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**HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS**

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QT Interval

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Summary

The electrocardiogram records the electrical activity of the heart, the depolarization and repolarization of the atria and ventricles. Deflections are all shown by the single features of the electrocardiogram: the P wave, the QRS complex, the T wave, the U wave, the PR interval and the QT. The QT interval represents the entire electrical activity of the left ventricle: it begins with the onset of ventricular depolarization (start of the Q wave) and is completed when ventricular repolarization ends (at the end of the T wave). Measurement of the QT interval is important because of the useful information it provides on the electrical activity of the heart; the length of the interval depends on various pathophysiological conditions, changes in electrolyte concentration, and the pharmacological action of toxic substances.

Key Words: ECG; QT Interval; QT measurement

1. Introduction

An electrocardiogram allow the measurement of the electrical activity of the heart: atrial depolarization and repolarization are consistent with contraction of the atria, whilst ventricular depolarization and repolarization correspond to contraction of the ventricles. These phenomena are followed by a recovery phase coinciding with the isoelectric line.

The single deflections of an electrocardiogram can be defined as follows:

- P wave: deflection consistent with atrial depolarization
- QRS complex: corresponding to ventricular depolarization comprising four types of waves:
 - Q wave: an initial negative deflection preceding the first positive deflection
 - R wave: first positive deflection
 - S wave: first negative deflection subsequent to an R wave
 - QS wave: a purely negative deflection unaccompanied by a positive wave
- T wave: deflection corresponding to ventricular repolarization

- U wave: deflection occurring after a T wave and elicited by repolarization of papillary muscles

The main intervals are:

- PR interval: corresponding to the duration of atrio-ventricular conduction
- QT interval: interval between the onset of ventricular depolarization (beginning of Q wave) and termination of ventricular repolarization (end of T wave).

The QT interval accounts for the entire electrical cycle of the left ventricle and is utilized in measuring the duration of ventricular repolarization.

The onset of ventricular depolarization is readily discernible, as it occurs concomitantly with the first QRS deflection. The onset of repolarization, on the other hand, is less easily definable, due to the fact that not all ventricular cells are repolarized simultaneously; so it is the electric systole, the QT interval, that is usually defined.

The electrocardiographic measurement of the QT interval is a procedure of major importance, as it provides information on the heart's electrical activity, which may be altered by a wide variety of physiopathological conditions, including electrolytic imbalance, and the action of drugs or toxic compounds on the heart. Conduction

Figure 1. QTc according to age and gender

| Age and gender | 1-15 years | Males | Females |
|----------------|------------|-----------|-----------|
| Normal | <440 msec | <430 msec | <450 msec |

abnormalities, including bundle branch blocks and pre-excitation, may produce repolarization alterations capable of influencing QT interval.

2. Measurement of the QT interval

The QT interval should be calculated from the initial deflection of the QRS complex. Incorrect calculations may be made when measuring QT at a single lead, as the initial QRS vectors may be located perpendicularly to the lead line, so abolishing the initial deflection and leading to an incorrect interpretation. Several authors suggest the advisability of obtaining steady measurements from leads V5 and V6, but the best way to achieve reliable results is to calculate QT using data obtained from all 12 leads, taking the longest measurement obtained as the final outcome [1, 3].

Distinguishing between T and U waves may prove to be a hard task, especially when the latter are pronounced. It may likewise be complicated to discriminate between a U wave situated close to a T wave of the type just mentioned, and a bifid T wave. When taking into account an entire bifid T wave, the resulting QT will be longer than that obtained measuring T as proximal and U as distal deflection. In view of the fact that the U wave is particularly evident in precordial leads, when a bifid T wave is observed across all leads it is feasible to assume that the wave is truly bifid and therefore calculate QT on the basis of the two deflections.

It should be stressed that some electrocardiographs are capable of calculating the QT interval automatically. The measurements so obtained are, however, thought to be unreliable; in more complex cases, such as those described previously, they may even provide totally incorrect readings.

The QT interval measured by single ECG leads may vary as a function of different recovery times recorded for specific heart regions: the difference between a prolonged and a shorter QT interval is commonly known as dispersion of the QT interval (QTd), and is applied in assessing disparity in ventricular repolarization. Values ranging between 20 and 40 msec are considered normal. An increased QTd has been reported in various heart disorders, including congestive heart failure, hypertrophic cardiomyopathy, prolapse of the mitral valve and ischaemic heart disease.

3. QT and heart rate

The QT interval is closely dependent on the heart rate, being shorter at a fast heart rate and prolonged when the heart rate is lower. Bazett's formula is applied in measuring Qt in relation to heart rate (QTc or corrected QT): [2]

$$QTc = QT / \sqrt{R-R \text{ interval}}$$

On assuming a duration of one second for the R-R interval, corresponding to a heart rate of 60 beats per minute (b/min), R-R is therefore equal to 1 and QTc identical in length to QT.

Mean normal QTc values of 0.430 sec are obtained for adult males; higher values are indicative of a pathological condition. In adult females normal values correspond to 0.450 sec. In pre-pubescent subjects a normal value of 0.440 sec is obtained, irrespective of gender (Table 1).

It should, however, be emphasized that the QT interval does not vary simultaneously with changes in heart rate, requiring a time-lag of 1-2 minutes to adapt, and varying on the basis of individual response. An incorrect measurement may be obtained if QT is assessed immediately after a change in heart rate.

4. Prolonged QT interval

Numerous conditions may underlie a prolonged QT interval – some acquired and others correlated with specific chromosomal alterations of a congenital nature.

Disorders featuring a congenital prolonged QT interval are classified in a group of disorders known as the Congenital long QT syndrome, comprising:

- an autosomal recessive disorder, the Jervell and Lange-Nielsen Syndrome, associated with deafness [6]
- an autosomal dominant disorder, the Romano-Ward Syndrome, not associated with hearing deficits [10, 15].

Numerous forms of long-QT syndrome have been identified, each featuring a specific physiognomy with regard to ion currents involved and mutated genes.

The most common forms taken by congenital long QT syndrome are LQTs1-LQTs2-LQTs3, accounting for 95% of forms, all associated with different genes.

LQTs1 is the most frequently expressed form, found in 70% of arrhythmias occurring during physical exertion.

In LQTs2 arrhythmias are more frequently associated

with an emotional cause.

In the LQTS3 form, 55% of arrhythmias take place during sleep. LQTS3 is increasingly associated with a fatal outcome.

From an electrocardiographic viewpoint, diagnostic screening is provided by ECG evidence of a prolonged QT, i.e. >450 msec in males and >460 msec in females. A diagnosis of LQTS in subjects displaying a prolonged QT at surface ECG is dependent on a wide array of clinical and instrumental parameters, as listed in Table 2 [11].

In this table a score of 1 denotes a subject at low risk of LQTS, a score of 2 or 3 indicates an intermediate

| Clinical and instrumental characteristics | Score |
|---|-------|
| QTc (msec) | |
| ≥480 | 3 |
| 460-470 | 2 |
| 450 (nei maschi) | 1 |
| VT torsades de pointes type | 2 |
| T wave alternans positive | 1 |
| T wave with engraver in three derivations | 1 |
| Relative for age bradycardia | 0.5 |
| Clinical history | |
| Stress syncope | 2 |
| Syncope without stress | 1 |
| Congenital deafness | 0.5 |
| Family history | |
| LQTS found | 1 |
| Sudden death before 30 years old | 0.5 |

probability of presenting LQTS and a score of 4 denotes a high risk of LQTS.

Patients affected by LQTS frequently remain asymptomatic throughout their entire lifetime, with sudden death occurring during the first episode ever to occur in 12% of cases.

Subjects featuring a past cardiac arrest should be treated by means of a defibrillator implant, whilst other patients may be given a prescription for drug treatments. The means of treatment varies according to the risk of arrhythmias.

5. Acquired prolonged QT

A prolonged QT interval may be the result of a genetic alteration of ion channels, whether drug-related or caused by an electrolyte imbalance.

5.1 Drugs

Many different drugs are capable of prolonging the QT interval. In particular, the effects produced by class I and class III anti-arrhythmic drugs and drugs acting on the central nervous system should be carefully noted. In some cases drugs may act on a predisposed substrate, delatentizing previously undetected ion current anomalies. An increased risk of fatal arrhythmias during the administration of anti-arrhythmic drugs inducing a prolonged QT interval is limited to the early stage of treatment. Administration of these drugs should therefore be initiated in a hospital setting, a precaution that has proved to be extremely cost-effective [12].

Table 3 lists drugs capable of prolonging the QT interval.

| | |
|---------------------------------|-----------------|
| Haloperidol | Neuroleptic |
| Amiodarone | Antiarrhythmic |
| Amitriptyline | Antidepressant |
| Ampicillin | Antibiotic |
| Azithromycin | Antibiotic |
| Chlorpromazine | Neuroleptic |
| Clomipramine | Antidepressant |
| Domperidone | Antiemetic |
| Erythromycin | Antibiotic |
| Flecainide | Antiarrhythmic |
| Fluoxetine | Antidepressant |
| Imipramine | Antidepressant |
| Indapamide | Diuretic |
| Ketoconazole | Antifungal |
| Metoclopramide | Antiemetic |
| Nortriptyline | Antidepressant |
| Procainamide | Antiarrhythmic |
| Sotalol | Antiarrhythmic |
| Tamoxifen | Anticancer |
| Trimethoprim - Sulfamethoxazole | Antimicrobial |
| Citalopram | Antidepressant |
| Droperidol | Neuroleptic |
| Felbamate | Anti epileptic |
| Levomopromazine | Neuroleptic |
| Lithium | Mood stabilizer |
| Methadone | Opiate |
| Olanzapine | Antipsychotic |
| Risperidone | Antipsychotic |

Table 3. Drugs capable of prolonging the QT interval

| | |
|-------------|-------------------|
| Sertraline | Antidepressant |
| Venlafaxine | Antidepressant |
| Tioridazine | Neuroleptic |
| Tizanidine | Muscle relaxation |
| | |

5.2 Electrolyte alterations

Hypokalaemia, hypocalcaemia and hypomagnesaemia are all conditions capable of eliciting a prolongation of QT. Prolonged QT in the context of hypokalaemia is associated with low voltage T waves and with U waves.

5.3 Ischaemic cardiopathy

During the evolution of a myocardial infarction giant negative T waves are associated with a long QT; their nature still needs to be clarified. This occurrence may be linked with an ischaemia-related action potential.

5.4 Other causes

Female gender [7, 8], hypothermia, total AV block, ventricular hypertrophy [13].

6. Arrhythmias associated with QT lengthening

Arrhythmias associated with QT lengthening include torsades de pointes (Figure 1) and ventricular fibrillation (Figure 2).

The above arrhythmias are elicited by oscillations of the membrane potential at times manifested during the 2nd and 3rd action potential stages. If the amplitude of these oscillations is sufficiently marked, extrasystolic beats potentially capable of triggering arrhythmias may occur. The onset of arrhythmia is correlated with a dispersion of repolarization facilitating the onset of the trigger factor.

A prolonged QT interval without any repolarization dispersion or the triggering of activities by membrane oscillations is not necessarily correlated with a significant risk of arrhythmic events. This is why some drugs, though they do prolong the QT interval, never, in the case of salbutamol, or rarely, as with amiodarone, induce arrhythmias [4, 5, 14].

In the course of an acquired long QT syndrome, ar-



Figure 1. Torsades de pointes

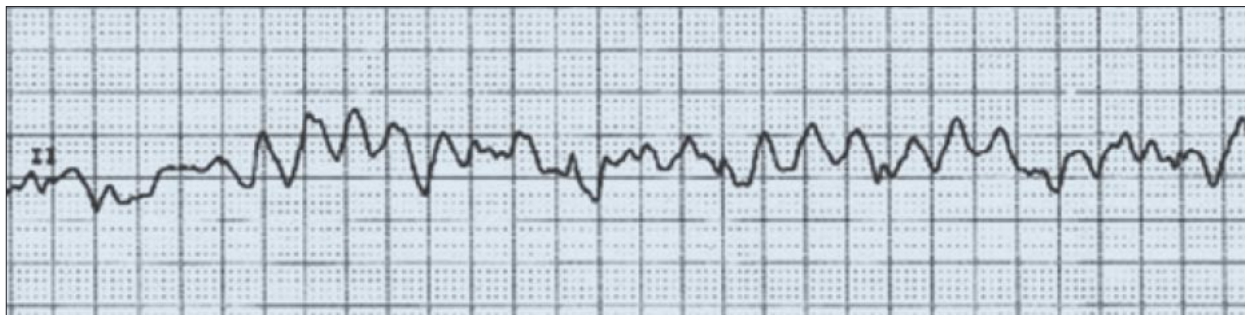


Figure 2. Ventricular fibrillation

rhythmias are often displayed without there being a low ventricular rate or any pauses. Conversely, arrhythmias correlated with a congenital long QT syndrome are induced through the involvement of the central nervous system.

In conclusion, recent studies providing evidence that a shortened QT interval may be correlated with arrhythmias and sudden death should be carefully noted. This electrophysiological alteration also correlates with genetic mutations that involve a malfunctioning of the potassium ion channel.

Three distinct forms of short QT syndrome linked with various gene mutations have been identified. Long QT is easy to define, because figures in excess of specific limit values are considered abnormal, but no clear-cut pathological limits have so far been defined for short QT.

A study performed to investigate short QT syndrome by applying the formula $QT_p = 656/(1+FC/100)$ in an attempt to establish a lower limit value for QT, provided evidence that, for a heart rate of 60 beats per minute, a QT below 361 msec should be considered pathological [9].

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