GENERAL UNIVERSITY HOSPITAL IN PRAGUE

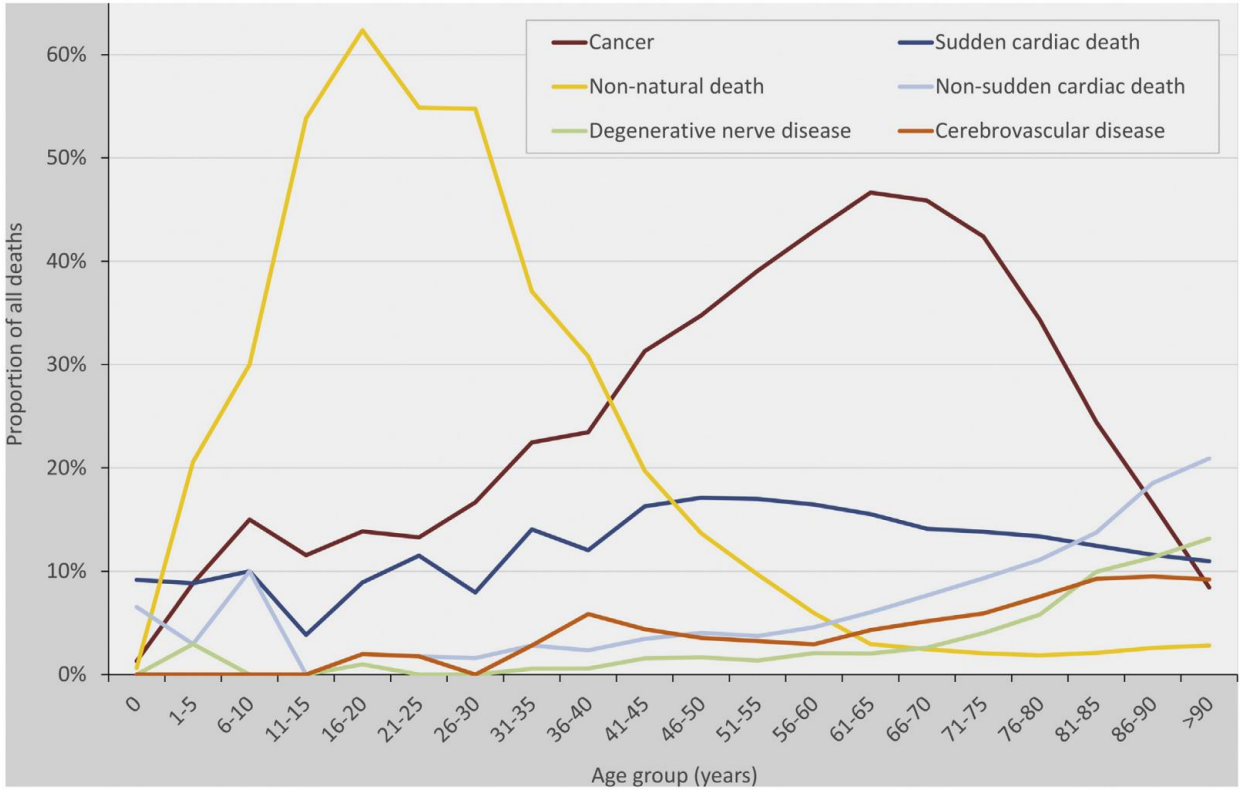
FIRST FACULTY OF MEDICINE
Charles University

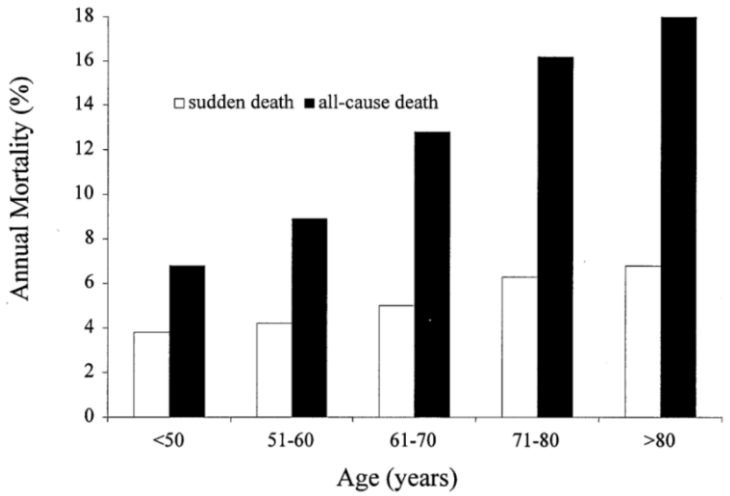
Provokační testy a elektrofyziologie

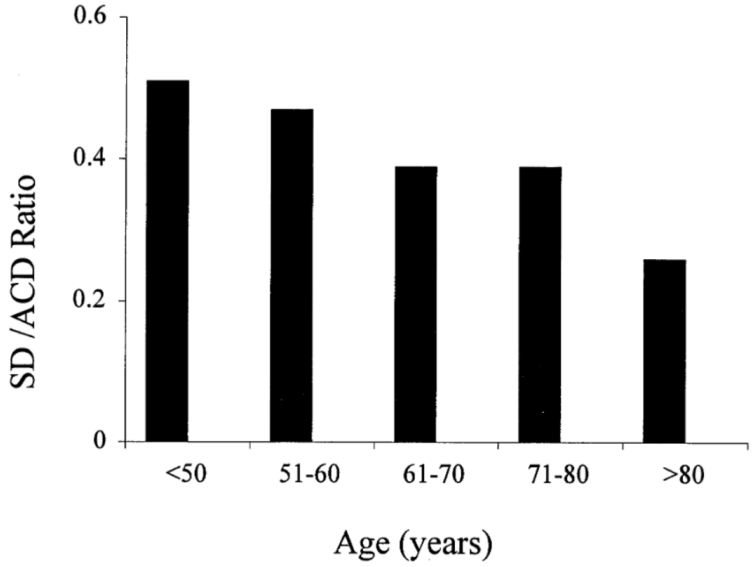
Štěpán Havránek

Podíl náhlé srdeční smrti (SCD) na celkové mortalitě

Příčiny úmrtí v Dánsku v roce 2010







Krahn AD. Diminishing of proprtional risk of sudden cardiac death with advancing age. Am Heart J 2004; 147:837-40
Lynge TH. Nationwide burden of SCD in Denmark. Heart Rhythm 2021

Diagnostika u nemocných s první manifestací KT bez známé kardiální anamnézy

Scénář 1: Náhodný záchyt nesetrvalé komorové tachykardie

Scénář 2: První manifestace setrvalé monomorfní komorové tachykardie

Scénář 3: Přeživší náhlou srdeční smrt

Scénář 4: Oběť náhlé srdeční smrti

Scénář 5: Příbuzný oběti náhlého úmrtí z arytmické příčiny

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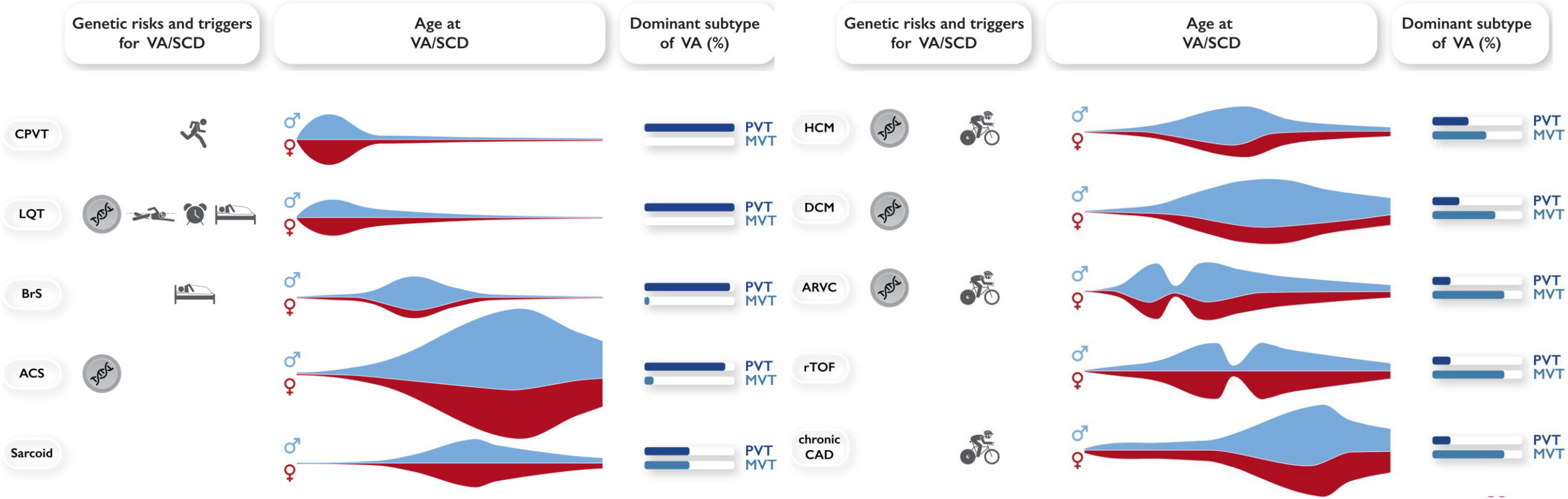
Etiologie náhlé srdeční smrti (SCD)



Mladší věk: Arytmické syndromy, kardiomyopatie, anomálie věnčitých tepen, myokaditida
Čtvrtá dekáda: Akutní koronární syndromy
Starší populace: Akutní a chronická ICHS, chlopenní vady, srdeční selhání

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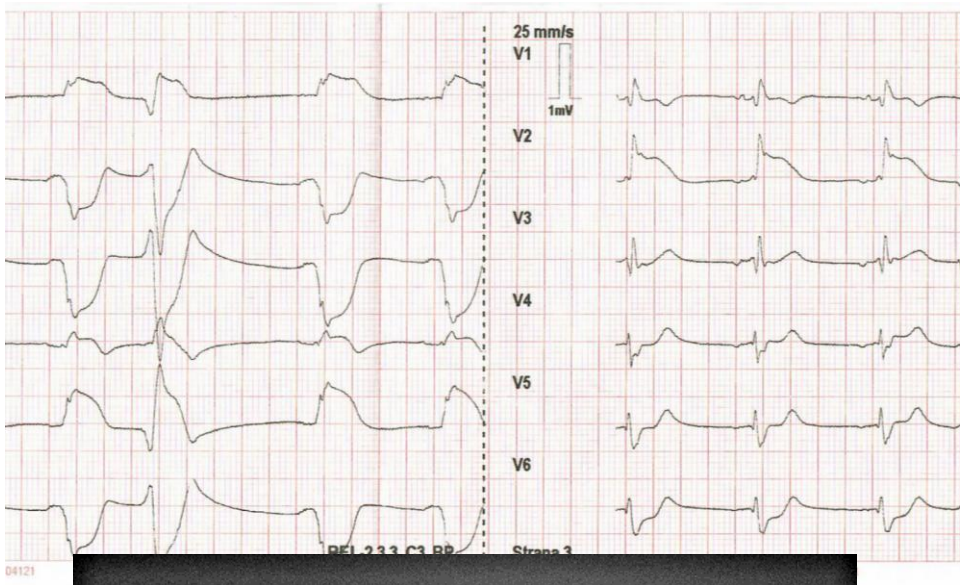

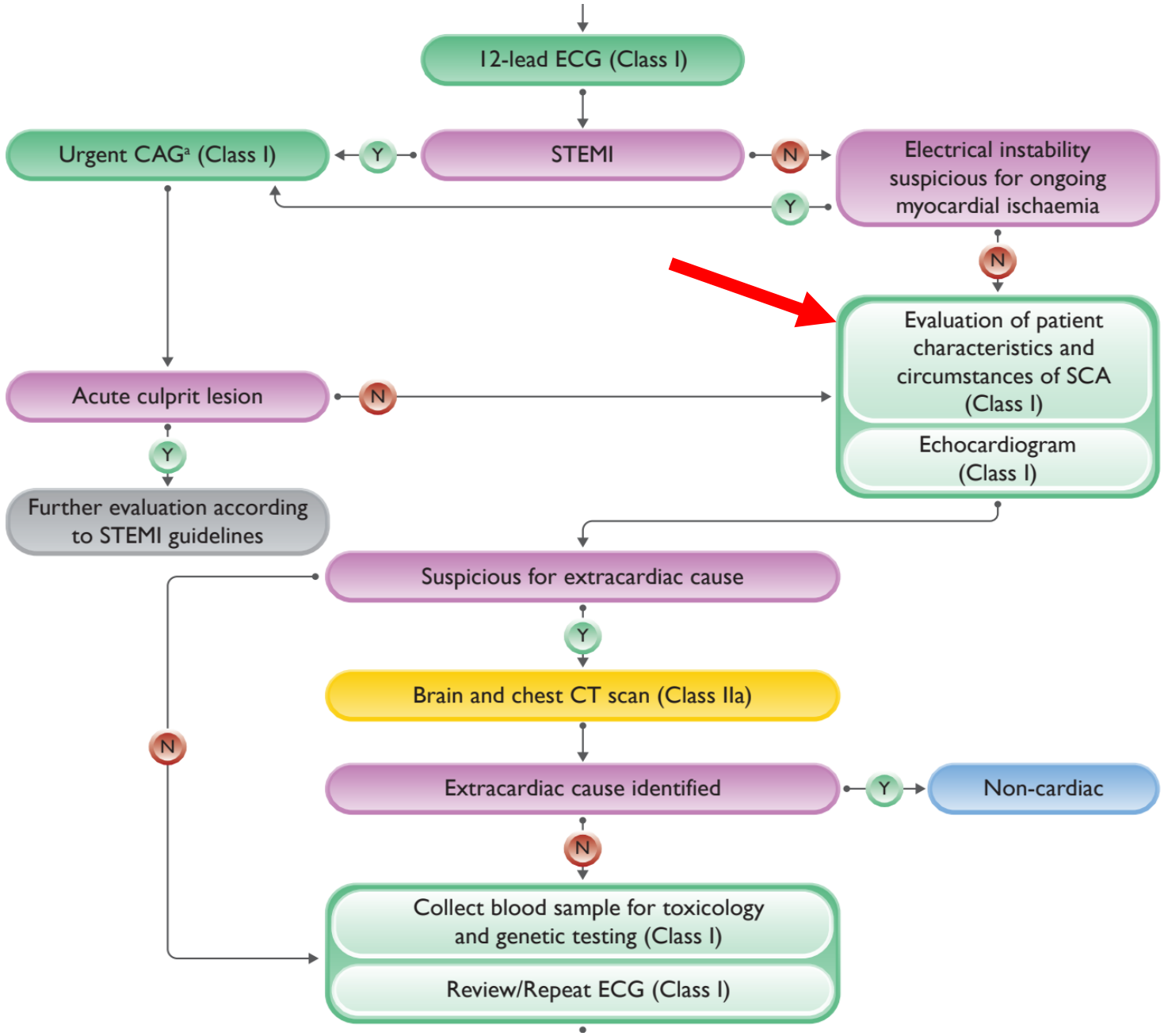

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Anamnéza a fyzikální nálezy

Anamnestické údaje

- Věk, pohlaví, předchozí osobní anamnéza
- Symptomy bezprostředně před zástavou
- Aktivita / emoční stav v okamžiku zástavy
    - spánek, sport, emoční vypětí
- Denní doba (ráno / noc)
- Prostředí zástavy (veřejné místo, domov)
- Užívaná medikace / alkohol / drogy
    - Antiarytmika, léky prodlužující QTi
- Detailní rodinná anamnéza, minimálně 3 generace

Odběry

- Kardiospecifické enzymy
- Markery zánětu
- Glykémie
- Elektrolyty
- Toxikologie
    - Etanol, opiáty, stimulanty
    - Medikace s potenciálem prodloužení QT, QRS, útlumem dechového centra
- DNA pro pozdější analýzu

Objektivní nález

- Obezita / xantelomata → ICHS
- “Woolly hair“, almoplantární keratoderma → ARVC
- Kontraktury → Emery-Dreifuss muskulární dystrofie
- Svalová slabost / atrofie → kardiomyopatie - lamin A/C; desmin
- Kloubní deformity; deformity hrudníku, vysoký vzrůst → Marfanův syndrom
- Mikrognacie, syndaktylie, klinodaktylie → Andrsen-Tawil and Timothy syndromy
- Horečka → Brugada syndrom
- Hypotermie, dehydratace, známky drogové závislosti
- Známky chronického srdečního selhání
- Fyzikální nález na srdci

EKG

- Vstupní rytmus / morfologie KT
- Výstup z AED
- Interogace CIEDs

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Význam CT hlavy a trupu (hrudníku) pro prognózu

Provedení SKG a/nebo CT

- Zpoždění přijetí na ARO / KJ o 180 minut (130-220)
- **Stanovení DG až u 60% pacientů s OHCA**

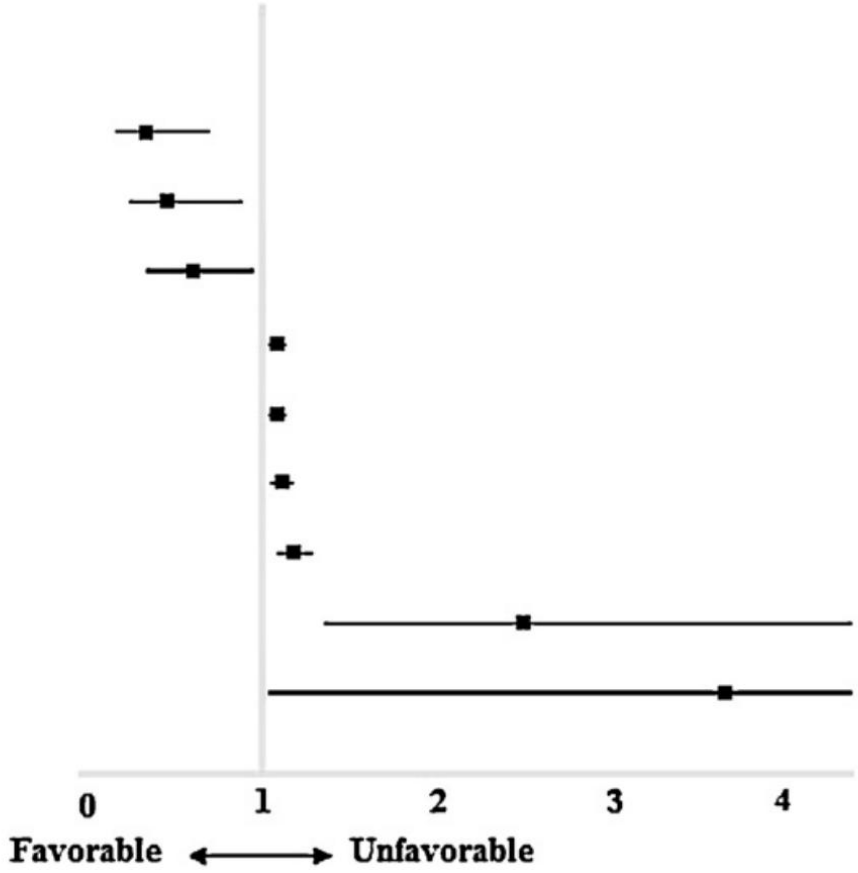
Coronary angiography *n* (%)
745 (83)

729 (98) immediate
16 (2) secondary

447 (61) positive
5 (31) positive

344 (77) PCI
3 (60) PCI

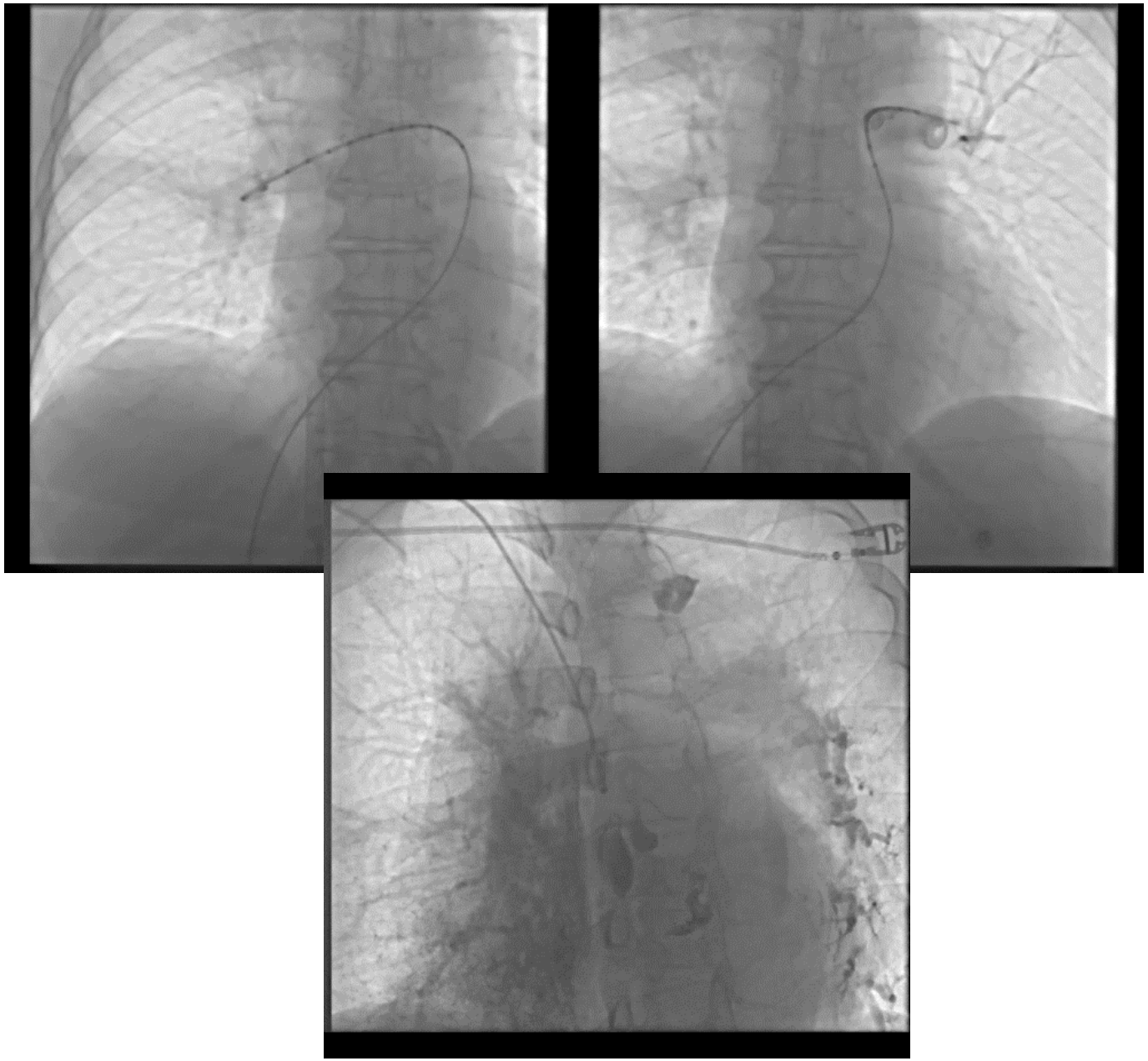
CT scan *n* (%)
355 (40)

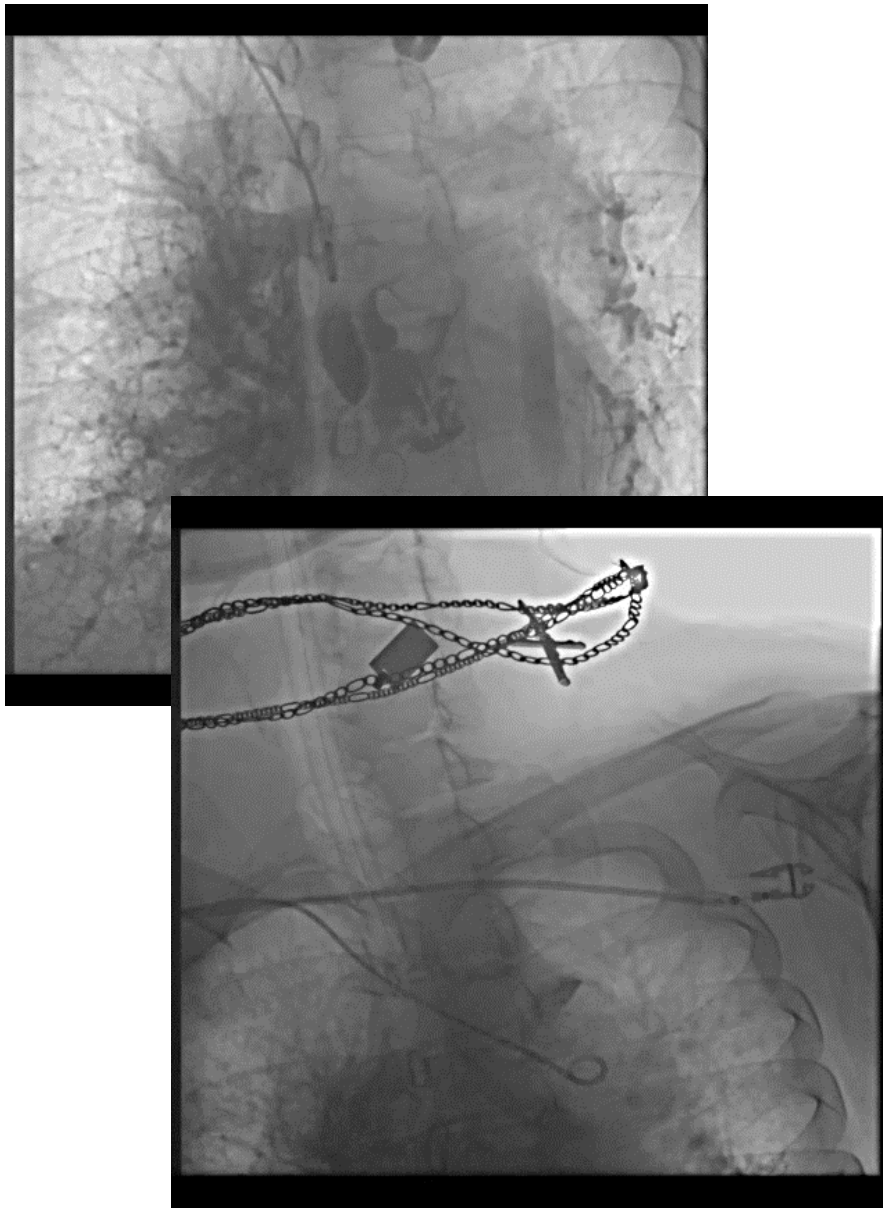


	OR	95% CI	p
VT / VF	0.40	0.24 - 0.68	0.001
Therapeutic hypothermia	0.53	0.32 - 0.87	0.01
Diagnosis by coronary angiography	0.64	0.41 - 0.99	0.047
Age > 60 years	1.04	1.02 - 1.05	< 0.001
Low flow duration	1.05	1.04 - 1.08	< 0.001
No flow duration	1.12	1.08 - 1.17	< 0.001
Arterial lactate level	1.16	1.10 - 1.23	< 0.001
Diabete mellitus	2.54	1.34 - 4.79	0.004
Diagnosis by CT-scan	3.68	1.02 - 13.3	0.046

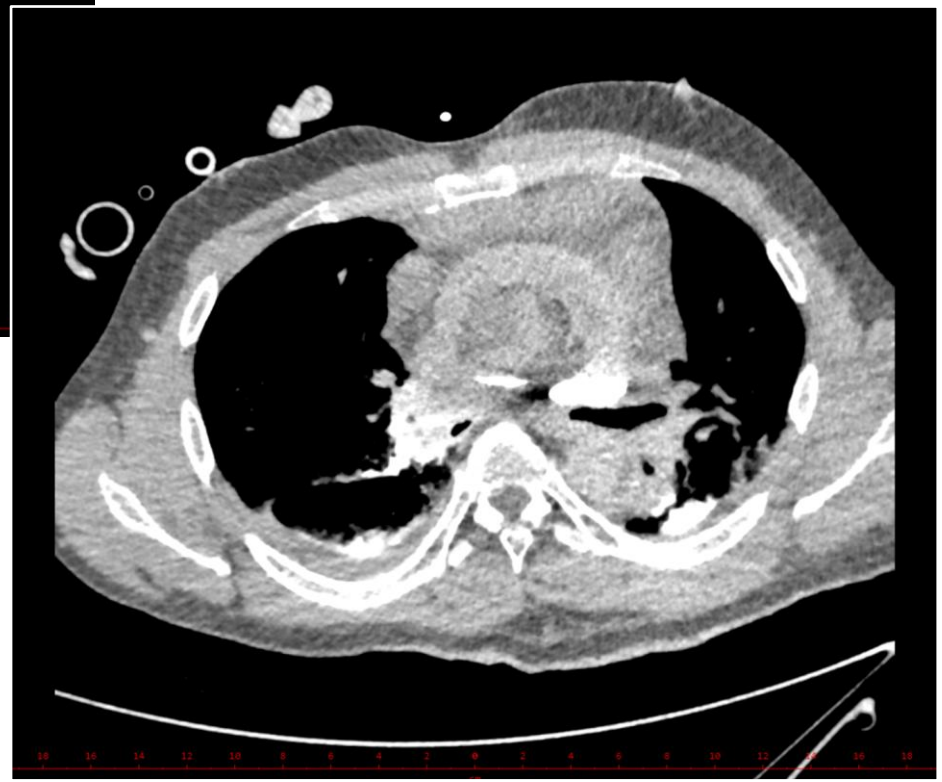
Chelly J. Benefit of an early and systematic imaging procedure after CA. Resuscitation 2012

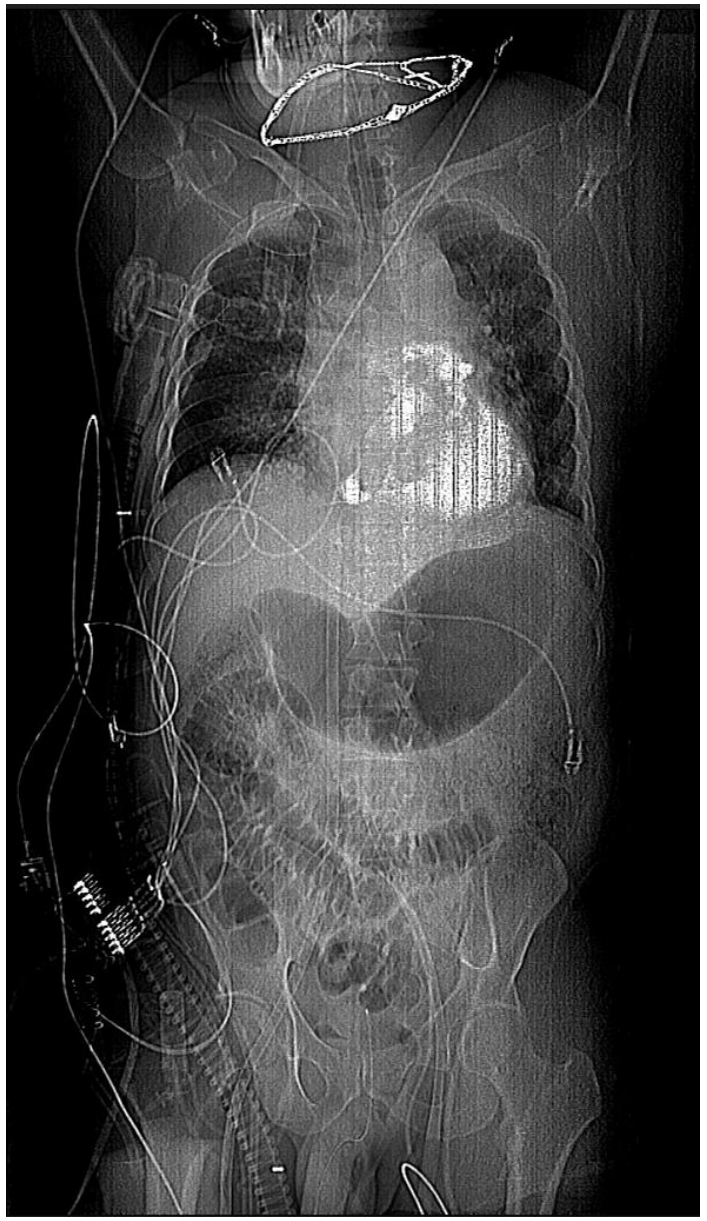
Angiografie plicnice a aortální disekce u refrakterní OHCA





CT nálezy u nemocných po oběhové zástavě u refrakterní OHCA





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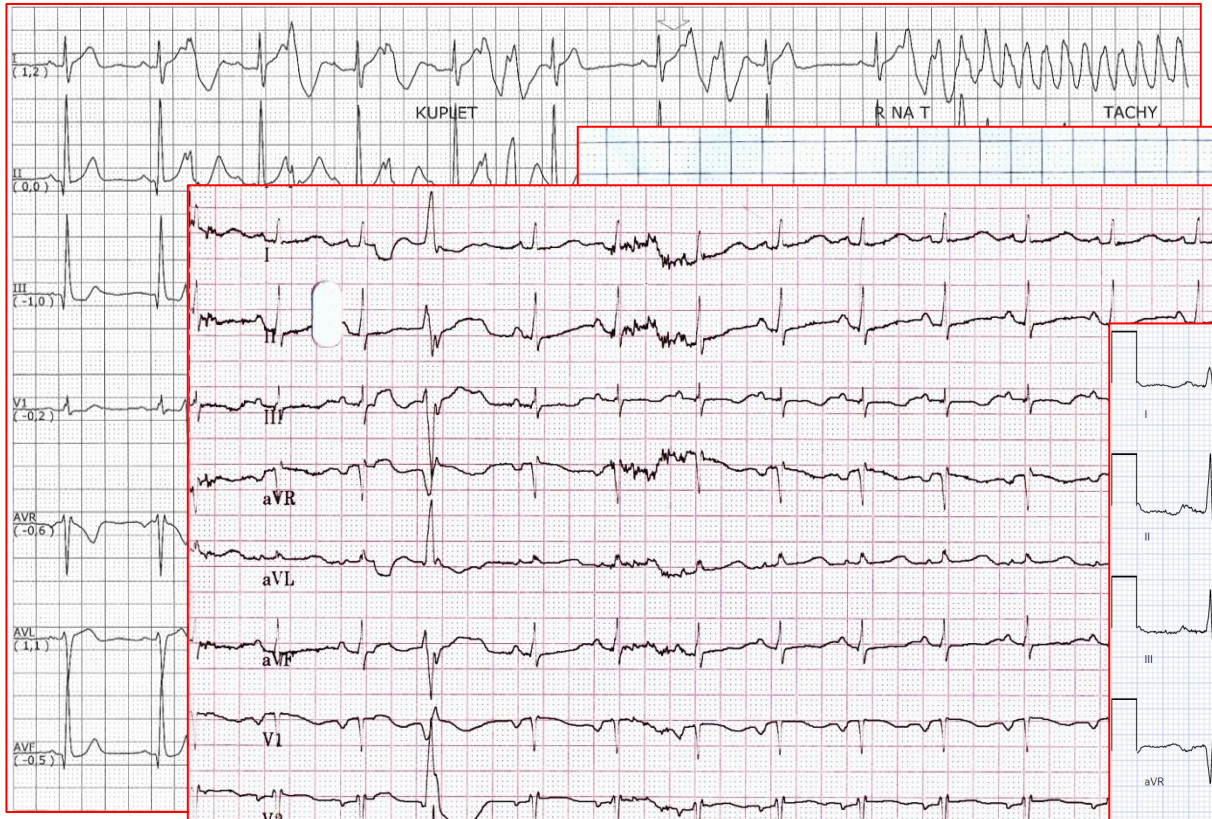
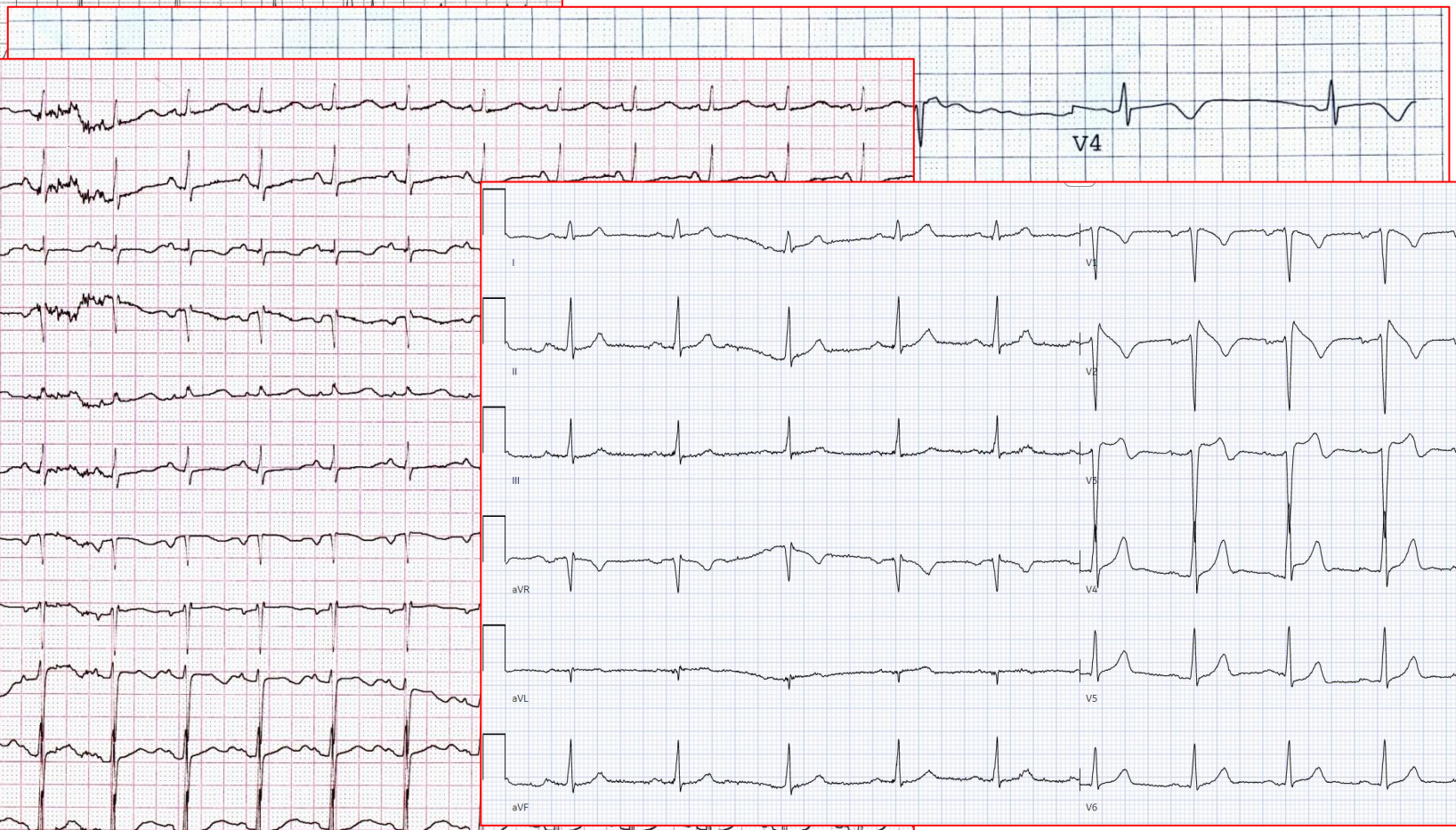
EKG – opakované, monitorování

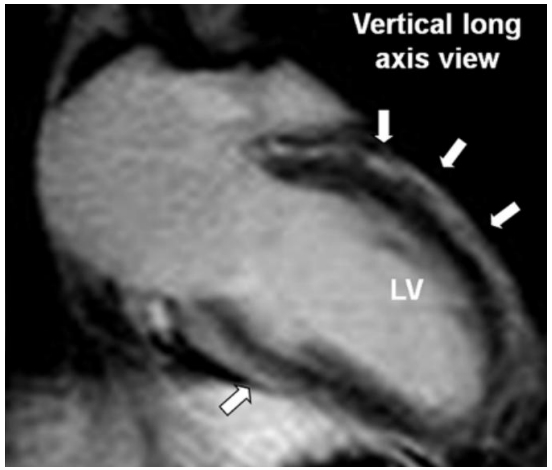
Short-couplet TdP

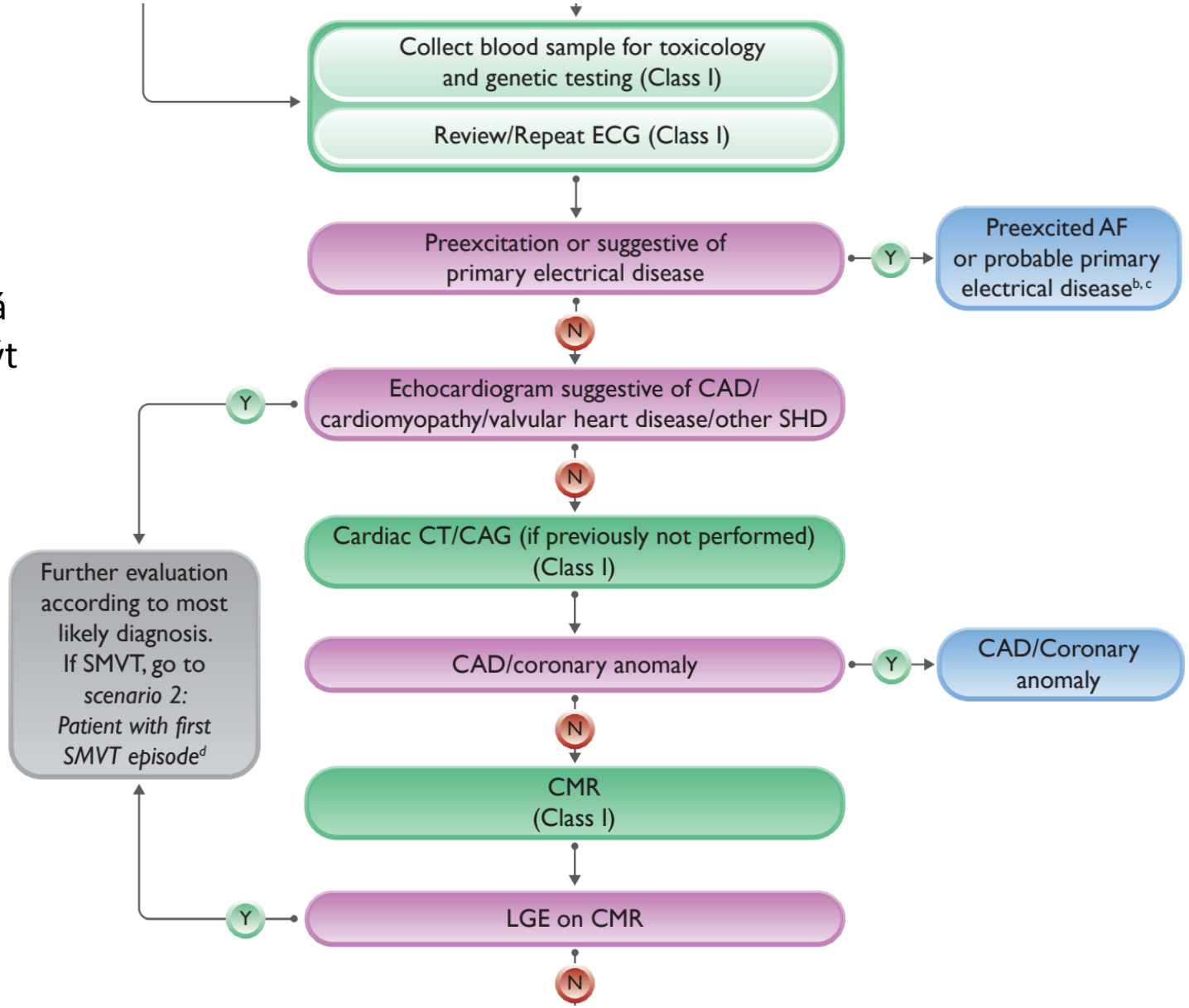


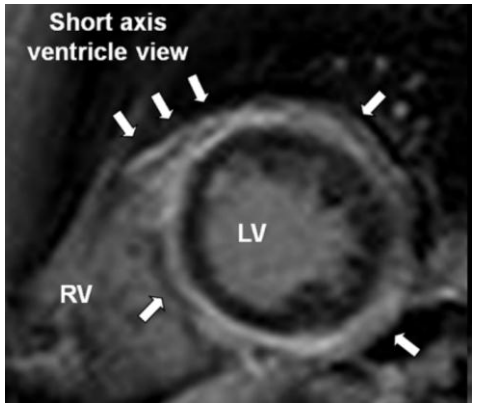
Long QT



Správně indikovaná SKG
– 61% pacientů po OHCA má přítomnu lézi, která může být zodpovědná za CA







Havranek S et al. BMC Cardiovasc Disord 2015; 15:18.
Chelly J. Benefit of an early and systematic imaging procedure after CA. Resuscitation 2012
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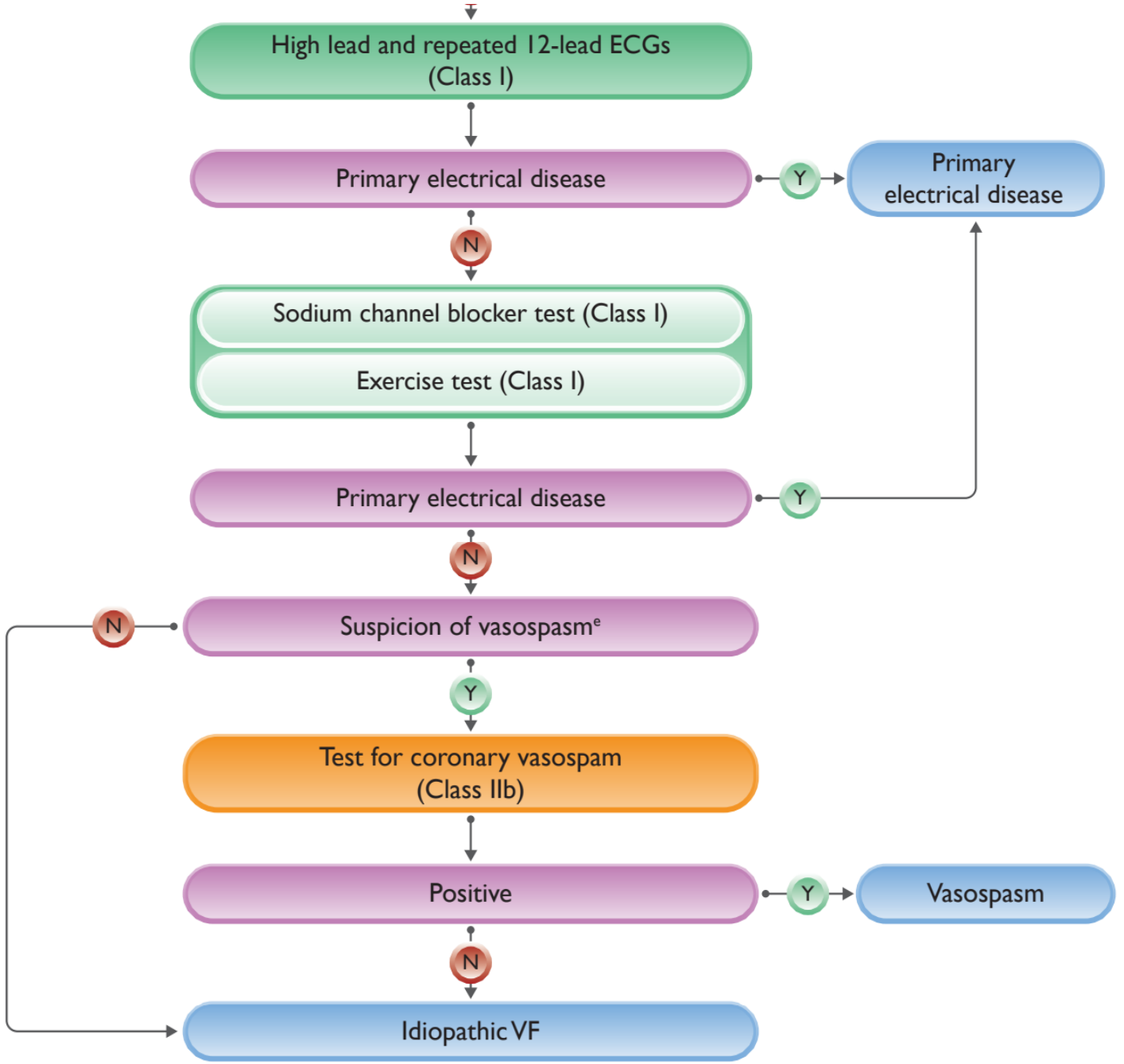

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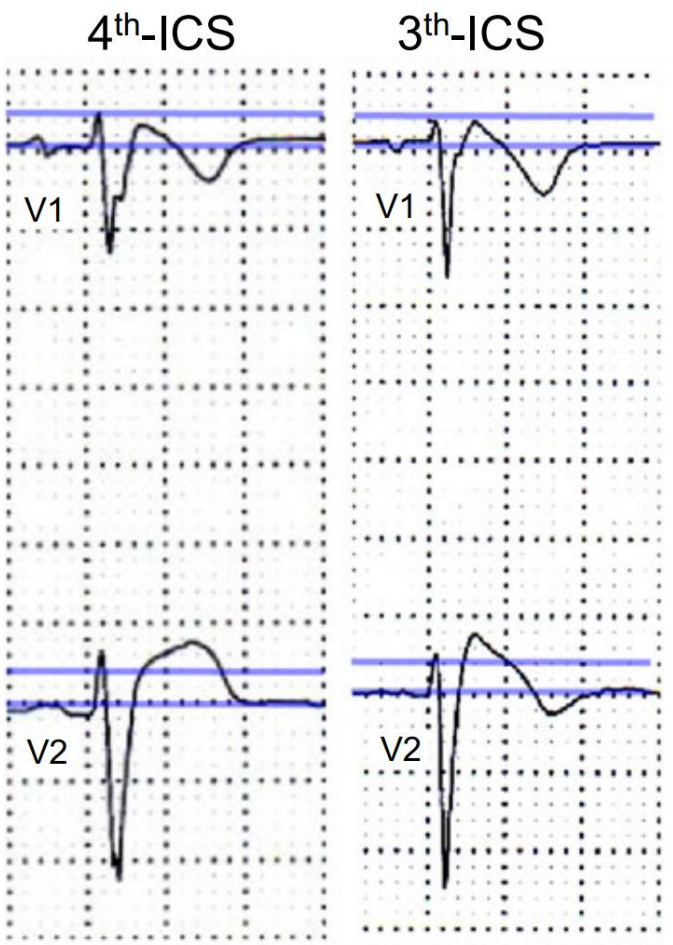
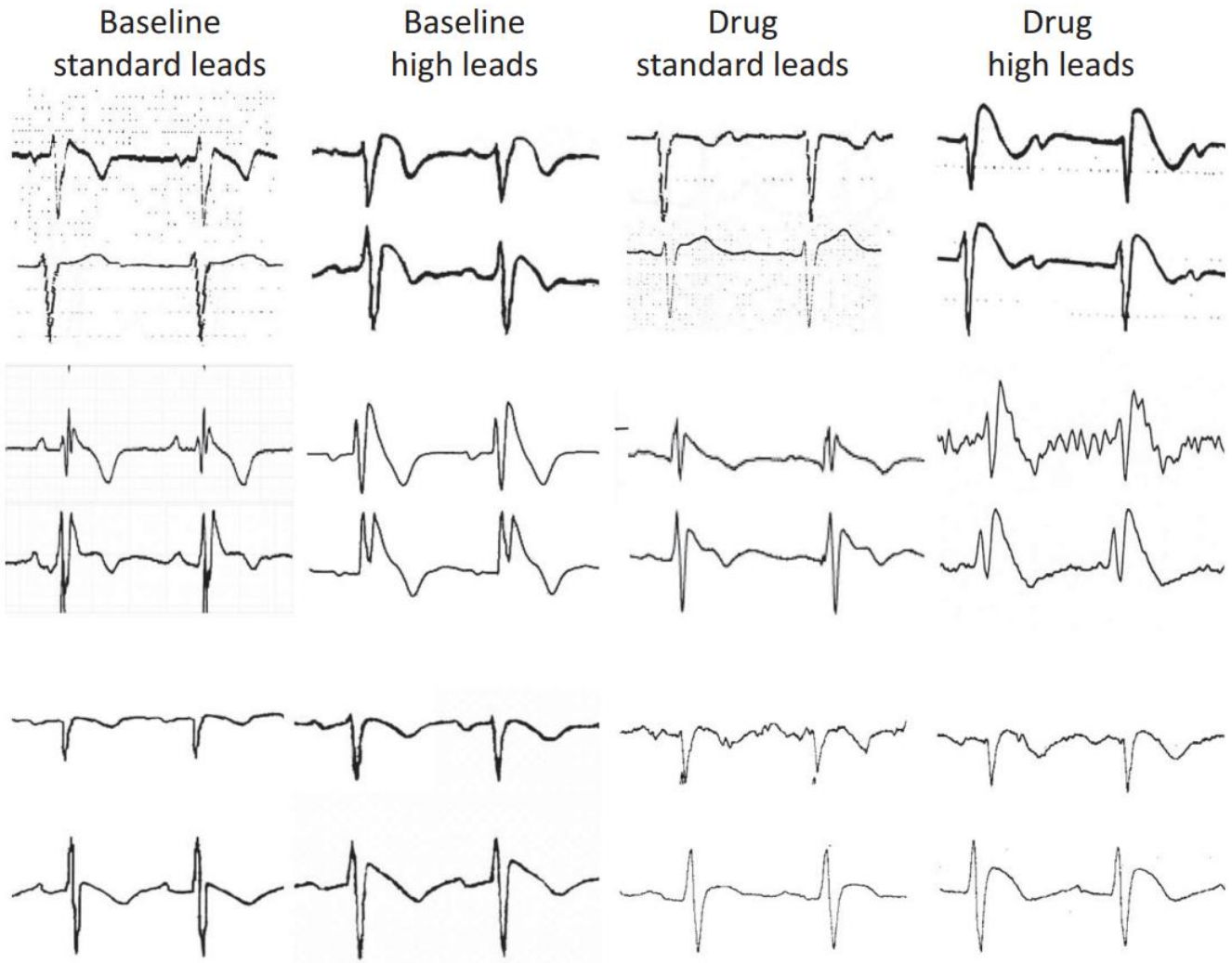
Brugada syndrom

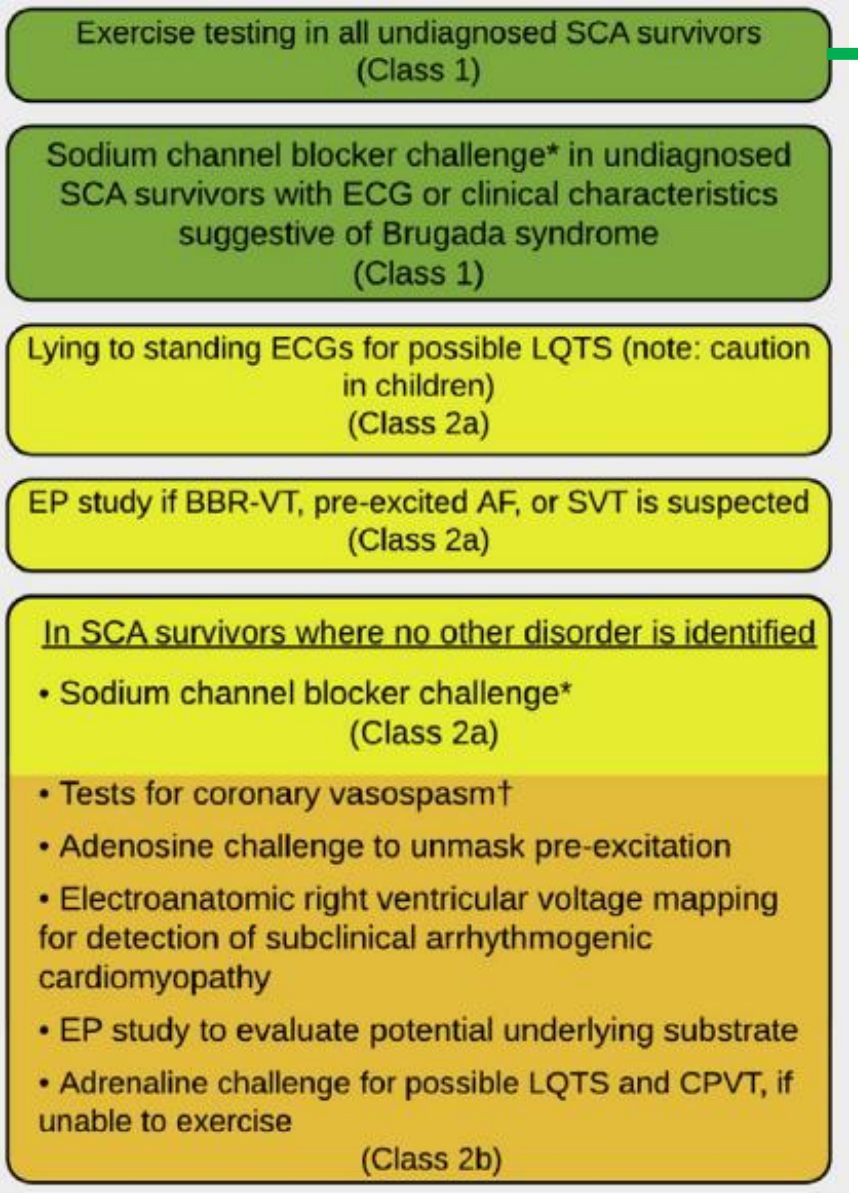
High precordial leads – Brugada syndrome





Curcio A et al. Clinical Presentation and Outcome of Brugada Syndrome Diagnosed with the New 2013 Criteria. JCE 2016; 27:937-43.

Zátěžové testy



Změny navozené adrenergním mechanismem

- Zátěží indukovaná KT (ARVC)
- Bidirecionální KT in CPVT
- Zátěží navozené Epsilon a Typ 1 Brugada
- QTC >480ms ve 4 min recovery - LQTS

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Zátěžové testy

Exercise testing in all undiagnosed SCA survivors
(Class 1)

Sodium channel blocker challenge* in undiagnosed SCA survivors with ECG or clinical characteristics suggestive of Brugada syndrome
(Class 1)

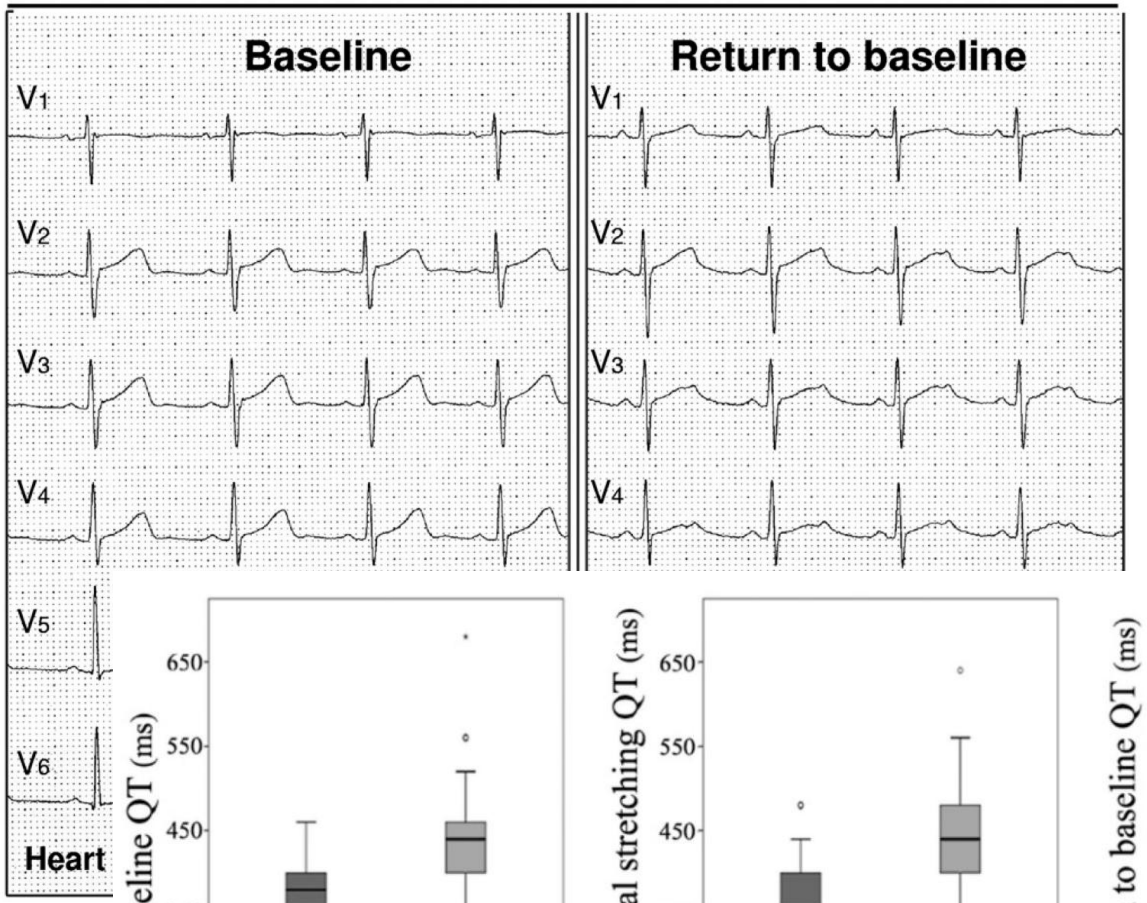
Lying to standing ECGs for possible LQTS (note: caution in children)
(Class 2a)

EP study if BBR-VT, pre-excited AF, or SVT is suspected
(Class 2a)

In SCA survivors where no other disorder is identified

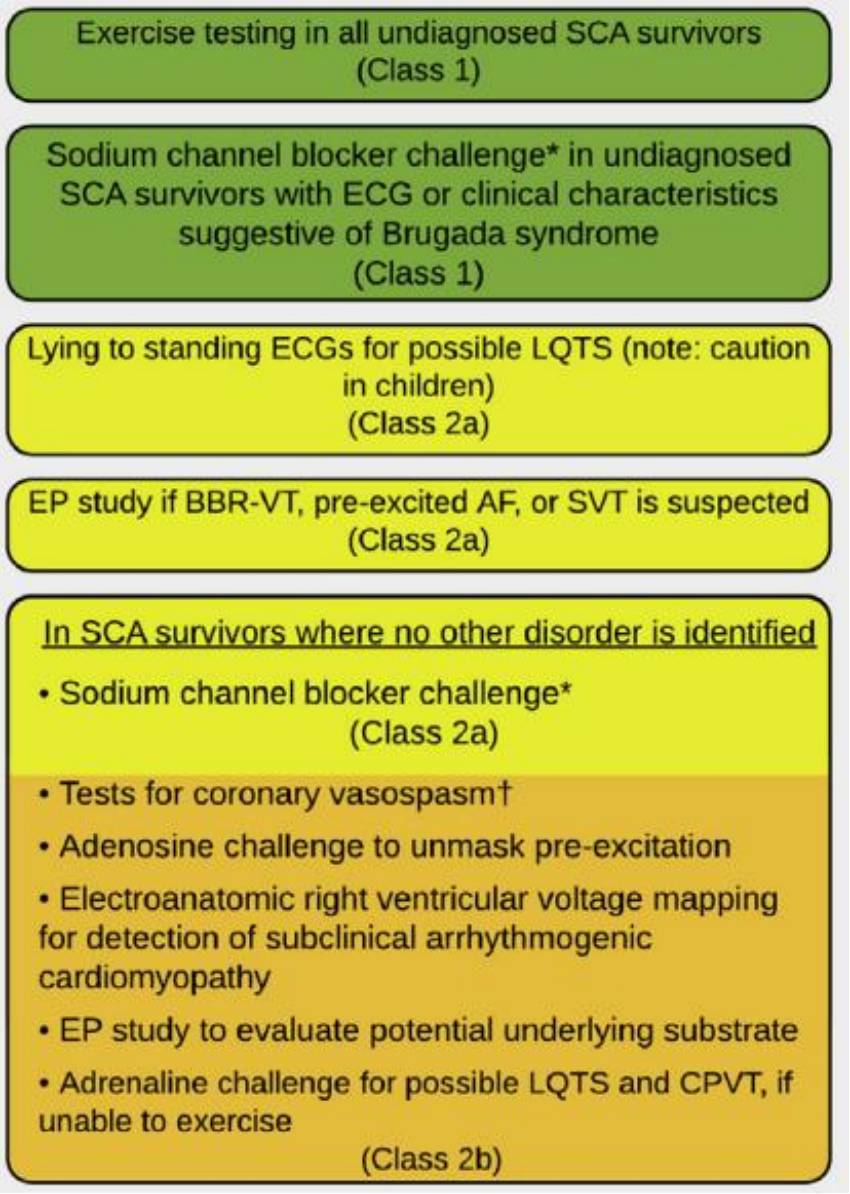
- Sodium channel blocker challenge*
(Class 2a)
- Tests for coronary vasospasm†
- Adenosine challenge to unmask pre-excitation
- Electroanatomic right ventricular voltage mapping for detection of subclinical arrhythmogenic cardiomyopathy
- EP study to evaluate potential underlying substrate
- Adrenaline challenge for possible LQTS and CPVT, if unable to exercise
(Class 2b)

Postavit se, vydržet 5 min; EKG



2020 APHRS/HRS expert consensus statement on the investigation of decedents with sudden unexplained death and patients with sudden cardiac arrest, and of their families.
Adler A et al. The phenomenon of QT stunning: The abnormal prolongation provoked by standing in patients with long QT syndrome. Heart Rhythm 2012; 9:301-8.

Provokační testy



Diagnostic test	Indication	Protocols Dose/infusion rate/duration	Positive test
Ajmaline	Family history of BrS or SADS. Resuscitated CA without SHD.	1 mg/kg over 5–10 min (maximum dose 100 mg) or 1 mg/kg at 10 mg/min. Record in standard and high precordial leads over 30 min.	BrS type 1 ECG.
Flecainide	Same as ajmaline.	2 mg/kg over 10 min (maximum dose 150 mg). Record in standard and high precordial leads over 30 min.	Same as ajmaline.

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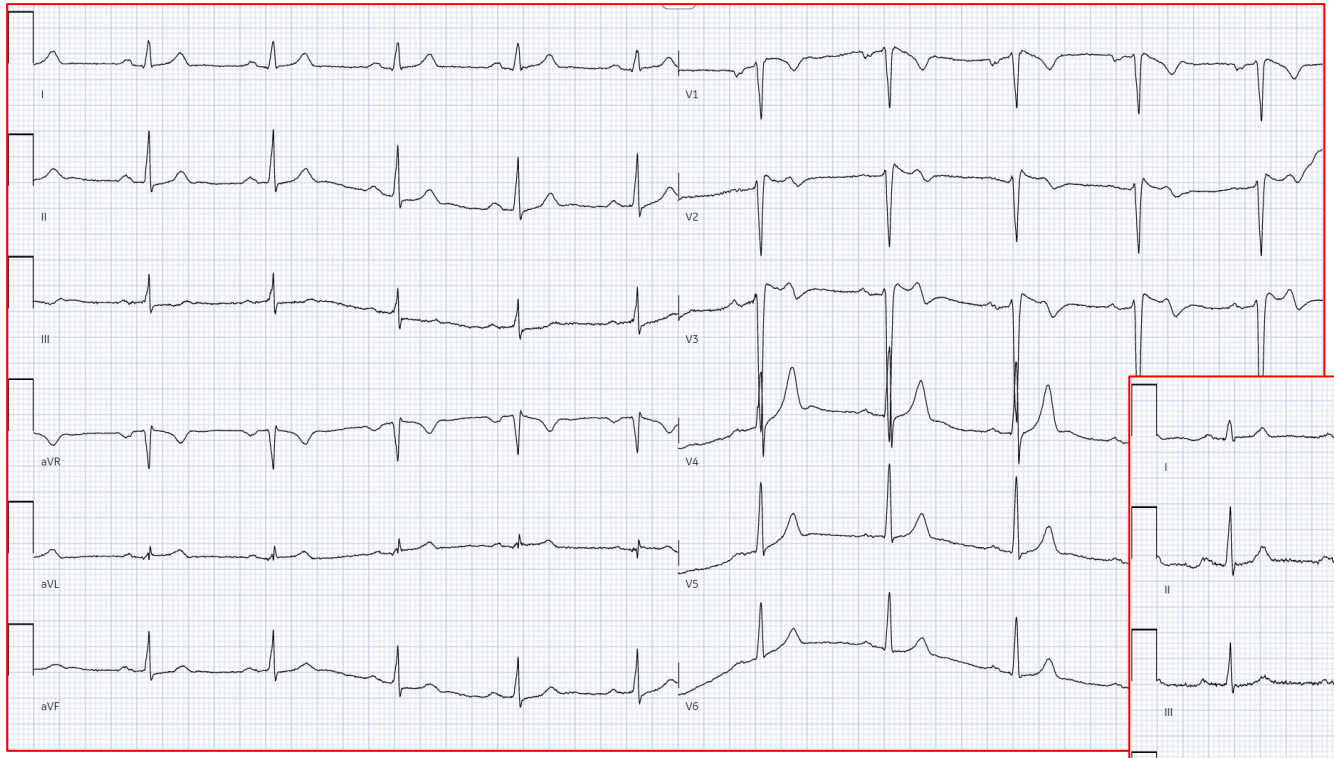
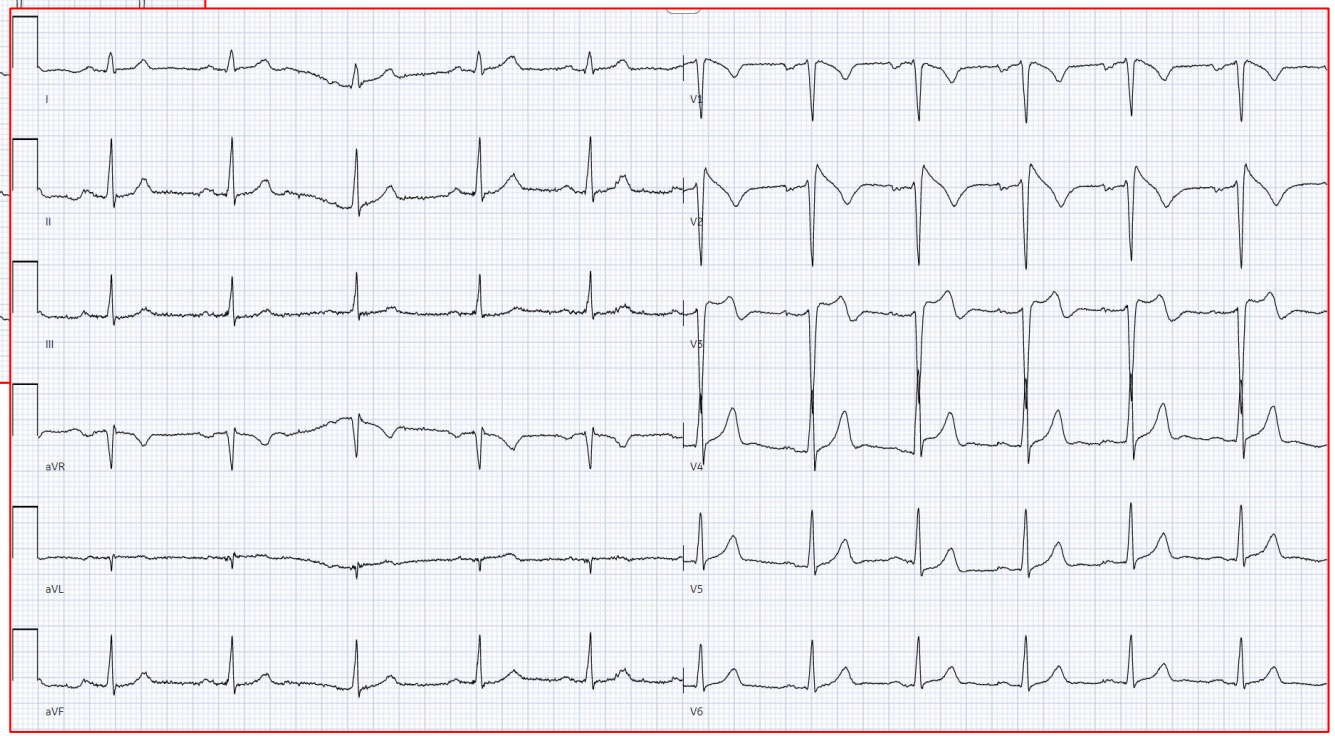
Provokační testy





Ajmalin / Flecainid test

Geneticky potvrzený Brugada Syndrom

Provokační testy

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(Class 2a)

EP study if BBR-VT, pre-excited AF, or SVT is suspected
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In SCA survivors where no other disorder is identified

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- Tests for coronary vasospasm†
- Adenosine challenge to unmask pre-excitation
- Electroanatomic right ventricular voltage mapping for detection of subclinical arrhythmogenic cardiomyopathy
- EP study to evaluate potential underlying substrate
- Adrenaline challenge for possible LQTS and CPVT, if unable to exercise
(Class 2b)

Diagnostic test	Indication	Protocols Dose/infusion rate/duration	Positive test
Adenosine	Exclude latent pre-excitation.	6, 12, 18 mg boluses up to maximum dose 24 mg or until AV block or pre-excitation occurs.	Identification of accessory pathway.
Epinephrine	CPVT and resuscitated CA with or without SHD when exercise test not feasible. Family history of SADS.	Rest 10 min. Start at 0.025 µg/ kg/ min for 10 min increase sequentially to 0.05, 0.1 and 0.2 µg/ kg/min in 5 min steps.	≥3 beats of PVT or bidirectional VT.

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(Class 2b)

Diagnostic test	Indication	Protocols Dose/infusion rate/duration	Positive test
Acetylcholine	Suspicion of coronary vasospasm.	Intracoronary injection: RCA: 20 and 50 µg. LCA: 20, 50, and 100 µg over 20 s. >3-min intervals between injections. Maximal dose of 50 µg in the RCA and 100 µg in the LCA.	Coronary artery spasm visualized during procedure.
Ergonovine	Same as acetylcholine.	Intracoronary stepwise injection: RCA (20–60 mg) LCA (20–60 mg) over a period of 2–5 min.	Same as acetylcholine

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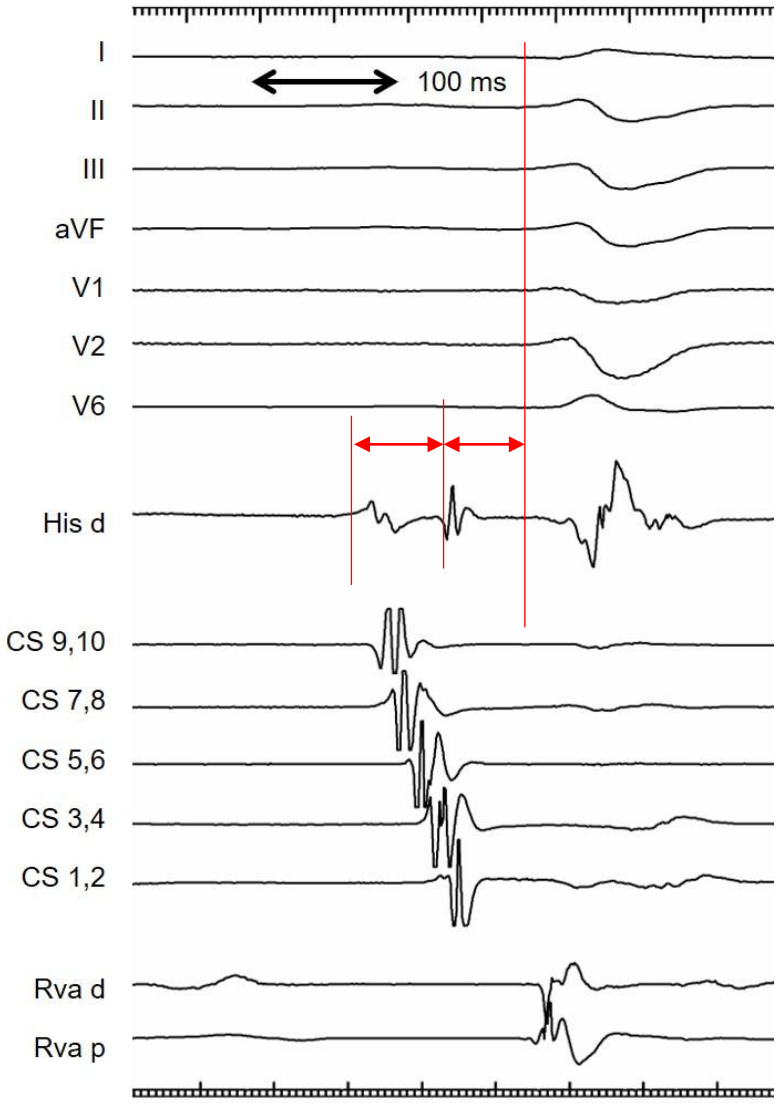
Elektrofyziologie & mapping

Součástí vyšetření

- Převodní intervaly AH, HV
- Programovaná stimulace
- Elektroanatomické mapování
- Podávání isoprenalinu

- Adenosin – rekonekce, provokace KES
- Hadgrip pro provokaci KES



Zdroj: Všeobecná fakultní nemocnice

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Základní změny guidelines

	2015	2022
Coronary artery disease		
In patients with syncope and previous STEMI, PES is indicated when syncope remains unexplained after non-invasive evaluation.	IIa	I
Intravenous amiodarone treatment should be considered for patients with recurrent PVT/VF during the acute phase of ACS.	I	IIa
In patients with CAD eligible for ICD implantation, catheter ablation may be considered just before (or immediately after) ICD implantation to decrease subsequent VT burden and ICD shocks.	IIa	IIb
PVC-induced cardiomyopathy		
In patients with a cardiomyopathy suspected to be caused by frequent and predominately monomorphic PVCs, catheter ablation is recommended.	IIa	I

DCM/HNDCM		
ICD implantation should be considered in patients with DCM/HNDCM, symptomatic heart failure (NYHA class II–III) and LVEF ≤35% after ≥3 months of OMT.	I	IIa
Catheter ablation in specialized centres should be considered in patients with DCM/HNDCM and recurrent, symptomatic SMVT, or ICD shocks for SMVT, in whom AADs are ineffective, contraindicated, or not tolerated.	IIb	IIa
ARVC		
ICD implantation should be considered in patients with definite ARVC and an arrhythmic syncope.	IIb	IIa
ICD implantation should be considered in patients with definite ARVC and severe RV or LV systolic dysfunction.	IIb	IIa

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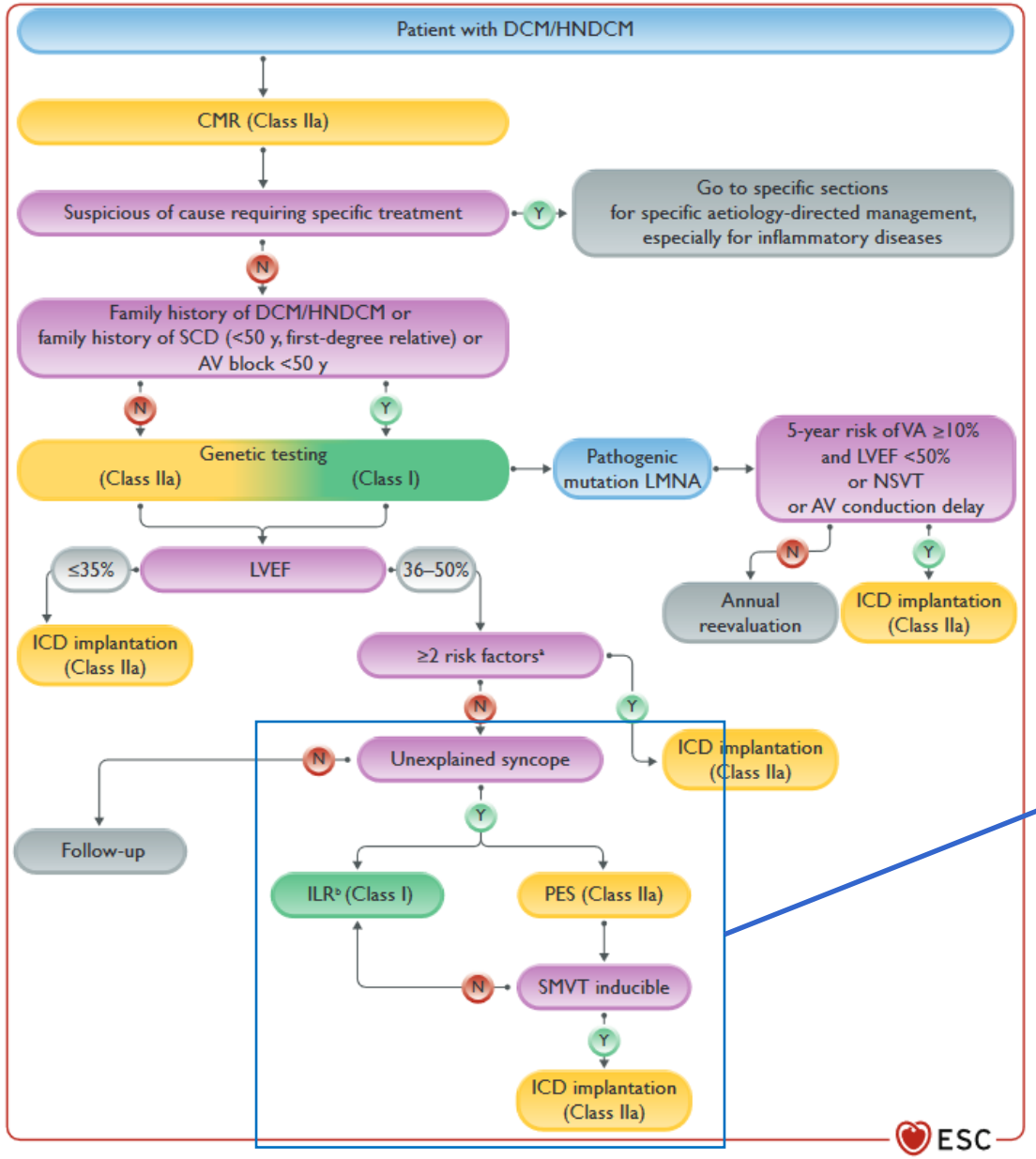

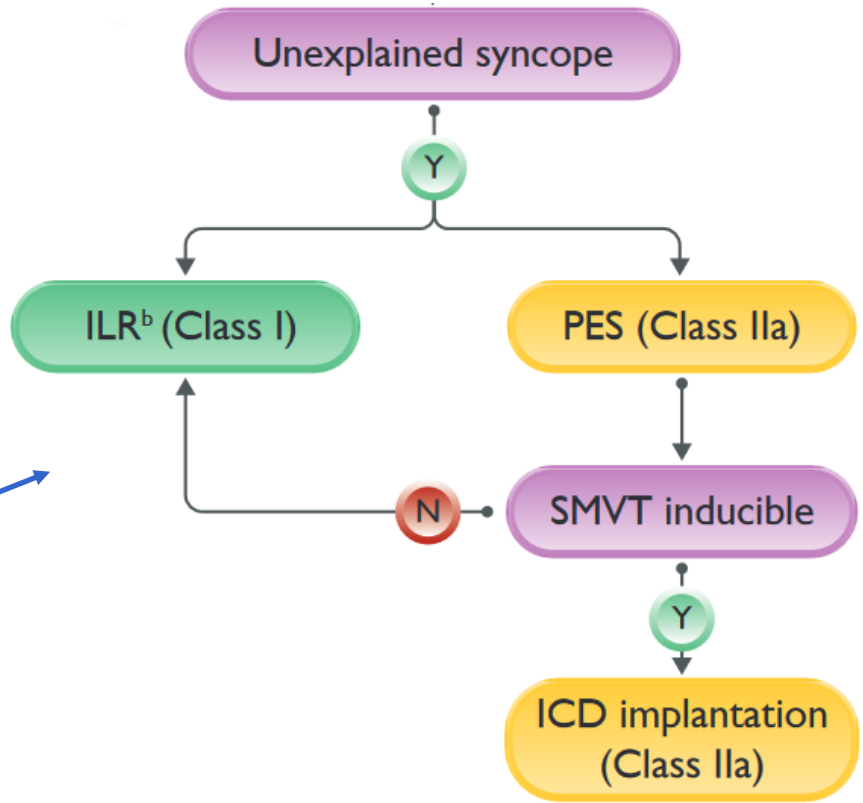

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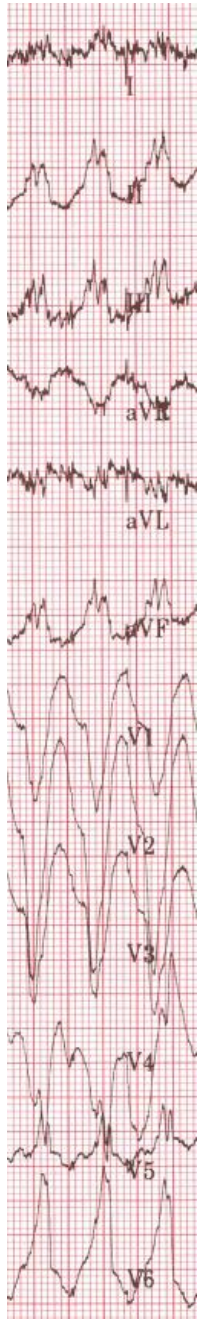
Elektrofyziologie & mapping



Jasný význam

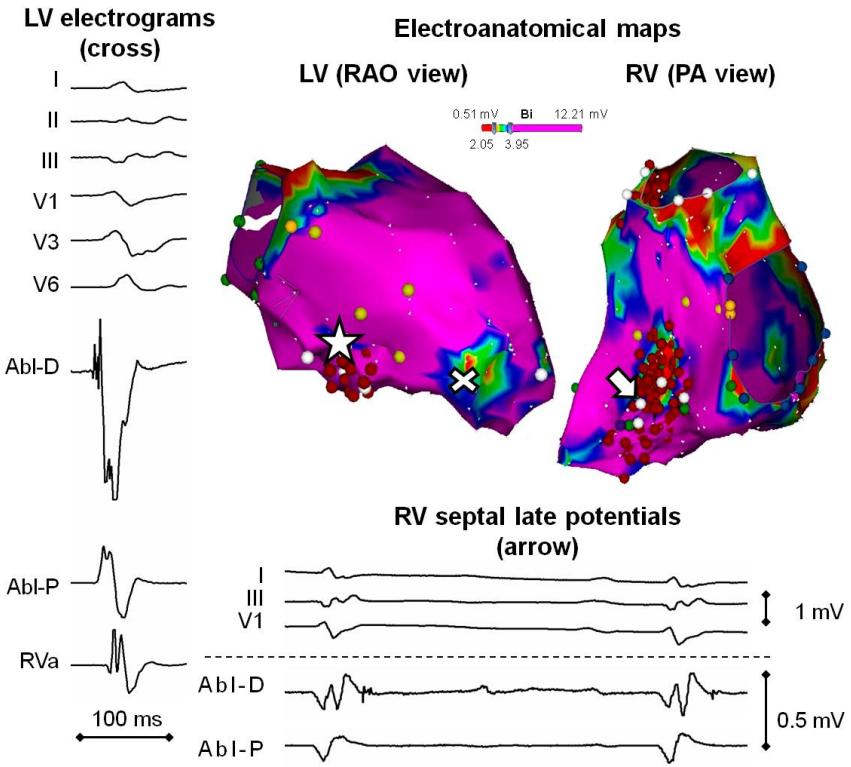
- Preexcitovaná fibrilace síní
- BBR-KT
- Rychlá SVT degenerující do VF
- Součást protokolu katetrizační ablace VT

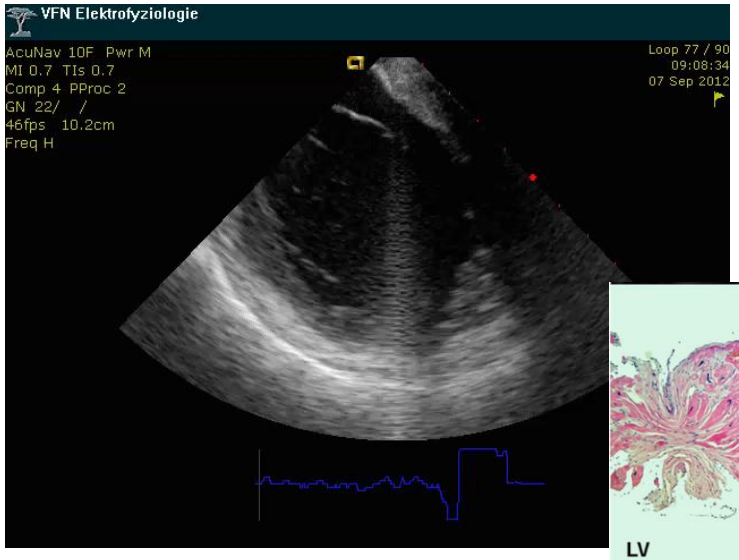
Potenciální význam

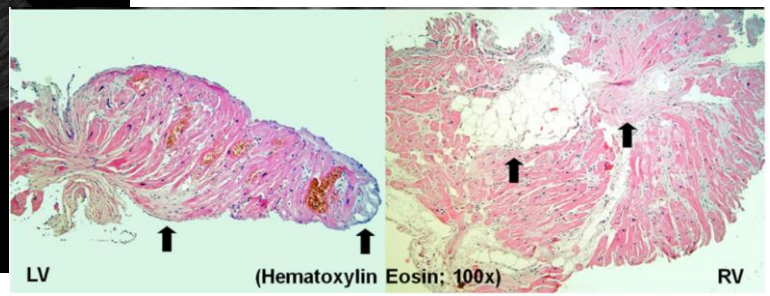
- Nejasná synkopa u pacienta se SHD s mrEF LK
- Brugada syndrom
- Myotonic dystrophy
- Sarkoidosa, ToF

Mapping

- Cíl pro katetrizační ablaci, Purkinje triggers
- Subklinická KMP (ARVC vs. OT VT)
- Cílení biopsie (ARVC, myocarditis, sarcoidosis…)







Havranek S et al. BMC Cardiovasc Disord 2015; 15:18. General University Hospital in Prague

2020 APHRS/HRS expert consensus statement on the investigation of decedents with sudden unexplained death and patients with sudden cardiac arrest, and of their families.

2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. EHJ (2022) 00,1-130

Vzácnější situace

Risk stratification, prevention of SCD and treatment of VA		
ICD implantation is recommended in patients with BrS who: (a) Are survivors of an aborted CA and/or (b) Have documented spontaneous sustained VT.[980,990–992]	I	C
ICD implantation should be considered in patients with type 1 Brugada pattern and an arrhythmic syncope.[990,992,996]	IIa	C
Implantation of a loop recorder should be considered in BrS patients with an unexplained syncope.[997,999]	IIa	C
Quinidine should be considered in patients with BrS who qualify for an ICD but have a contraindication, decline, or have recurrent ICD shocks.[922,1006,1007]	IIa	C
Isoproterenol infusion should be considered in BrS patients suffering electrical storm.[1008]	IIa	C
Catheter ablation of triggering PVCs and/or RVOT epicardial substrate should be considered in BrS patients with recurrent appropriate ICD shocks refractory to drug therapy.[1010–1015]	IIa	C
PES may be considered in asymptomatic patients with a spontaneous type I BrS ECG.[155]	IIb	B
ICD implantation may be considered in selected asymptomatic BrS patients with inducible VF during PES using up to 2 extra stimuli.[155]	IIb	C
Catheter ablation in asymptomatic BrS patients is not recommended.	III	C

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Prevence náhlé srdeční smrti u ICHS

Risk stratification and primary prevention of SCD		
In patients with syncope and previous STEMI, PES is indicated when syncope remains unexplained after non-invasive evaluation.[146,584]	I	C
ICD therapy is recommended in patients with CAD, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% despite ≥3 months of OMT.[354,356]	I	A
ICD therapy should be considered in patients with CAD, NYHA class I, and LVEF ≤30% despite ≥3 months of OMT.[354]	IIa	B
ICD implantation should be considered in patients with CAD, LVEF ≤40% despite ≥3 months of OMT, and NSVT, if they are inducible for SMVT by PES.[355]	IIa	B

Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in patients without ongoing ischaemia with documented VF or haemodynamically not-tolerated VT occurring later than 48 h after MI.[349–351]	I	A
In patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite chronic amiodarone therapy, catheter ablation is recommended in preference to escalating AAD therapy.[471]	I	B

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Genetické testování

Recommendations	Class[a]	Level[b]
Genetic testing is recommended when a condition is diagnosed in a living or deceased individual with a likely genetic basis and a risk of VA and SCD.[56,183]	I	B
When a putative causative variant is first identified, evaluation for pathogenicity is recommended using an internationally accepted framework.[176]	I	C
When a Class IV or Class V variant has been identified in a living or deceased individual with a condition that carries a risk of VA and SCD, genetic testing of first-degree and symptomatic relatives and obligate carriers is recommended.	I	C
It is recommended that genetic testing and counselling on its potential consequences should be undertaken by an expert multidisciplinary team.[179]	I	C
It is recommended that Class III (variants of uncertain significance) and Class IV variants should be evaluated for segregation in families where possible, and the variant re-evaluated periodically.	I	C
It is not recommended to undertake genetic testing in index patients with insufficient evidence of a genetic disease.	III	C

Optimální je, aby výsledek ovlivnil

- Finální diagnózu
- Další management
- Rodinný screening

Indikované

- Diagnostikované či vysoce suspektní geneticky vázané onemocnění na podkladě fenotypu
- Geny s robustní „gene-disease association“

Není benefit

- Fenotyp s jasnou negenetickou příčinou

Mutation class	Variant	
I	Benign	Nondiagnostic
II	Likely benign	
III	A variant of uncertain origin	Re-evaluation
IV	Likely pathogenic	Diagnostic
V	Pathogenic	

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Genetické testování

			LQTS	BrS	CPVT	Idiopathic VF	ERS
	Genetic test		Class I[a]	Class I	Class I[a]	Class IIb	Class IIb
Proband	**Initial clinical test**	**Cornerstone for diagnosis**	ECG Exercise test	ECG and high precordial lead ECG Sodium channel blockers provocative test[c]	Exercise test	See *Section 5.2.3*, scenario 3	ECG
		Other tests/processes	Exclude acquired LQTS	Exclude phenocopy[b]	Exclude phenocopy[b]/SHD		Holter Echocardiography
	Follow-up		1–3 years dependent on level of risk				
Relatives	**Clinical screening**		ECG Exercise test (when feasible) From birth	ECG and high precordial lead ECGs: start at 10 years Sodium channel blockers provocative test[c]: start >16 years unless clinically indicated[180,181]	ECG Exercise test From birth	ECG and high precordial lead ECGs Exercise test Echocardiogram[182]	ECG Echocardiogram
	Follow-up	Positive phenotype and/or Class IV/V variant	1–3 years dependent on level of risk				
		Negative phenotype and no Class IV/V variant	Discharge				

Genetické testování a management

- Long QT syndrom → β-blokátor
- Long QT3 syndrom → Na+ blokátor
- CPVT → flecainide
- ARVC / ALVC → exercise restrictions

Další zásadní diagnózy

- DKMP (lamin A/C gene, PLN, FLNC, RBM20)
- HKMP (sarkomerická mutace)

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Závěr

Pacient po oběhové zástavě

Akutní management k zvládnutí kritického stavu

Identifikace a odstranění reverzibilních příčin

Odstranění pokračující etiologie zástavy

Dlouhodobý management k objasnění příčiny a dlouhodobé zajištění

Význam pro pacienta i rodinu nemocného

Děkuji za pozornost!