Abstract on QT time, QTc time calculation, general principles and psychotropic drug-associated QTc interval prolongation - ECG measurement - The paper on QT, QTc time calculation, general principle and conclusions:

The determination of the QT interval is particularly difficult if the amplitude of the T-wave is low and therefore the end of the T-wave is difficult to be defined.

The intervals should be measured manually from a 12-lead ECG (usually from limb lead II) and then the mean value from three to five beats is to be calculated. Since the repolarization period shortens with increasing heart rate, a frequency correction of the QT interval should be done.

The most frequently used correction formula according to **Bazett (QTc = QT/RR0.5**) should only be applied in a relatively narrow frequency range of **HR 60-80 bpm**. For higher heart rates **up from HR 80 bpm**, the **Fridericia** correction formula **(QTc = QT/RR0.33)** is more suitable.

General principles of QT time in relation to relative QT time:

QTc

Instead of comparing the QT time read (or calculated) on the ECG strip with a frequency-related normal value, it is also possible to go the other way round and specify it as a frequency-corrected QT time (QTc), which would corresponds to the QT time at 60bpm. It is normally less than 440ms (= 390ms + 13%) and is calculated (in seconds) as

$$QTc[s] = \frac{QT[s]}{\sqrt{\frac{RR[s]}{s}}}$$

If RR is exchanged again for the frequency f, the result is:

$$QTc[s] = \frac{QT[s]}{\sqrt{\frac{60s/min}{f[1/min]} \cdot \frac{1}{s}}}$$

For HR = 60 bpm the formula QTc = QT, e.g. the formula always converts the QT time read off to the corresponding QT time that would be obtained at a frequency (HF) of 60 bpm. In this way, the QT times can be compared at different frequencies. The QTc formulae are the same as above with QTc[s] = 0.39s. If a tolerance limit of about +13% upwards is applied the result is a limit of 440ms (0.39s + 13%) as the limit for long QT.

Meaning of the QT time and the relative QT time (QTc)

Prolongation of the QT time (QTc > 440ms) increases the risk of ventricular extrasystole entering the vulnerable phase of the T-wave (R to T phenomenon) with the possible consequence of dangerous Torsades de pointes (TdP) tachycardia. There is also an increased risk of sudden cardiac death (PHT), sudden infant death syndrome (SIDS) and of syncopated rhythm.

QTc Prolongation by Psychotropic Drugs and the Risk of Torsade de Pointes
Many psychotropic drugs can delay cardiac repolarization and thereby prolong the rate-corrected QT interval (QTc). A prolonged QTc often arouses concern in clinical practice, as it can be followed, in rare cases, by the life-threatening polymorphic ventricular tachyarrhythmia called torsade de pointes (TdP). Drugs, that prolongate the QT time are e.g. neuroleptics, anti-depressants, macrolide antibiotics, fluoroquinolones, azole antifungals, antimalarials, antivirals (e.g. foscarnet, amantadine), second generation antihistamines, 5-HT3 antagonists (especially dolasetron), triptans, antiarrhythmics, sympathomimetics, etc.) These psychotropic drugs can delay cardiac repolarization and thereby prolong the rate-corrected QT interval (QTc). A prolonged QTc often arouses concern in clinical practice, as it can be followed, in rare cases, by the life-threatening polymorphic ventricular tachyarrhythmia called torsade de pointes (TdP).

Method, published by Wenzel-Seifert, Katharina; Wittmann, Markus; Haen, Ekkehard:
We searched PubMed for pertinent literature on the risk of QTc prolongation and/or TdP associated with commonly used psychotropic drugs.

Results, published by Wenzel-Seifert, Katharina; Wittmann, Markus; Haen, Ekkehard:
Thioridazine and ziprasidone confer the highest risk of QTc prolongation and/or TdP. There is also a clinically significant risk associated with haloperidol given intravenously in high doses. TdP has been reported in a few cases in association with the use of newer antipsychotic drugs (mainly quetiapine and amisulpride), most of the tri- and tetracyclic antidepressants, and the selective monoamine reuptake inhibitors citalopram, fluoxetine, paroxetine, and venlafaxine. As a rule, however, QTc prolongation and/or TdP occur only in the presence of multiple additional risk factors, such as age over 65 years, pre-existing cardiovascular disease, bradycardia, female sex, hypokalemia, hypomagnesemia, a supratherapeutic or toxic serum concentration, or the simultaneous administration of other drugs that delay repolarization or interfere with drug metabolism.

Standard values QTc length
The average QTc length in healthy people is about 400 ms. While a maximum length of 460 ms in women and 450 ms in men is still considered as being normal, QTc intervals of more than 500 ms are considered as a clear risk factor for the occurrence of TdP (Torsades de pointes / Source: Abstract Wenzel-Seifert et.al - Psychotropic drugs and QTc time)

Conclusion:

Background: The repolarisation-prolonging effect of many psychotropic drugs, among others - as indicated by a prolongation of the heart rate-corrected QT interval (QTc) - often leads to uncertainty in the everyday clinical practice, as seldom, it can lead to life-threatening polymorphic ventricular tachyarrhythmias, so-called Torsade de Pointes (TdP), see definition of TdP on last page.

If now QTc is set as physiological standard value from 400 ms to approx. 450 ms and calculates QTc frequency corrected according to Bazett (at HR up to 80 bpm) and Fridericia (at HR > 80 bpm), it is also possible to calculate the deviation from the defined limit value 450 ms in % and from the risk factor for the occurrence of Torsades de Pointes (TdP) > 500 ms in %.

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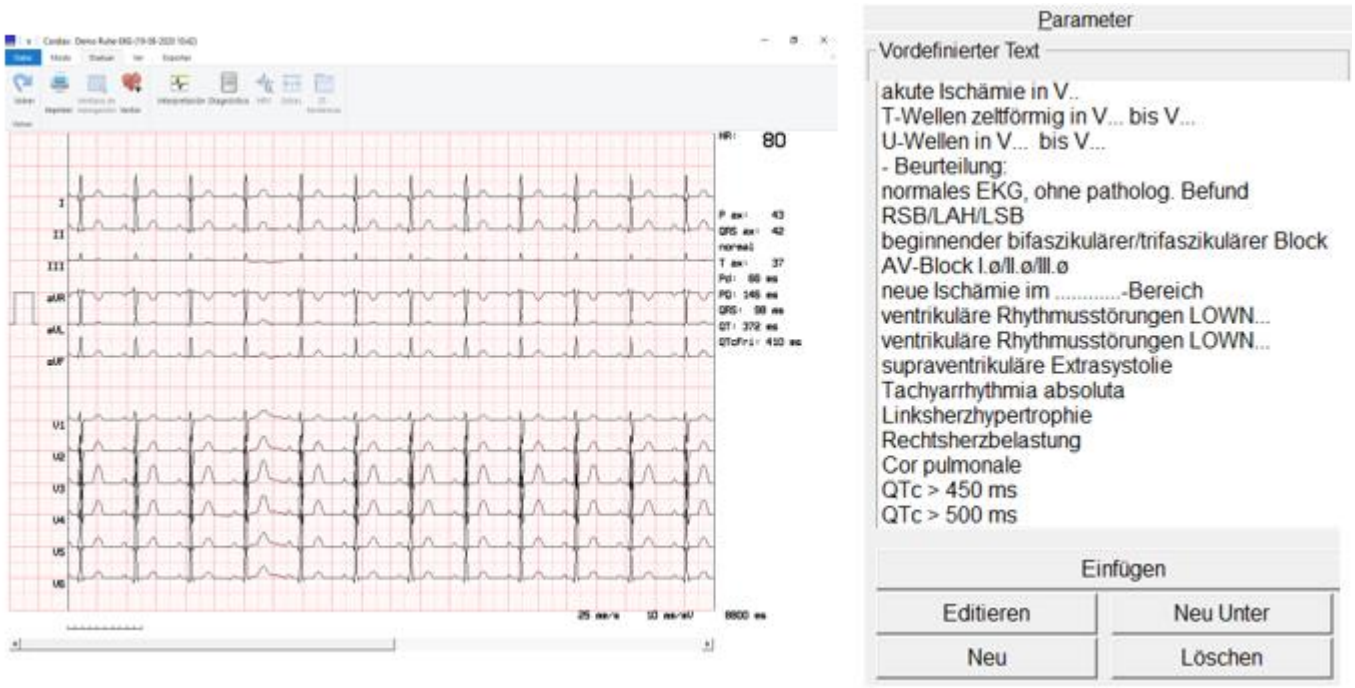
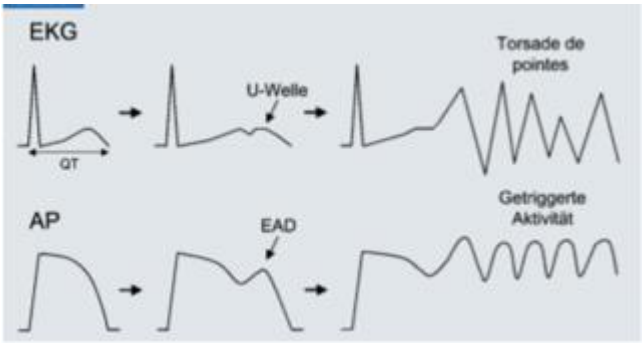
In view of this relatively high variability or prolongation of the QTc times when psychotropic drugs, such as antidepressants or generally other QTc impairing drugs, are administered, there is an entry in the editable diagnosis window of and ECG, here the CARDIAX PC ECG measurement program possible. In addition to the essential cardiological parameters, the correlating "text blocks" from the publication “by Wenzel-Seifert, Katharina; Wittmann, Markus, Haen, Ekkehard”**,** are integrated here with reference to the definitions of prolonged QTc times QTc > 450 ms and QTc > 500 ms, too.

Picture of an ECG measurement incl. detection of QTc length

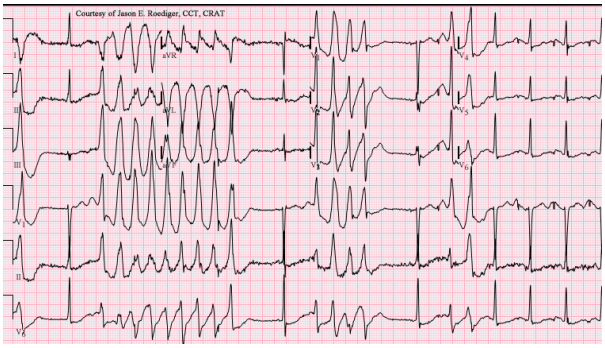


Definition from Wikipedia for Torsades de Pointes (TdP):

Torsades de pointes, **torsade de pointes** or **torsades des pointes** (**TdP**) (French: translated as "twisting of peaks") is a specific type of abnormal heart rhythm that can lead to sudden cardiac death. It is a polymorphic ventricular tachycardia that exhibits distinct characteristics on the electrocardiogram (ECG). It was described by the French physician François Dessertenne in 1966. Prolongation of the QT interval can increase a person's risk of developing this abnormal heart rhythm.



Scheme for the development of TdP



View of TdP in the ECG

Literature source reference:
Abstract: Psychopharmacaassociated QTc-Interval Prolongation and Torsade de Pointes
Wenzel-Seifert, Katharina; Wittmann, Markus; Haen, Ekkehard
published by Dr. med. Katharina Wenzel-Seifert, Klinische Pharmakologie, Klinik und Poliklinik für Psychiatrie, Psychosomatik und Psychotherapie der Universität Regensburg Universitätstraße 84, 93053 Regensburg, Fassung vom 10.03.2011

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