ECG

CONGENTIAL SHORT QT SYNDROME : ABBREVIATED REPOLARIZATION

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OUTLINE

Congenital short QT syndrome : Abbreviated repolarization

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O SQTS Thou are a young entity.

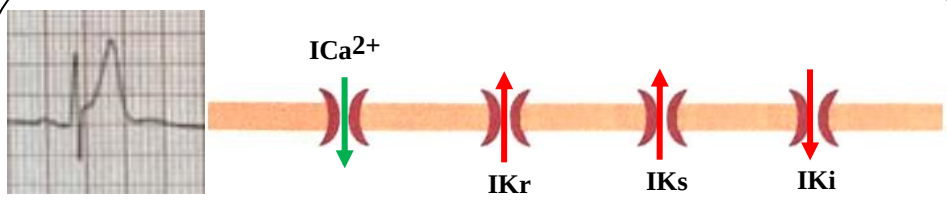
- ☐ **Mutational alteration to a gene may be linked to 'Abbreviated repolarisation'**
- ☐ **With the loss of electrophysiological wisdom , protective guarding of QTc is shadowed leaving behind the murmuring of nothing but alarming nuisance**

The Seers of medical science are making their endless efforts to witness thy outskirting from within – a searching mission with a spotlight of knowledge to conquer the shadowy imprints so casted and tented.

1. Introduction

Short QTc syndrome (SQTS) is a very rare genetically determined heterogeneous disease with inherent mutation defects producing an electrophysiological pattern –'Abbreviated repolarisation pattern'. The first report of short QT syndrome came in the knowledge of the medical science with its publication in 2000, revealing a family with SQTS on the 12-lead ECG which also described atrial fibrillation occurring at a younger age and also revealed its association with sudden cardiac death. As the time progressed in the pages of the history such in 2003, there was further found an association between short QTs and sudden cardiac death. It was the year 2004 when the first genetic association with this condition was uncovered. The criteria for diagnosing this condition were proposed and laid down in 2011. Now the medical scientists are working on the animal model with short QT to reveal its secrecy more in depth.

It has been recently reported that there exist genotype variants with mutation to Ca^{2+} channel or K^+ channel subunits , as simplified with the following sketch :



ICa^{2+} : Reduced influx of calcium during the plateau phase of the action potential leading **to shortening of QT interval**

IKr
IKs
IKi

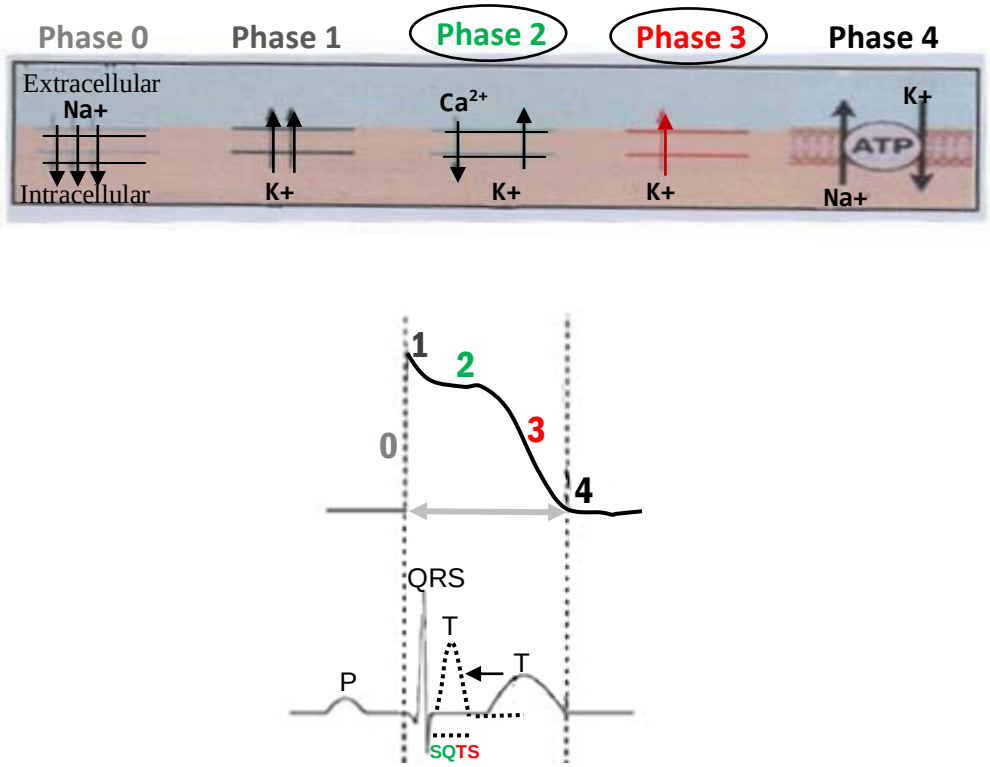
Increased potassium efflux (Ikr , IKs) and rapid inflow of IKi current inside during the repolarization lead to more rapid ventricular repolarisation with **shortening of the QT interval and taller –narrower T wave**

The potassium channels represent a family of the delayed rectifier potassium channels (IK) , being active during repolarization are **IKr, IKs, IKi**. The first two IKr (rapidly evolving current) and IKs (slowly evolving current) allow a sustained K^+ efflux during repolarization. The inward rectifier current **IKi** pushes the K ions inside the cardiac cell and hence the nomenclature.

Fig. 1.1

2. Electrophysiological basis

Further to explore, the following sketch might be more helpful to understand the nature of this syndrome :



SQTS genotypes, 1-3 : with increased potassium dynamics leading to more rapid ventricular repolarization with **marked shortening of the QT interval and taller - narrower T wave**

SQTS genotypes, 4-6 : with reduced influx of calcium during the plateau phase of the action potential leading to **modest shortening of the QT interval**

Fig. 1.2

This sketch demonstrates hypofunction of calcium current and hyperfunction of delayed rectifier potassium current.

Several mutations have been characterized so far , all of which seems to be inherited as an autosomal dominant.

It has long been detected that species of Kangaroo that are prone to sudden cardiac death (SCD) exhibit abbreviated ventricular action potential and shortening of QT interval on the ECG.

SQTS	Channels	Action
Potassium Channels		
SQTS1	KCNH2	Increase in I_{Kr} current
SQTS2	KCNQ1	Increase in I_{Ks} current
SQTS3	KCNJ2	Increase in the I_{K1} current
Calcium Channels		
SQTS4	CACNA1C	Reduction in L Type Ca-Channel current
SQTS5	CACNB2	Reduction in L Type Ca-Channel current
SQTS6	CACNA2D1	Reduction in L Type Ca-Channel current
Carnitine Deficiency		
		Altered regulation of the potassium channels

Nowadays there is ongoing mutational defects being detected in SQTS. And therefore , recently more several genotypes SQTS have been described.

3. Phenotype presentation

- **Age** : median age 30 years but ranges from a few months to sixth decade of life.
- **Sex** : Male sex is found to be associated with a higher penetrance in SQTS. Due to the relative lack of large scale samples analysis there exists a limited interpretation of sex in SQTS (low oestradiol levels among females and high testosterone level among males have been associated with a higher incidence of SCD).
- **Symptoms** : Palpitation , syncope , sudden cardiac death , family history of syncope. Some observers have observed the following conclusions from their pooled analysis :
  (i) The clinical profile with presenting symptoms among female population is comparable to that of male , but marked predominance of syncope among males.
  (ii) There is no significant differences in age distribution when patient presented initially with SCD.

4. Changes over 12-lead ECG

The basic change is the shortening of QT interval due to abbreviated repolarization phase. The salient features are described as below :

- ☐ A constant QT values and lack of adaptation to heart rate. ST segment is short or even absent , with T initiating immediately after the S wave. T is usually taller and narrower compared to normal population (Obviously seen mainly over precordial leads).
- ☐ The immediate inscription of T wave irrespective of the heart rate is the main reason of QTc being constant. At fast heart rates , the calculated QTc may appear normal (‘Pseudo normal’ QTc). Even with a decrease in the heart rate, the QTc typically fails to prolong.

- ☐ Serial ECGs or Holter monitoring may be needed to capture short QT intervals during periods of relative bradycardia (the preferred heart rate for the calculation is 60-80 bpm). This is to be mentioned here that Bazett's formula overcorrects QT interval at slow heart rate.
- ☐ Exercise testing may demonstrate lack of adaptation of QT interval , recorded with different heart rates. A Holter strip is always useful to record the constancy of QTc at different rates.

> - Males with QTc < 330 ms and females with QTc < 340 ms should be taken as a diagnostic marker with SQTS even if the person concerned is asymptomatic (these values are very rare in healthy population).
> - QTc interval shorter than 360 and 370 ms (males and females respectively) are the diagnostic pointers of SQTS when supported by symptoms or family history (it is to mention here that overlap of these QTc values with healthy population warrants the need of symptoms or family history to be further added in this context).

- ☐ Symptomatic patients have been reported with shorter Jpoint-Tpeak<120 ms interval. This finding is suggestive of augemented transmural dispersion of the ventricular mass , as encountered with SQTS.
- ☐ Depression of the PQ segment due to a heterogenous abbreviation of atrial repolarisation , most commonly observed in inferior and anterior leads.
- ☐ Often a prominent U wave can be observed , being separated by an isoelectric T-U segment.
- ☐ These patients are prone to have episodes of tachyarrhythmias (atrial fibrillation , ventricular tachycardia and ventricular fibrillation).
- ☐ Now there is a growing evidence that some cases of SQTS may have an 'overlap syndrome', associated concurrence with Brugada, Early Repolarization Syndrome or even Sick Sinus Syndrome , as a combined phenotype partership.

In nutshell , the much shortening of the QTc – T wave appearing immediately after the QRS complex is being reflected with the different accompanying changes on 12-lead surface ECG, as mentioned above. **Abbreviated repolarization phase accompanied by local dispersion of repolarization** is the main fact behind the story of ECG changes.

5. Mechanism of arrhythmogenesis in SQTS

The combination of shorter effective refractory period and transmural dispersion of repolarization is the foundation stone for the tachyarrhythmias.

The mechanism , occurring as the dispersion of repolarization , is encountered because the action potential shortening associated with this condition occurs to a greater extent in some layers of the cardiac walls than in others. It thereby indicates that some layers of the cardiac cycles are fully repolarized and so they are ready to contract and the reverse is also true to say that other regions are only partially repolarized and so remaining within their absolute refractory period, unable to be re-excited. A triggering impulse in the presence of short effective refractory period may be met with a critical point of the cardiac cycle where

electrical impulse is being conducted in some regions but is blocked in others, potentially creating a wavebreak with resultant re-entrant arrhythmias.

The entire concept is summarized with the following table :

ARRHYTHMOGENESIS IN SQTS

- **Short ventricular effective refractive period** (usually manifest as a short QT interval on ECG)
- **Transmural dispersion of repolarization** i.e. the different layers of myocardium (endocardium, epicardium and M cells) repolarize a different rates
- **Impulse arrives at critical point in the cardiac cycle**, and the resultant electrical wave is conducted in some regions but blocked in others, potentially resulting in wavebreaking with re-entrant tachyarrhythmias.

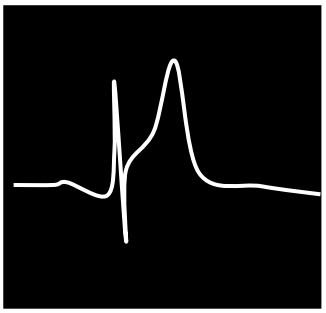


Fig. 1.3

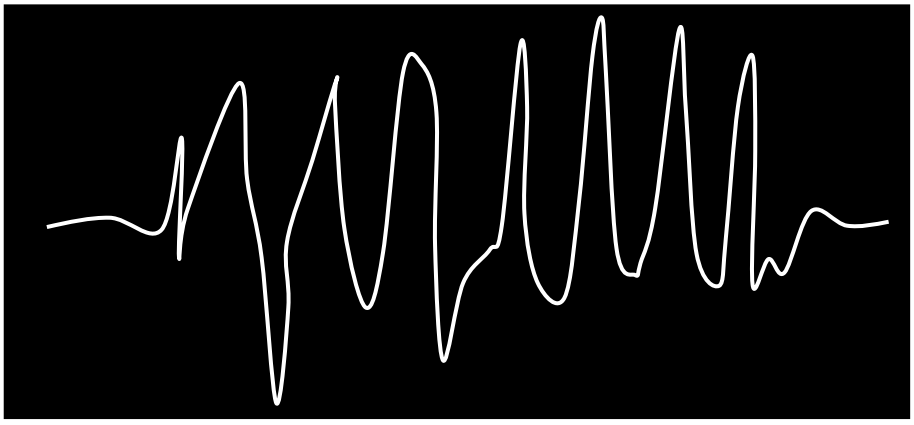


Fig. 1.4

6. A diagnostic approach

With the foregoing discussion the following consideration should come in mind while making a diagnosis of SQTS.

- Shorter QTc with accompanying tall and narrower T
- Jpoint-Tpeak interval / Tpeak-Tend intervals to access the ventricular dispersion
- Clinical history
  - Sudden cardiac arrest
  - Documented evidence of tachyarrhythmias (atrial fibrillation, ventricular tachycardia or ventricular fibrillation) ± syncope of unknown nature.
- Positive Family history in first or second degree relatives.

☐ **Gollop-Redpath and Roberts in 2011 laid down the following diagnostic criteria to diagnose SQTS**. By their scoring system a score of 4 or more was considered to indicate a high diagnostic probability of SQTS (please see on the next page).

The Short QT Syndrome : Diagnostic Scoring Scheme

	Points
QTc, ms	
<370	1
<350	2
<330	3
Jpoint-Tpeak interval <120 ms	1
Clinical history	
History of sudden cardiac arrest	2
Documented polymorphic VT or VF	2
Unexplained syncope	1
Atrial fibrillation	1
Family history	
First- or second-degree relative with high-probability SQTS	2
First- or second-degree relative with autopsy-negative sudden cardiac death	1
Sudden infant death syndrome	1
Genotype	
Genotype positive	2
Mutation of undetermined significance in a culprit gene	1

The above scoring system is not having the universal acceptance

☐ **According to the guidelines in effect HRS/EHRA/APHRS Expert Consensus 2013**

1. SQTS **is diagnosed** in the presence of a QTc≤330 ms.

2. SQTS can be diagnosed in the presence of a QTc<360 ms and one or more of the following : a pathogenic mutation, family history of SQTS , family history of a sudden deathat age ≤40, survival of a VT/VF episode in the absence of heart disease.

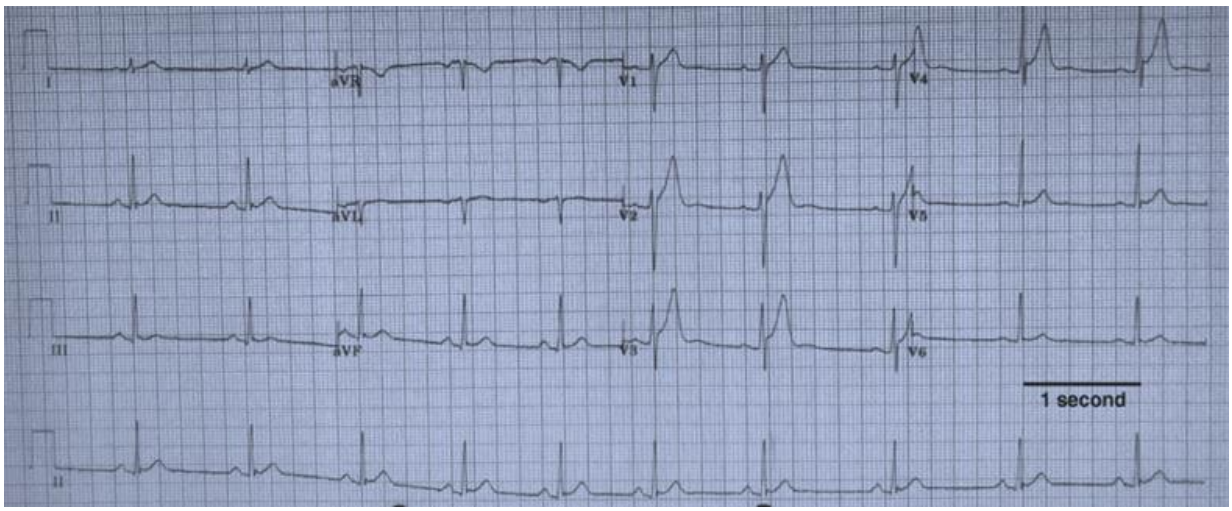
7. Lone-tachyarrhythmias

This is to be noted here that some people with short QT syndrome never experience any major problem associated with this condition. Sometimes only one meets with episodes of tachyarrhythmias and these may point towards the strong probability of SQTS.

- Atrial fibrillation presenting in a new born child should raise the suspicion of short QT syndrome. A useful analogy can be made here with familial atrial fibrillation in another members of the family.
- Considering the high incidence of atrial fibrillation associated with these patients, it should be kept in mind that **'Lone-atrial fibrillation' , specially in young individuals might be in some cases associated with a short QT syndrome**.
- The episodes of ventricular tachycardia on 12-lead surface ECG specially in younger generation without the known exciting factors should also raise the suspicion of SQTS.

8. Illustration by ECG

Short QTc syndrome



Source : Global Heart Rhythm Forum (15.05.2019) by Dr. R. Rajasekar , Eminent Diabetologist and Senior Consultant in Medicine , Kumbakonam

A young adult male who experienced cardiac arrest

ECG findings :

I. QT and QTc intervals respectively : 0.32 and 0.32 ms both are equal and unchanged.
II. Tall / peaked T , best seen over precordial leads V1-V4.

Discussion (in general) :

1. Short QT syndrome (SQTS) is a very rare genetically determined heterogeneous disease with inherent mutation defect producing a typical pattern on ECG.
2. QTc interval shorter than 0.36 and 0.37s in males and females respectively with tall / peaked T wave is the diagnostic pointers of SQTS when supported by symptoms or family history

The sketch to explain SQTS :

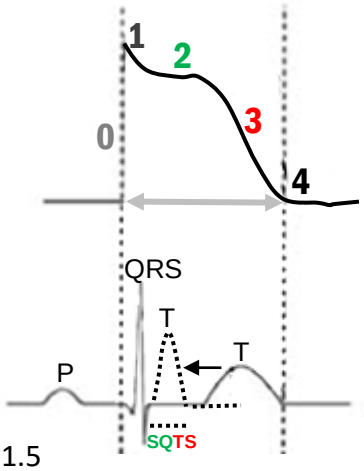


Fig. 1.5

This sketch demonstrates hypofunction of the calcium current and the hyperfunction of the delayed rectifier potassium current.

9. Concluding remark

The much rarity of this SQTS in general population warns the clinician to be familiar with its nature if one encounters with this condition in clinical practice. A short QTc interval with taller and narrower T wave immediately after the QRS complex should raise the strong suspicion of this syndrome in the concerned patient. And a sincere effort should be enforced in action to confirm this , as discussed in the foregoing pages.

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