Jak na primární elektrické syndromy

Peter Kubuš

Dětské kardiocentrum 2. LF UK
v Praze a FN v Motole, Praha

European Heart Journal (2011) **32**, 983–990
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Nationwide study of sudden cardiac death in persons aged 1–35 years

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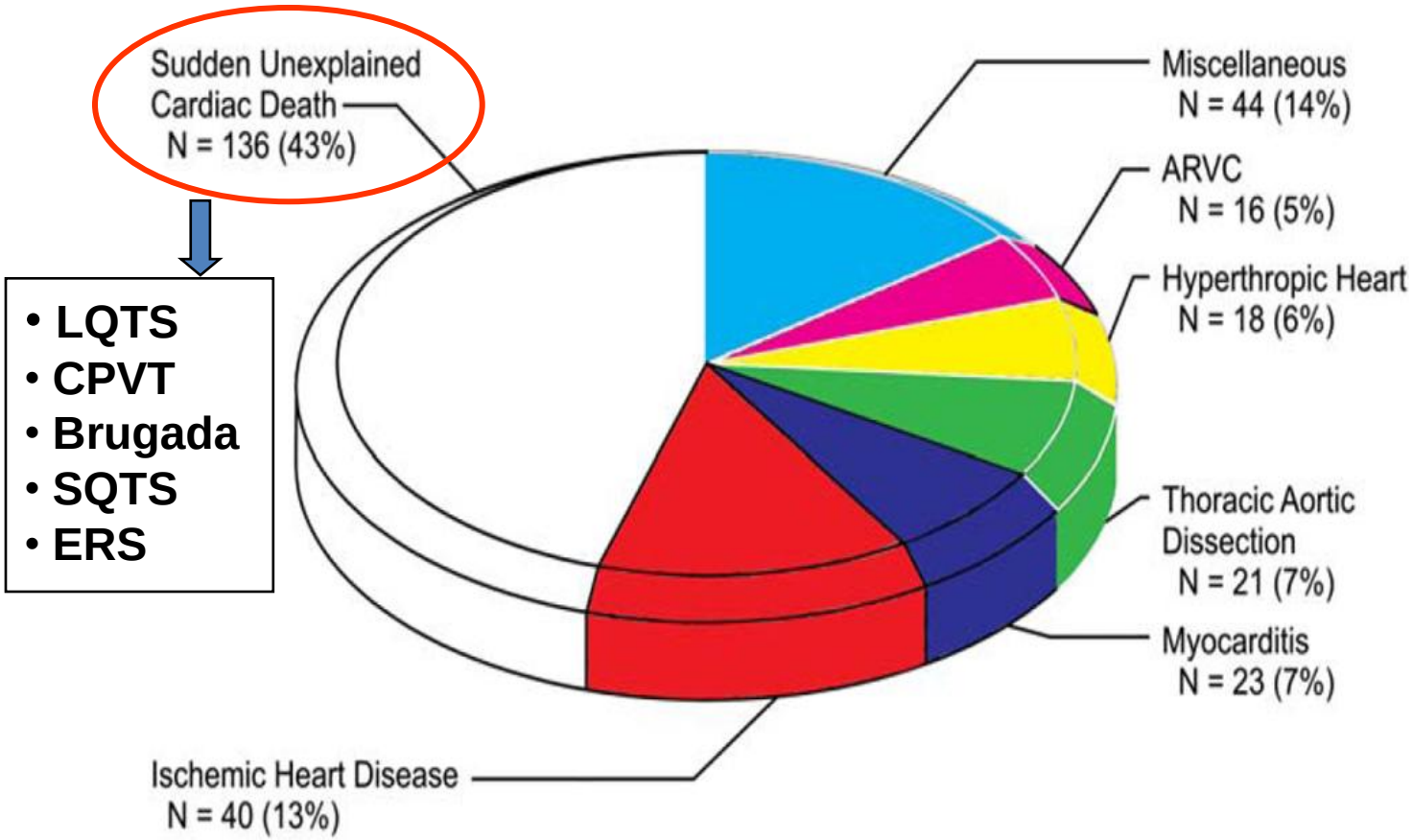

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HRS/EHRA EXPERT CONSENSUS STATEMENT

HRS/EHRA Expert Consensus Statement on the State of Genetic Testing for the Channelopathies and Cardiomyopathies

This document was developed as a partnership between the Heart Rhythm Society (HRS) and the European Heart Rhythm Association (EHRA)

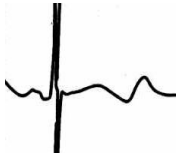
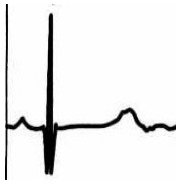
Ackerman MJ et al.

Table 2 Summary of Common Cardiac Channelopathy/Cardiomyopathy-Associated Genes (>5% of Disease)

Gene	Locus	Protein	% of Disease
Section I – Long QT Syndrome (LQTS)			
KCNQ1 (LQT1)	11p15.5	I_{Ks} potassium channel alpha subunit (Kv7.1)	30%–35%
KCNH2 (LQT2)	7q35-q36	I_{Kr} potassium channel alpha subunit (Kv11.1 or hERG)	25%–40%
SCN5A (LQT3)	3p21	Cardiac sodium channel alpha subunit (NaV1.5)	5%–10%
Section II – Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)			
RYR2 (CPVT1)	1q42.1-q43	Ryanodine receptor 2	60%
Section III – Brugada Syndrome (BrS)			
SCN5A	3p21	Cardiac sodium channel alpha subunit (NaV1.5)	20%–30%
Section IV – Cardiac Conduction Disease (CCD)			
SCN5A	3p21	Cardiac sodium channel alpha subunit (NaV1.5)	5%

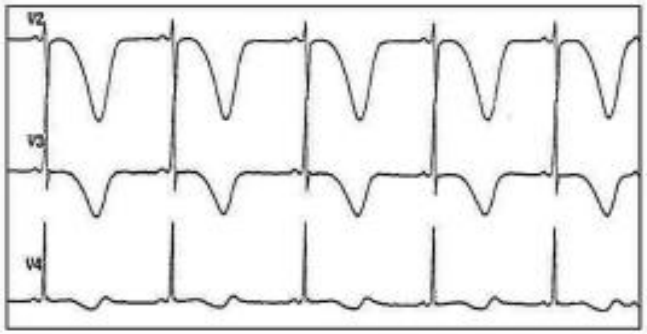
Syndrom dlouhého QT intervalu (LQTS)

(příslušné geny identifikovány v ~ 75 % případů)

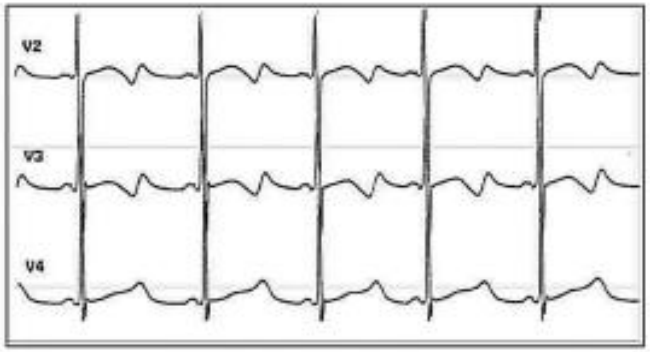
Typ	Gen/Chromozom	Iontový kanál	Distrib.	T vlna	Spouštěč
LQT1	*KvLQT1* / 11	Slowly activating delayed rectifier current Iks	54 %		zátěž emoce
LQT2	*HERG* / 7	Rapidly activating delayed rectifier current Ikr	35 %		zátěž emoce
LQT3	*SCN5A* / 3	Defective Na channel with repetitive reopenings	10 %		spánek klid zvuky
LQT4	*?* / 4				
LQT5	*KCNE1, minK* / 21				
LQT6	*KCNE2, MiRP1*/21				

Měření QT

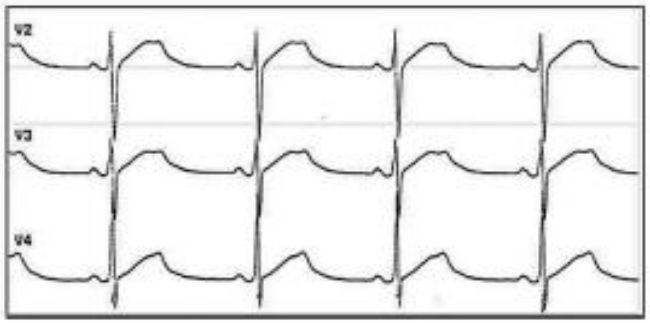
PROBAND
G.T., 7 yrs
QTc = 630 ms



SISTER
S.T., 10 yrs
QTc = 605 ms



FATHER
V.T., 37 yrs
QTc = 584 ms



QTc Behavior During Exercise and Genetic Testing for the Long-QT Syndrome

Peter J. Schwartz, MD; Lia Crotti, MD, PhD

Figure. Different T wave morphologies in affected members of the same family. The proband had a documented cardiac arrest as first manifestation of LQTS. His sister is still asymptomatic, whereas his father has had 2 syncopal episodes. From: Schwartz PJ, Priori SG, Napolitano C. The long-QT syndrome. In: Zipes DP, Jalife J, eds. *Cardiac Electrophysiology: From Cell to Bedside.* 3rd ed. Philadelphia: WB Saunders Co. 2000:597–615. Reproduced with permission. Copyright © 2000, Elsevier.

LQTS Klinická manifestace

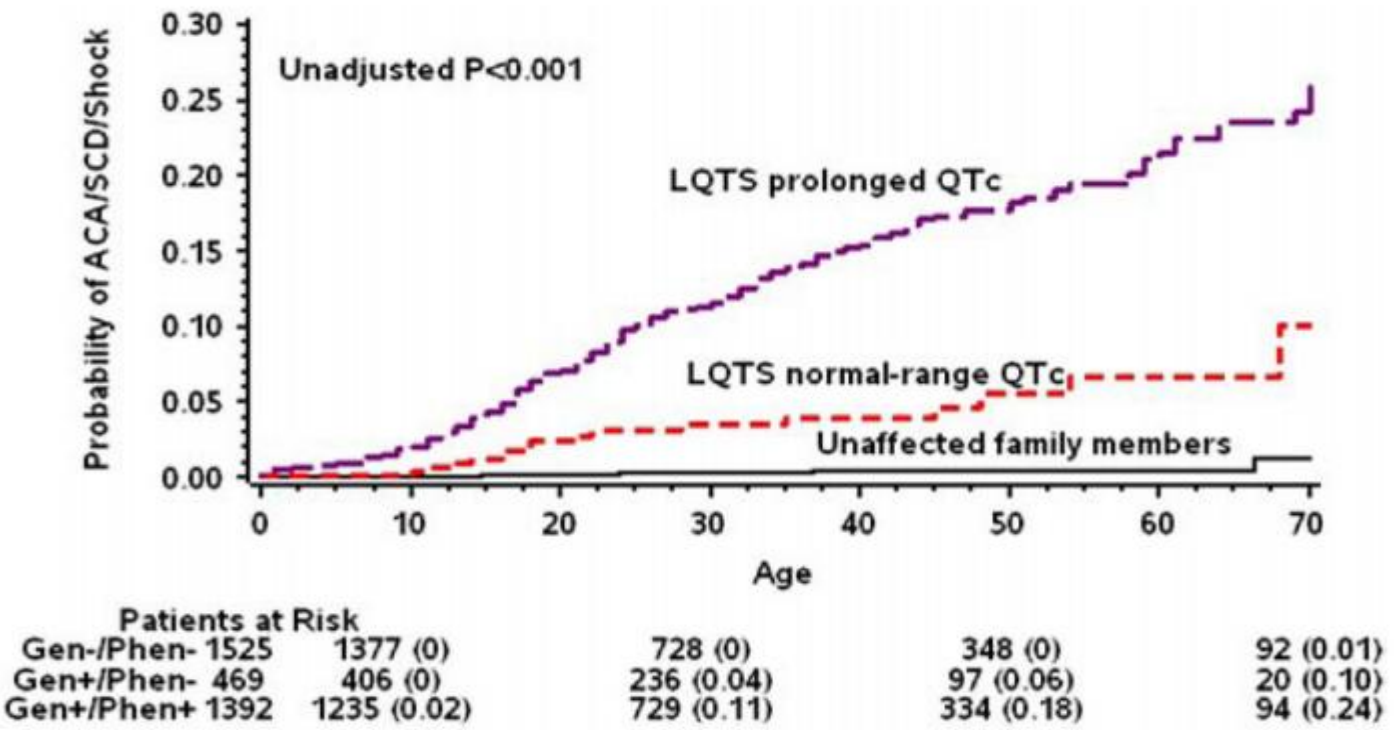
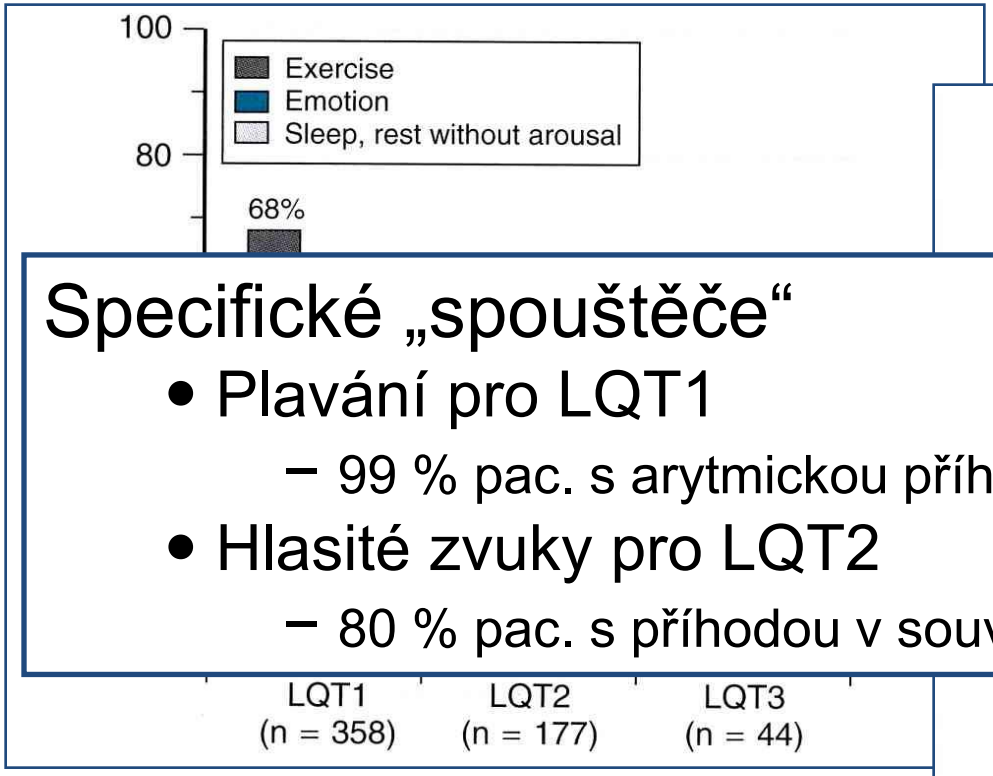


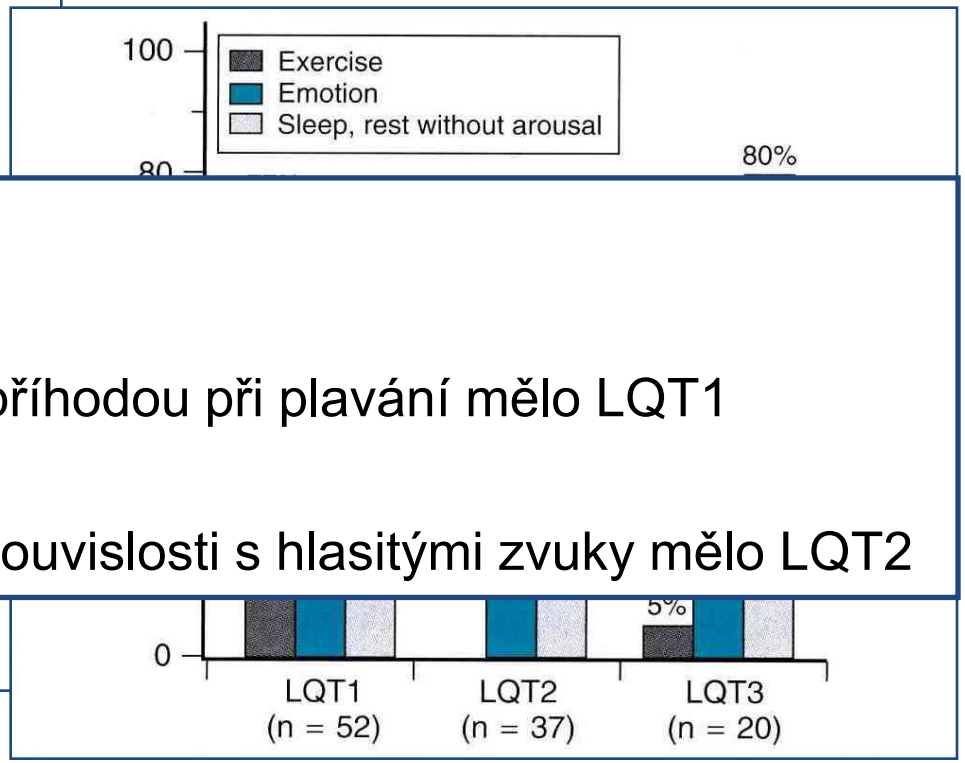
Figure 2. Rate of ACA or SCD by Genotype and QTc Category
Kaplan-Meier cumulative probabilities of aborted cardiac arrest (ACA) and sudden cardiac death (SCD) by genotype and corrected QT (QTc) subgroup. LQTS = long-QT syndrome.

[3]Goldenberg I et al. JACC 2011

Spouštěcí faktory arytmických příhod u LQTS



Všechny arytmické příhody
(letální i non-letální)



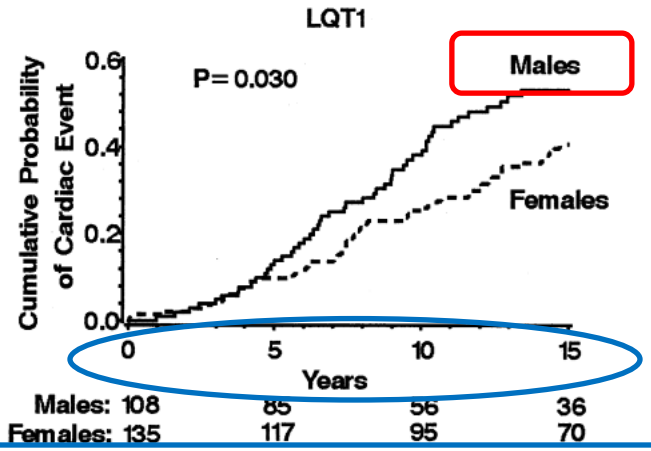
Jen letální arytmické příhody

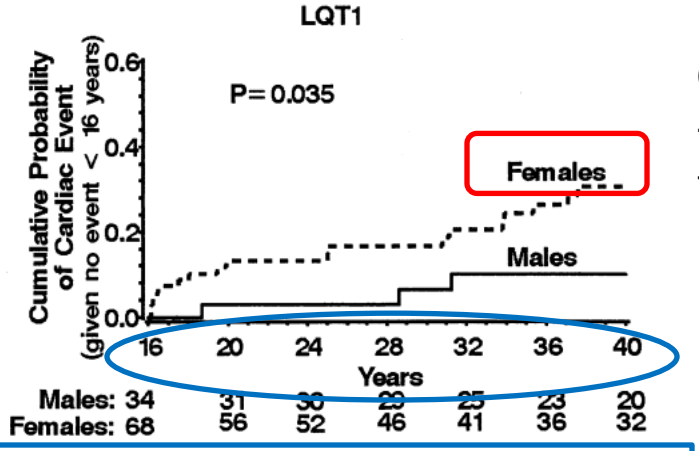
Specifické „spouštěče“

- Plavání pro LQT1
  - 99 % pac. s arytmickou příhodou při plavání mělo LQT1
- Hlasité zvuky pro LQT2
  - 80 % pac. s příhodou v souvislosti s hlasitými zvuky mělo LQT2

Schwartz PJ et al. Circulation 2001

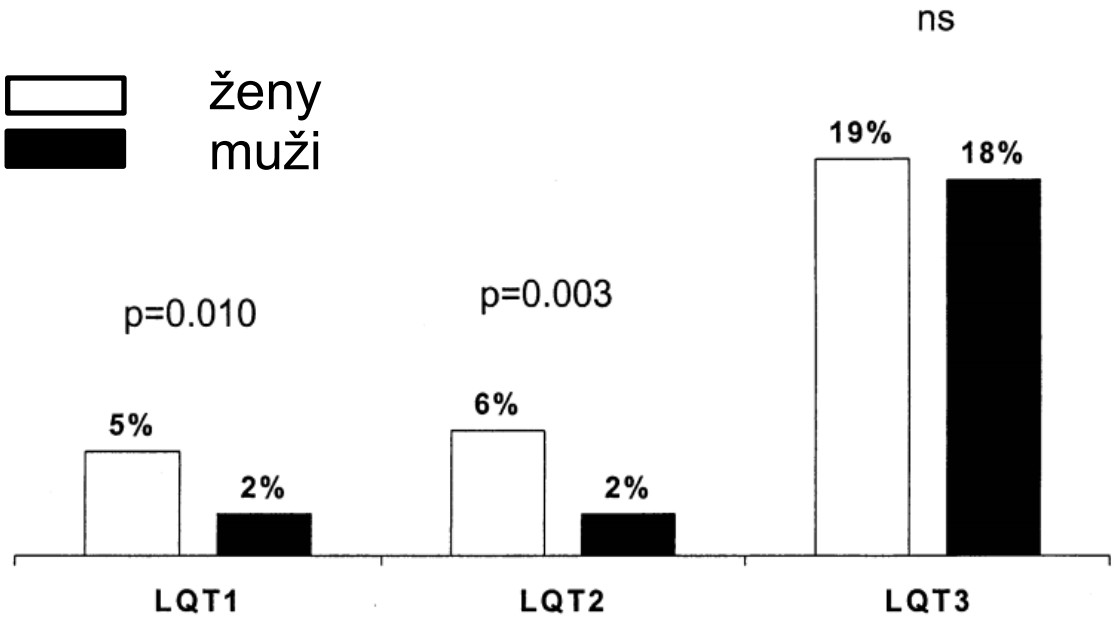
LQT 1





Cardiac event:
- Synkopa/ACA
- SCD

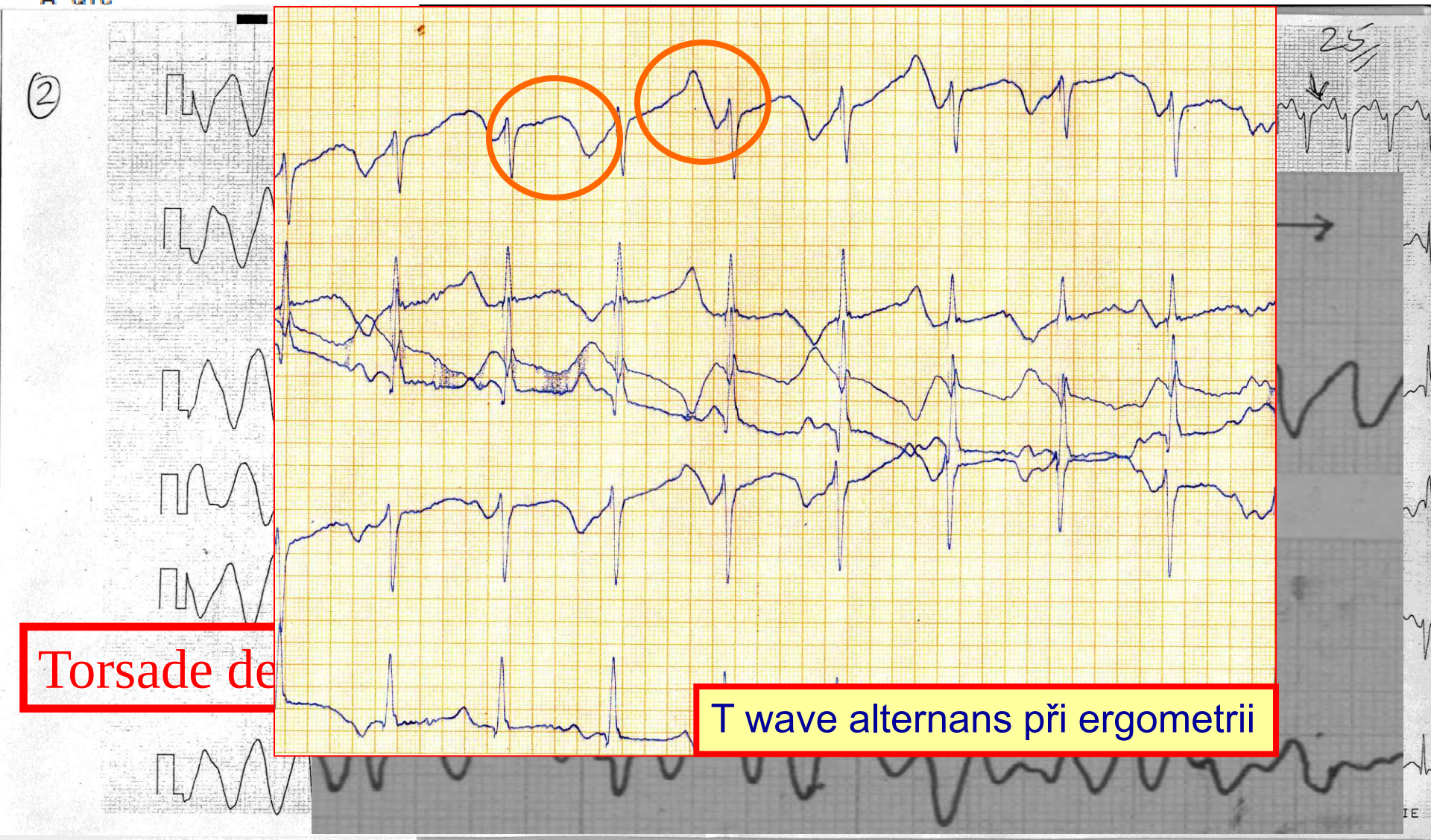
Úmrtí při první příhodě



Zareba W et al.
JACC, 2003

Table 2. 1993–2011 LQTS Diagnostic Criteria

	Points
Electrocardiographic findings #	
A QTc*	



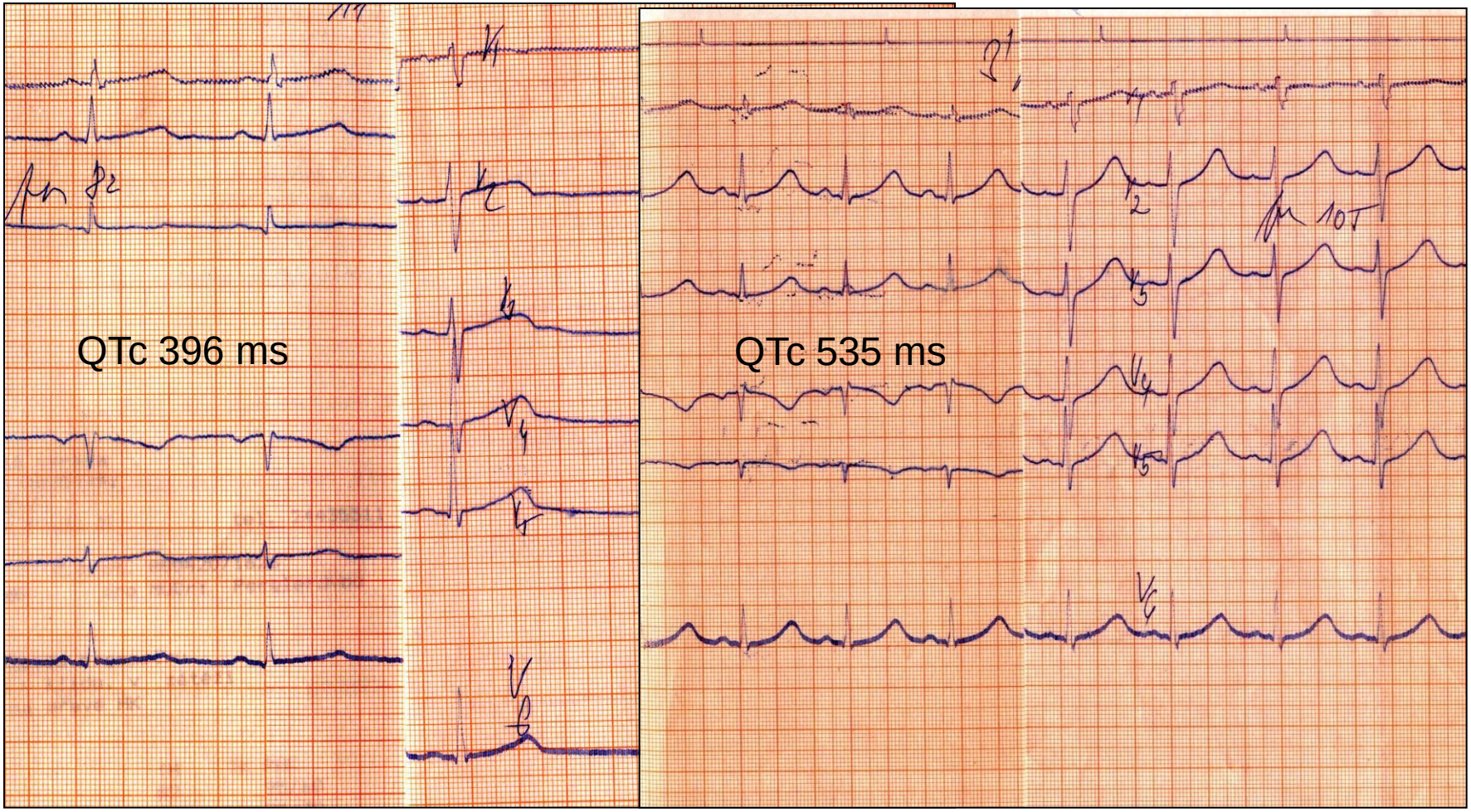
Torsade de

T wave alternans při ergometrii

LQTS: ergometrie

Klidové EKG

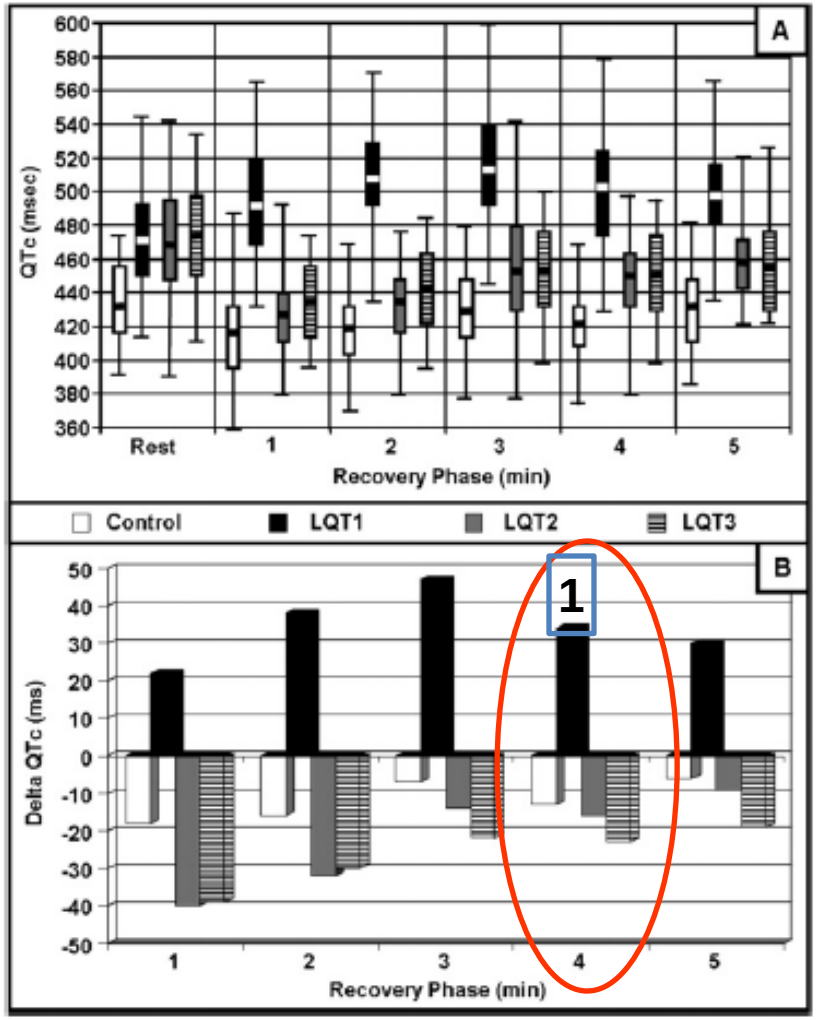
3. min. zotavné fáze



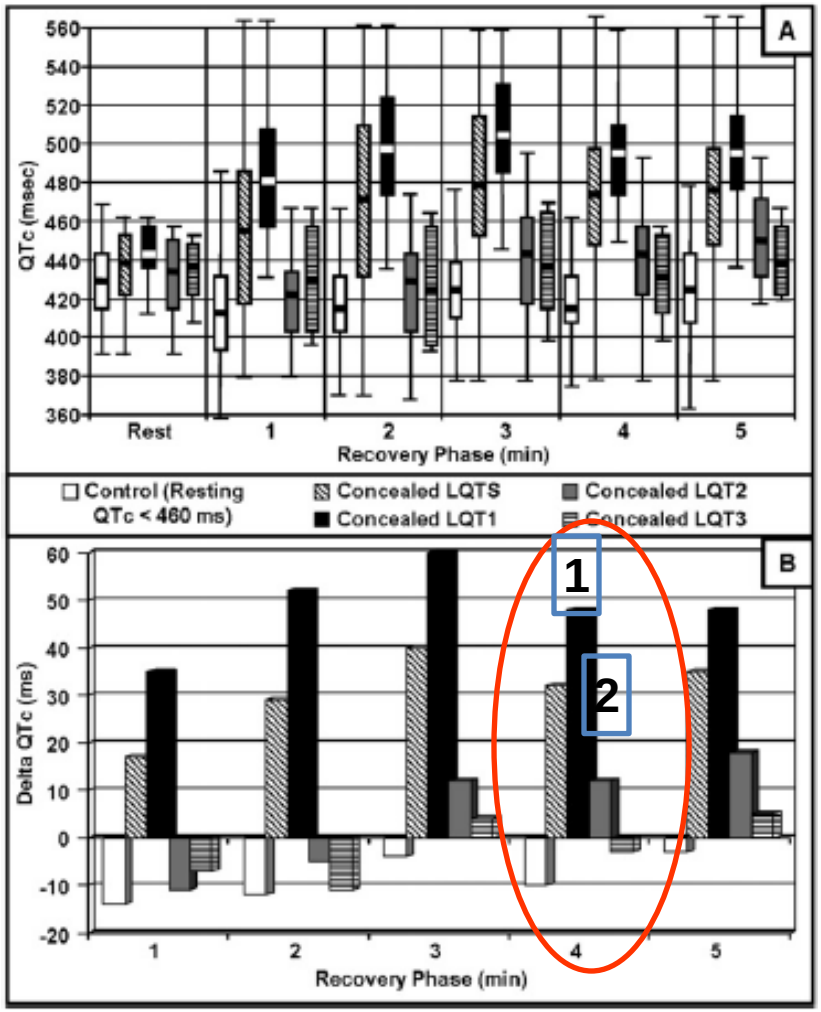
3. – 7. min. zotavné fáze!

LQTS: ergometrie
zotavná fáze

LQTS



Concealed LQTS



ΔQTc

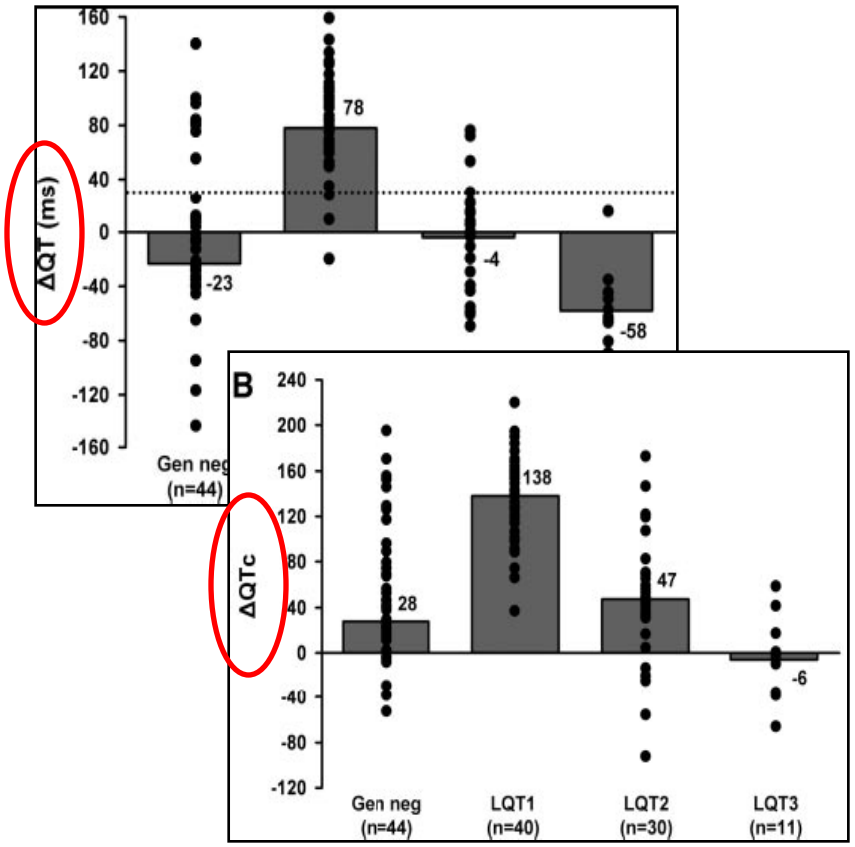
zotavení (min.)

Horner et al., Heart Rhythm, 2011

LQTS: adrenalinový test

Dávka: 0,025 – 0,1 μg/kg/min

- LQT1
  - Prodloužení QT ≥ 30 ms
    - Pozitivní prediktivní hodnota 76 %
    - Negativní prediktivní hodnota 96 %
- LQT2
  - Dikrotické T vlny s T2 > T1



Priori SG et al. NEJM 2003
Ackermann MJ et al. Mayo Clin Proc 2002
Vyas H et al. Circulation 2006
Khositseth A et al. Heart Rhythm 2005

European Heart Journal (2015) 36, 2793–2867
doi:10.1093/eurheartj/ehv316

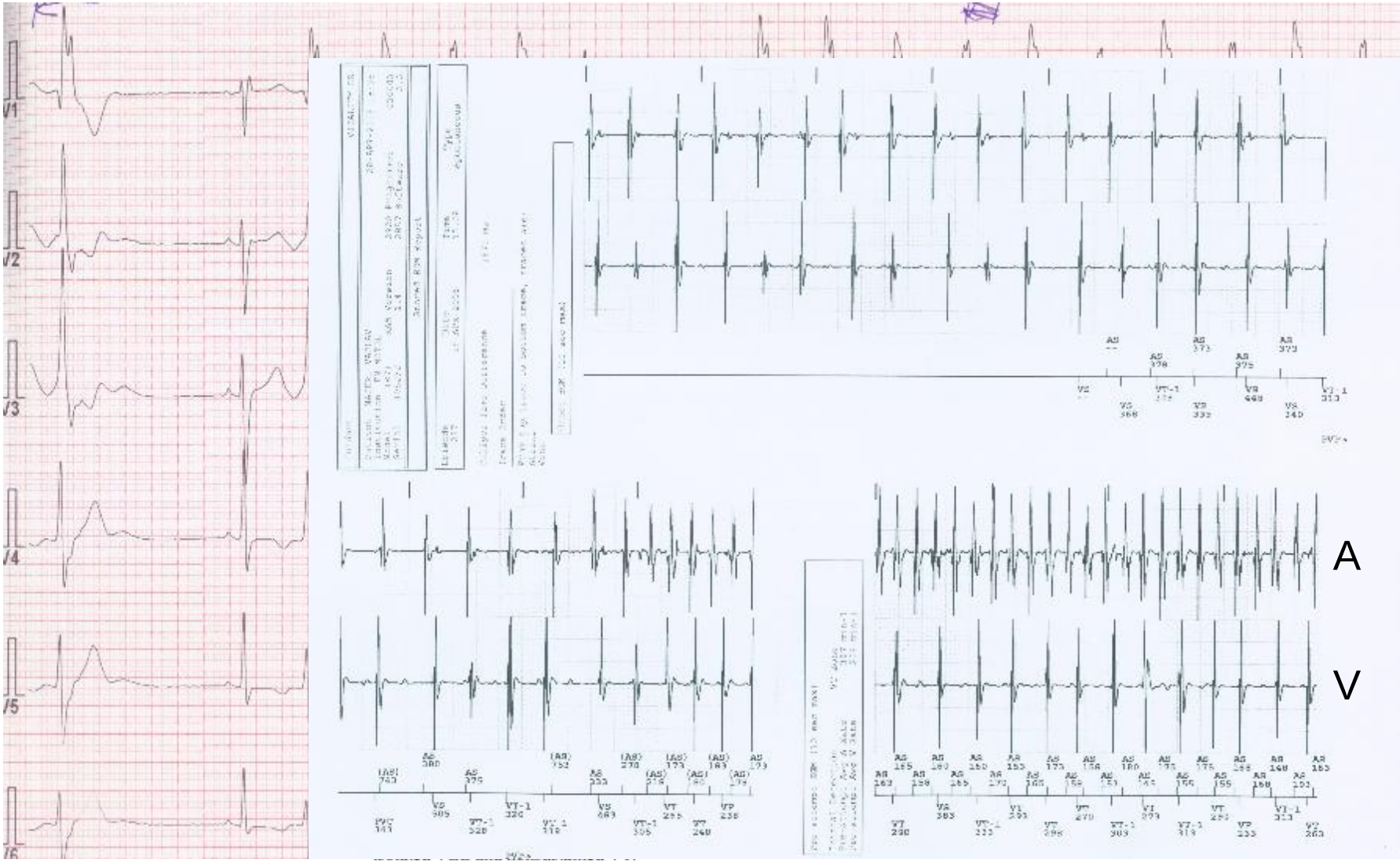
2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Priori SG et al.

Risk stratification and management in Long QT Syndrome

Recommendations	Class[a]	Level[b]	Ref.[c]
The following lifestyle changes are recommended in all patients with a diagnosis of LQTS: (a) Avoidance of QT-prolonging drugs (http://www.crediblemeds.org). (b) Correction of electrolyte abnormalities (hypokalaemia, hypomagnesaemia, hypocalcaemia) that may occur during diarrhoea, vomiting or metabolic conditions. (c) Avoidance of genotype-specific triggers for arrhythmias (strenuous swimming, especially in LQTS1, and exposure to loud noises in LQTS2 patients).	I	B	434
Beta-blockers are recommended in patients with a clinical diagnosis of LQTS.	I	B	435
ICD implantation with the use of beta-blockers is recommended in LQTS patients with previous cardiac arrest.	I	B	436–438
Beta-blockers should be considered in carriers of a causative LQTS mutation and normal QT interval.	IIa	B	67
ICD implantation in addition to beta-blockers should be considered in LQTS patients who experienced syncope and/or VT while receiving an adequate dose of beta-blockers.	IIa	B	439
Left cardiac sympathetic denervation should be considered in patients with symptomatic LQTS when (a) Beta-blockers are either not effective, not tolerated or contraindicated; (b) ICD therapy is contraindicated or refused; (c) Patients on beta-blockers with an ICD experience multiple shocks.	IIa	C	440
Sodium channel blockers (mexiletine, flecainide or ranolazine) may be considered as add-on therapy to shorten the QT interval in LQTS3 patients with a QTc >500 ms.	IIb	C	441–443
Implant of an ICD may be considered in addition to beta-blocker therapy in asymptomatic carriers of a pathogenic mutation in *KCNH2* or *SCN5A* when QTc is >500 ms.	IIb	C	67

Katecholaminergní polymorfní komorová tachykardie (CPVT)



Europace (2017) 0, 1–7
doi:10.1093/europace/euw389

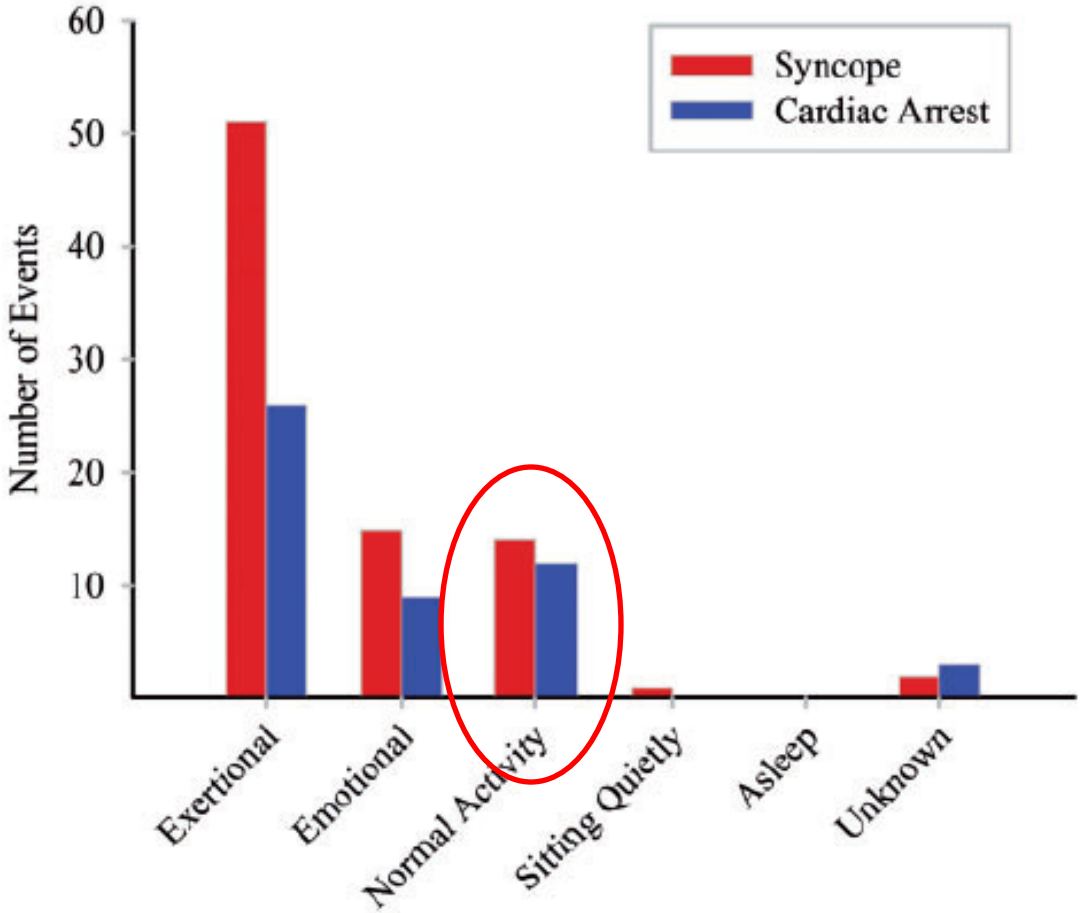


Figure 3 Circumstances immediately preceding all life-threatening events defined as syncope and/or cardiac arrest.

- N = 236
  - dg. CPVT < 19 let
  - příbuzní 1. st. s fenotypem CPVT

RyR2 mutace u 60 %

	Cardiac arrest events (n = 52)[a]
	8 (16%)
	11 (21%)
	12 (23%)
	9 (17%)
	8 (15%)
	4 (8%)
	21 (42%)
	13 (26%)
	8 (16%)
	3 (6%)
	5 (10%)

European Heart Journal (2015) 36, 2793–2867
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2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Priori SG et al.

Diagnosis of catecholaminergic polymorphic ventricular tachycardia

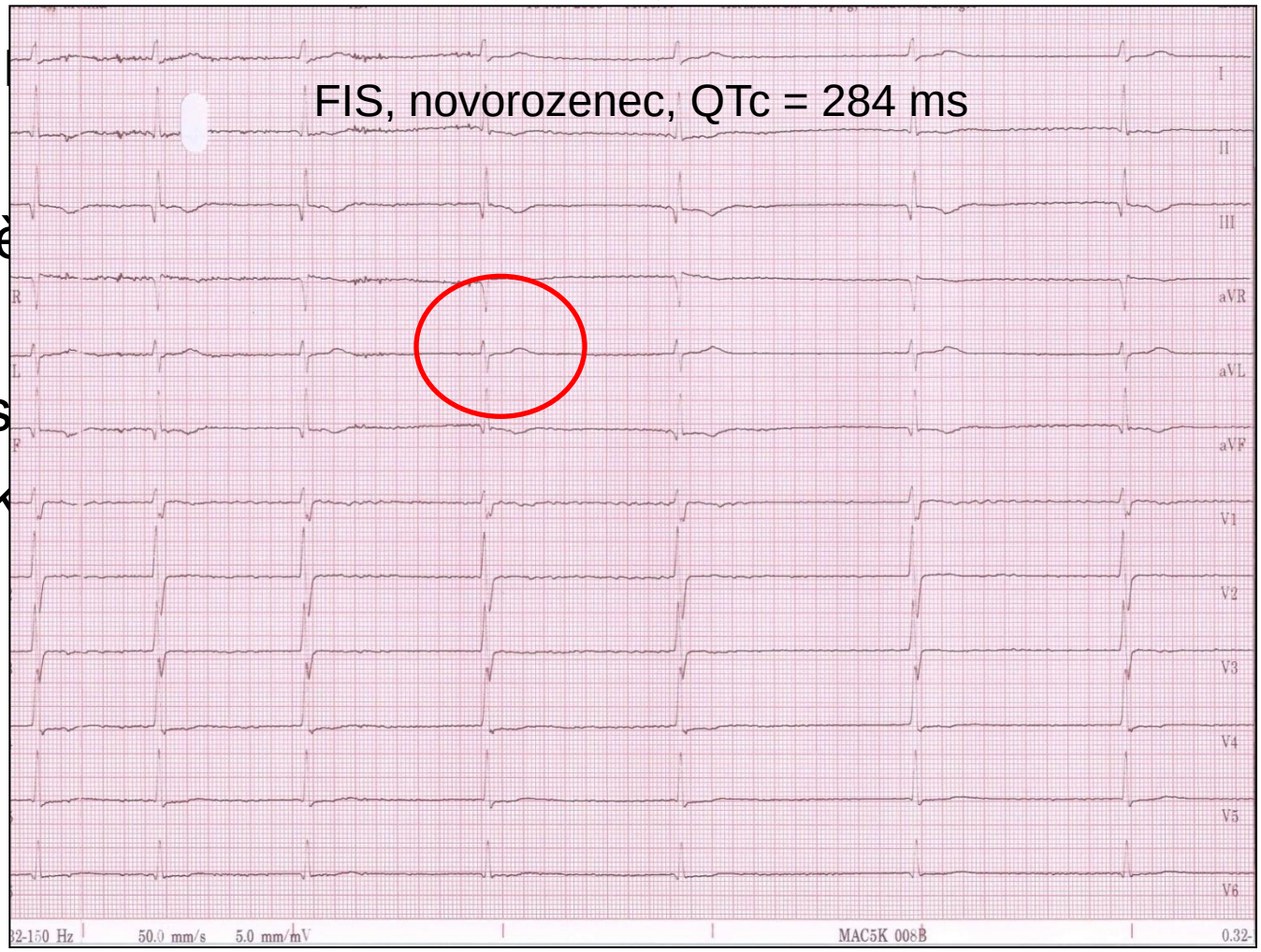
Recommendations
CPVT is diagnosed in the presence structurally normal heart, normal E and exercise- or emotion-induced bidirectional or polymorphic VT.
CPVT is diagnosed in patients who carriers of a pathogenic mutation(s the genes *RyR2* or *CASQ2*.

Risk stratification and management in Catecholaminergic Polymorphic Ventricular Tachycardia

Recommendations	Class[a]	Level[b]	Ref.[c]
The following lifestyle changes are recommended in all patients with a diagnosis of CPVT: avoidance of competitive sports, strenuous exercise and stressful environments.			
Beta-blockers are recommended in all patients with a clinical diagnosis of CPVT, based on the presence of documented spontaneous or stress-induced VAs.			
ICD implantation in addition to beta-blockers with or without flecainide is recommended in patients with a diagnosis of CPVT who experience cardiac arrest, recurrent syncope or polymorphic/bidirectional VT despite optimal therapy.			
Therapy with beta-blockers should be considered for genetically positive family members, even after a negative exercise test.	IIa	C	461, 462
Flecainide should be considered in addition to beta-blockers in patients with a diagnosis of CPVT who experience recurrent syncope or polymorphic/bidirectional VT while on beta-blockers, when there are risks/ contraindications for an ICD or an ICD is not available or rejected by the patient.	IIa	C	463
Flecainide should be considered in addition to beta-blockers in patients with a diagnosis of CPVT and carriers of an ICD to reduce appropriate ICD shocks.	IIa	C	463

Syndrom krátkého QT intervalu (SQTS)

- Zkrácení repolarizace jako arytmogenní substrát
- Pravděpodob
  kategoriích
  - > 40 % do vè
    - reporting
  - Rekurence s
  - Nejasné rizik



European Heart Journal (2015) 36, 2793–2867
doi:10.1093/eurheartj/ehv316

2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Priori SG et al.

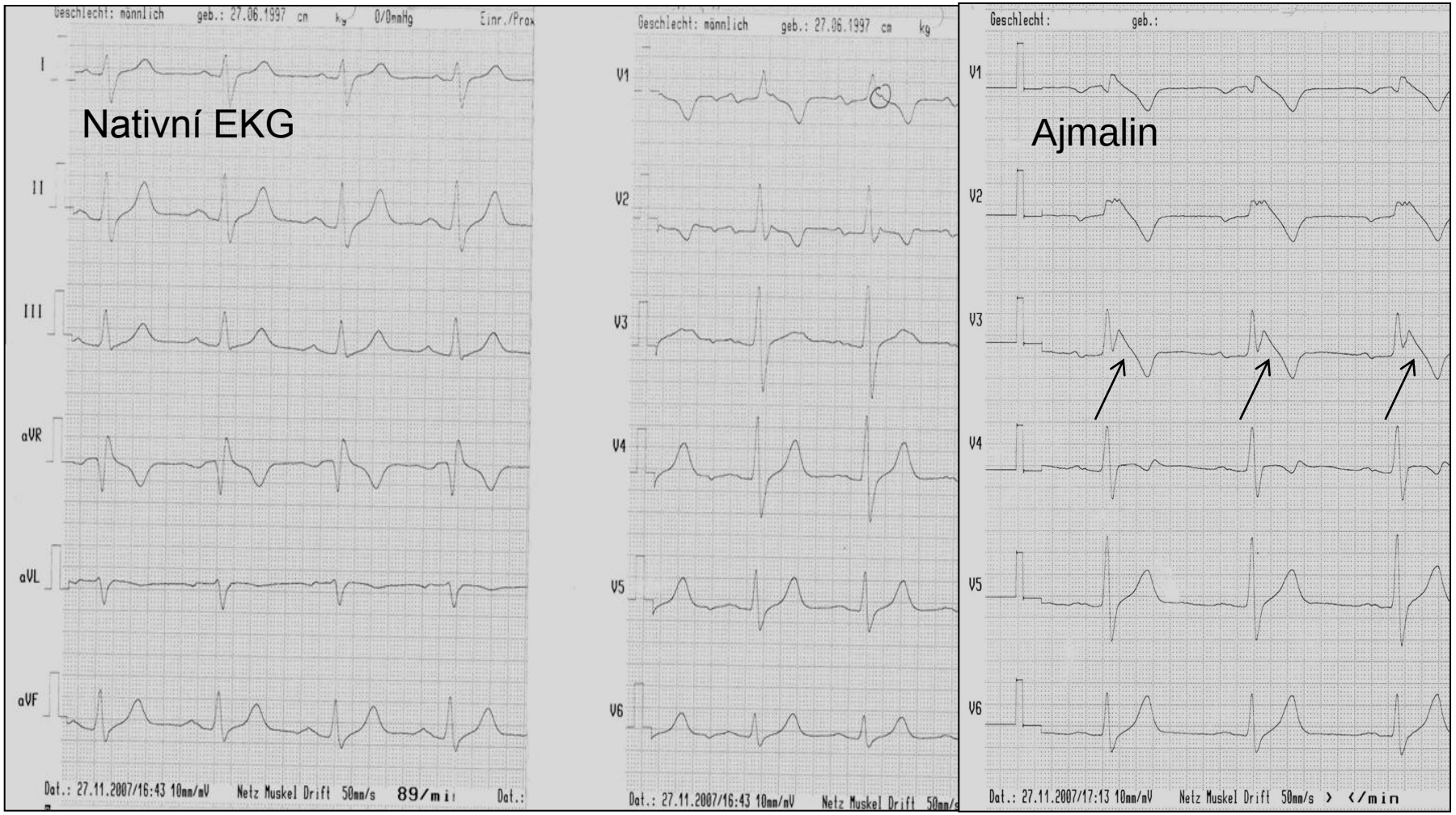
Diagnosis of Short QT Syndrome

Recommendations	Class[a]	Level[b]	Ref.[c]
SQTS is diagnosed in the presence of a QTc ≤340 ms.	I	C	This panel of experts
SQTS should be considered in the presence of a QTc ≤360 ms and one or more of the following: (a) A confirmed pathogenic mutation (b) A family history of SQTS (c) A family history of sudden death at age <40 years (d) Survival from a VT/VF episode in the absence of heart disease.	IIa	C	This panel of experts

Risk stratification and management in Short QT Syndrome

Short QT Syndrome			
Recommendations	**Class[a]**	**Level[b]**	**Ref.[c]**
ICD implantation is recommended in patients with a diagnosis of SQTS who (a) Are survivors of an aborted cardiac arrest, and/or (b) Have documented spontaneous sustained VT.	I	C	119, 447
Quinidine or sotalol may be considered in patients with a diagnosis of SQTS who qualify for an ICD but present a contra-indication to the ICD or refuse it.	IIb	C	118, 448
Quinidine or sotalol may be considered in asymptomatic patients with a diagnosis of SQTS and a family history of SCD.	IIb	C	118, 448

Syndrom Brugadových



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2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Priori SG et al.

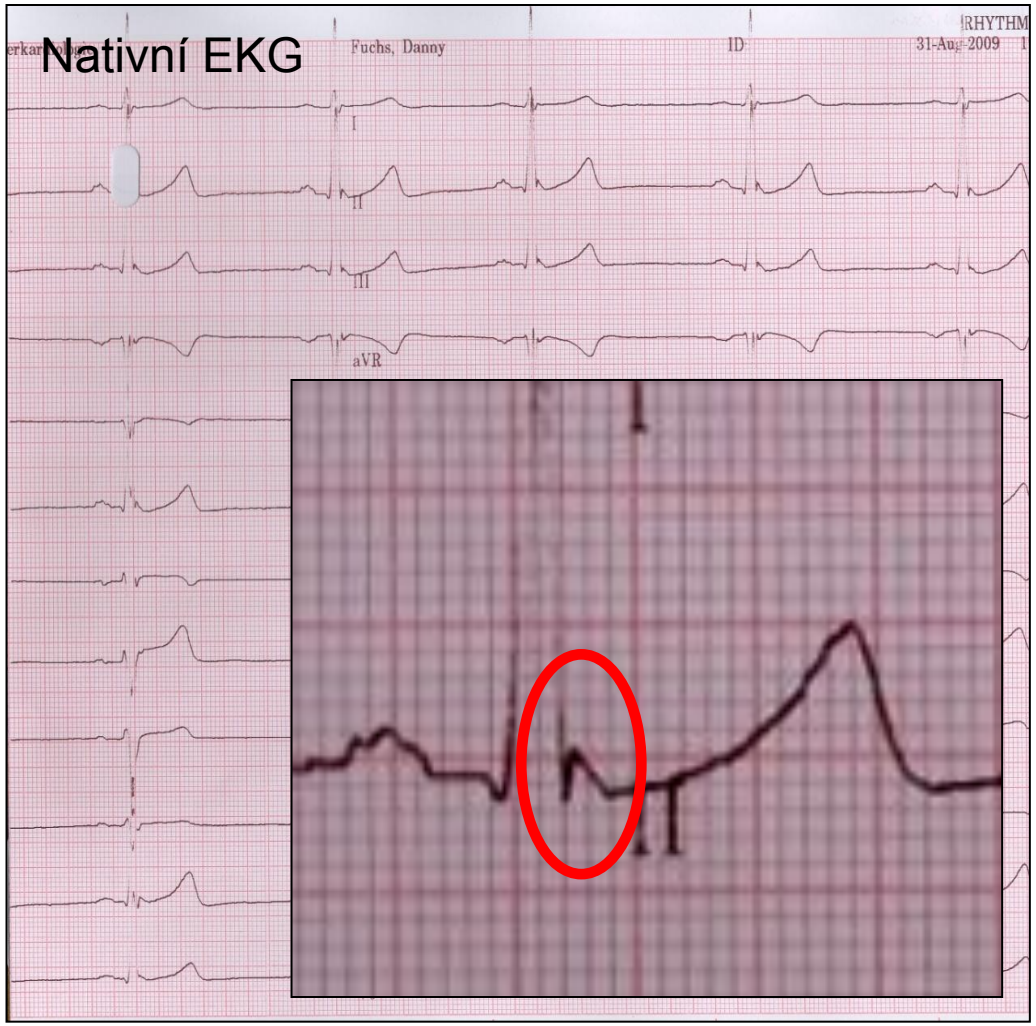
Diagnosis of Brugada Syndrome

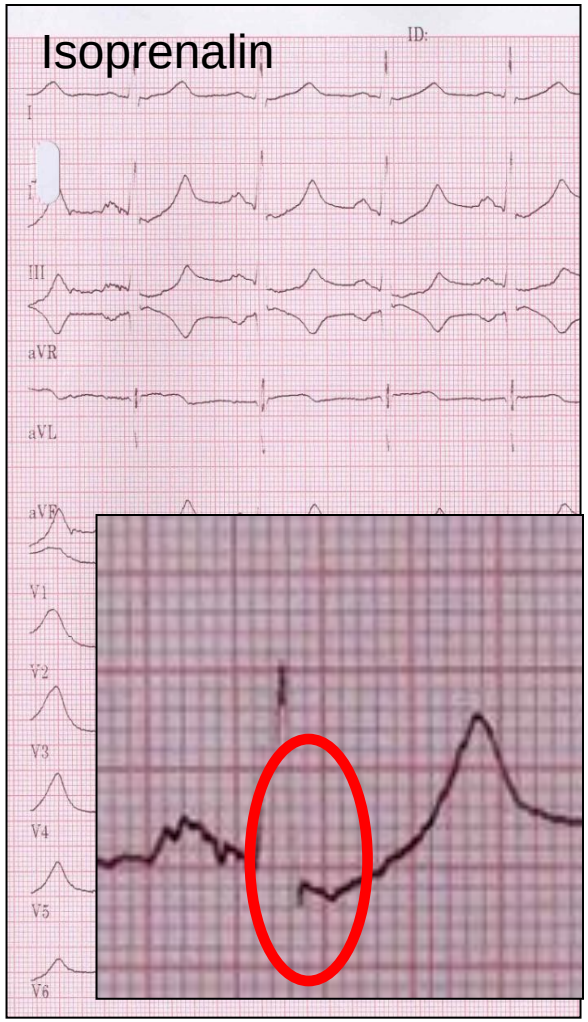
Recommendations	Class[a]	Level[b]	Ref.[c]
Brugada syndrome is diagnosed in patients with ST-segment elevation with type 1 morphology ≥2 mm in one or more leads among the right precordial leads V1 and/or V2 positioned in the second, third, or fourth intercostal space, occurring either spontaneously or after provocative drug test with intravenous administration of sodium channel blockers (such as ajmaline, flecainide, procainamide or pilsicainide).	I	C	This panel of experts

Risk stratification and management in Brugada Syndrome

Recommendations	Class[a]	Level[b]	Ref.[c]
The following lifestyle changes are recommended in all patients with a diagnosis of Brugada syndrome: (a) Avoidance of drugs that may induce ST-segment elevation in right precordial leads (http://www.brugadadrugs.org) (b) Avoidance of excessive alcohol intake and large meals (c) Prompt treatment of any fever with antipyretic drugs.	I	C	This panel of experts
ICD implantation is recommended in patients with a diagnosis of Brugada syndrome who (a) Are survivors of an aborted cardiac arrest and/or (b) Have documented spontaneous sustained VT.	I	C	451
ICD implantation should be considered in patients with a spontaneous diagnostic type I ECG pattern and history of syncope.	IIa	C	451
Quinidine or isoproterenol should be considered in patients with Brugada syndrome to treat electrical storms.	IIa	C	453
Quinidine should be considered in patients who qualify for an ICD but present a contraindication or refuse it and in patients who require treatment for supraventricular arrhythmias.	IIa	C	454

Syndrom časné repolarizace (ERS)





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2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death

Priori SG et al.

8.5 Early repolarization syndrome

8.5.1 Definitions and epidemiology

The presence of an early repolarization pattern in the inferior and/or lateral leads has been associated with idiopathic VF in case–control studies.[467,468] Owing to the high incidence of the early repolarization pattern in the general population, it seems reasonable to diagnose an 'early repolarization syndrome' only in patients with a pattern who are resuscitated from a documented episode of idiopathic VF and/or polymorphic VT.

The genetics of early repolarization are probable polygenic in many instances. No clear evidence of familial transmission of the early repolarization syndrome exists.

Given the uncertainties in the interpretation of the early repolarization pattern as a predictor of SCD, this panel of experts has decided that there is insufficient evidence to make recommendations for management of this condition at this time.

Děkuji za pozornost