Syncope dilemma's:

a 16 year old with a 480ms QTc

Venice Arrhythmias 2015

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Disclosures

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MY CONFLICTS OF INTEREST ARE:

None

The case

A 16 year old female

with a history of abrupt TLOC without warning supine or upright, with or without exertion.

The corrected QT is 480.

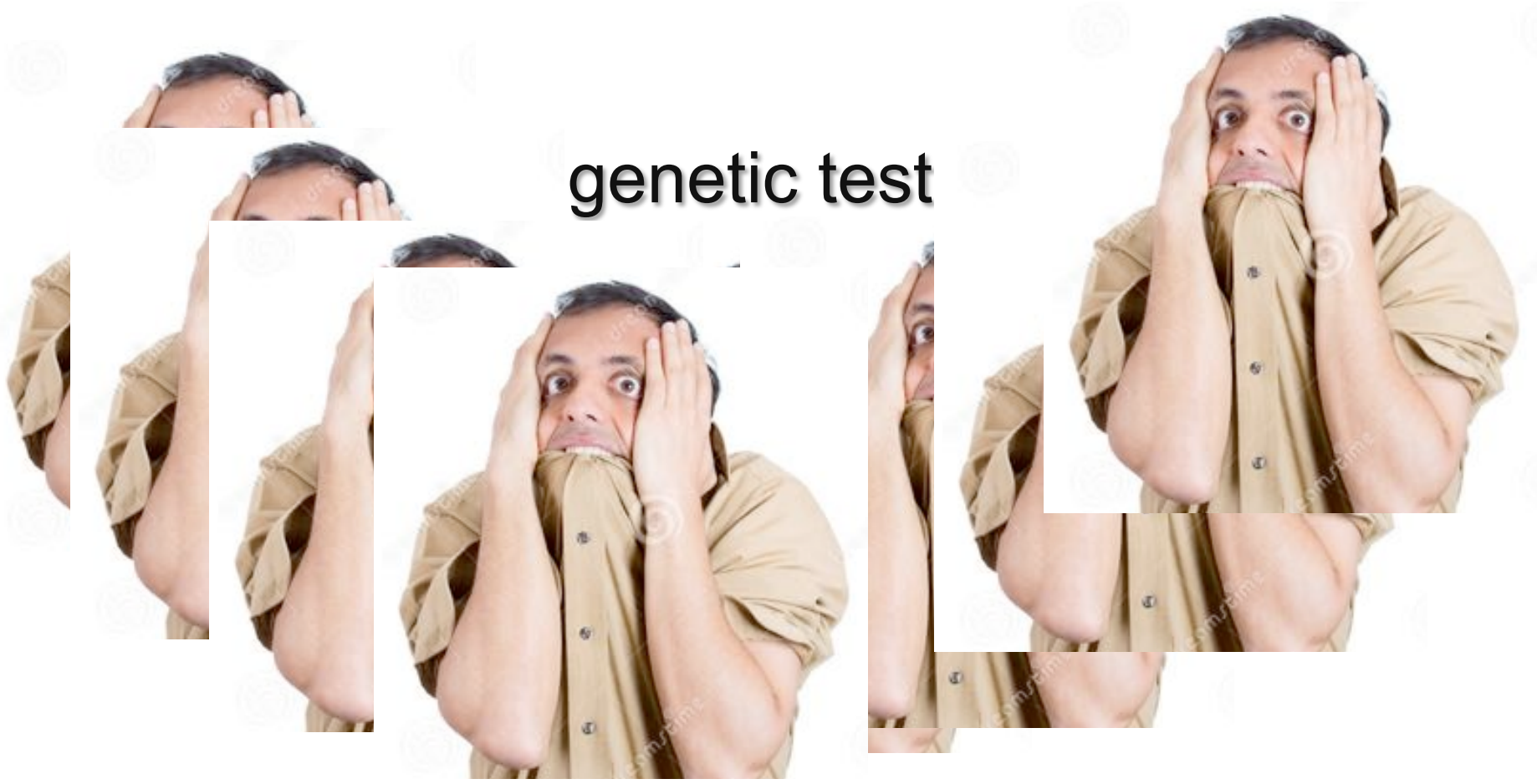
She has a family history of faints on her mother's side.

What is the next step? Genetic testing?

The easy way out?

- Sure, do some genetic test …

The easy way out?

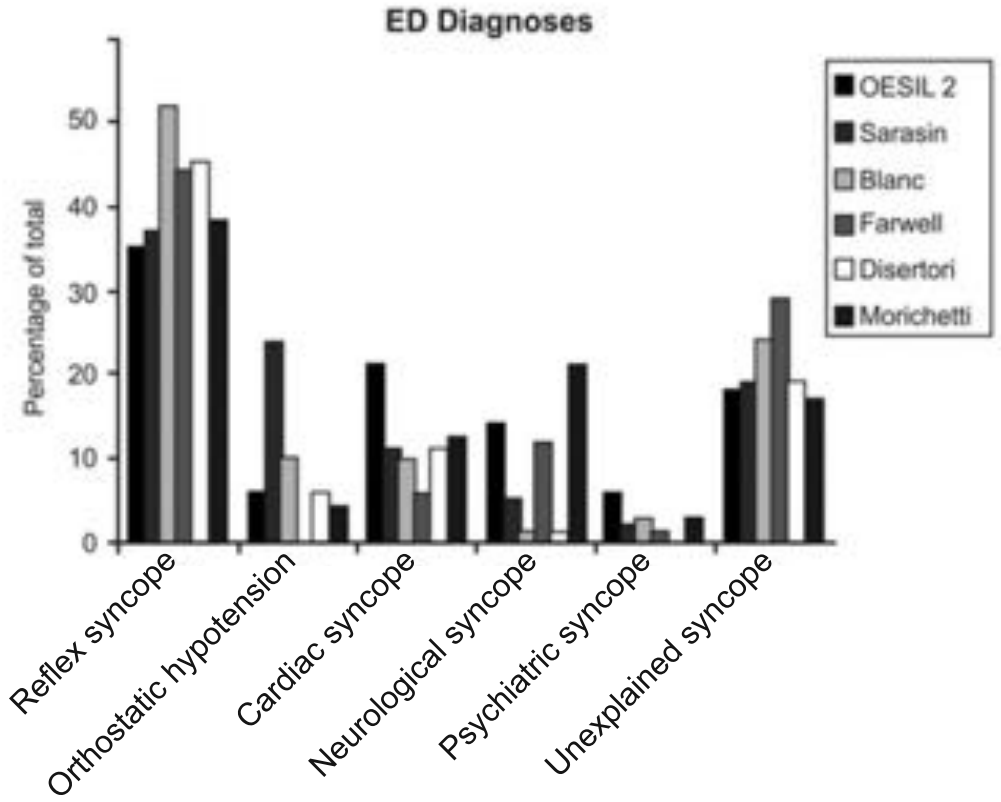


What is in there?

- History taking TLOC
- Determination of the abnormal/LQTS QT
- Value of family history
- Genetic testing as *THE* next step

History taking TLOC

- Prevalence of syncope/TLOC in the young
  - Estimates ranging from 15-40% (!)



Brignole ea. Europace 2004, Ganzeboom ea. Am J Cardiol 2003, Colman ea. Europace 2009, Wieling ea. EHJ 2015

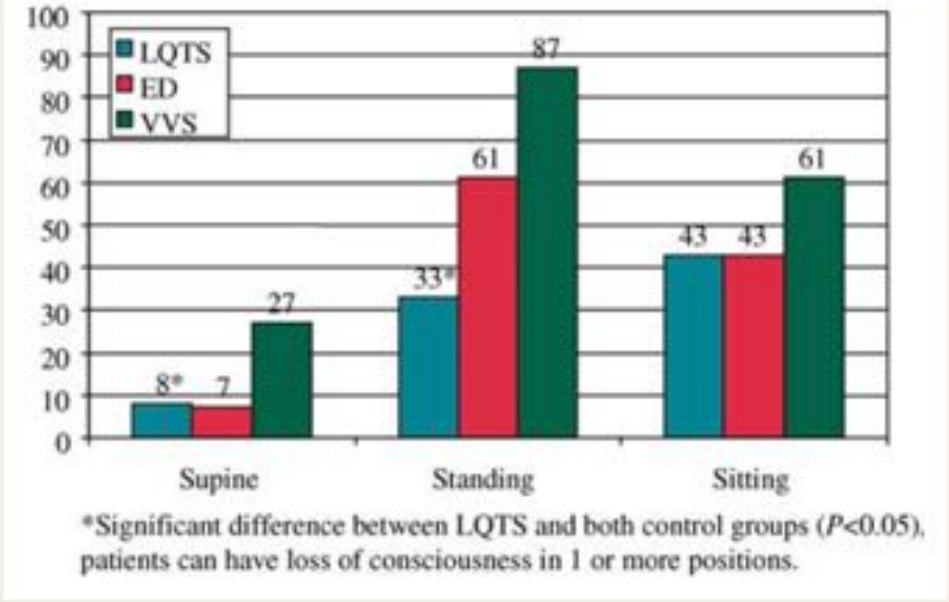
A few key features

Table 1 Skill set of syncope experts

Basic
Listen to the patient and take enough time. Put the patient at ease.
Be face-to-face with the patient. Seek unspoken clues.
Build with the patient rather than take a history from the patient
Details
Determine the timelines of symptoms; how did the day progress?
Expand the timeline with the story of one or more witnesses
What medications might have played a role?
Seek a witness. Obtain a video of an episode.
Overall
Build hypotheses, practice pattern recognition, develop illness scripts
Use analytic reasoning to check intuitive thinking
Development
Learn and invoke circulatory physiology that may contribute to T-LOC
Reflect on the skill set used in each syncope patient, and on what it would take to expand it.
Learn to read beat-to-beat heart rate and blood pressure tracings like an ECG.

Wieling ea. EHJ 2015

What's in that trigger?



*Significant difference between LQTS and both control groups ($P<0.05$). patients can have loss of consciousness in 1 or more positions.

Figure 1 Percentages of patients with postural triggers.

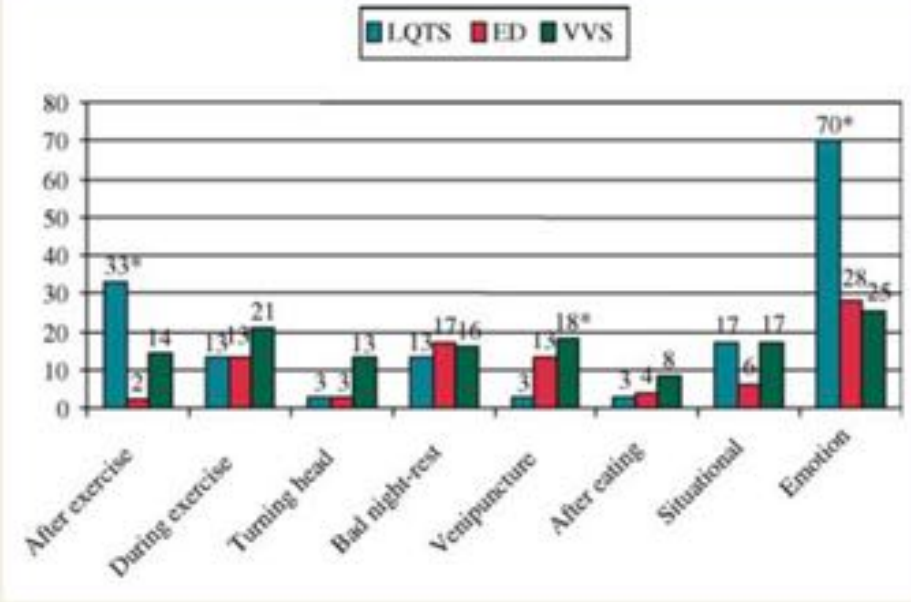


Figure 2 Percentages of patients with miscellaneous triggers.

Colman ea. Europace 2009

Does the (type of) TLOC matter?

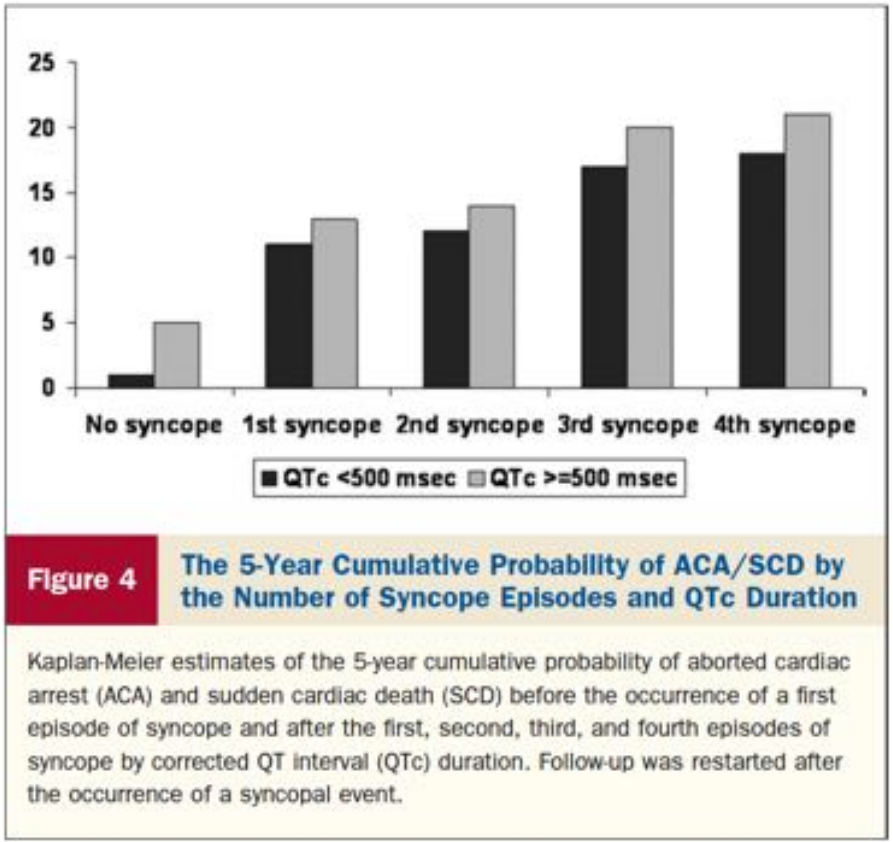


Figure 4 **The 5-Year Cumulative Probability of ACA/SCD by the Number of Syncope Episodes and QTc Duration**

Kaplan-Meier estimates of the 5-year cumulative probability of aborted cardiac arrest (ACA) and sudden cardiac death (SCD) before the occurrence of a first episode of syncope and after the first, second, third, and fourth episodes of syncope by corrected QT interval (QTc) duration. Follow-up was restarted after the occurrence of a syncopal event.

Age 0-20 years

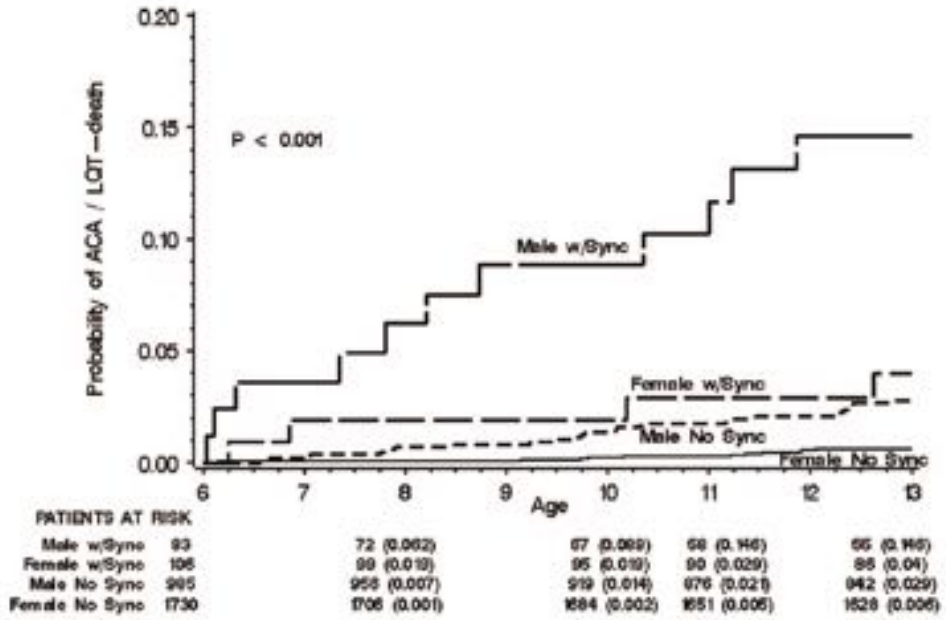
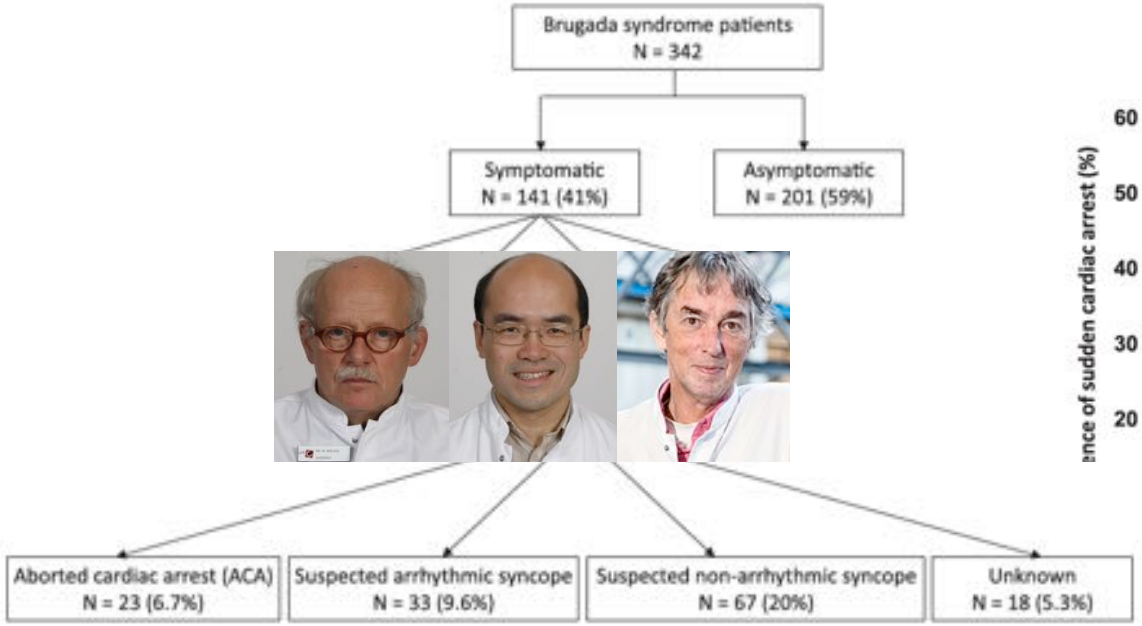
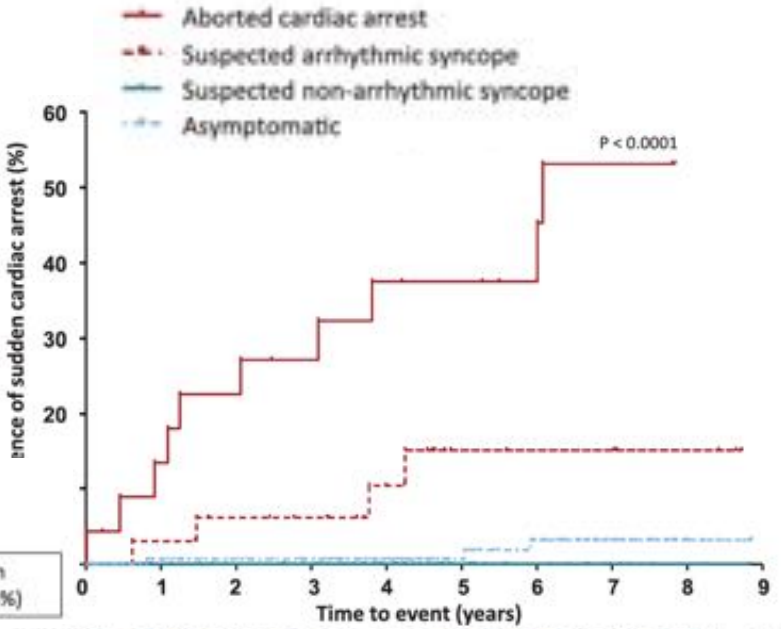


Figure 3. Kaplan–Meier estimates of the probability of ACA or SCD after 6 years of age by gender and a history of syncope before the sixth birthday (values in parentheses are event rates). W/Sync indicates with syncope.

Liu ea. JACC 2013, Goldenberg ea. Circ 2008

Does the (type of) TLOC matter?





ACA during follow-up occurred in 43% (10/23) ACA patients (8.7% per year) and in 12% (4/33) suspected arrhythmic syncope patients (2.2% per year). ACA did not occur in suspected nonarrhythmic syncope patients. ACA occurred in 1.5% of patients (3/201) who were asymptomatic at diagnosis (0.3% per year). One of these patients (baseline type 1 BrS ECG) had a suspected arrhythmic syncope during follow-up, for which he received ICD placement and multiple appropriate ICD shocks 5 years later. The 2 other patients (no baseline type 1 BrS ECG) had suspected arrhythmic syncope and underwent implantable loop recorder placement, which recorded sustained VT in 1 (followed by ICD placement), and symptomatic AV block and sinus node dysfunction in the other (followed by pacemaker implantation).

Olde Nordkamp ea. Heart Rhythm 2014

TLOC and QT

This misinterpretation of vasovagal symptoms as being consistent with congenital LQTS was particularly accentuated for patients with "borderline" findings on ECG. More than one third (35%) of patients found in our clinic to have No-LQTS had a history of a vasovagal "spell" (including near-syncope) and a QTc <460 ms.

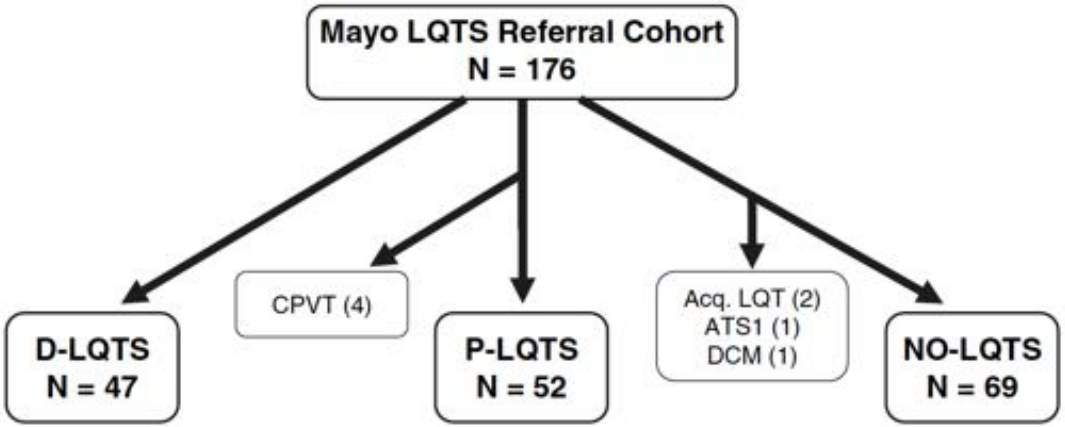


Figure 2. Diagnostic outcome of LQTS referral cohort. CPVT indicates catecholaminergic polymorphic ventricular tachycardia; ATS1, type 1 Andersen-Tawil syndrome; and DCM, dilated cardiomyopathy.

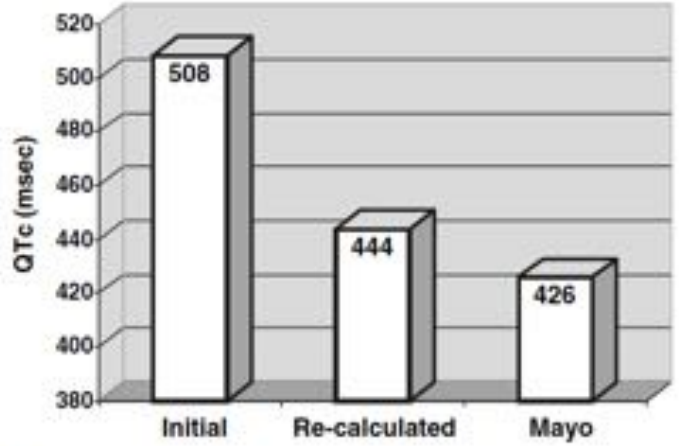
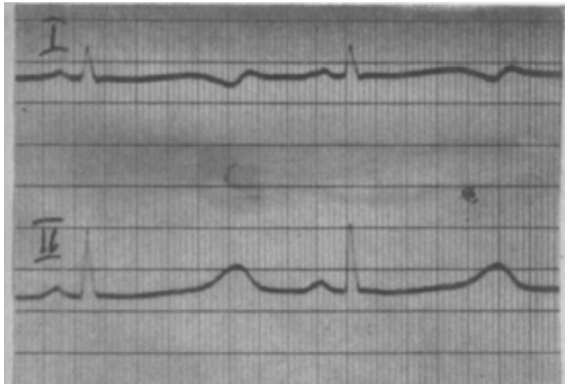


Figure 3. Overestimation of QTc among patients in the No-LQTS cohort.

Taggart ea. Circ 2007

Recognizing the abnormal QT



I find it tempting to say that, when dealing with a possible case of long QT syndrome, one does not measure the QT interval, one looks at it.

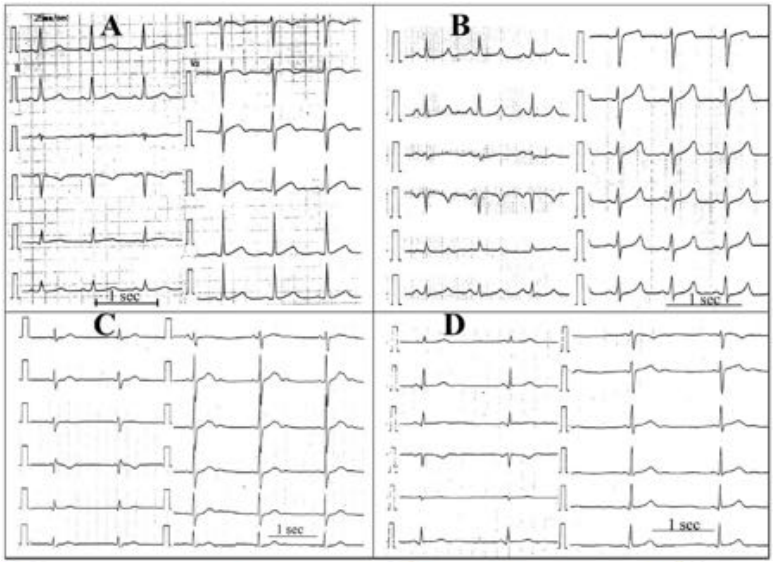
Peter J. Schwartz, 1989

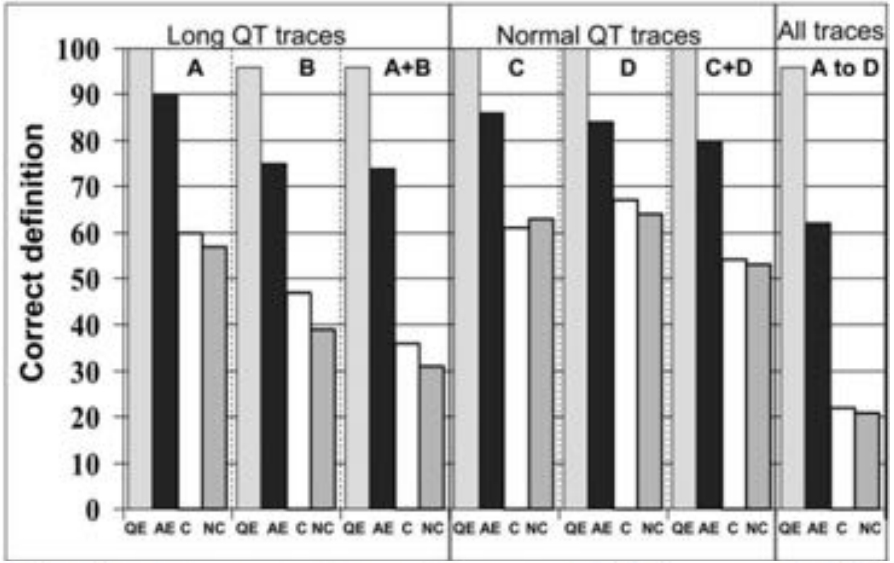
Inaccurate electrocardiographic interpretation of long QT: The majority of physicians cannot recognize a long QT when they see one

Sami Viskin, MD,* Uri Rosovski, MD,* Andrew J. Sands, MPhil, MB, BCh,†

Jervell & Lange-Nielsen AHJ 1957, Schwartz 1989, Viskin ea. Heart Rhythm 2005

Recognizing the abnormal QT





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Viskin ea. Heart Rhythm 2005

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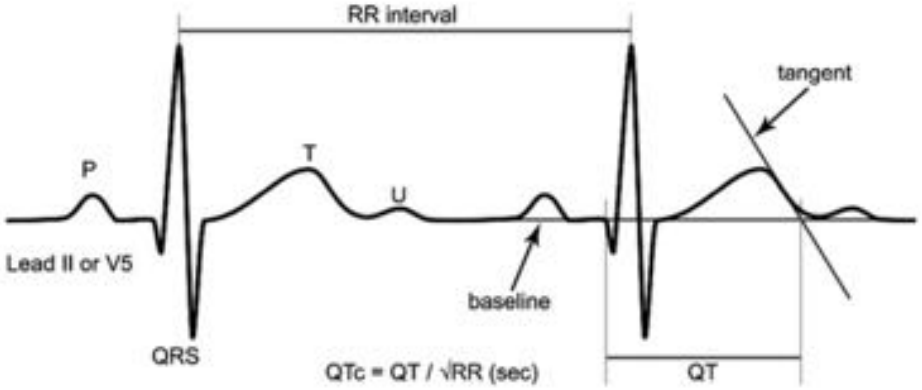
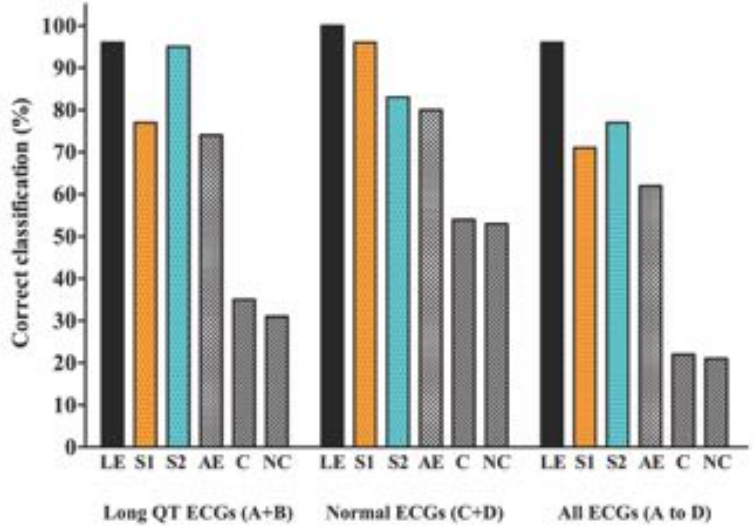


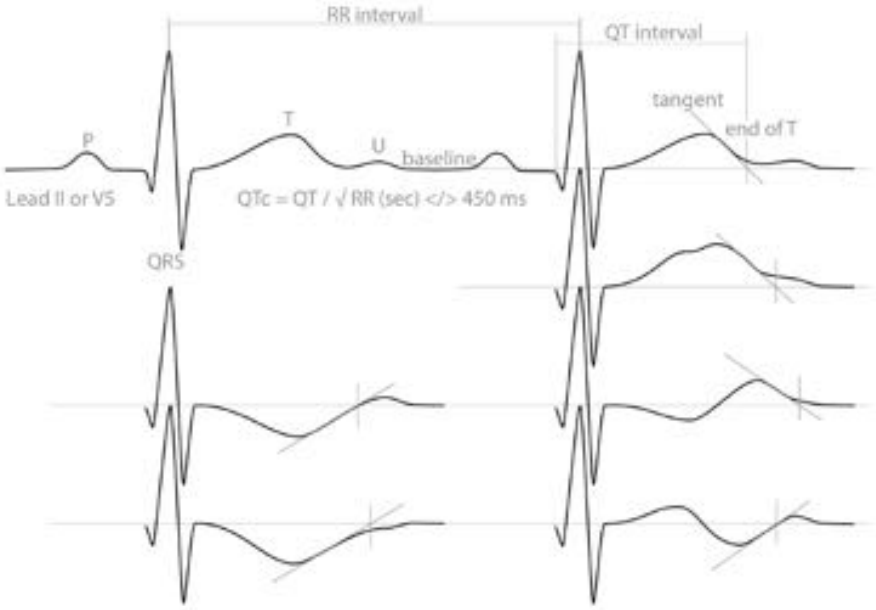


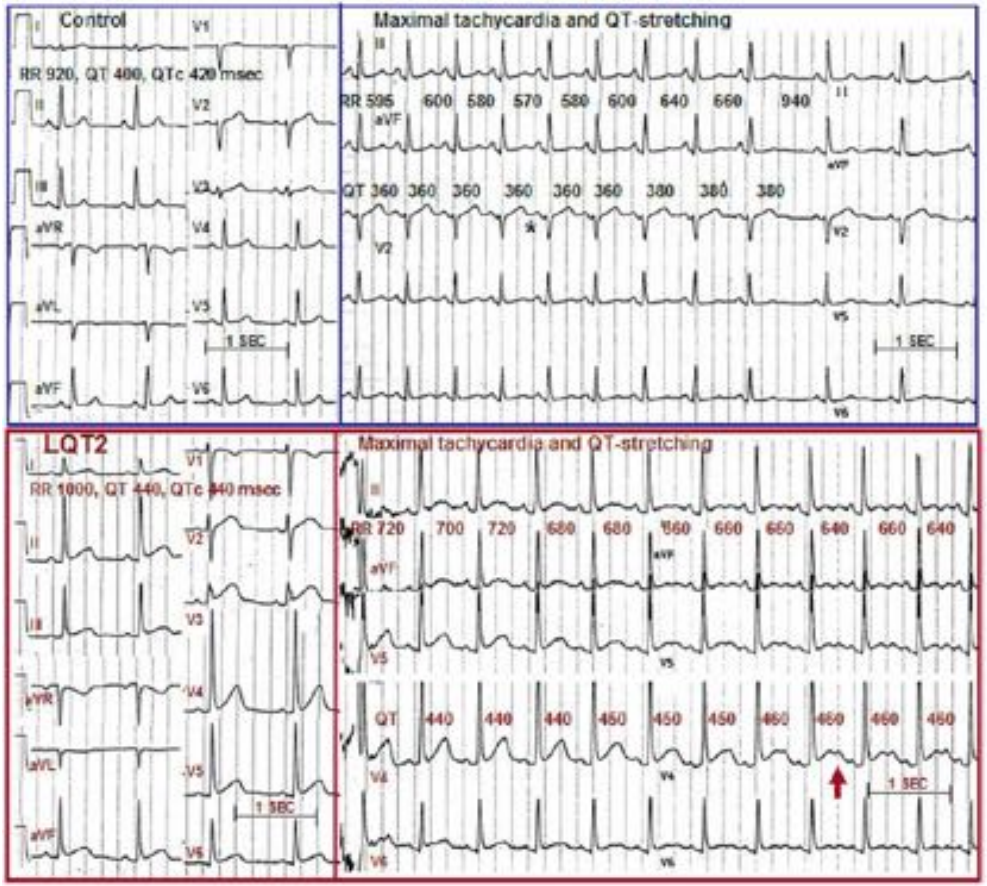
Accurate electrocardiographic assessment of the QT interval: Teach the tangent

Pieter G. Postema, MD, Jonas S.S.G. De Jong, MD, Ivo A.C. Van der Bilt, MD, Arthur A.M. Wilde, MD, PhD

Postema ea. Heart Rhythm 2008

Recognizing the abnormal QT





Postema ea. Curr Cardiol Rev 2014, Viskin ea. JACC 2010

Diagnosing LQTS

Table I 1993–2012 long QT syndrome diagnostic criteria

			Points
Electrocardiographic findings[a]			
A	QTc[b]	≥480 ms	3
		460–479 ms	2
		450–459 (male) ms	1
B	QTc[b] 4th minute of recovery from exercise stress test ≥480 ms		1
C	Torsade de pointes[c]		2
D	T-wave alternans		1
E	Notched T-wave in three leads		1
F	Low heart rate for age[d]		0.5
Clinical history			
A	Syncope[c]	With stress	2
		Without stress	1
B	Congenital deafness		0.5
Family history			
A	Family members with definite LQTS[e]		1
B	Unexplained sudden cardiac death below age 30 among immediate family members[e]		0.5

SCORE: ≤1 point: low probability of LQTS. 1.5 to 3 points: intermediate probability of LQTS. ≥3.5 points high probability.
[a]In the absence of medications or disorders known to affect these electrocardiographic features.
[b]QTc calculated by Bazett's formula where QTc = QT/√RR.
[c]Mutually exclusive.
[d]Resting heart rate below the 2nd percentile for age.
[e]The same family member cannot be counted in A and B (from ref.[13]).

2. Long QT Syndrome (LQTS)

Expert Consensus Recommendations on LQTS Diagnosis

1. LQTS is diagnosed:
   a. In the presence of an LQTS risk score ≥3.5 in the absence of a secondary cause for QT prolongation *and/or*
   b. In the presence of an unequivocally pathogenic mutation in one of the LQTS genes *or*
   c. In the presence of a QT interval corrected for heart rate using Bazett's formula (QTc) ≥500 ms in repeated 12-lead electrocardiogram (ECG) and in the absence of a secondary cause for QT prolongation.
2. LQTS can be diagnosed in the presence of a QTc between 480–499 ms in repeated 12-lead ECGs in a patient with unexplained syncope in the absence of a secondary cause for QT prolongation and in the absence of a pathogenic mutation.

Diagnosis of Long QT Syndrome (in the absence of secondary causes for QT prolongation)

Recommendations	Class[a]	Level[b]	Ref.[c]
LQTS is diagnosed with either – QTc ≥480 ms in repeated 12-lead ECGs or – LQTS risk score >3.[431]	I	C	This panel of experts
LQTS is diagnosed in the presence of a confirmed pathogenic LQTS mutation, irrespective of the QT duration.	I	C	This panel of experts
ECG diagnosis of LQTS should be considered in the presence of a QTc ≥460 ms in repeated 12-lead ECGs in patients with an unexplained syncopal episode in the absence of secondary causes for QT prolongation.	IIa	C	This panel of experts

ECG = electrocardiogram; LQTS = long QT syndrome; QTc = corrected QT.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Schwartz and Ackerman EHJ 2013, Priori ea. Heart Rhythm 2013, Priori ea. Europace 2015

What about the family history?

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Clinical history			
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And what about genetic testing?

Table 1 Summary of Expert Consensus Recommendations

STATE OF GENETIC TESTING FOR LONG QT SYNDROME (LQTS)

Class I (is recommended)

Comprehensive or LQT1-3 (*KCNQ1*, *KCNH2*, and *SCN5A*) targeted LQTS genetic testing is recommended for any patient in whom a cardiologist has established a strong clinical index of suspicion for LQTS based on examination of the patient's clinical history, family history, and expressed electrocardiographic (resting 12-lead ECGs and/or provocative stress testing with exercise or catecholamine infusion) phenotype.

Comprehensive or LQT1-3 (*KCNQ1*, *KCNH2*, and *SCN5A*) targeted LQTS genetic testing **is recommended** for any asymptomatic patient with QT prolongation in the absence of other clinical conditions that might prolong the QT interval (such as electrolyte abnormalities, hypertrophy, bundle branch block, etc., i.e., otherwise idiopathic) on serial 12-lead ECGs defined as QTc >480 ms (prepuberty) or >500 ms (adults).

Mutation-specific genetic testing **is recommended** for family members and other appropriate relatives subsequently following the identification of the LQTS-causative mutation in an index case.

Class IIb (may be considered)

Comprehensive or LQT1-3 (*KCNQ1*, *KCNH2*, and *SCN5A*) targeted LQTS genetic testing **may be considered** for any asymptomatic patient with otherwise idiopathic QTc values >460 ms (prepuberty) or >480 ms (adults) on serial 12-lead ECGs.

Ackerman ea. Heart Rhythm 2011

In conclusion

A 16 year old female

with a history of abrupt TLOC without warning supine or upright, with or without exertion.

The corrected QT is 480.

She has a family history of faints on her mother's side.

What is the next step? Genetic testing?

In conclusion

Many thanks

for your kind attention

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