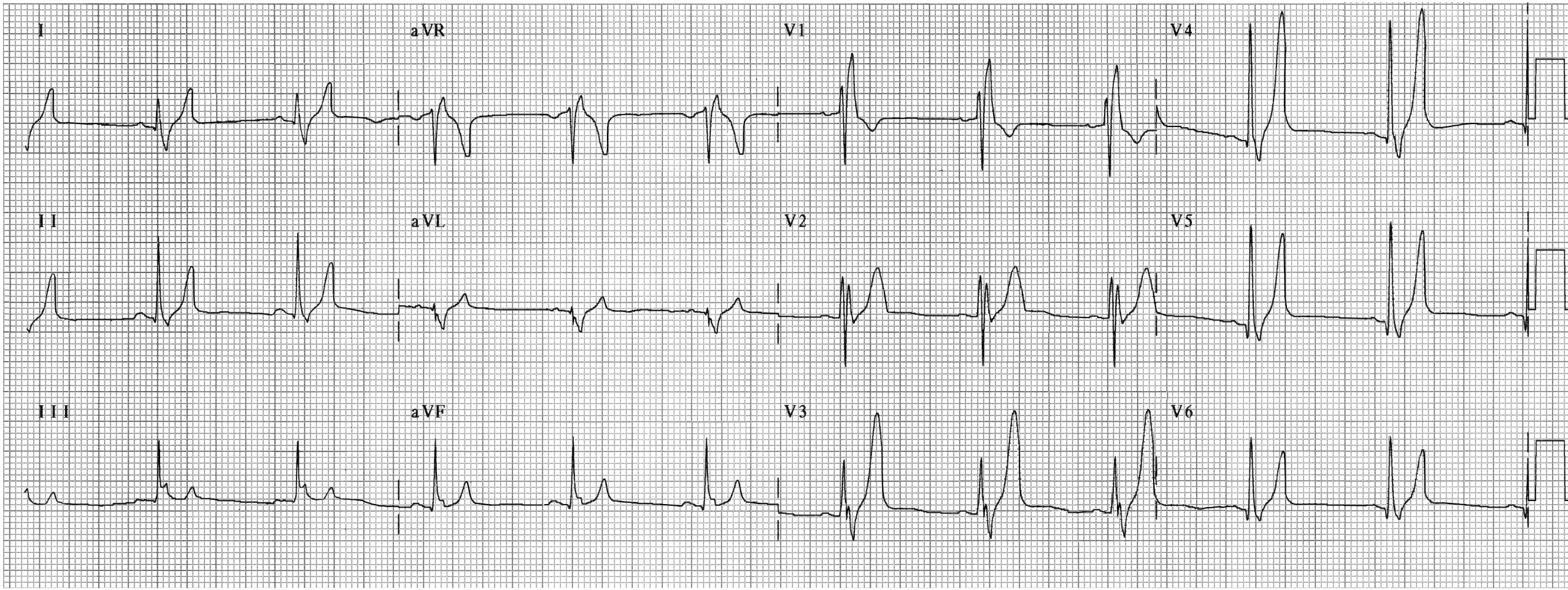
- **SQT2:** the T waves appear to be symmetrical, but not as tall and narrow (15;16).

- **SQT3:** asymmetrical T waves with a rather normal ascending ramp and a remarkable rapid descending terminal ramp (17).

Peaked and symmetrical with a narrow base T waves ("tent-shaped") are characteristic of mild hyperpotasssemia. Usually, this is the earliest sign of hyperkalaemia. This morphological T waves are observed with slightly increased serum potassium levels(potassium level > 5.5 mEq/L and < 6.0 mEq/L). It is present only in 22% of the cases of hyperkalemia. Not too sensitive but quite specific. Similar T waves are registered eventually in congenital short QT syndrome. Additionally, peaked and symmetrical with a narrow base T waves ("tent-shaped") are observed also in metabolic acidosis and without hyperkalemia (18). Peaked, symmetrical T waves, with broad base is an early sign of hyperacute phase of myocardial infarction (19).

Figure 10

Name: JSVB; **Age**: 27; **Sex**: Male; **Race**: White; **Weight**: 67 Kg.
Height: 1.72 m. **Date**: 06/24/2004; **Medication in use**: none.

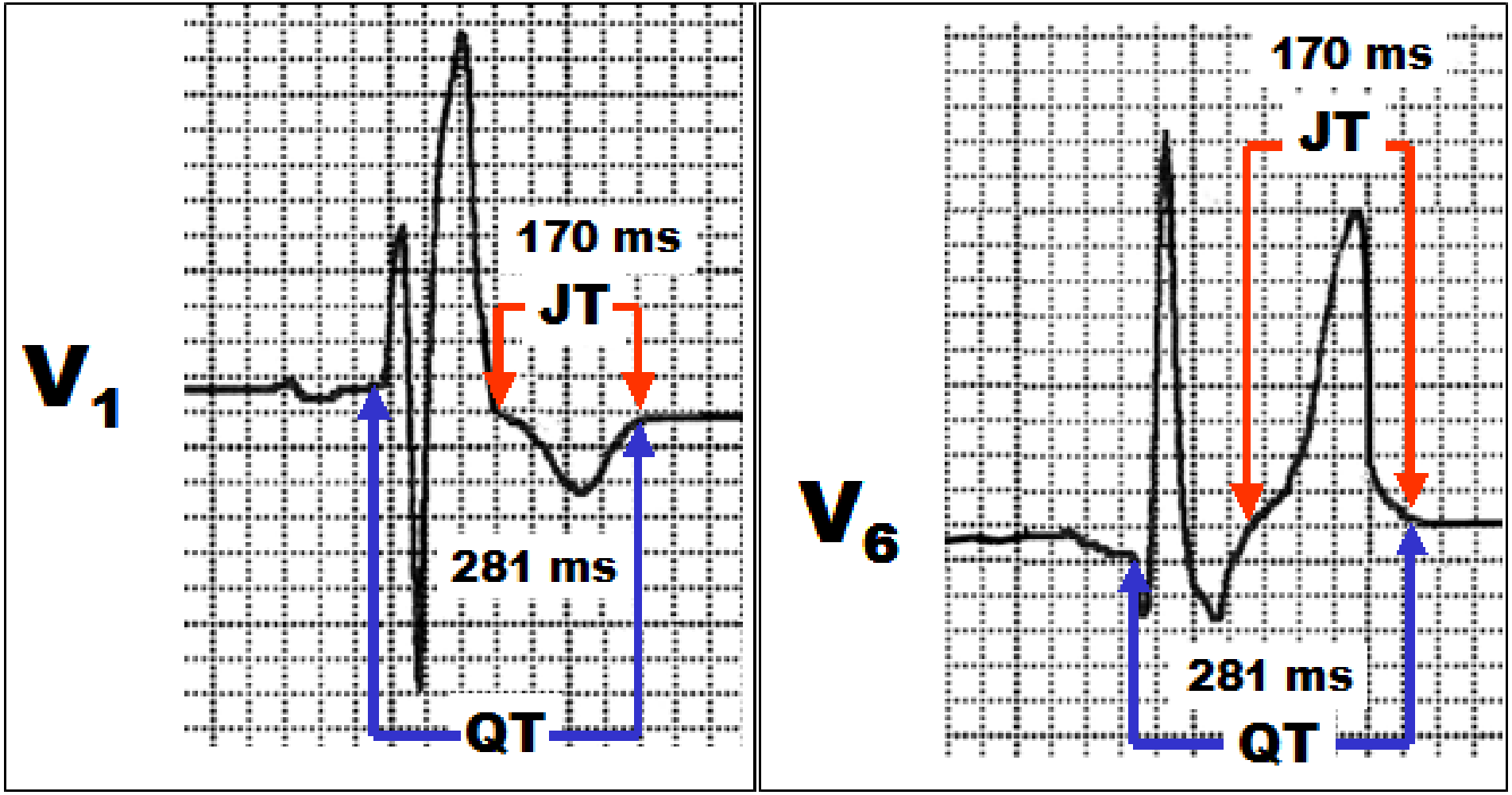


Rhythm: sinus; HR: 65 bpm; P wave: SAP axis: +54º in the FP and to the front in the HP; Duration: 80 ms; Voltage: 1 mm; PR interval: 134 ms; QRS: SAQRS: +106º; in the FP and to the front in the HP; QRS duration (QRSD): 120 ms; QRS morphology: triphasic rSR' pattern in V1 and broad S wave in left leads *DI, aVL V5 and V6 (right terminal forces)*; intrinsic deflection in V1 > 50 ms.

T wave: morphology: tall T wave from V3 through V5 with narrow base and a tendency to be symmetrical (the patient does not have serum potassium increase); SAT: +42º in the FP and discretely heading to the front and below in the HP; QT/QTc interval: 302/315: short for this rate (the inferior limit for a 67 bpm heart rate in men is 324ms (20);

Characteristics of JT and QT intervals in congenital short QT syndrome

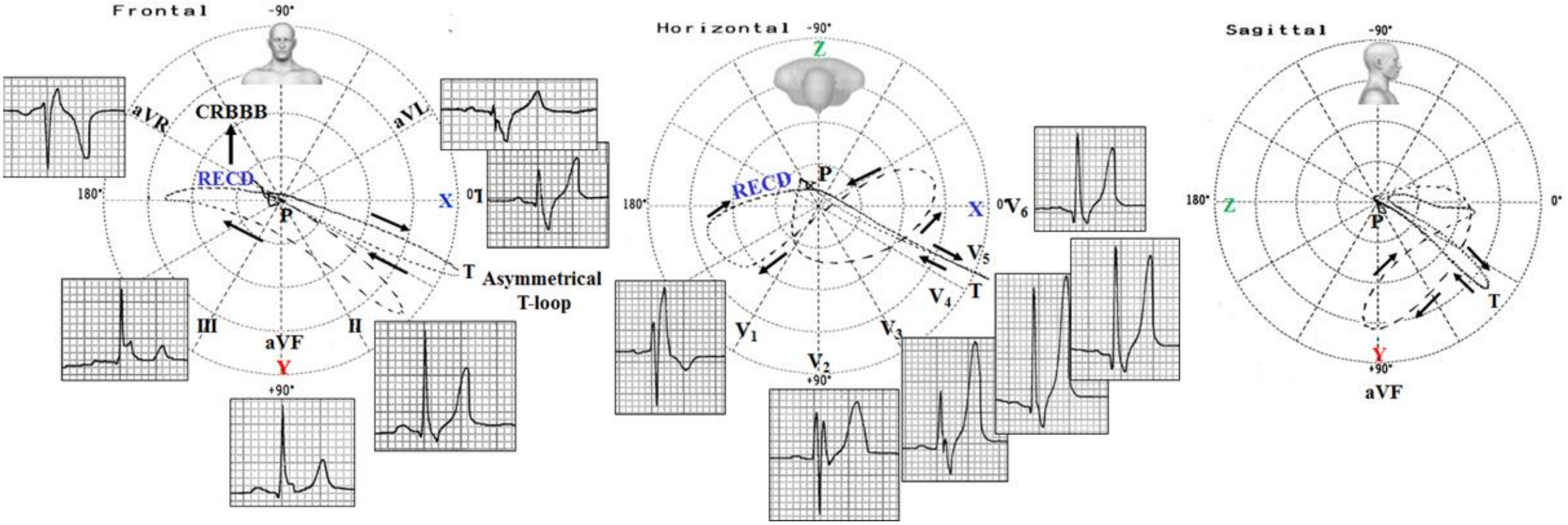
Figure 11



JT/JTc interval: 182/199 ms: extremely short (QT-QRSD = JT. 302-120 = 182 ms). (The inferior limit for a 67 bpm heart rate in men is 224 ms). Conclusion: 1) CRBBB; 2) Increase of QRS duration; 3) Short QT interval with no use of drugs, electrolytic disorders or any associated pathophysiological state; 4) Very short JT interval; 5) Probable early repolarization pattern.

ECG/VCG correlation

Figure 12



FP - QRS loop duration 120 ms. Right End Conduction Delay (RECD) located on top right quadrant near aVR lead. Asymmetrical T-loop SÂT +20º.

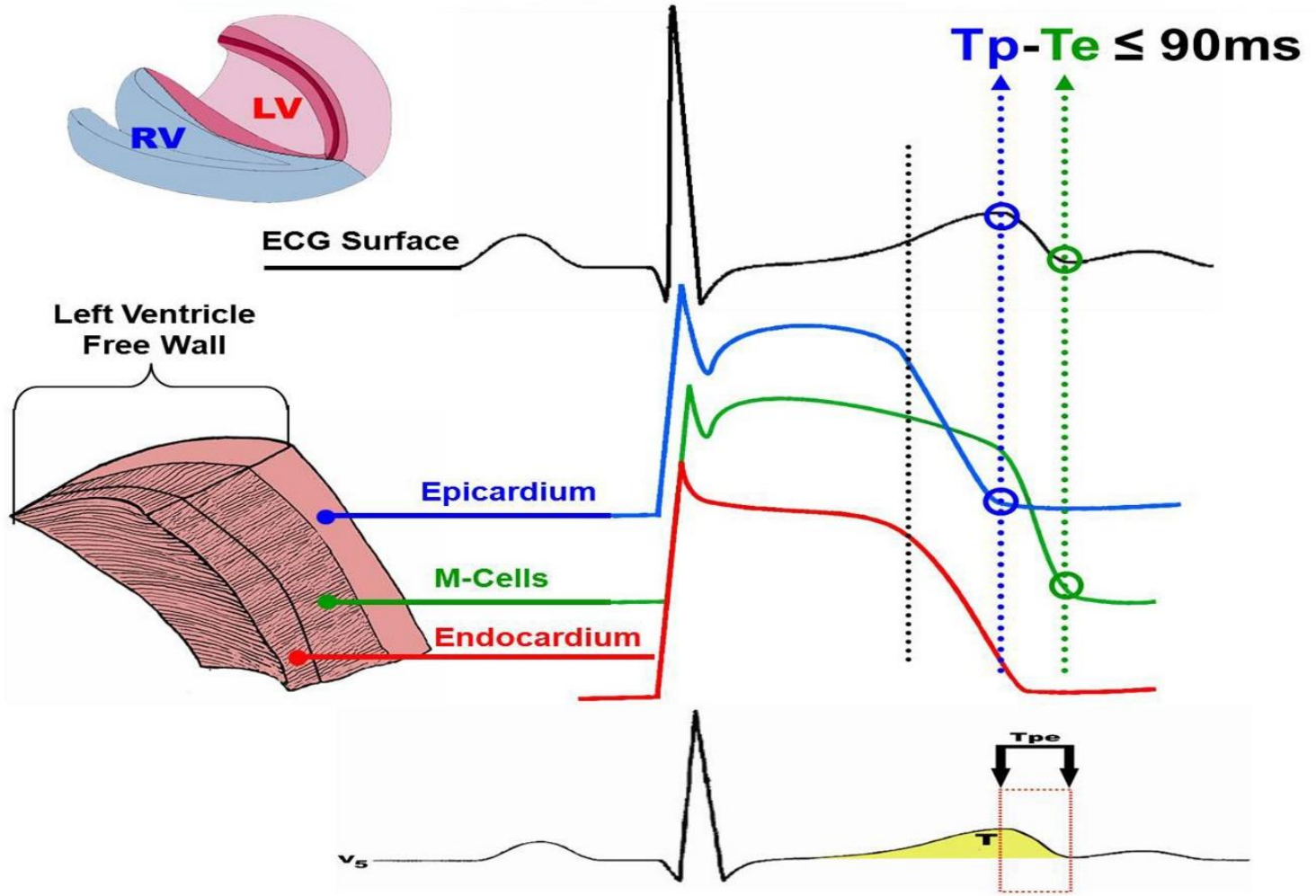
HP – Triphasic QRS pattern in V1-V2 and broad final S-wave in V5-V6: CRBBB. VCG Grishman-type of CRBBB: afferent loop behind the X line; triphasic rSR' pattern; short QT interval; tall T waves with narrow base from V_3 through V_5.

RSP – Asymmetrical T loop heading down and to the front.

Observation: The VCG is conclusive that T-wave is not symmetrical because efferent limb has tears very close one another, on the other hand, the afferent limb has tears more separated from each other.

Prolongation of T peak/Tend interval (Tpe)

Figure 13



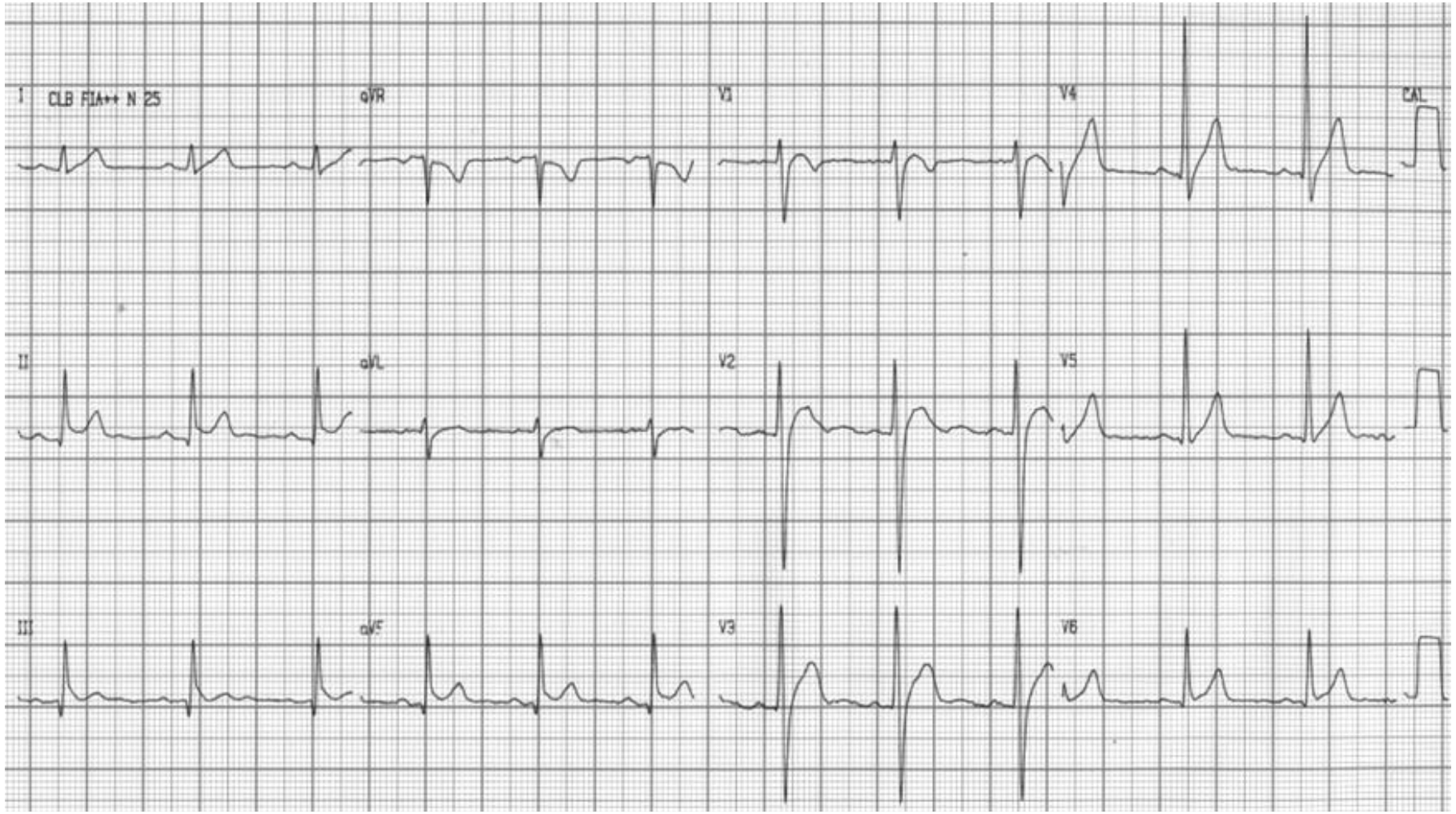
*T*he possible substrate for the development of ventricular tachyarrhythmias may be a significant transmural dispersion of the repolarisation due to a heterogeneous abbreviation of the action potential duration. *Normally T peak/Tend interval is 94 ms in men and 92 in women when measured in the V5 lead. In SQTS this parameter is prolonged > 92ms in women and > 94ms in men with the measurement in V5.* In SQT1 patients the T waves in the precordial leads, appear often tall, narrow and symmetrical, with a relatively prolonged Tpeak-Tend interval (14).

High prevalence of early repolarization. It associated with arrhythmic events

There is a high prevalence of early repolarization in patients with SQTS. Additionally, early repolarization may be useful in identifying risk of cardiac events in SQTS (21).

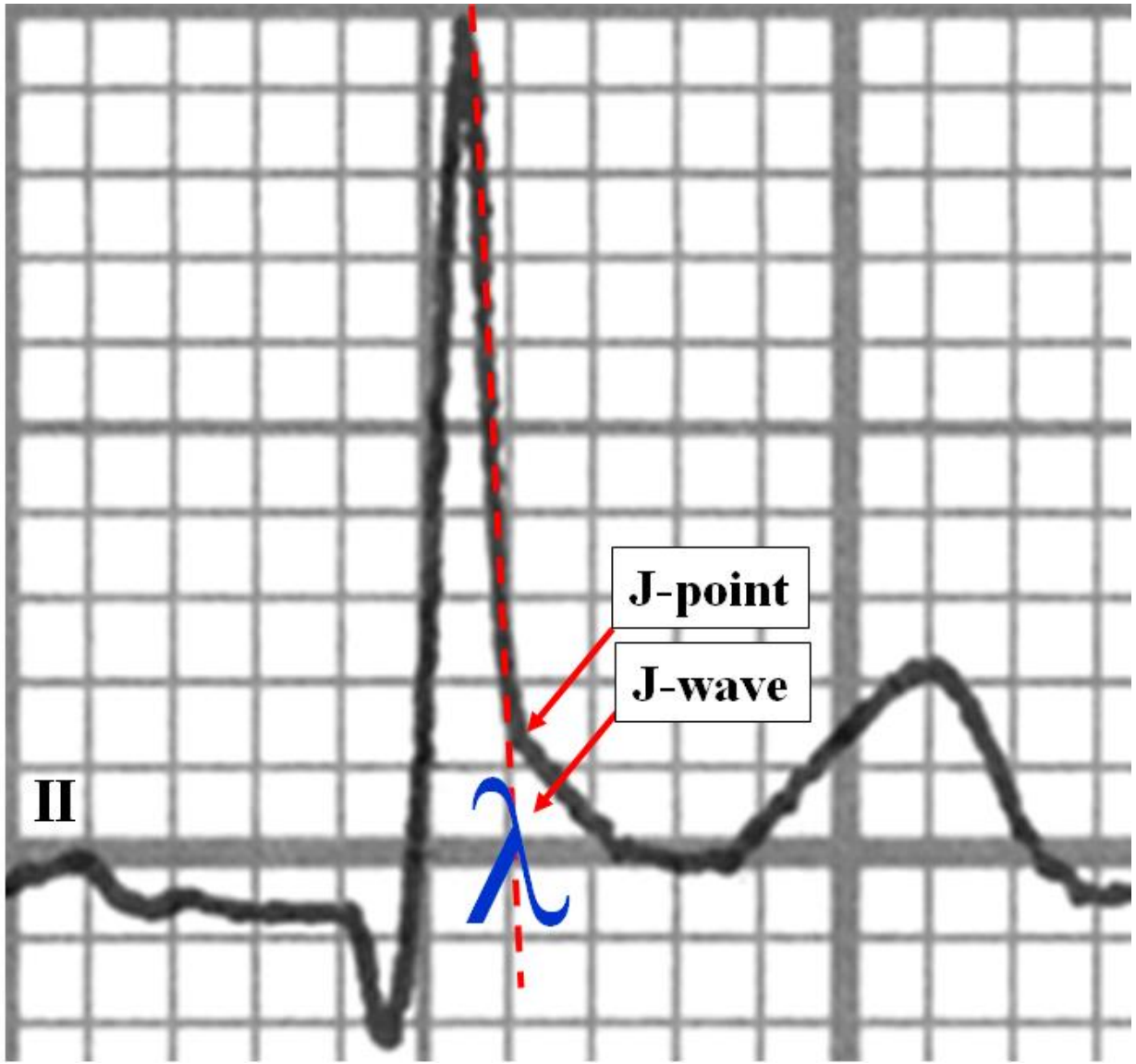
Figure 14

Example of SQTS associated with early repolarization



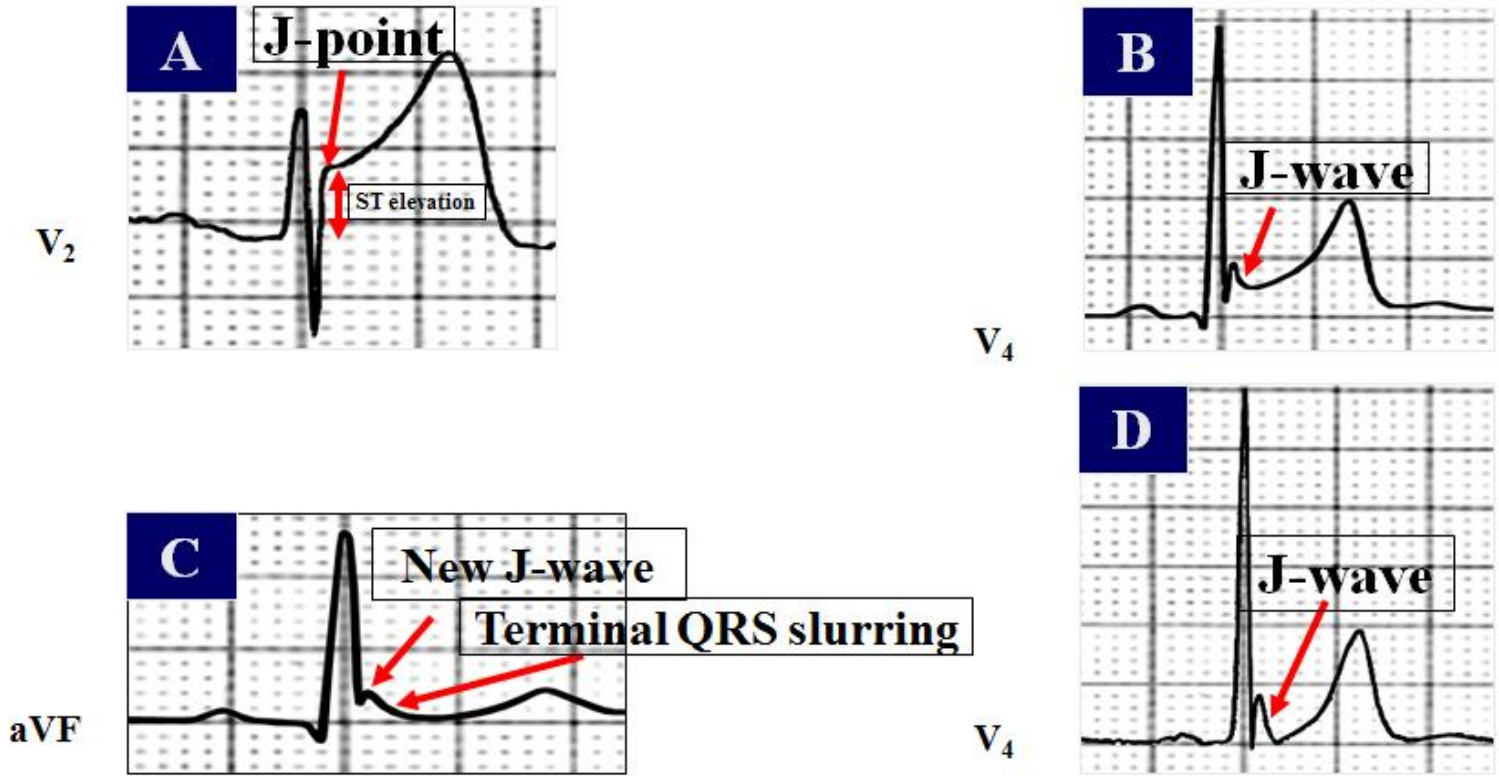
HR= 68bpm; QT=340ms; RR=880ms; QTc=362ms

Figure 15



The first point of inflection of R wave descendent ramp is considered the real J-point. In these cases "The tangent line" method is ideal. ST-segment elevation = 0.8mm. We considered an atypical C type variant of early repolarization pattern. The lambda aspect is a marker of fatal arrhythmias.

Figure 16



Classic definition of ERP always with ST segment elevation

A. ERP with only ST segment elevation
B. ERP with ST segment elevation and J-point at the end of J wave.

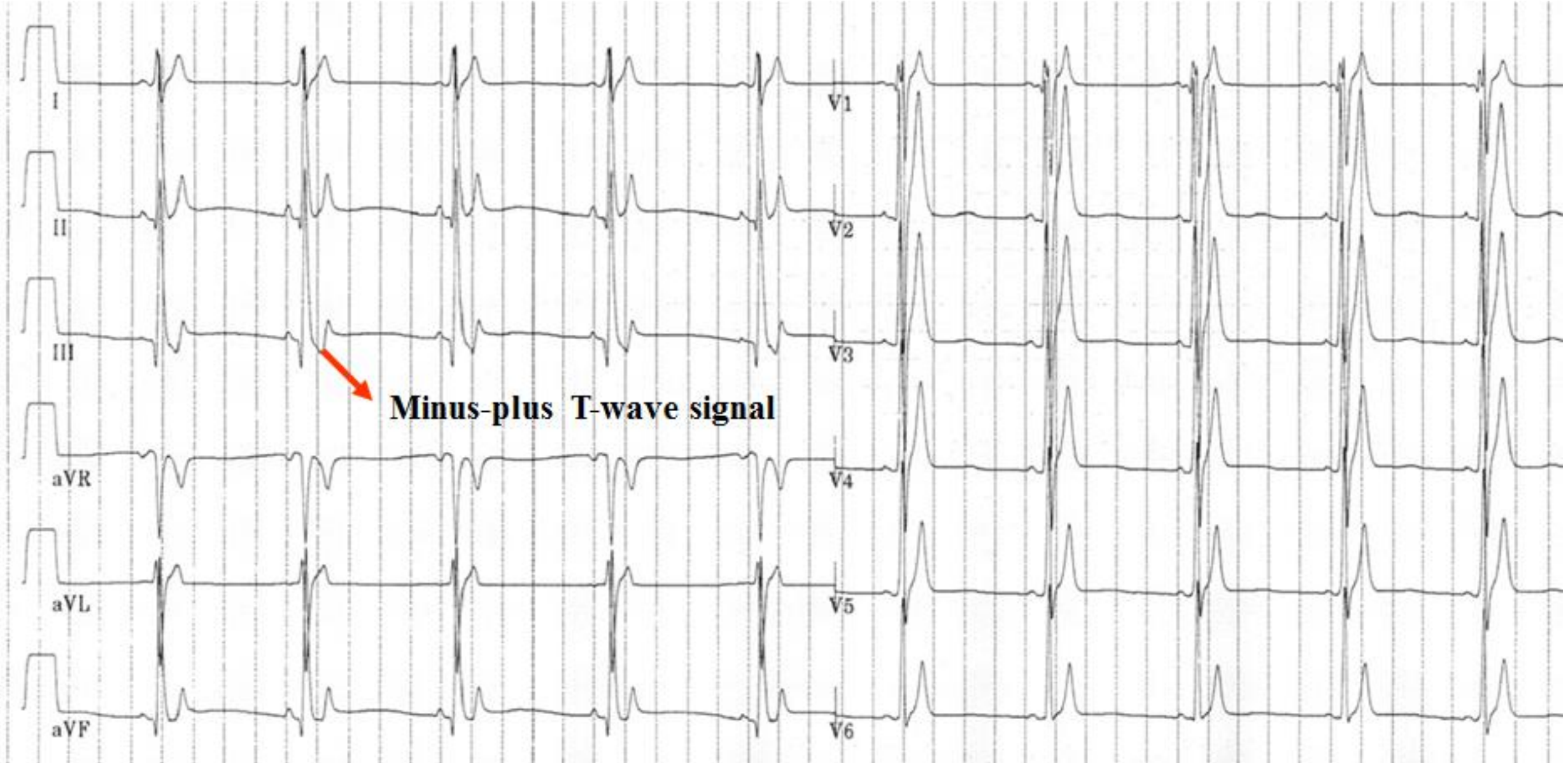
New definition of ERP without ST segment elevation

C. J-point elevation and terminal QRS slurring without ST segment elevation. The first point of inflection of R wave descendent ramp is considered the real J-point. In these cases "The tangent line" method is ideal.
D. J-wave without ST segment elevation (22).

Usually, PRs (end of P wave up to QRS complex onset), STs (from J point or the end of QRS up to the beginning of the T wave) and TP (from the end of the T wave up to the P wave of the following cycle) segments are at the same level. The figure shows a normal ECG and a line of dots pointing out the level of the three segments: PR, ST and TP.

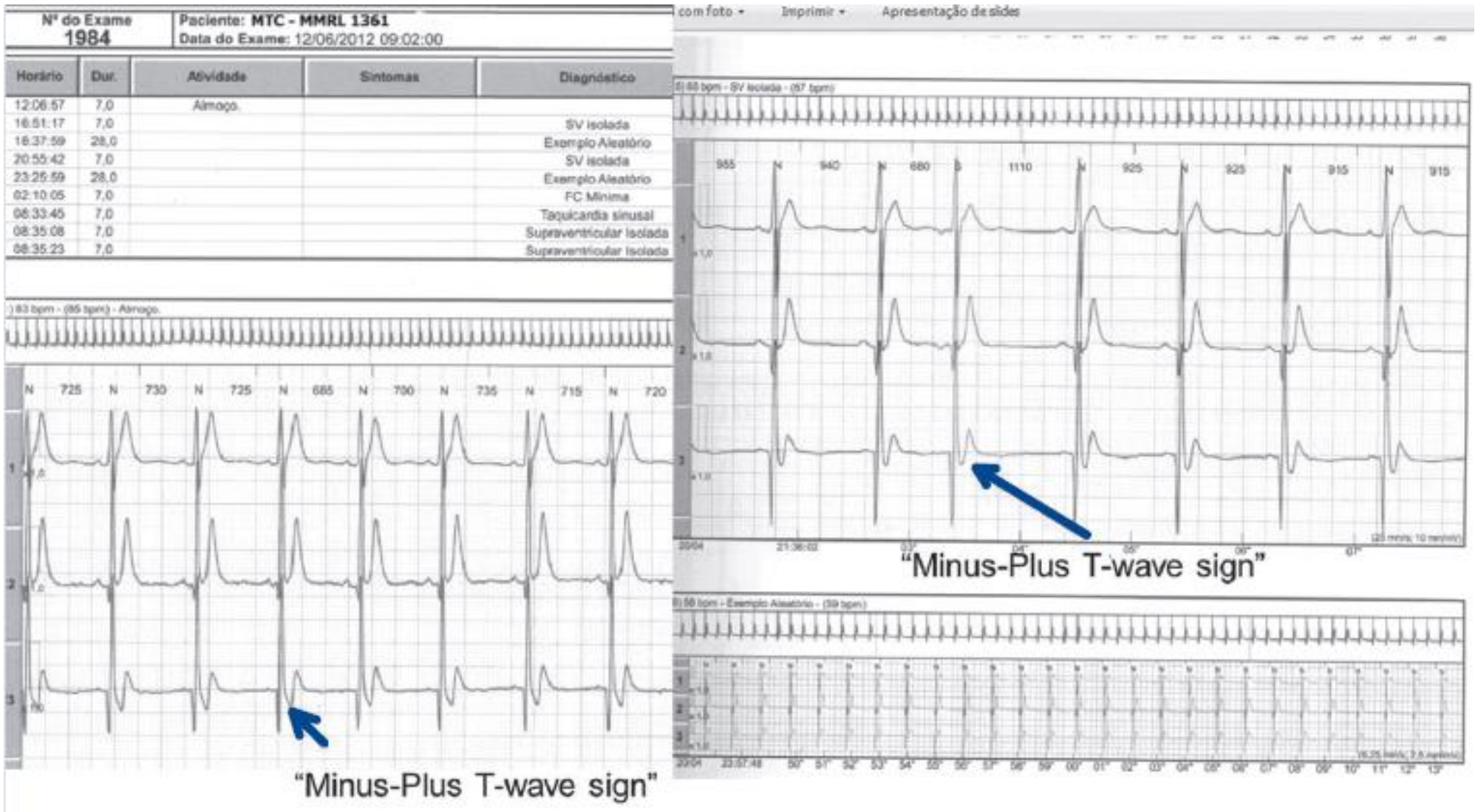
Minus-plus T-wave signal (see next ECG and Holter)

Figure 17



The minus-plus T-wave signal or negative-positive-T wave without ST segment observed in III in a patient with SQT1 variant (23).

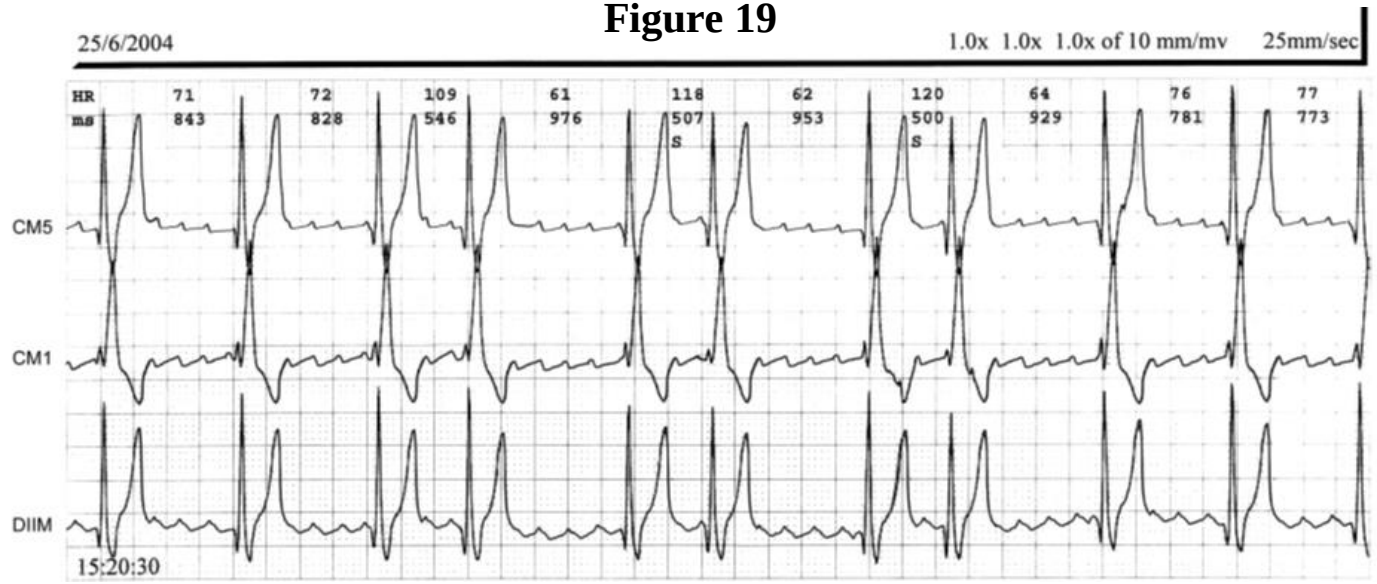
Figure 18



The "minus-plus T-wave sign" observed in a Holter recording in a patient from Latin America (Brazil). Caveolin mutation. Unpublished.
"Minus-plus T-wave signal": The initial part of the T wave is recorded immediately after the QRS complex (absence or minimal ST segment) shows a negative initial polarity in some leads (red arrow) that we denominated "minus-plus" T-wave signal (negative-positive). Coincidentally, the CAV3 mutation that causes gain-of-function of late I_{to} without affecting other cardiac ion channels corresponds to J point and the initial negative portion of the T wave on the surface ECG. There would be a genetypic/phenotypic relationship?

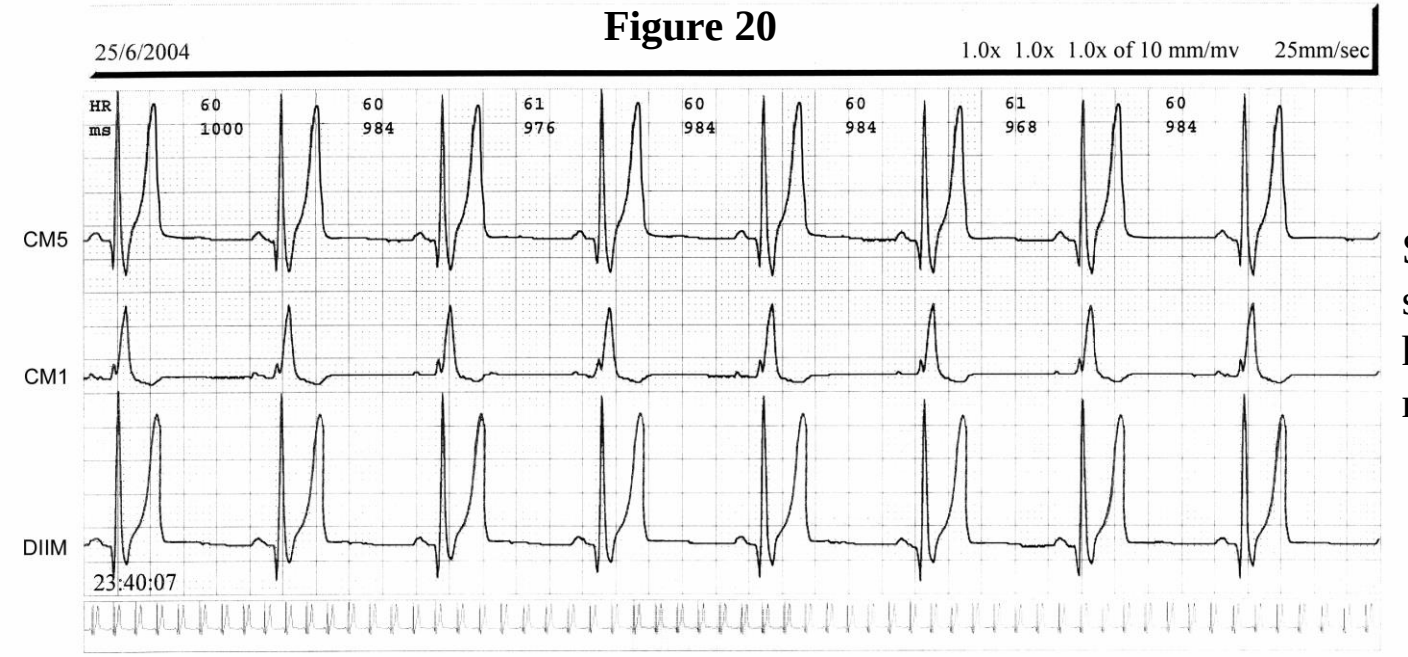
Holter monitoring

Figure 19



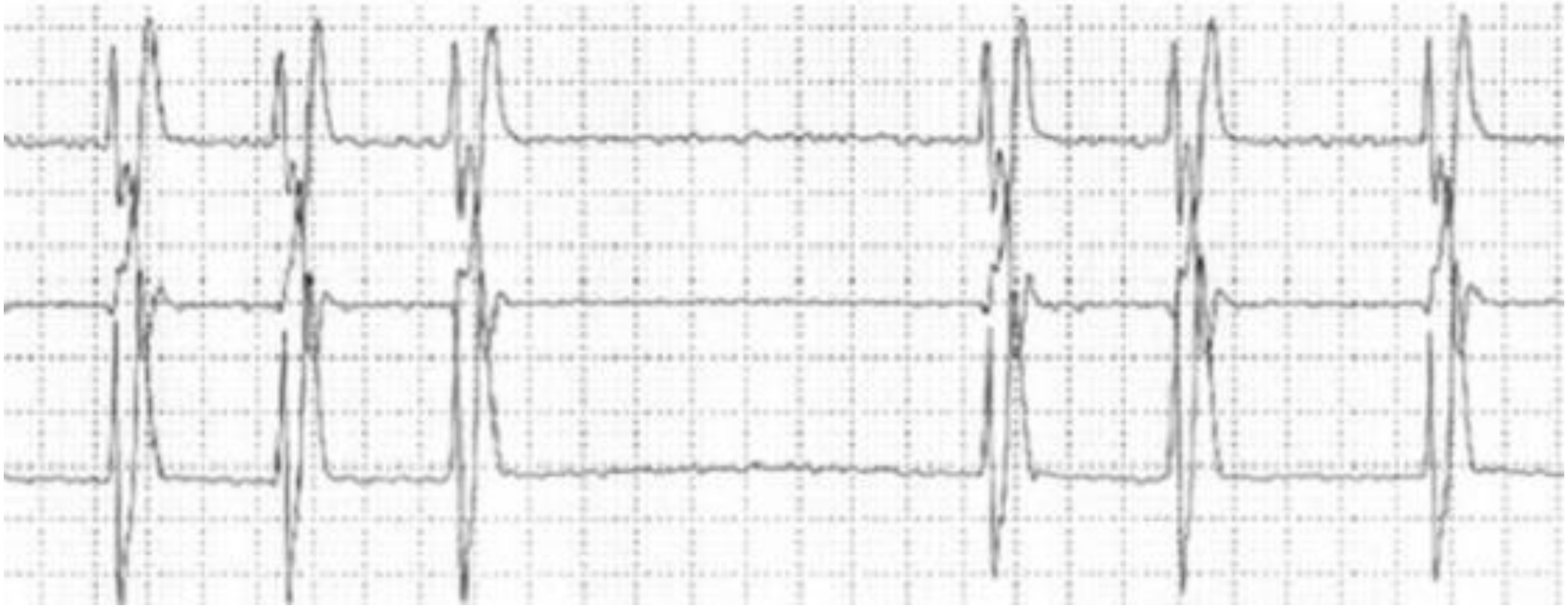
In this tracing we can see a short period of gross atrial fibrillation. The patient described palpitations. Congenital short QT syndrome is associated to high incidence of paroxysmal atrial fibrillation, the electrophysiological mechanism of which would be caused by very short action potential with heterogeneous shortening of the cardiac potential and refractory period of atrial cardiomyocytes.

Figure 20



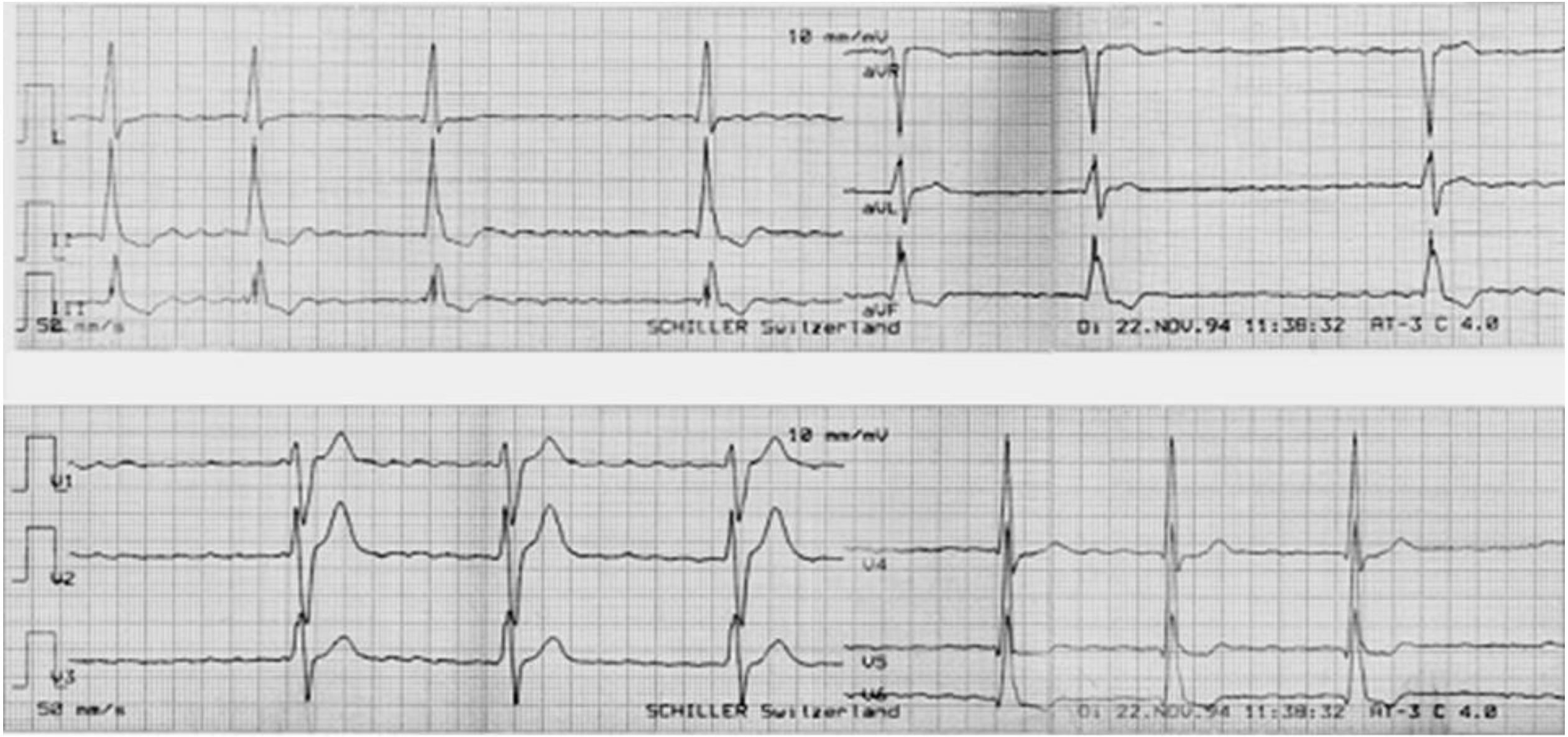
Sinus rhythm, tall/ peaked, narrow-based T waves or pseudo symmetrical T-wave in a patient with SQTS. Approximately 8 hours later during the same test, the patient spontaneously reversed into sinus rhythm (24).

Figure 21



Twelve-lead ECG Holter recording showing atrial fibrillation (heart rate,120 bpm) with markedly shortened QT interval (QT 200 ms, paper speed 25 mm/s).
Twelve-lead ECG Holter recording showing atrial fibrillation (heart rate, 60 bpm) with short QT interval (QT 200 ms).
The flat relationship between heart rate and QT interval indicates lack of adaptation of QT interval to changes in cycle length.

Figure 22



* Presentation named Supraventricular tachycardias and Brugada Syndrome from Brugada Syndrome Consensus Conference held in Lake Placid – NY – September 11-14 2003 by Prof. Martin Borggrefe MD, Ph.D.

Healthy kangaroos are prone to sudden death (SD). To investigate possible causes of this phenomenon, echocardiographic and ECG studies were conducted in 7 healthy sedated kangaroos aged 1.5-5 years weighing 5.5-48 kg (25). As in human hypertrophic cardiomyopathy (HCM), kangaroos showed relative LVH measured as a ratio of (internal LV end-diastolic diameter)/(septal + posterior wall thickness. Peak LV diastolic filling velocity is smaller in kangaroos and HCM than in normal man. The end of T wave occurred earlier than the closing of aortic valve (before U wave). The U wave is the only component of the ventricular complex on the electrocardiogram (ECG) that cannot be derived from the ventricular action potential. This may explain many competing hypotheses on the origin of the U wave. The last enigma of the ECG (26). The inability to find a universally acceptable hypothesis has not caused major impediments in use of the ECG in practice and research because the small deflection conveys no significant diagnostic information and is rarely included in routine ECG analysis (27).
The QTc interval is shorter than the normal value for man. Kangaroos have cardiac hypertrophy of unknown aetiology, with impaired diastolic function, as in non-obstructive HCM patients. Additionally, QTc interval is very short. These echocardiographic and ECG findings may explain the mechanism of SD in kangaroos, a species which may be used as an experimental model of non-obstructive HCM and short QT syndrome in man.

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