Iskustva sa Flekanidom u svakodnevnoj kliničkoj praksi

Doc. dr Nebojša Mujović
Dr Milan Marinković

Odeljenje za elektrofiziologiju srca
UKCS

Indikacije za primenu Flekanida

Za prevenciju aritmija na "zdravom srcu":

- Prevencija paroksizmalne i perzistentne AF
- Idiopatske VES, kratkotrajne i dugotrajne VT
- SVT, WPW sindrom, SVES i AT

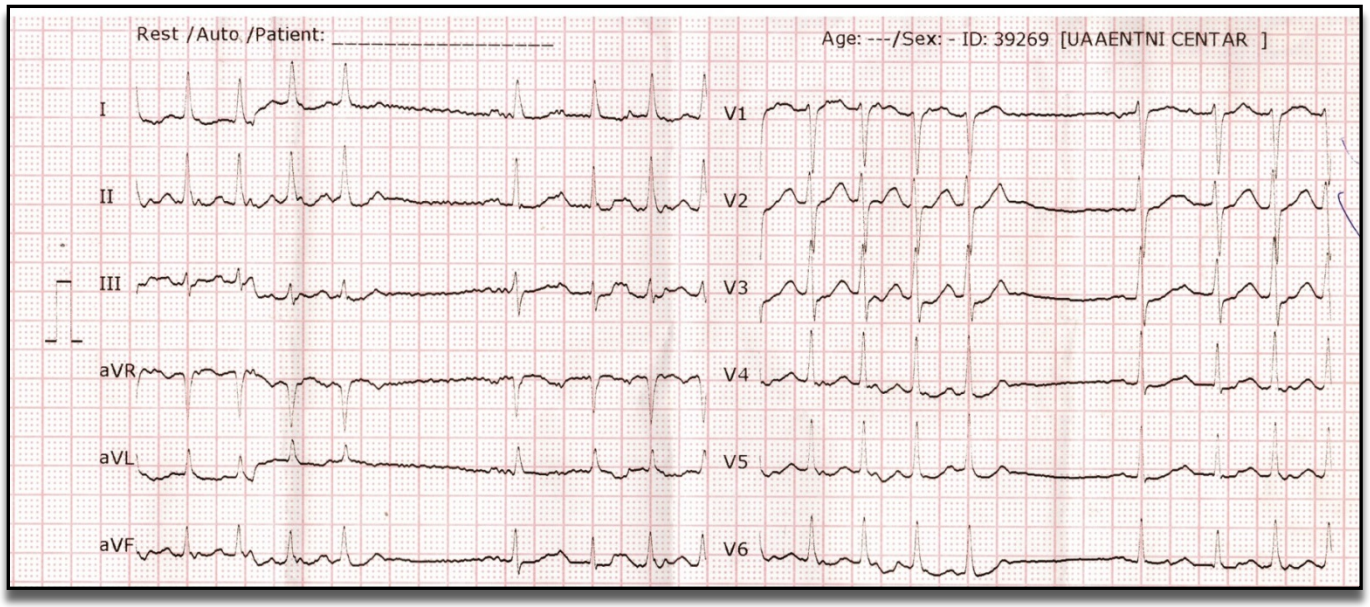
ATRIJALNA FIBRILACIJA

Moj pacijent sa AF…

- Paroks. AF

Istorija bolesti:
Muškarac, 55 god
Česti paroksizmi AF, salve SVES
Hipertenzija, dijabetes tip 2
Eho srca: LK EF = 60%, LP = 43 mm

Terapija:
Bisoprolol 5 mg
Telmisartan 80 mg
Varfarin (INR 2-3)
Metformin 2x1000 mg

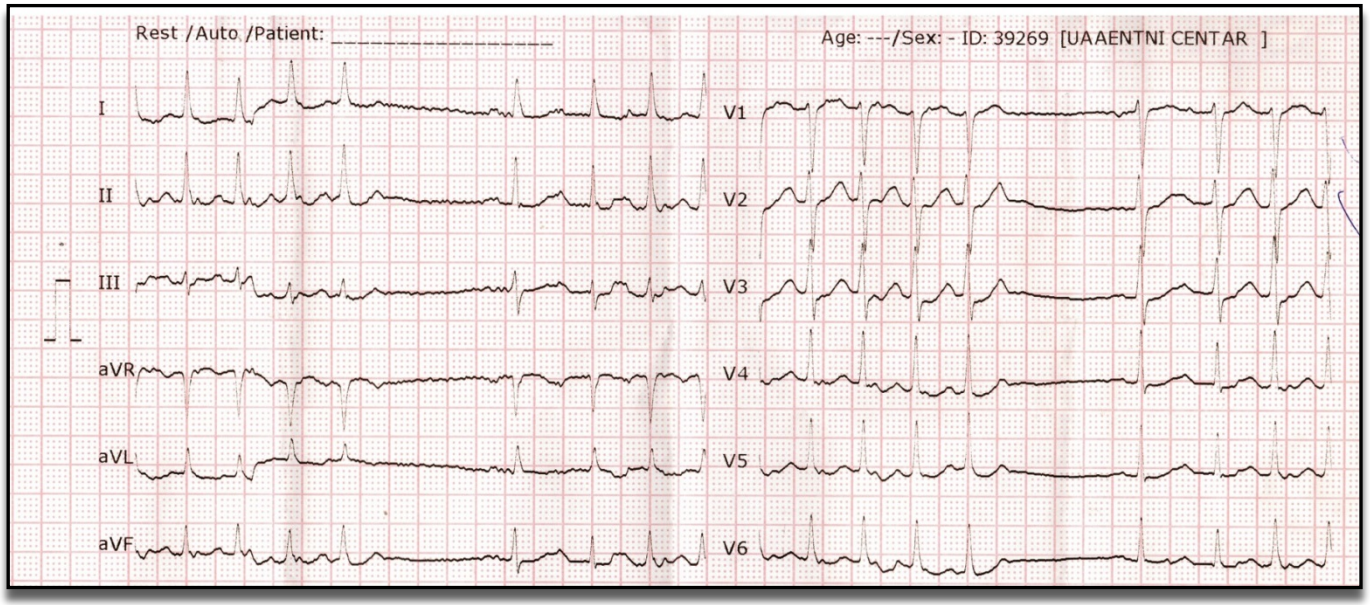


Izbor antiaritmika kod AF

- AF

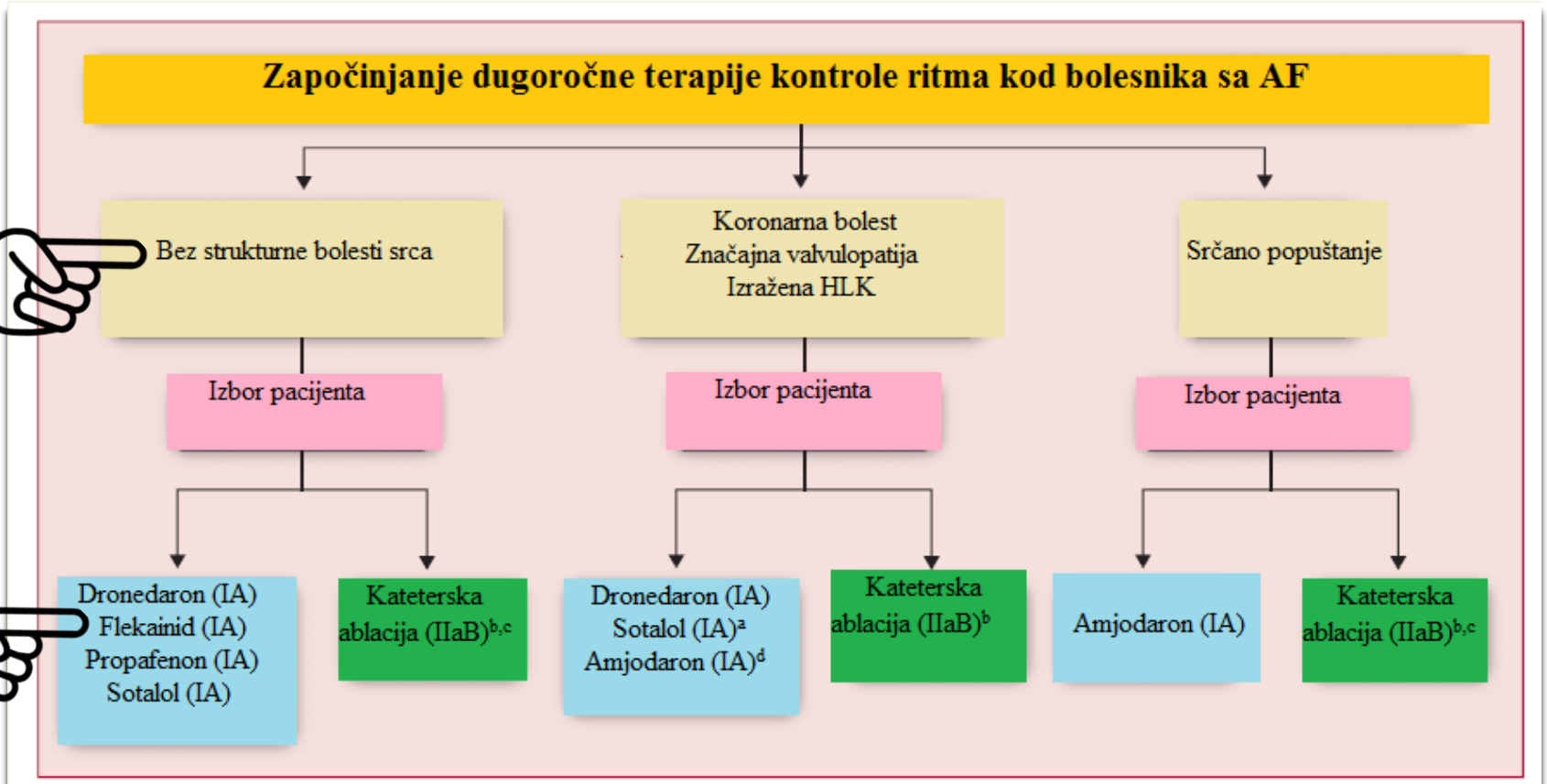
Terapijske opcije:

- **IC klasa (Flekainid, Propafenon)…….IA klasa**
- III klasa (Sotalol, Dronedaron)……IA klasa
- Amiodaron ???
- Kateterska ablacija (izolacija plućnih vena)……..IIaB klasa



Preporuke za lečenje AF, ESC 2016

- AF , prevencija epizoda AF – pravilan izbor leka



AF=atrijalna fibrilacija; HLK=hipertofija leve komore.
[a] Primena sotalola zahteva pažljivu procenu proaritmijskog rizika.
[b] Kateterskom ablacijom treba izolovati plućne vene i ona može se izvesti upotrebom katetera sa radiofrekventnom energijom ili kriobalonom.
[c] Kateterska ablacija je terapija izbora kod bolesnika sa srčanim popuštanjem i tahikardiomiopatijom.
[d] Amjodaron je terapija drugog reda zbog svojih ekstrakardijalnih toksičnih efekata.

Figura 17 Kontrola ritma kod atrijalne fibrilacije skorašnjeg početka.

Propafenon vs Flekainid

European Heart Journal (1995) **16**, 1943–1951

Safety of flecainide versus propafenone for the long-term management of symptomatic paroxysmal supraventricular tachyarrhythmias

Report from the Flecainide and Propafenone Italian Study (FAPIS) group

M. Chimienti, M. T. Cullen Jr.,* G. Casadei† for the Flecainide and Propafenone Italian Study Investigators‡

200 bolesnika sa PAF

Flekainid 200 mg/d vs. Propafenon 450 mg/d

Flekainid značajno efikasniji za održavanje sinusnog ritma nakon 1 god: 79% vs 63%

Table 7 Life table analysis of efficacy (per-protocol)

				Day 0	15	30	90	180	270	360	
PAF	Flecainide 100 mg b.i.d.	No. of patients		77	71	70	62	58	53	50	$P<0.02$
		Probability			0·93	0·93	0·86	0·84	0·79	0·79	
	Propafenone 150 mg t.i.d.	No. of patients		82	69	63	53	50	48	45	
		Probability			0·84	0·79	0·70	0·69	0·67	0·63	

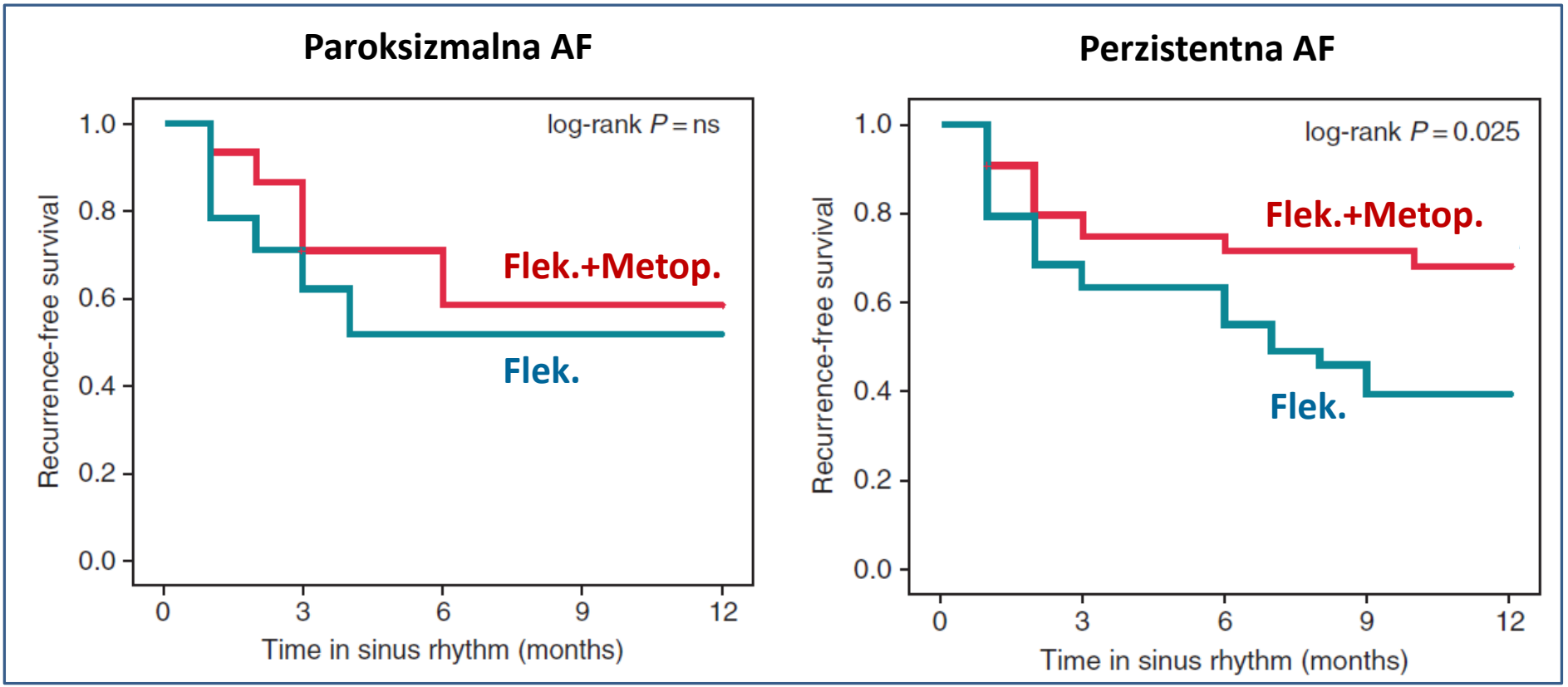
Razlike između Flekanida i Propafena

- Slični elektrofiziološki efekti – **razlike u farmakokinetici**

	Propafen	**Flekanid**
Bioraspoloživost	50%	**90%**
β1 β2 blokatorsko dejstvo	**Da** (5%) • HOBP, • perif. art. bolest	Ne
Put eliminacije	Jetra • Brzi i spori metabolizeri	**Bubreg** • bubrežna slabost
Poluvreme eliminacije	2-10 h • doziranje 2-3 x dnevno	20 h • **doziranje 1 x dnevno,** • **bolja komplijansa**

Kombinacija Flekainid + Metoprolol

- 173 bolesnika sa PAF i Pe-AF
- Dodavanje Metoprolola Flekainidu pojačava efekat u prevenciji AF i toleranciju leka
- Kombinacija posebno doprinosi boljoj prevenciji Pe-AF

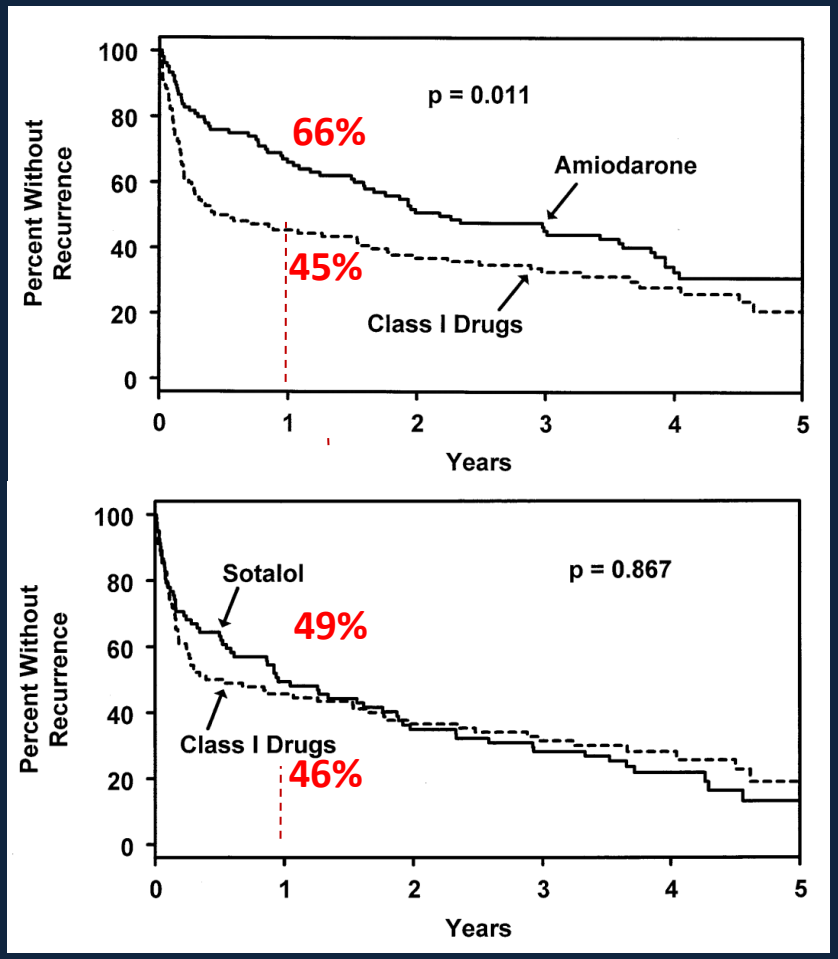


Capucci et al. Flecainide-metoprolol combination reduces atrial fibrillation recurrences and improves tolerability at 1-year follow-up in persistent symptomatic atrial fibrillation. Europace 2016;18:1698-1704

AMJODARON ?

Prevencija AF, relativna efikasnost antiaritmika:

- Amiodaron znacajno efikasniji od svih ostalih antiaritmika, AFFIRM JACC 2003
- Ozbiljna kardijalna i ekstrakardijalna toksičnost amiodarona



AMJODARON ?

Toxicity	Incidence	Screening/monitoring	Therapeutic recommendation
Cardiac ▪ Bradycardia ▪ QT prolongation ▪ Torsades DP	▪ 5% ▪ all ▪ <1%	▪ ECG before therapy and at least once during the "loading" phase, then once a year	▪ dose reduction ▪ if QT >550 ms or torsades occur - discontinuation of amiodarone
Thyroid ▪ Hyperthyroidism ▪ Hypothyroidism	▪ 3% ▪ 20%	▪ FT4/TSH before therapy, every 3 months during the first year, then every 6 months ▪ anti-TPO antibodies before therapy	▪ avoid amiodarone in pre-existing thyroid disease ▪ tionamides for type 1, corticosteroides for type 2 hyperthyroidism ▪ thyroid hormone replacement therapy (levo-thyroxine)
Pulmonary	▪ <3%	▪ pulmonary function tests (CO diffusion capacity), ▪ Chest X-ray before therapy, than at 6-12 months	▪ immediate cessation of amiodarone for suspected pulmonary toxicity ▪ corticosteroid therapy
Hepatic	▪ 15%	▪ obtain AST/ALT before amiodarone introduction, then every 6 months	▪ avoid drug in case of an existing liver disease ▪ cessation of therapy in case of double AST/ALT ↑
Ophthalmological ▪ Keratopathy ▪ Optic neuropathy	▪ 80% ▪ <1%	▪ ophthalmological examination before therapy, then according to symptoms	▪ continue therapy ▪ stop the amiodarone
Neurological	▪ 3-30%	▪ as needed	▪ dose reduction or cessation
Dermatological	▪ 25-75%	▪ examination in case of skin changes	▪ avoid the sunlight ▪ sunglasses and UV protection factor

Mujovic et al. Pharm Research 2019 (in press)

Indikacije za kat-ablaciju PAF

Table 2 Indications for catheter (A and B) and surgical (C, D, and E) ablation of atrial fibrillation

	Recommendation	Class	LOE
Indications for catheter ablation of atrial fibrillation			
A. Indications for catheter ablation of atrial fibrillation			
Symptomatic AF refractory or intolerant to at least one Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is recommended.	I	A
	Persistent: Catheter ablation is reasonable.	IIa	B-NR
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-LD
Symptomatic AF prior to initiation of antiarrhythmic therapy with a Class I or III antiarrhythmic medication	Paroxysmal: Catheter ablation is reasonable.	IIa	B-R
	Persistent: Catheter ablation is reasonable.	IIa	C-EO
	Long-standing persistent: Catheter ablation may be considered.	IIb	C-EO

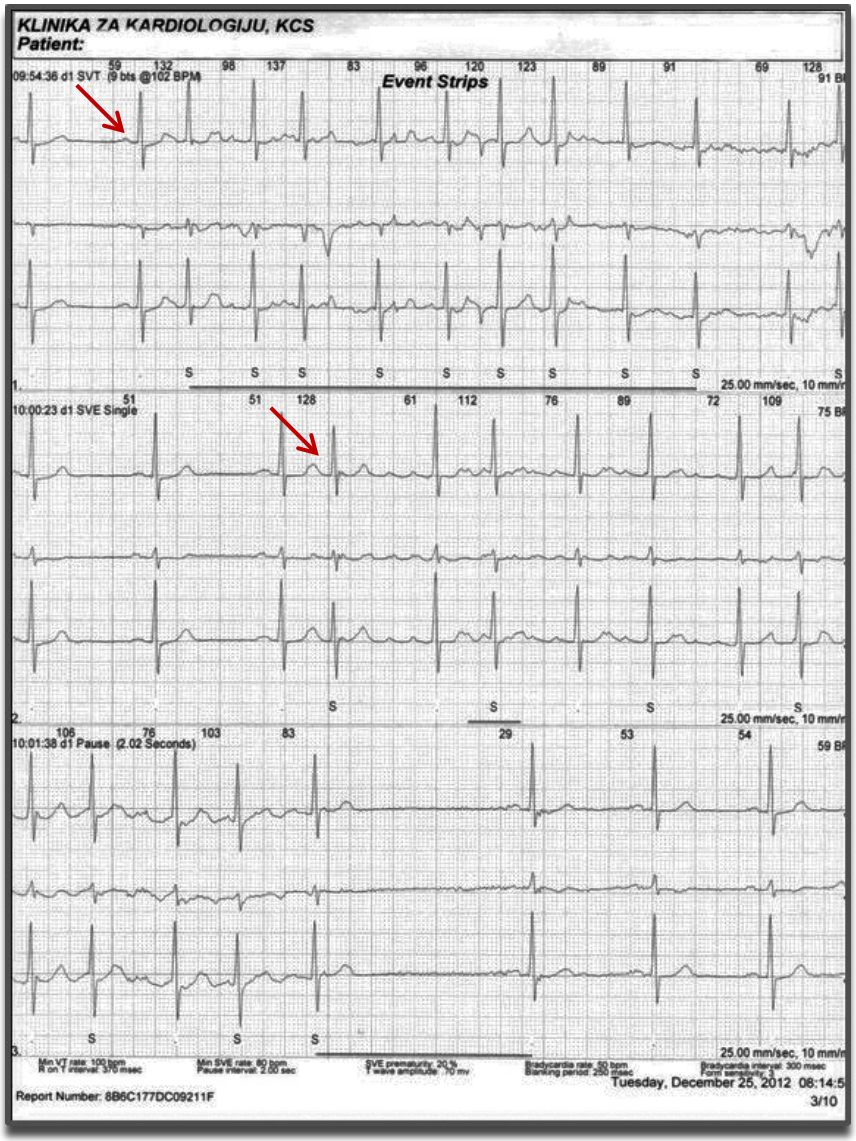
2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation

Hugh Calkins, MD (Chair),[1] Gerhard Hindricks, MD (Vice-Chair),[2]*

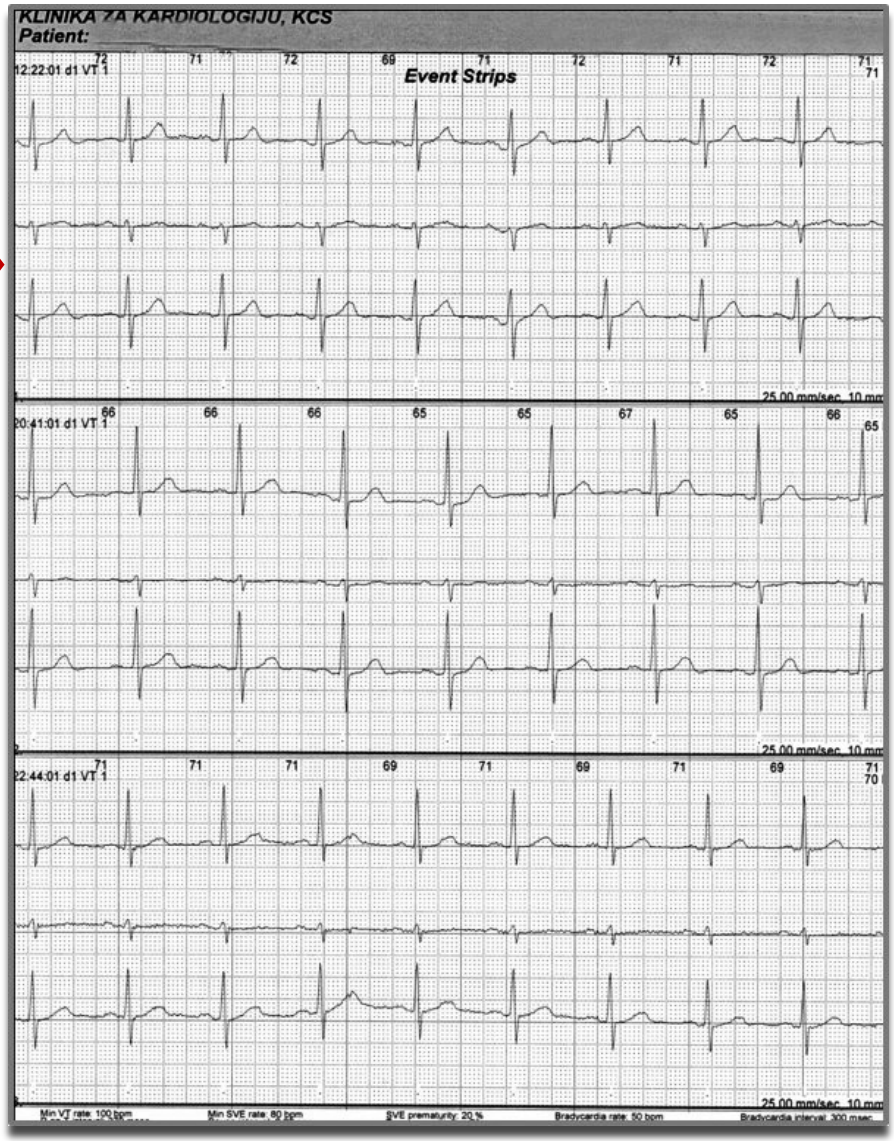
Europace (2017) **00**, 1–160

.....moj pacijent sa AF → Flekainid

Bez antiaritmika



Flekanid 200 mg



KOMORSKE ARITMIJE

Moj pacijent sa VT…

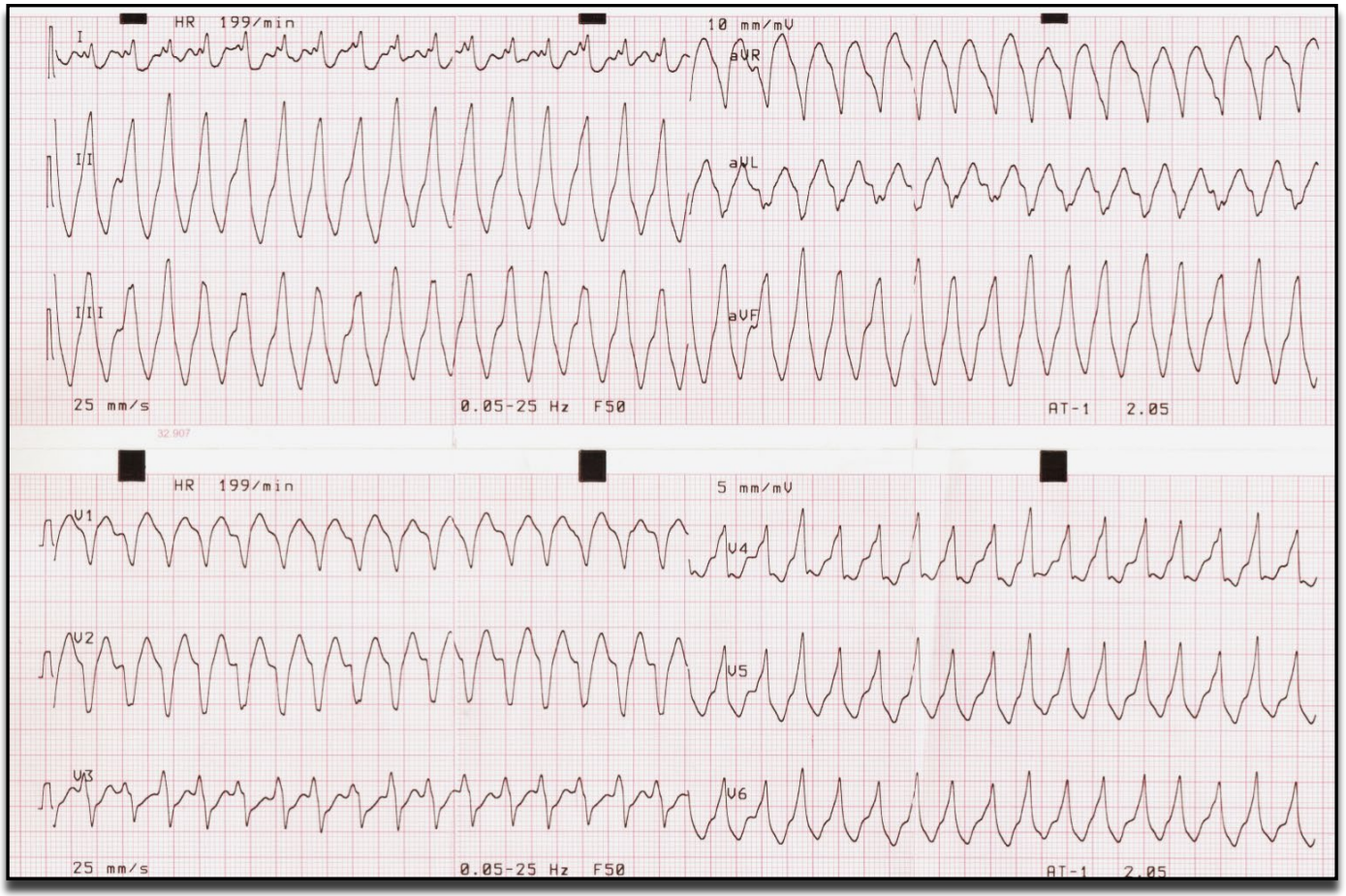
- VES, VT , na “zdravom srcu”

  - Devojka,18 god.
  - **Sinkopa** tokom paroksizma tahikardije
  - 12-kanalni EKG: sinusni ritam, normalan
  - Eho srca normalan: LK 48/27 mm, EF 70%
  - Ergometrija normalna
  - Holter-EKG 24h, oko 12.000 VES (VTNS + dugotrajna VT)

  - **Bisoprolol 2.5 mg**

Moj pacijent sa VT….

- VES, VT , na “zdravom srcu”
  - EKG: dugotrajna monomorfna VT 200/min **(inferior axis, LBBB)**
  - Fokus **u izlaznom traktu DK (RVOT)**, trigerovani automatizam



Moj pacijent sa VT…

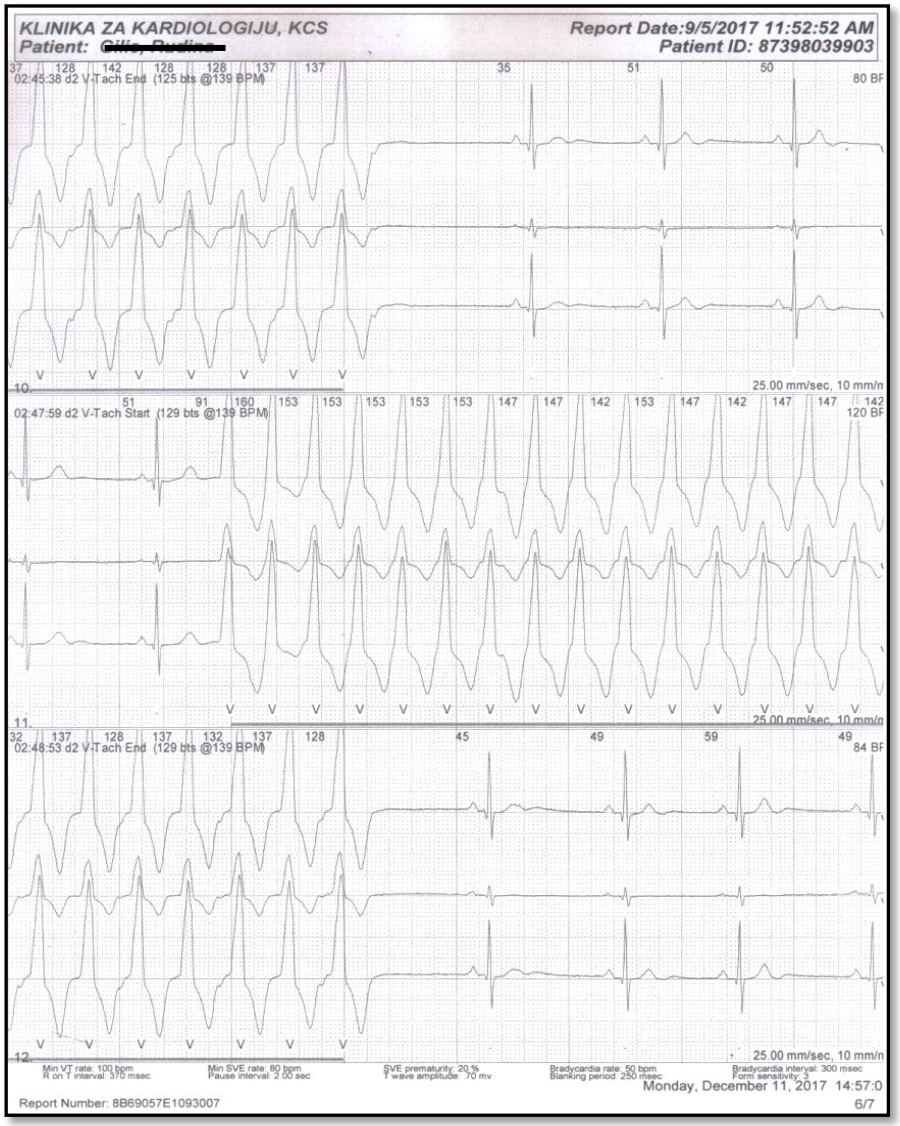
- VES, VT , na “zdravom srcu”

Holter 24h:

(4004 VES, 60 epizoda VTNS)

Invazivno EP ispitivanje:

- Neinducibilna VT
- Odustalo se od ablacije



Terapijske opcije ?

- VES, VT , na “zdravom srcu”

Terapijske opcije (antiaritmici) :

- Amiodaron
- Sotalol
- Verapamil
- Meksiletin
- **IC klasa (Flekainid ili Propafenon)**
- Kateterska ablacija
- ICD

Odabir antiaritmika za idiopatske VA

- VES, VT , na "zdravom srcu" (ESC 2015 Guidelines for VA)

Table 3 Non-sustained ventricular tachycardia with apparent normal heart

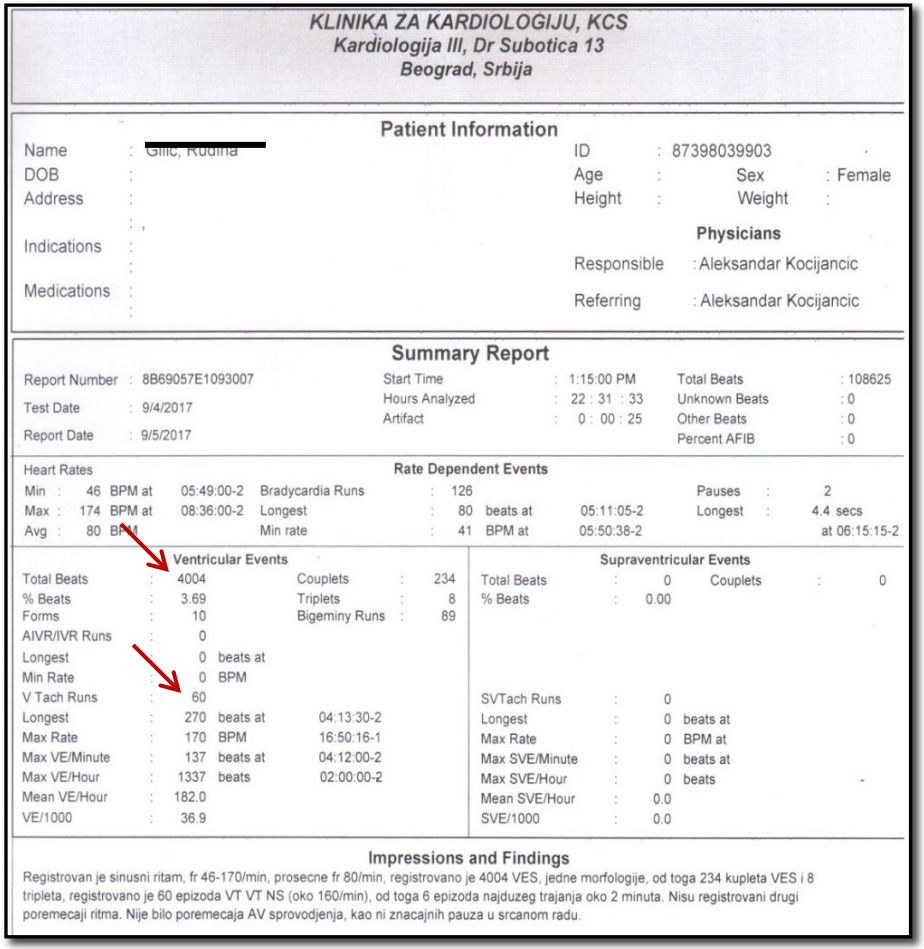
NSVT clinical presentation	ECG	Risk of sudden cardiac death	Diagnostic evaluation	Alternative diagnostic considerations	Treatment	Treatment to be considered	Key references
Typical RVOT	LBBB, inf axis, axis transition V3–V4	Very rare	Standard	Differentiate from ARVC	Beta-blocker, verapamil, IC drugs with symptoms	Catheter ablation	Latif *et al.*[62]
Typical LVOT	Inferior axis, transition <V3	Very rare	Standard	RVOT VT	Beta-blocker, verapamil, IC drugs with symptoms	Catheter ablation	Latif *et al.*[62]
Idiopathic reentrant LV tachycardia	RBBB, LS axis	Very rare	Standard EP testing	Ischaemic heart disease, CM	Verapamil if symptomatic	Catheter ablation	Latif *et al.*[62]
Other focal VT	Multiple morphologies, monomorphic	Uncommon	Exercise testing or catecholamine stimulation	Ischaemic heart disease, CM	Beta-blocker for the arrhythmia	Catheter ablation	Latif *et al.*[62]
Exercise	Multiple	Increased risk when NSVT in recovery	Ischaemic heart disease, cardiomyopathy	CPVT	Underlying disease	Beta-blockers, flecainide	Jouven *et al.*[65], Frolkis *et al.*[66]
Athlete	Multiple	If it disappears with increased exercise low risk	Evaluate for latent HCM or ischaemic heart disease	HCM	No treatment training can continue	None	Biffi *et al.*[67,68]
Hypertension valvular disease	Multiple morphology	As without arrhythmia	Consider ischaemic heart disease	Ischaemic heart disease, CM	Treat HTN	Beta-blocker	
Polymorphic VT	Polymorphic	High	Evaluated for CAD, CPVT, inherited arrhythmia syndromes	Purkinje fibre triggering focus	Underlying disease	Revascularization, ICD, beta-blocker, catheter ablation	Zipes *et al.*[60]
TdP VT	Long QT, TdP	High	Medications, congenital LQTS	Medications, K^+, Mg^{++}, Ca^{++}	Stop medications, correct electrolytes	ICD, beta-blocker	Sauer and Newton-Cheh[69]

ARVC, arrhythmogenic right ventricular cardiomyopathy; CAD, coronary artery disease; CM, cardiomyopathy; CPVT, catecholaminergic polymorphic ventricular tachycardia; HCM, hypertrophic cardiomyopathy; HTN, hypertension; ICD, implantable cardioverter-defibrillator; LS, left-superior; LV, left ventricular; LVOT, left ventricular outflow tract; NSVT, non-sustained ventricular tachycardia; RBBB, right bundle branch block; RVOT, right ventricular outflow tract; TdP, torsade de pointes; VT, ventricular tachycardia.

…moj pacijent sa VT

- VES, VT , na “zdravom srcu”

Bez antiaritmika



KLINIKA ZA KARDIOLOGIJU, KCS
Kardiologija III, Dr Subotica 13
Beograd, Srbija

Patient Information

Name : [redacted]
DOB :
Address :
Indications :
Medications :
ID : 87398039903
Age : Sex : Female
Height : Weight :
Physicians
Responsible : Aleksandar Kocijancic
Referring : Aleksandar Kocijancic

Summary Report

Report Number : 8B69057E1093007
Test Date : 9/4/2017
Report Date : 9/5/2017
Start Time : 1:15:00 PM
Hours Analyzed : 22 : 31 : 33
Artifact : 0 : 00 : 25
Total Beats : 108625
Unknown Beats : 0
Other Beats : 0
Percent AFIB : 0

Heart Rates
Min : 46 BPM at 05:49:00-2
Max : 174 BPM at 08:36:00-2
Avg : 80 BPM

Rate Dependent Events

Bradycardia Runs : 126
Longest : 80 beats at 05:11:05-2
Min rate : 41 BPM at 05:50:38-2
Pauses : 2
Longest : 4.4 secs at 06:15:15-2

Ventricular Events

Total Beats	4004	Couplets	234
% Beats	3.69	Triplets	8
Forms	10	Bigeminy Runs	89
AIVR/IVR Runs	0		
Longest	0 beats at		
Min Rate	0 BPM		
V Tach Runs	60		
Longest	270 beats at	04:13:30-2	
Max Rate	170 BPM	16:50:16-1	
Max VE/Minute	137 beats at	04:12:00-2	
Max VE/Hour	1337 beats	02:00:00-2	
Mean VE/Hour	182.0		
VE/1000	36.9		

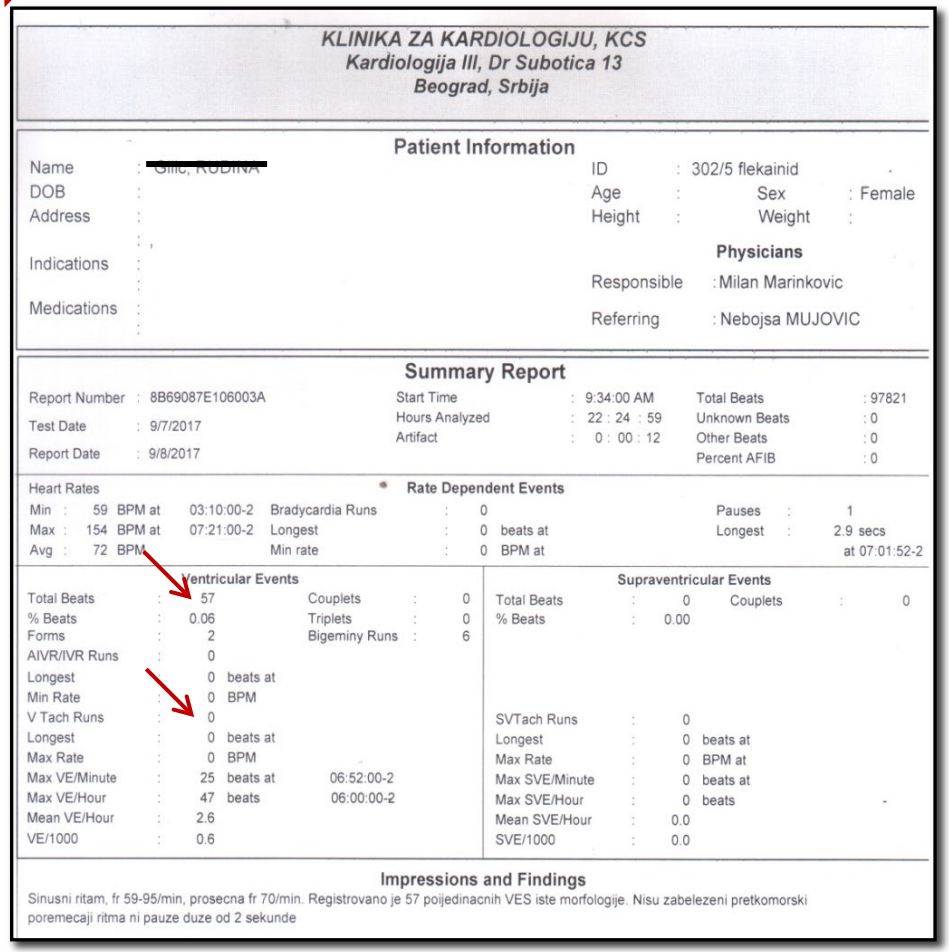
Supraventricular Events

Total Beats	0	Couplets	0
% Beats	0.00		
SVTach Runs	0		
Longest	0 beats at		
Max Rate	0 BPM at		
Max SVE/Minute	0 beats at		
Max SVE/Hour	0 beats		
Mean SVE/Hour	0.0		
SVE/1000	0.0		

Impressions and Findings

Registrovan je sinusni ritam, fr 46-170/min, prosecne fr 80/min, registrovano je 4004 VES, jedne morfologije, od toga 234 kupleta VES i 8 tripleta, registrovano je 60 epizoda VT VT NS (oko 160/min), od toga 6 epizoda najduzeg trajanja oko 2 minuta. Nisu registrovani drugi poremecaji ritma. Nije bilo poremecaja AV sprovodjenja, kao ni znacajnih pauza u srcanom radu.

Flekanid 200 mg



KLINIKA ZA KARDIOLOGIJU, KCS
Kardiologija III, Dr Subotica 13
Beograd, Srbija

Patient Information

Name : [redacted]
DOB :
Address :
Indications :
Medications :
ID : 302/5 flekainid
Age : Sex : Female
Height : Weight :
Physicians
Responsible : Milan Marinkovic
Referring : Nebojsa MUJOVIC

Summary Report

Report Number : 8B69087E106003A
Test Date : 9/7/2017
Report Date : 9/8/2017
Start Time : 9:34:00 AM
Hours Analyzed : 22 : 24 : 59
Artifact : 0 : 00 : 12
Total Beats : 97821
Unknown Beats : 0
Other Beats : 0
Percent AFIB : 0

Heart Rates
Min : 59 BPM at 03:10:00-2
Max : 154 BPM at 07:21:00-2
Avg : 72 BPM

Rate Dependent Events

Bradycardia Runs : 0
Longest : 0 beats at
Min rate : 0 BPM at
Pauses : 1
Longest : 2.9 secs at 07:01:52-2

Ventricular Events

Total Beats	57	Couplets	0
% Beats	0.06	Triplets	0
Forms	2	Bigeminy Runs	6
AIVR/IVR Runs	0		
Longest	0 beats at		
Min Rate	0 BPM		
V Tach Runs	0		
Longest	0 beats at		
Max Rate	0 BPM		
Max VE/Minute	25 beats at	06:52:00-2	
Max VE/Hour	47 beats	06:00:00-2	
Mean VE/Hour	2.6		
VE/1000	0.6		

Supraventricular Events

Total Beats	0	Couplets	0
% Beats	0.00		
SVTach Runs	0		
Longest	0 beats at		
Max Rate	0 BPM at		
Max SVE/Minute	0 beats at		
Max SVE/Hour	0 beats		
Mean SVE/Hour	0.0		
SVE/1000	0.0		

Impressions and Findings

Sinusni ritam, fr 59-95/min, prosecna fr 70/min. Registrovano je 57 poijedinacnih VES iste morfologije. Nisu zabelezeni pretkomorski poremecaji ritma ni pauze duze od 2 sekunde

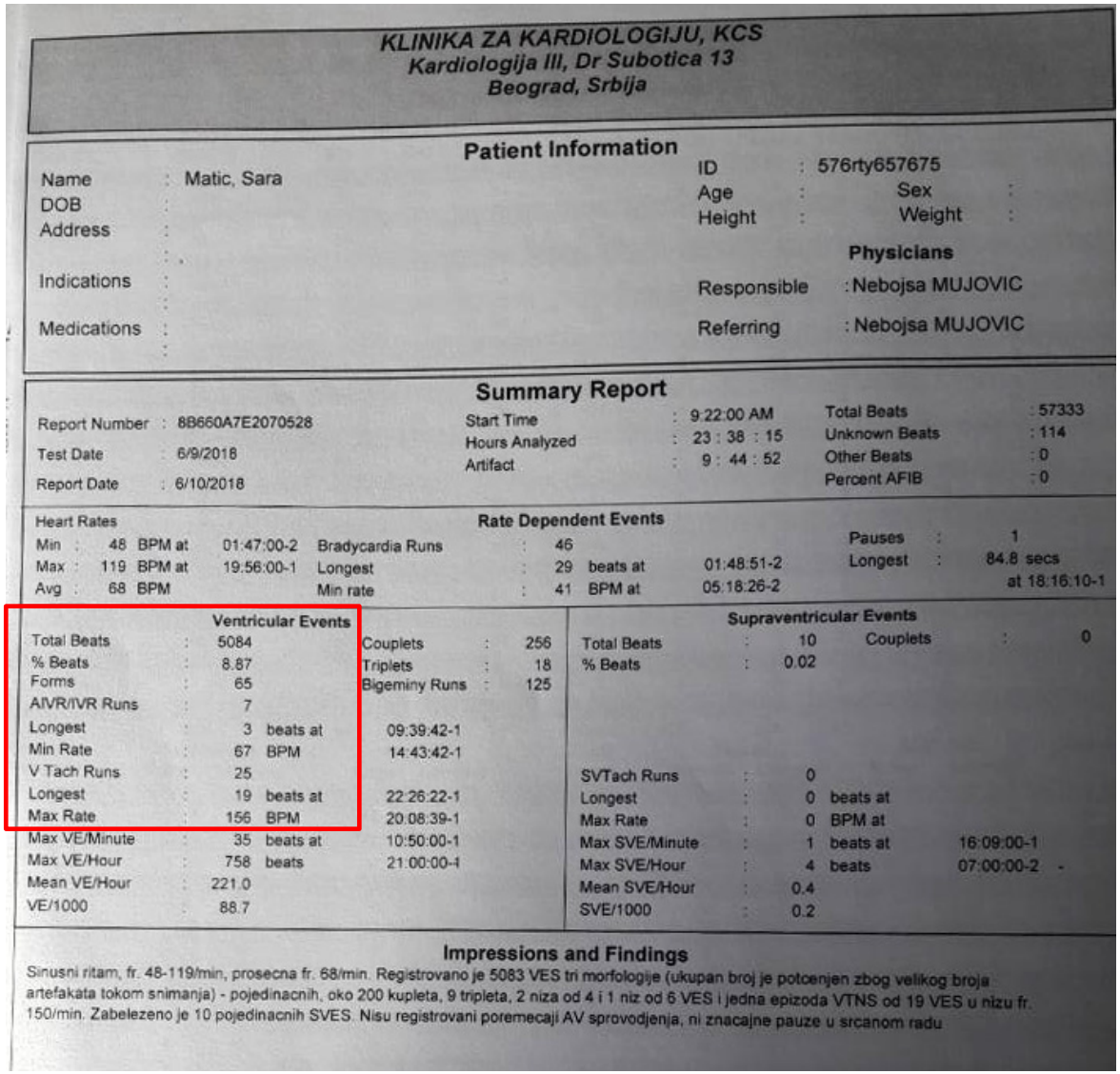
Pacijent sa VTNS

- Devojka, 21 god., 50 kg
- Primljena radi evaluacije VES aritmije
- Polimorfne VES (simptomatske)
- Nema strukturnu bolest srca
- Porodična istorija naprasne smrti

- Beta-blokator (metoprolol 2x50 mg)

Pacijent 4°

Metoprolol 100 mg: 24h Holter, oko 5000 polimorfnih VES, repetitivne VTNS



KLINIKA ZA KARDIOLOGIJU, KCS
Kardiologija III, Dr Subotica 13
Beograd, Srbija

Patient Information

Name : Matic, Sara
DOB :
Address :
Indications :
Medications :

ID : 576rty657675
Age : Sex :
Height : Weight :

Physicians

Responsible : Nebojsa MUJOVIC
Referring : Nebojsa MUJOVIC

Summary Report

Report Number : 8B660A7E2070528
Test Date : 6/9/2018
Report Date : 6/10/2018

Start Time : 9:22:00 AM
Hours Analyzed : 23 : 38 : 15
Artifact : 9 : 44 : 52

Total Beats : 57333
Unknown Beats : 114
Other Beats : 0
Percent AFIB : 0

Heart Rates

Min : 48 BPM at 01:47:00-2
Max : 119 BPM at 19:56:00-1
Avg : 68 BPM

Rate Dependent Events

Bradycardia Runs : 46
Longest : 29 beats at 01:48:51-2
Min rate : 41 BPM at 05:18:26-2

Pauses : 1
Longest : 84.8 secs at 18:16:10-1

Ventricular Events

Total Beats	5084		
% Beats	8.87		
Forms	65		
AIVR/IVR Runs	7		
Longest	3	beats at	09:39:42-1
Min Rate	67	BPM	14:43:42-1
V Tach Runs	25		
Longest	19	beats at	22:26:22-1
Max Rate	156	BPM	20:08:39-1
Max VE/Minute	35	beats at	10:50:00-1
Max VE/Hour	758	beats	21:00:00-1
Mean VE/Hour	221.0		
VE/1000	88.7		

Couplets : 256
Triplets : 18
Bigeminy Runs : 125

Supraventricular Events

Total Beats : 10
% Beats : 0.02
Couplets : 0

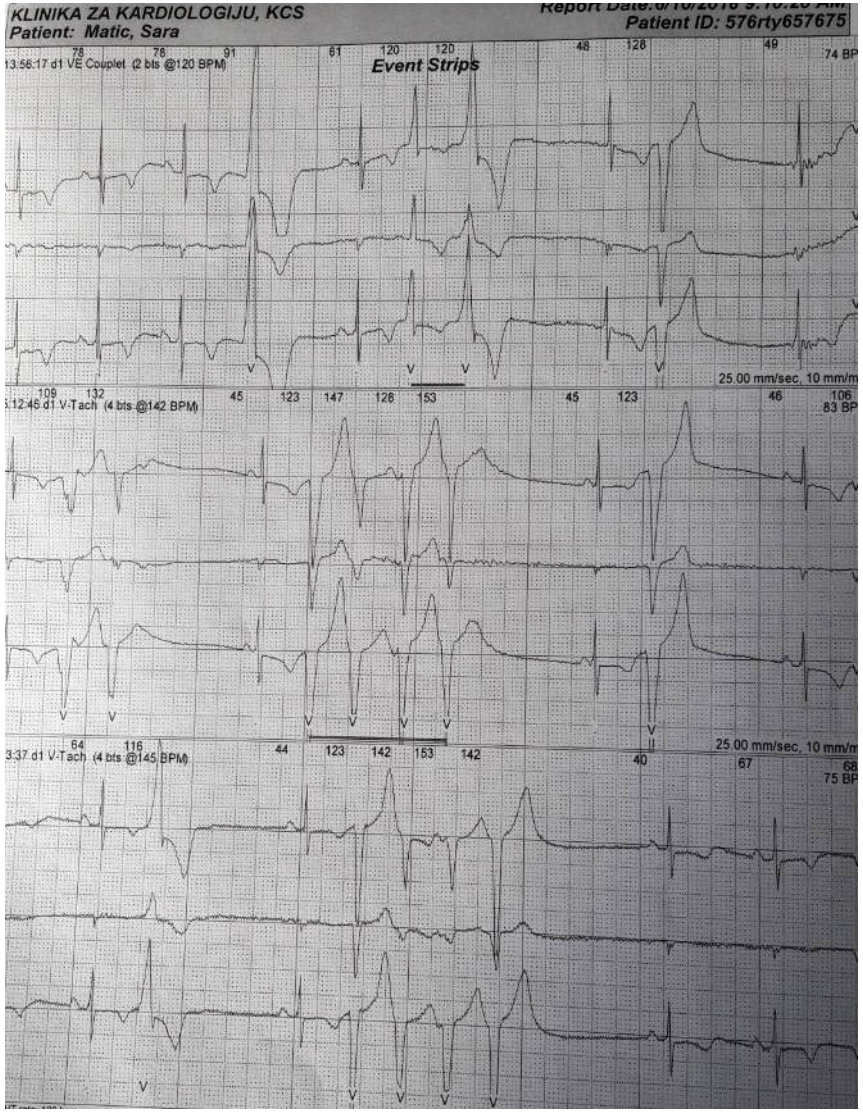
SVTach Runs : 0
Longest : 0 beats at
Max Rate : 0 BPM at
Max SVE/Minute : 1 beats at 16:09:00-1
Max SVE/Hour : 4 beats 07:00:00-2
Mean SVE/Hour : 0.4
SVE/1000 : 0.2

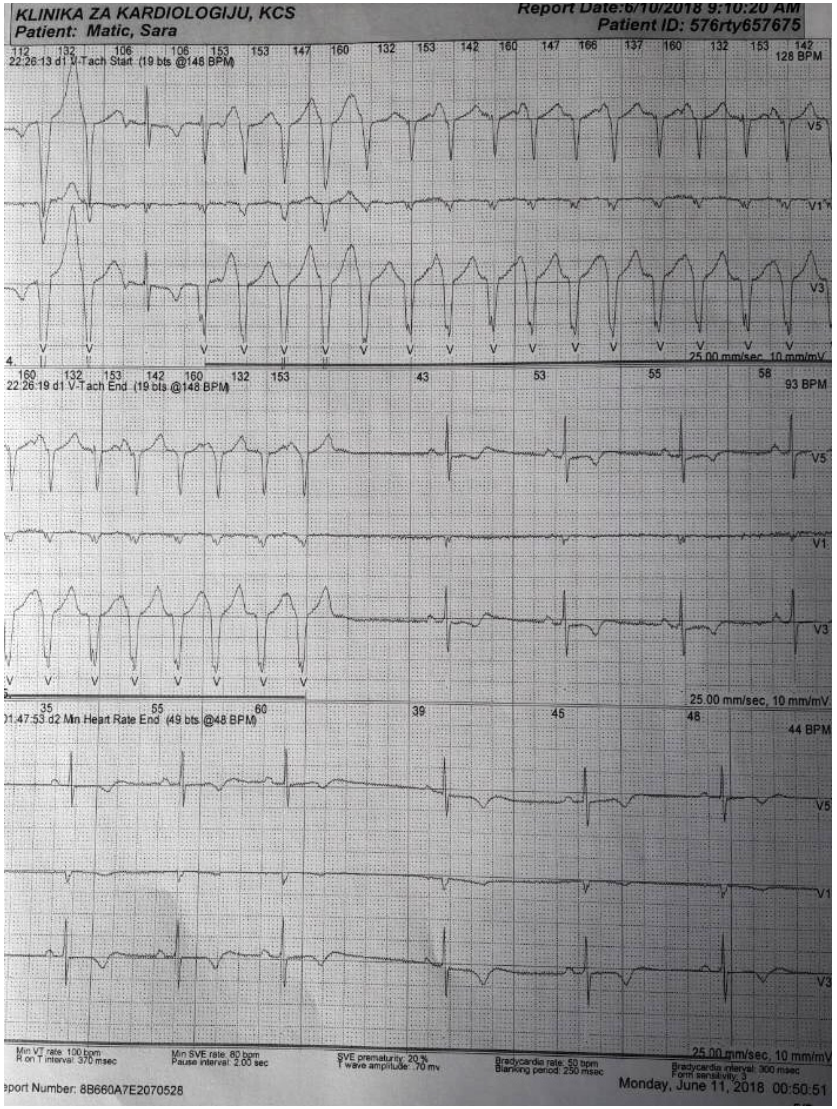
Impressions and Findings

Sinusni ritam, fr. 48-119/min, prosecna fr. 68/min. Registrovano je 5083 VES tri morfologije (ukupan broj je potcenjen zbog velikog broja artefakata tokom snimanja) - pojedinacnih, oko 200 kupleta, 9 tripleta, 2 niza od 4 i 1 niz od 6 VES i jedna epizoda VTNS od 19 VES u nizu fr. 150/min. Zabelezeno je 10 pojedinacnih SVES. Nisu registrovani poremecaji AV sprovodjenja, ni znacajne pauze u srcanom radu

Pacijent 4°

Metoprolol 100 mg: 24h Holter, oko 5000 polimorfnih VES, repetitivne VTNS





Pacijent 4°

Metoprolol 100 mg: ergometrija prekinuta na I° zbog malignih poremećaja ritma ?

Broj protokola:/18 Datum:08.06.2018.

KABINET ZA ERGOMETRIJU I STRESEHOKARDIOGRAFIJU

Prezime, Ime:Matic Sara 21god TT 50kg TV 160cm MB:1302997786015
Adresa i telefon:JNA 34, Jasika, Krusevac tel:062/8565372 zanimanje:student
Indikacije za test:VES
Dg:VES-I49.3
Intervencije:/
FR:hereditet
Th:Presolol 50+25mg 1x1

SMF 169/min

Vreme (min)	Opterećenje	TA	Puls	EKG	LVEDVI	LVESVI	WMSI	EF	B linije
Mir	Mir	100/70	84						
3	I stepen	110/70	113						
6	II stepen								
9	III stepen								
12	IV stepen								
15	V stepen								
Odmor 1	1.min	110/70	85						
5	5.min								
CF rest									
CF stres				CFR=					

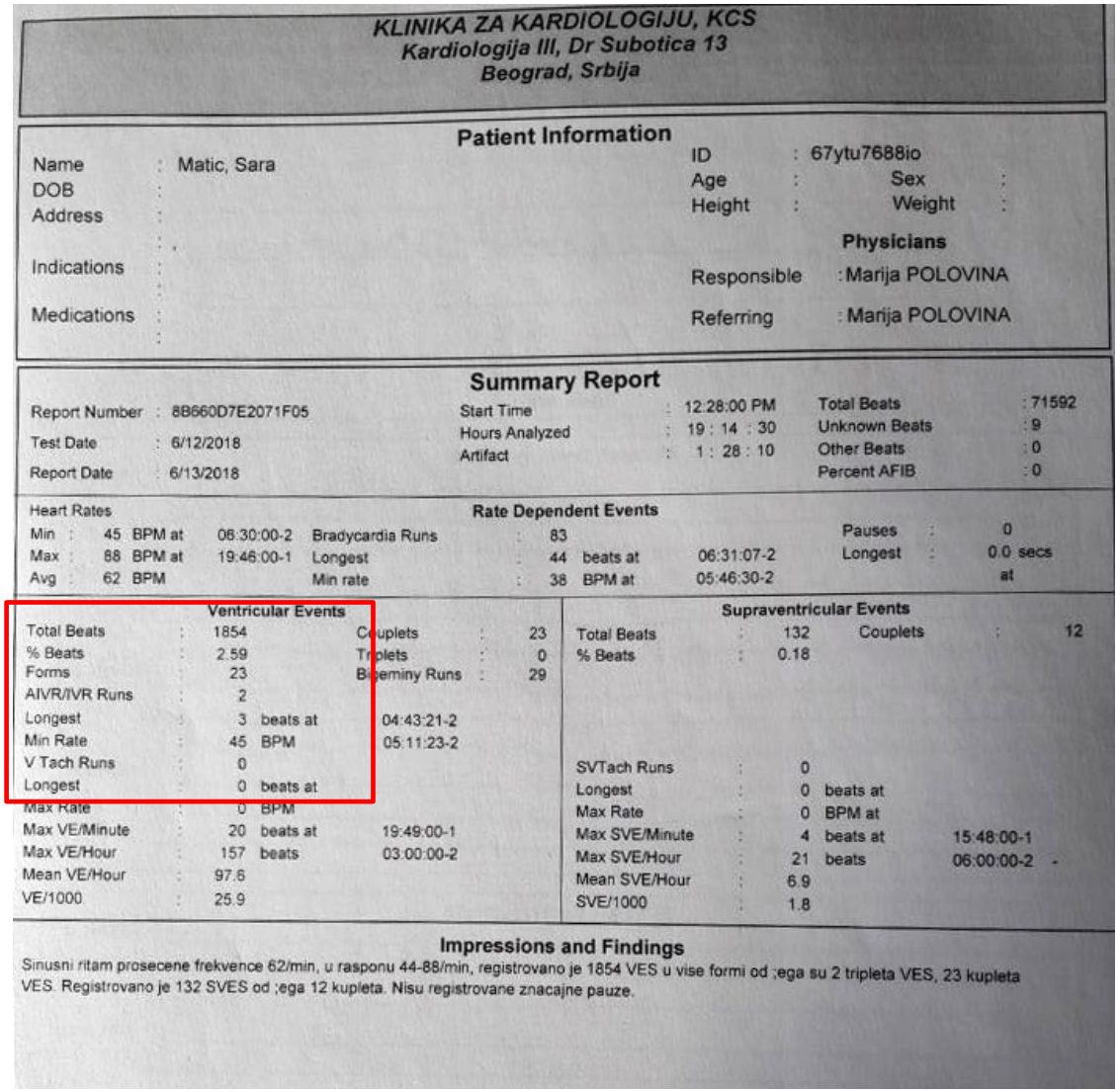
ZAKLJUČAK: ERGO test opterećenja po Bruce protokolu prekinut u 2. min I stepena zbog cestih VES iz vise fokusa, parova i VT pre dostizanja SMF pri Fr 113/min. Subjektivno bez tegoba tokom testa.

EKG: s.r. fr 84/min, neg.T u v4-V6, pojedinacne VES i VES u paru. U naporu ceste VES iz vise fokusa, parovi i VT, koji se registruju i u oporavku. Dat Presolol iv.

Naporom se indikuju maligni poremecaji ritma.

Pacijent 4°

FLEKAINID 200 mg + Metoprolol 100 mg: Holter, oko 1800 pojedinačnih VES ali bez VTNS



KLINIKA ZA KARDIOLOGIJU, KCS
Kardiologija III, Dr Subotica 13
Beograd, Srbija

Patient Information

Name	: Matic, Sara	ID	: 67ytu7688io
DOB	:	Age	: Sex :
Address	:	Height	: Weight :
Indications	:	**Physicians**	
		Responsible	: Marija POLOVINA
Medications	:	Referring	: Marija POLOVINA

Summary Report

Report Number	: 8B660D7E2071F05	Start Time	: 12:28:00 PM	Total Beats	: 71592
Test Date	: 6/12/2018	Hours Analyzed	: 19 : 14 : 30	Unknown Beats	: 9
Report Date	: 6/13/2018	Artifact	: 1 : 28 : 10	Other Beats	: 0
				Percent AFIB	: 0

Heart Rates

Min	: 45 BPM at	06:30:00-2	
Max	: 88 BPM at	19:46:00-1	
Avg	: 62 BPM		

Rate Dependent Events

Bradycardia Runs	: 83		
Longest	: 44 beats at	06:31:07-2	
Min rate	: 38 BPM at	05:46:30-2	

Pauses	: 0	
Longest	: 0.0 secs	
	at	

Ventricular Events

Total Beats	: 1854		Couplets	: 23	
% Beats	: 2.59		Triplets	: 0	
Forms	: 23		Bigeminy Runs	: 29	
AIVR/IVR Runs	: 2				
Longest	: 3	beats at	04:43:21-2		
Min Rate	: 45	BPM	05:11:23-2		
V Tach Runs	: 0				
Longest	: 0	beats at			
Max Rate	: 0	BPM			
Max VE/Minute	: 20	beats at	19:49:00-1		
Max VE/Hour	: 157	beats	03:00:00-2		
Mean VE/Hour	: 97.6				
VE/1000	: 25.9				

Supraventricular Events

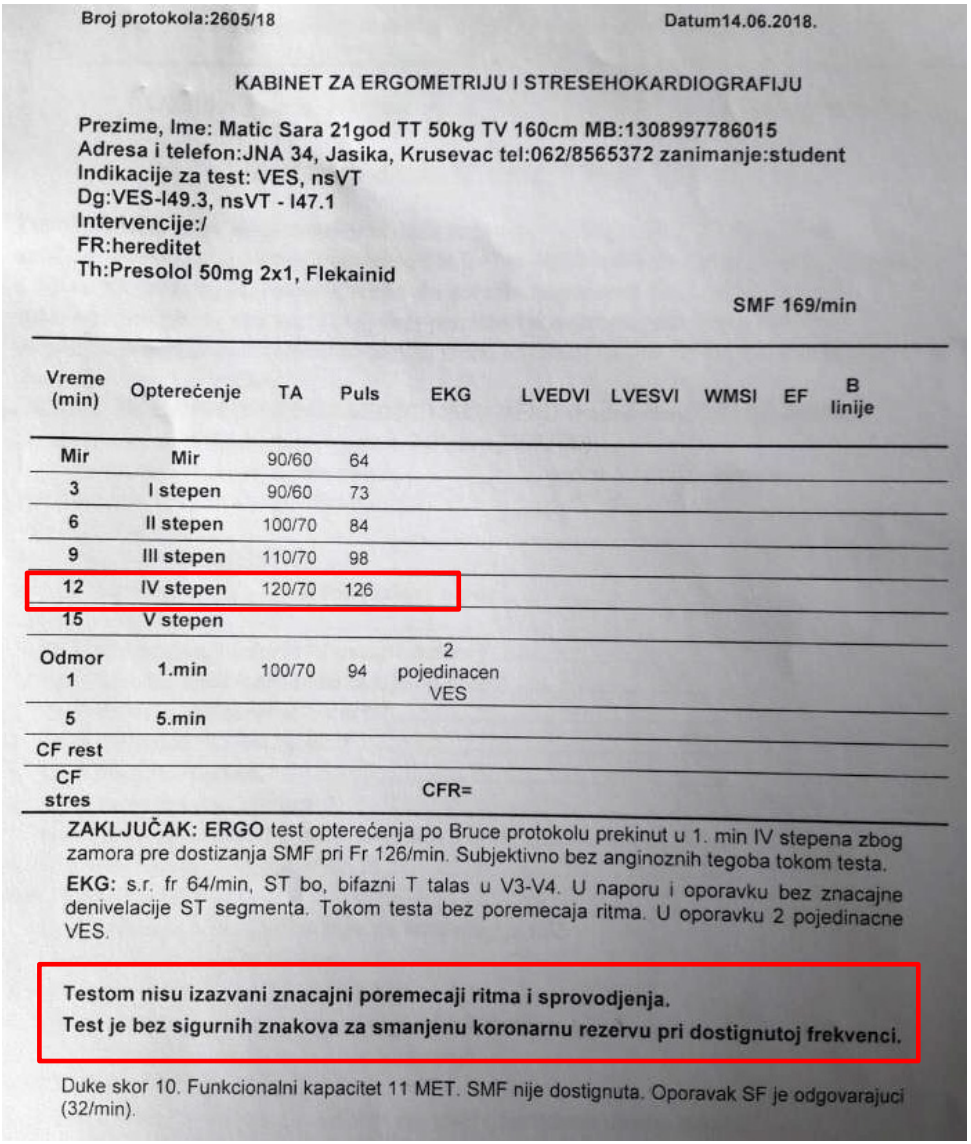
Total Beats	: 132		Couplets	: 12	
% Beats	: 0.18				
SVTach Runs	: 0				
Longest	: 0	beats at			
Max Rate	: 0	BPM at			
Max SVE/Minute	: 4	beats at	15:48:00-1		
Max SVE/Hour	: 21	beats	06:00:00-2		
Mean SVE/Hour	: 6.9				
SVE/1000	: 1.8				

Impressions and Findings

Sinusni ritam prosecene frekvence 62/min, u rasponu 44-88/min, registrovano je 1854 VES u vise formi od ;ega su 2 tripleta VES, 23 kupleta VES. Registrovano je 132 SVES od ;ega 12 kupleta. Nisu registrovane znacajne pauze.

Pacijent 4°

FLEKAINID 200 mg + Metoprolol 100 mg: ergometrija, IV° - bez značajne VES aritmije



Broj protokola:2605/18 Datum14.06.2018.

KABINET ZA ERGOMETRIJU I STRESEHOKARDIOGRAFIJU

Prezime, Ime: Matic Sara 21god TT 50kg TV 160cm MB:1308997786015
Adresa i telefon:JNA 34, Jasika, Krusevac tel:062/8565372 zanimanje:student
Indikacije za test: VES, nsVT
Dg:VES-I49.3, nsVT - I47.1
Intervencije:/
FR:hereditet
Th:Presolol 50mg 2x1, Flekainid

SMF 169/min

Vreme (min)	Opterećenje	TA	Puls	EKG	LVEDVI	LVESVI	WMSI	EF	B linije
Mir	Mir	90/60	64						
3	I stepen	90/60	73						
6	II stepen	100/70	84						
9	III stepen	110/70	98						
12	IV stepen	120/70	126						
15	V stepen								
Odmor 1	1.min	100/70	94	2 pojedinacen VES					
5	5.min								
CF rest									
CF stres				CFR=					

ZAKLJUČAK: ERGO test opterećenja po Bruce protokolu prekinut u 1. min IV stepena zbog zamora pre dostizanja SMF pri Fr 126/min. Subjektivno bez anginoznih tegoba tokom testa.

EKG: s.r. fr 64/min, ST bo, bifazni T talas u V3-V4. U naporu i oporavku bez znacajne denivelacije ST segmenta. Tokom testa bez poremecaja ritma. U oporavku 2 pojedinacne VES.

Testom nisu izazvani znacajni poremecaji ritma i sprovodjenja.
Test je bez sigurnih znakova za smanjenu koronarnu rezervu pri dostignutoj frekvenci.

Duke skor 10. Funkcionalni kapacitet 11 MET. SMF nije dostignuta. Oporavak SF je odgovarajuci (32/min).

Pacijent 4°

- Otpuštena sa 200 mg FLEKAINIDA + 100 mg Metoprolola

- Vanredna kontrola posle 3 nedelje
- Duple slike, vrtoglavica
- Redukovana doza Flekainida sa 200 mg na 100 mg
- I dalje odlična kontrola VES aritmije, bez sporednih efekata
- Praćenje >12 meseci

- dg kateholaminima posredovane VT (?), genetsko ispitivanje
- Specifičan efekat Flekainida na rianodinske receptore

KONTRAINDIKACIJE ZA PRIMENU FLEKAINIDA I UVODJENJE LEKA

KONTRAINDIKACIJE

Flekainid (IC klasa) je kontraindikovan kod:

- **ishemijske bolesti srca, i**
- **srčane slabosti**

i, potreban je oprez kod:

- starijih osoba
- oštećene bubrežne i hepatične funkcije
- poremećaja AV provođenja (AV blok I, blok grane)

Uvođenje i doziranje Flekainida

…kod datog bolesnika….

1. Da li uvesti lek ambulantno ili u bolničkim uslovima ?

2. Koja je početna, a koja ciljna doza ?
   (kada povećati dozu leka ?)

Kapsule, 6 x 10 kom.

50 mg, 100 mg i 200 mg

Uvođenje i doziranje Flekainida

Ambulantno uvođenje leka:

- Mlađi bolesnici
- Normalan EKG
- Normalna bubrežna funkcija
- **Početi** za **AF 100-200 mg**, za **VA 200 mg**
- **Ciljna doza** za **AF 200 mg**, za **VA 200 - 400 mg**
- Povećanje doze za 3-4 dana

Uvođenje i doziranje Flekainida

Hospitalno uvođenje leka:

- Stariji bolesnici
- Pejsmeker (povećava prag kapture)
- Bradikardija, produžen PQ ili blok grane
- Početna HLK (<12 mm)
- Oštećen klirens kreatinina (<35 mL/min/1.73 m^2)
- Početi sa 50-100 mg,
- Eventualno povećati na 100-200 mg posle 4-5 dana

DISKUSIJA…

“SIVE ZONE” - DILEME OKO PRIMENE FLEKAINIDA

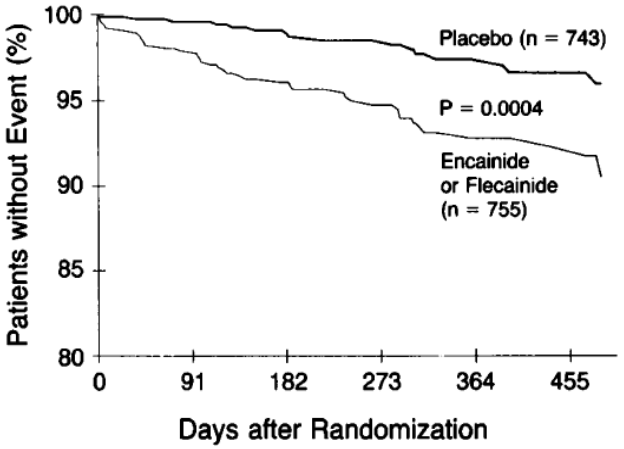
KONTRAINDIKACIJE

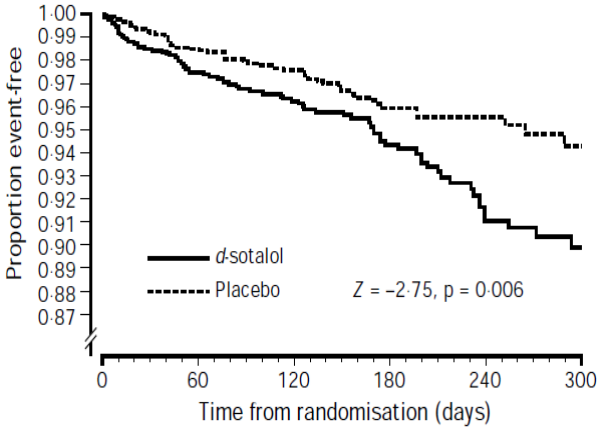
- **IC klasa**, **sotalol** i **dronedaron** povećavaju smrtnost u kongest.srčanoj slabosti [1-3]

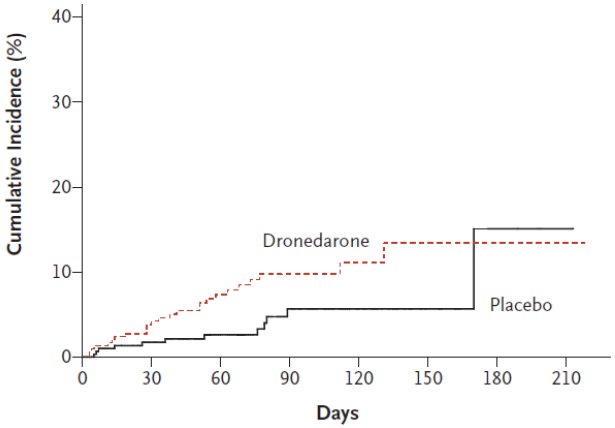
CAST I (1991)
- 1498 pts
- Post IM LV EF≤40%, ≥6 VPBs/h
- Flecainide (IC class) vs placebo
- Excess of death due to **arrhythmia and acute MI with shock** (8.3% vs 3.1%, p=0.01)

SWORD (1996)
- 3121 pts
- Post IM LV EF≤40%, CHF
- Sotalol vs placebo
- Higher **total mortality** (5% vs 3.1%), **cardiac mortality and arrhythmic death** (p=0.008)

DRONEDARONE (2003)
- 627 pts
- NYHA III-IV, EF<35%
- Dronedarone vs placebo
- Higher CV mortality due to **worsening HF** (8.1% vs 3.8%, p<0.01)







1. Echt DS et al. Mortality and morbidity in pts receiving encainide, flecainide or placebo. The Cardiac Arrhythmia Supression Trial. N Engl J Med 1991; 324: 781-8.
2. Waldo AL et al. SWORD Investigators. Effect of d-sotalol on mortality in patients with left ventricular dysfunction after recent and remote myocardial infarction. Lancet 1996; 348: 7-12.
3. Kober L et al. Dronedarone Study Group. Increased mortality after dronedarone therapy for severe heart failure. N Engl J Med 2008; 358: 2678-87.

KONTRAINDIKACIJE

Muškarac, **88 god**.

AF/AFL, 15 god.

PCI – Cx, pre 7 god.

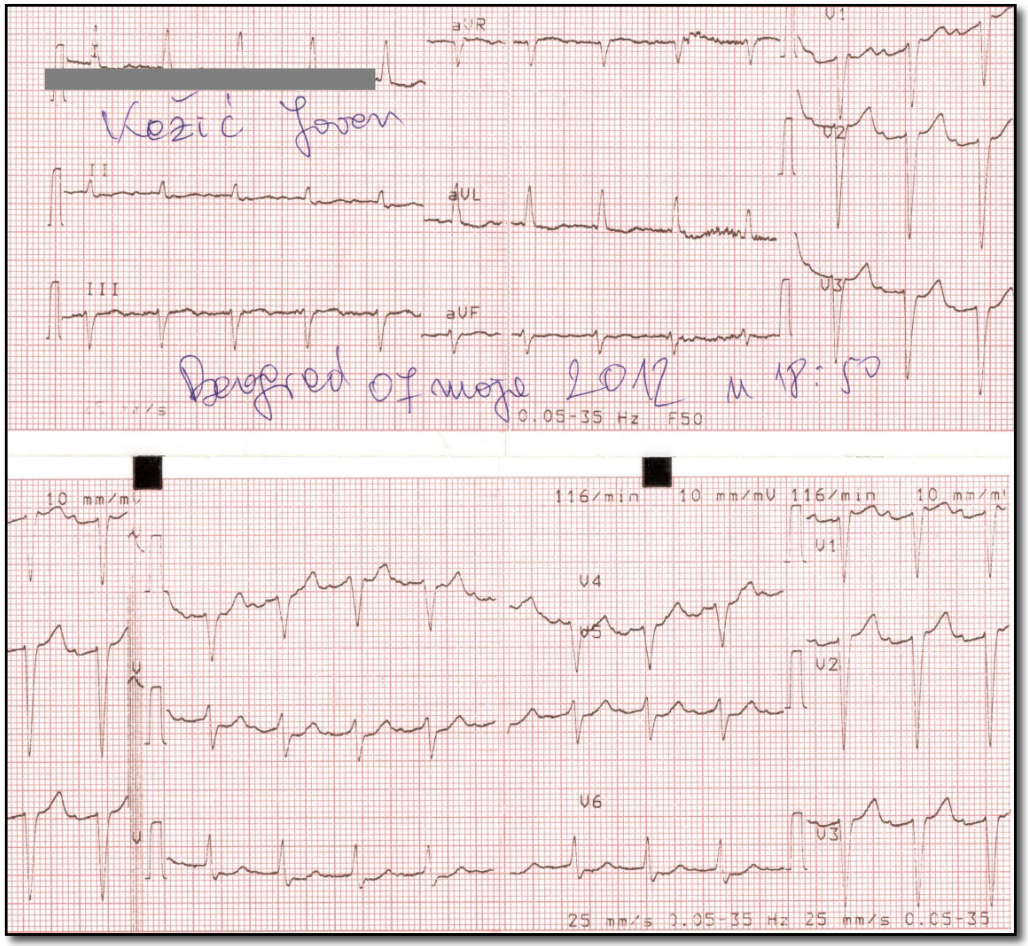
Eho srca: LK 59/49 mm,
akinezija donjeg zida,
EF 33%

Tx.

Amiodaron (tireotox.)

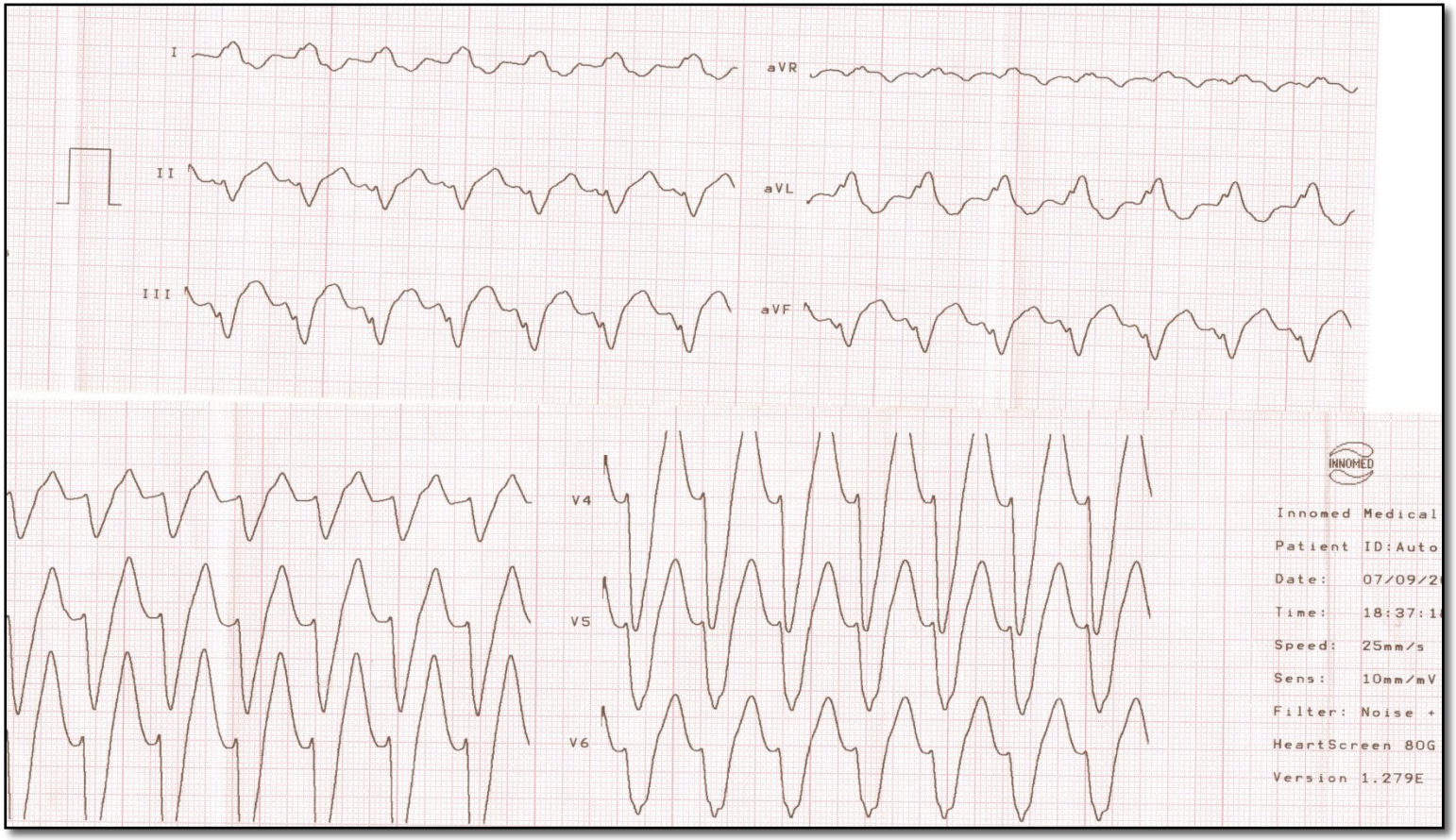
Flekainid 3x50 mg (1 mesec)

EKG pre uvođenja Flekainida: AF/AFL



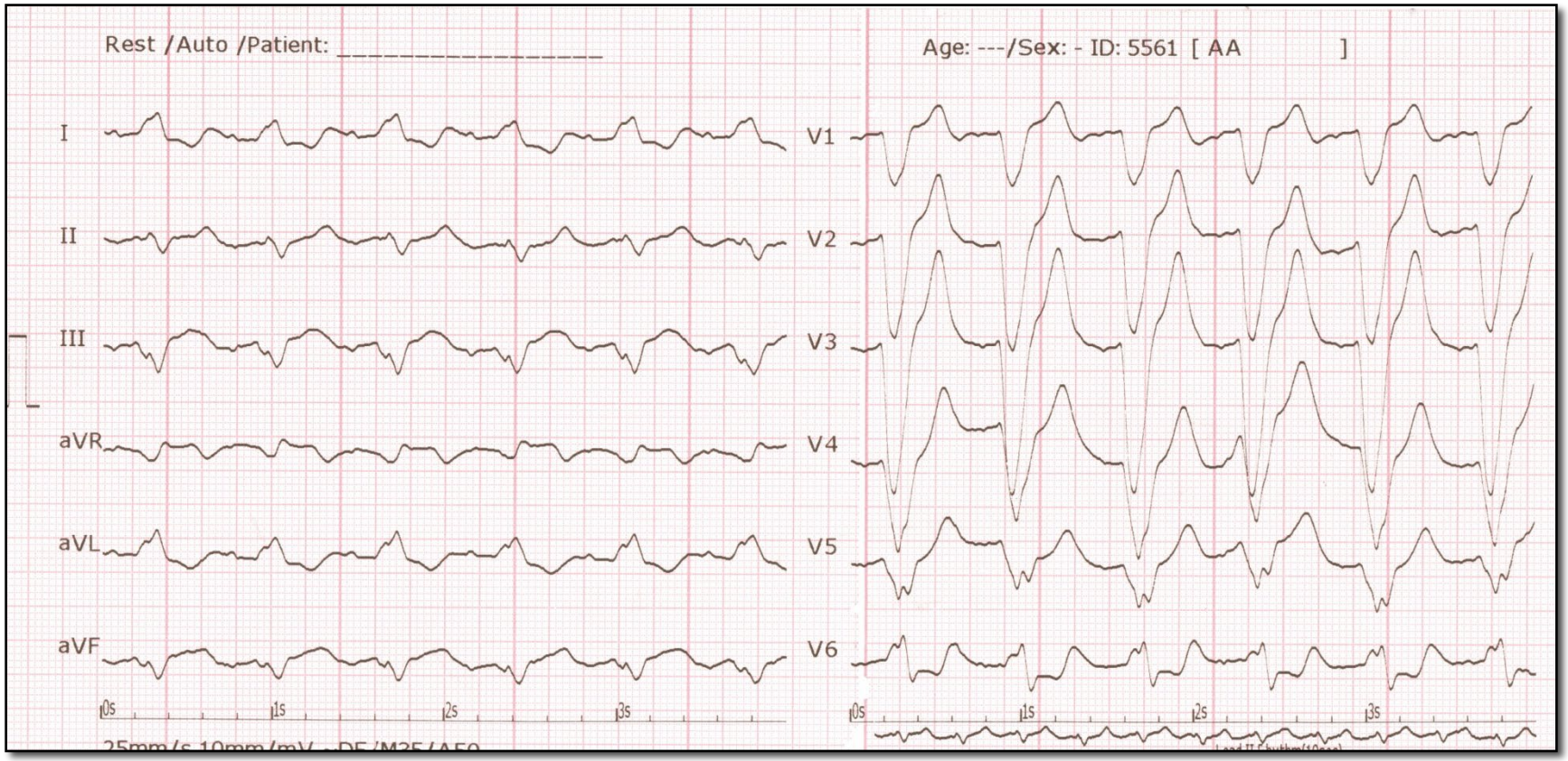
KONTRAINDIKACIJE

- 2 nedelje posle uvođenja Flekainida, progresivno zamaranje
- Prijem UC: tahikardija sa širokim QRS = VT
- Somnolentan, TA 90/60 mmHg



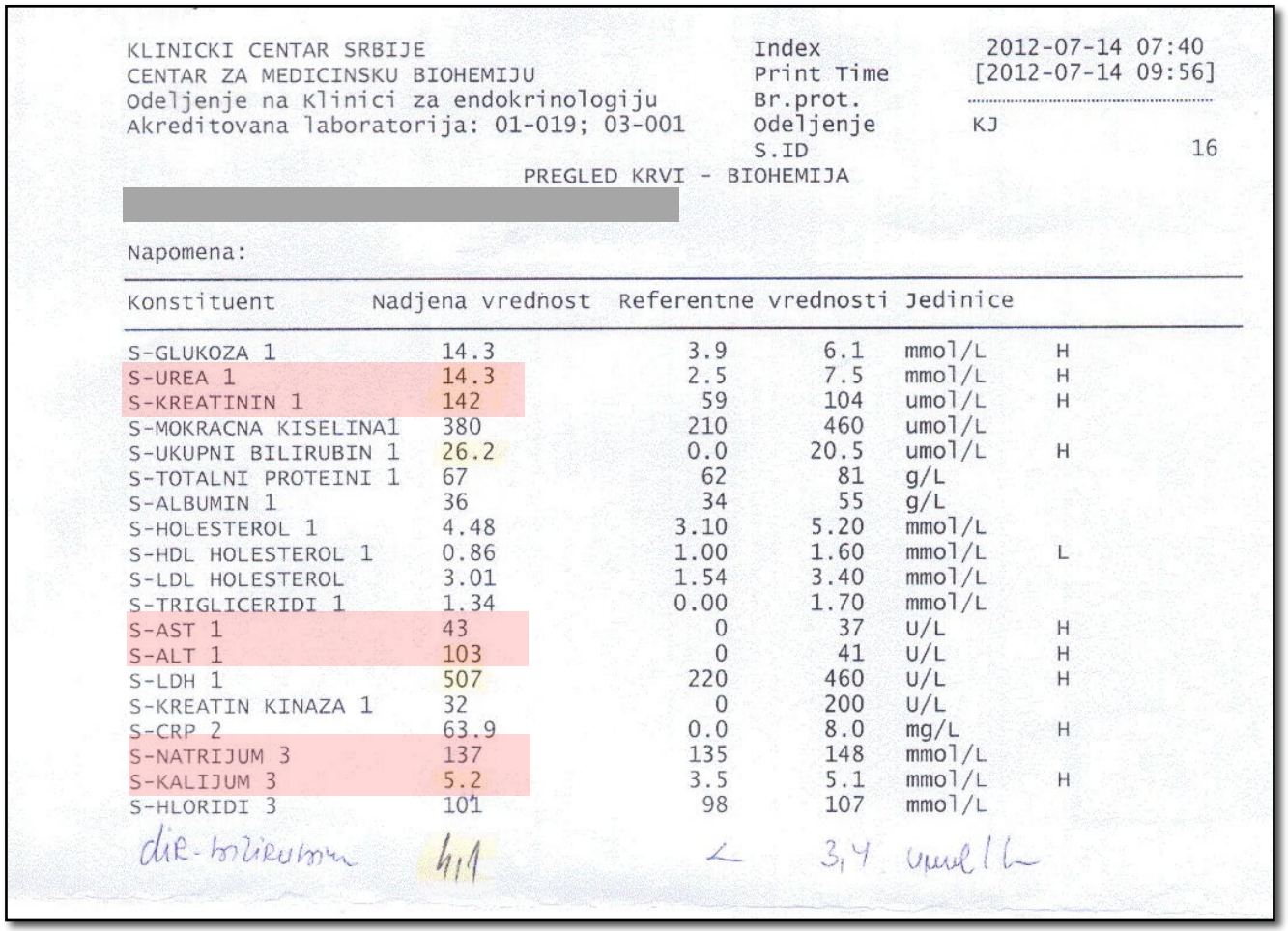
KONTRAINDIKACIJE

- Ponavljana sinhrona elektrokonverzija: 100, 150, 200, 270 J
- EKG: sinusni ritam, AV blok I, blok leve grane



KONTRAINDIKACIJE

- Normalni elektroliti, oštećena bubrežna funkcija



KLINICKI CENTAR SRBIJE
CENTAR ZA MEDICINSKU BIOHEMIJU
Odeljenje na Klinici za endokrinologiju
Akreditovana laboratorija: 01-019; 03-001

Index 2012-07-14 07:40
Print Time [2012-07-14 09:56]
Br.prot. .....
Odeljenje KJ
S.ID 16

PREGLED KRVI - BIOHEMIJA

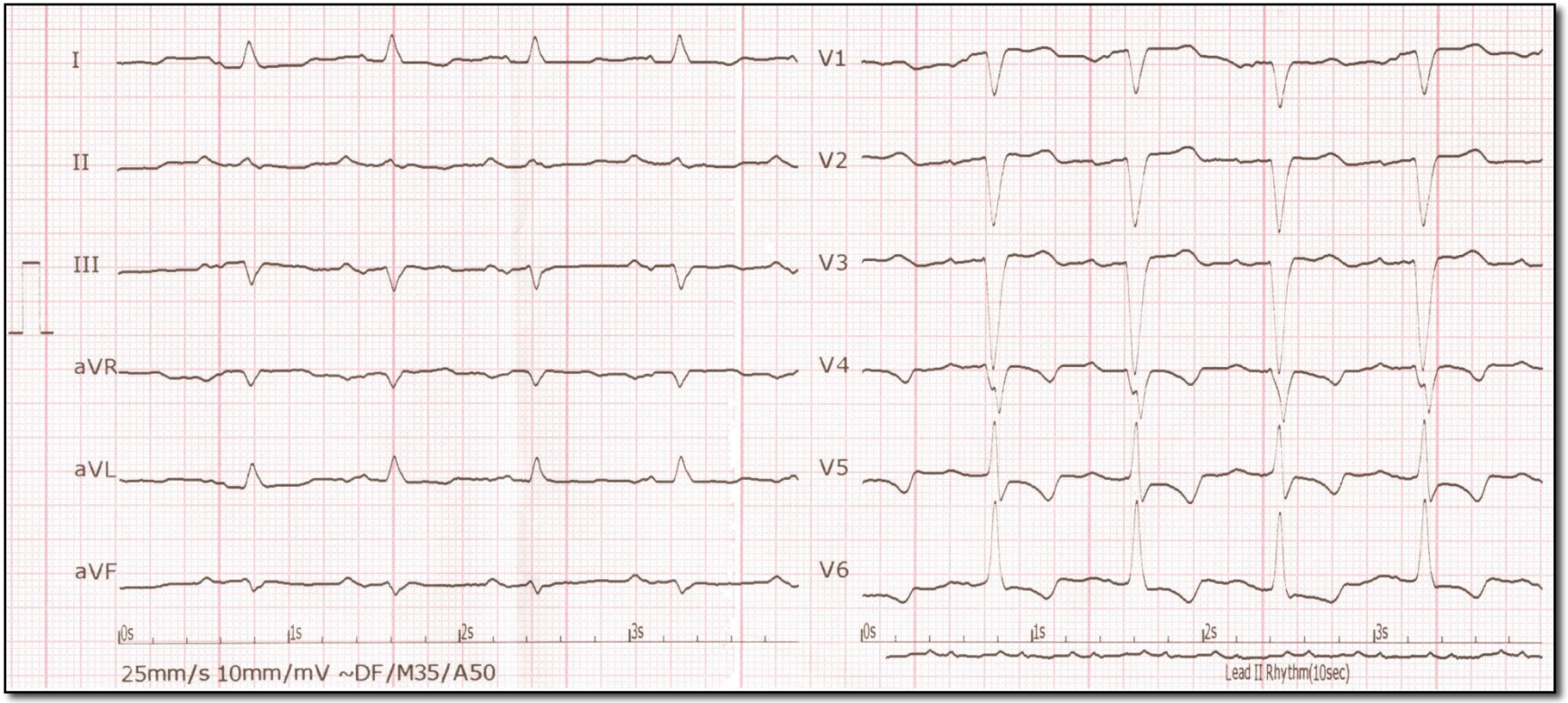
[redacted]

Napomena:

Konstituent	Nadjena vrednost	Referentne vrednosti		Jedinice	
S-GLUKOZA 1	14.3	3.9	6.1	mmol/L	H
S-UREA 1	14.3	2.5	7.5	mmol/L	H
S-KREATININ 1	142	59	104	umol/L	H
S-MOKRACNA KISELINA1	380	210	460	umol/L	
S-UKUPNI BILIRUBIN 1	26.2	0.0	20.5	umol/L	H
S-TOTALNI PROTEINI 1	67	62	81	g/L	
S-ALBUMIN 1	36	34	55	g/L	
S-HOLESTEROL 1	4.48	3.10	5.20	mmol/L	
S-HDL HOLESTEROL 1	0.86	1.00	1.60	mmol/L	L
S-LDL HOLESTEROL	3.01	1.54	3.40	mmol/L	
S-TRIGLICERIDI 1	1.34	0.00	1.70	mmol/L	
S-AST 1	43	0	37	U/L	H
S-ALT 1	103	0	41	U/L	H
S-LDH 1	507	220	460	U/L	H
S-KREATIN KINAZA 1	32	0	200	U/L	
S-CRP 2	63.9	0.0	8.0	mg/L	H
S-NATRIJUM 3	137	135	148	mmol/L	
S-KALIJUM 3	5.2	3.5	5.1	mmol/L	H
S-HLORIDI 3	101	98	107	mmol/L	
dir. bilirubin	4,1	<	3,4	umol/L	

KONTRAINDIKACIJE

- EKG posle 2 sata od elektrokonverzije
- Normalizacija PQ intervala i sužavanje QRS kompleksa



Pacijent 1°

- Žena, 58 god.
- Dijabetes tip 1, Hiperlipidemija, Hipertenzija
- Eho srca: LP 43 mm, LK bez segmentnih ispada, EF 60%
- Angina pektoris, simptomatski paroksizmi AF
- Amjodaronska hipertireoza u remisiji
- Koronarografija: jednosudovna bolest (proks. RCA - 80%)
- Urađena PCI – RCA
- Pokušano sa Sotalolom…. i dalje paroksizmi AF

Pacijent 1°

Terapijske opcije:

- Amjodaron (visok rizik tireoidne toksičnosti ?)
- Dronedaron (nedostupan ?)
- Kateterska ablacija (odbija ?)
- IC klasa (Flekainid) - (bezbednost ?)

IC klasa i CAST studija

The New England
Journal of Medicine

Volume 324 MARCH 21, 1991 Number 12

MORTALITY AND MORBIDITY IN PATIENTS RECEIVING ENCAINIDE, FLECAINIDE, OR PLACEBO

The Cardiac Arrhythmia Suppression Trial

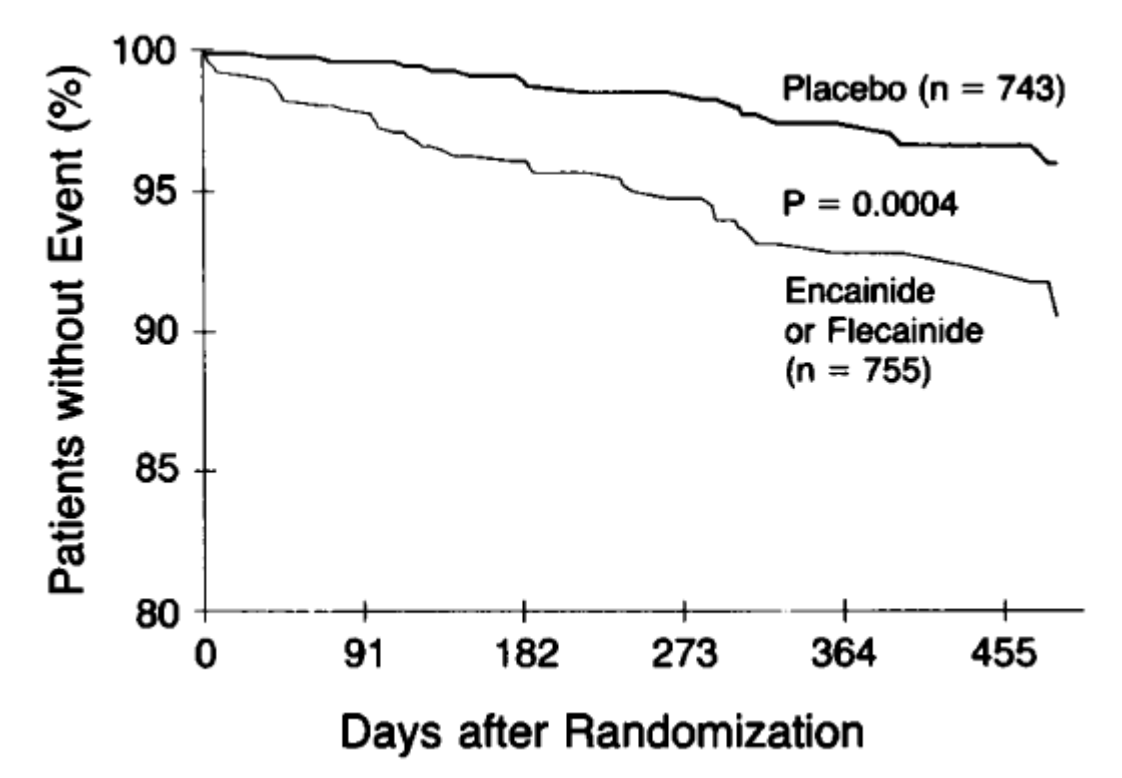
DEBRA S. ECHT, M.D., PHILIP R. LIEBSON, M.D., L. BRENT MITCHELL, M.D., ROBERT W. PETERS, M.D., DULCE OBIAS-MANNO, R.N., ALLAN H. BARKER, M.D., DANIEL ARENSBERG, M.D., ANDREA BAKER, R.N., LAWRENCE FRIEDMAN, M.D., H. LEON GREENE, M.D., MELISSA L. HUTHER, DAVID W. RICHARDSON, M.D., AND THE CAST INVESTIGATORS*

- 1498 bolesnika
- Post-IM sa čestim VES (≥6 VES/min ili VTNS)
- Hipoteza: supresija VES antiaritmikom moze smanjiti rizik od naprasne smrti ?

IC klasa i CAST studija

Studija je obustavljena posle 10 meseci zbog ekscesa ukupne smrtnosti kod bolesnika lecenih IC klasom antiaritmika:

- Smrtnost zbog aritmije, sust-VT ili VF (p=0.0004)
- Smrtnost usled akutnog IM sa kardiogenim sokom (p=0.01)



Pacijent 1°

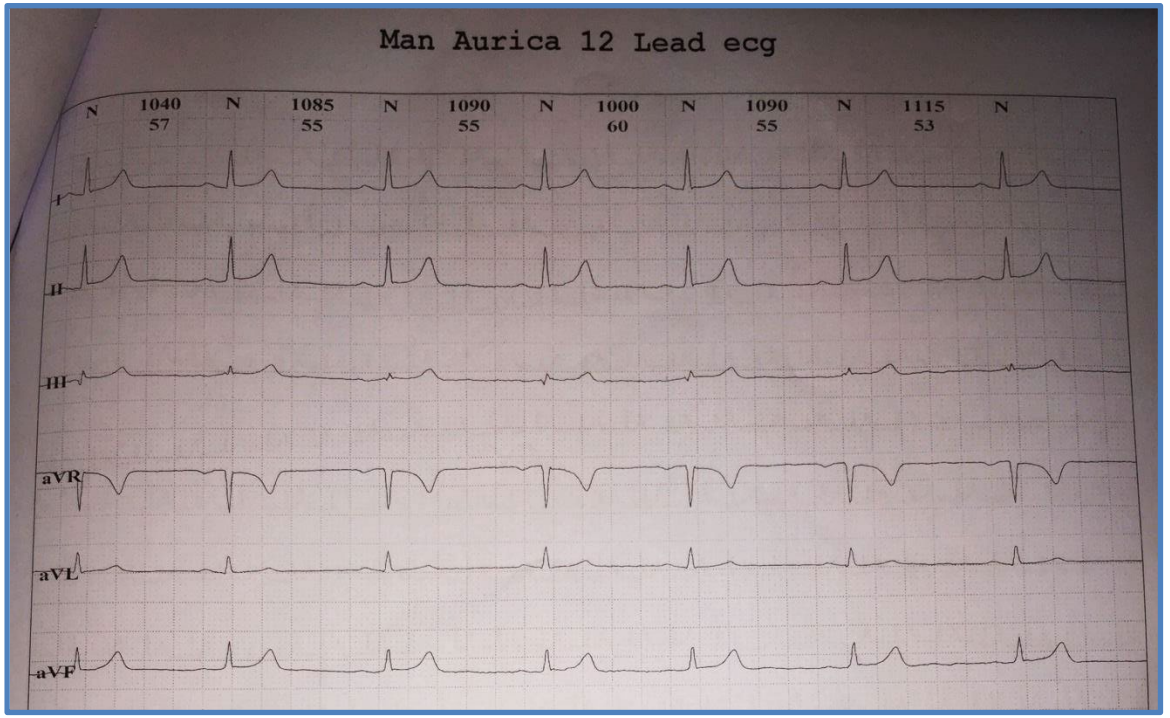
CAST:

- Rizik (HR) od **proaritmije sličan** kod **EF <40% i >40%**
- HR je **7.9** posle **non-Q IM**, i **1.8** posle **Q-IM (kontraindikovan posle IM)**

- **Nema podataka o (ne)bezbednosti Flekanida kod bolesnika sa stabilnom koronarnom bolešću koji nisu preboleli IM, koji nemaju ishemiju a koji imaju očuvanu sistolnu funkciju LK, i koji nemaju komorske ekstrasistole !!!**

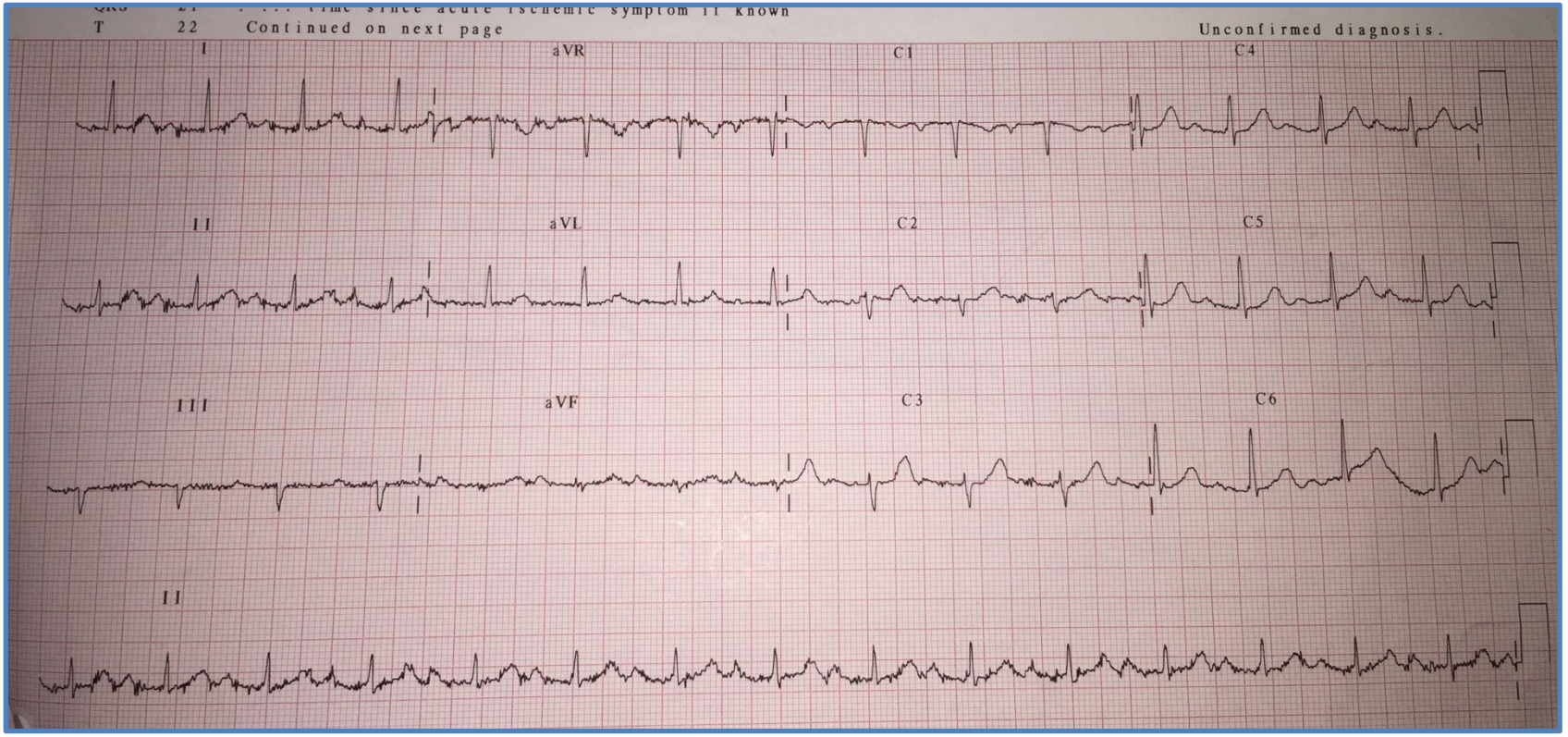
Pacijent 2°

- Žena, 61 god.
- Simptomatske VES
- Eho srca: EF 60%, blaga SOAS (23 mmHg), AR 2+
- EKG: s.r., normalan PQ-QRS



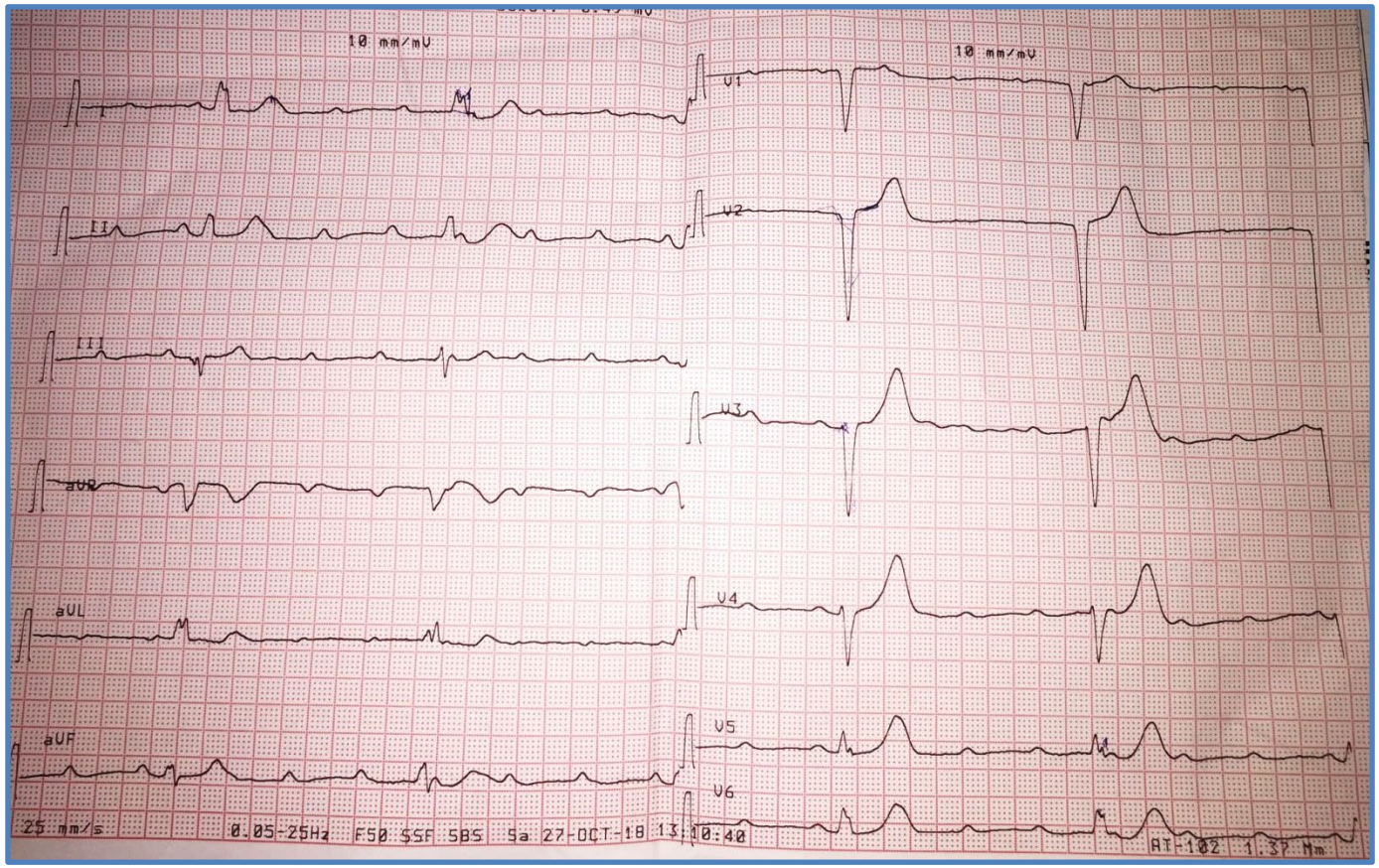
Pacijent 2°

- Flekainid 100 mg
- EKG: s.r., AV blok I° (PQ 280 ms)
- ……i dalje simptomatske VES (?)



Pacijent 2°

- Ambulantno povećan Flekainid sa 100 mg na 200 mg (?)
- UC: nesvestice…..
- EKG: AV blok III° (sa širokim QRS – blok ispod Hisa !!!)

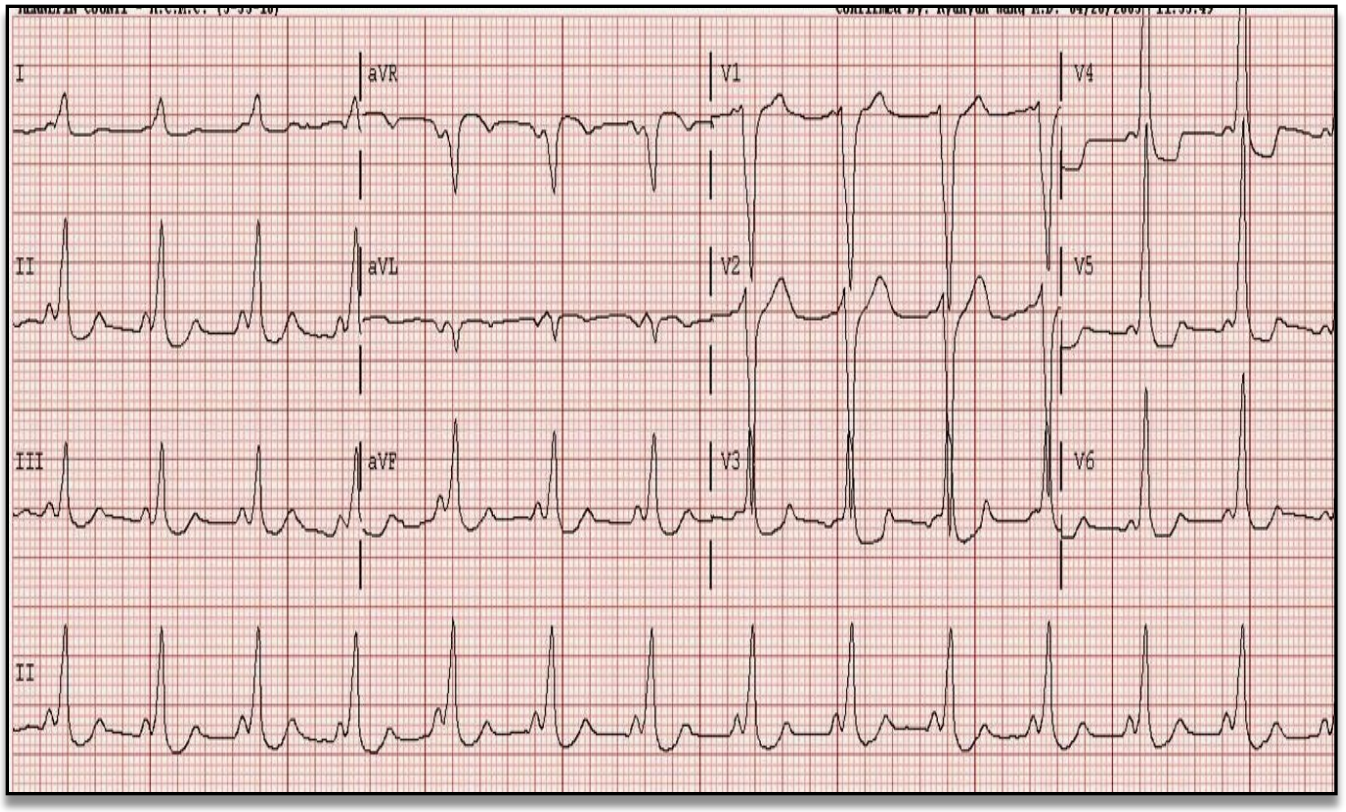


Pacijent 3°

- <u>WPW sindrom</u>

  Dečko, 10 godina, 35-40 kg

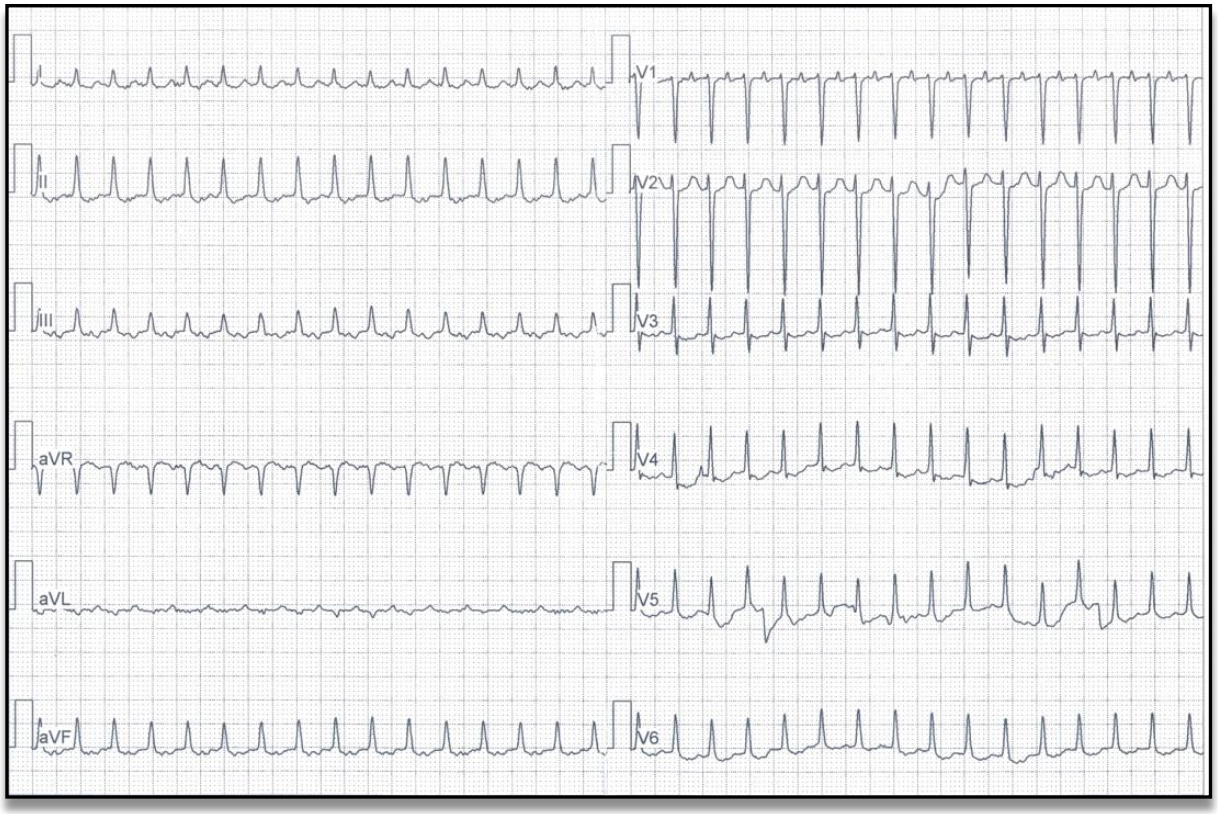
  Palpitacije, nije imao sinkopu, na EKG-u otkrivena komorska preekscitacija

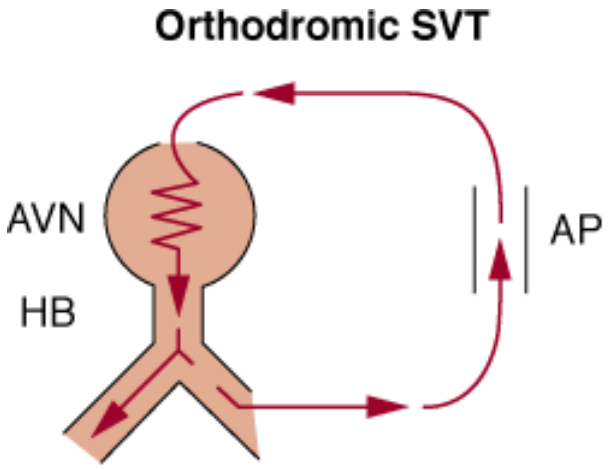


Pacijent 3°

- <u>WPW sindrom</u>

  Registrovana SVT, fr. 200/min





Pacijent 3°

- WPW sindrom

Terapijske opcije:

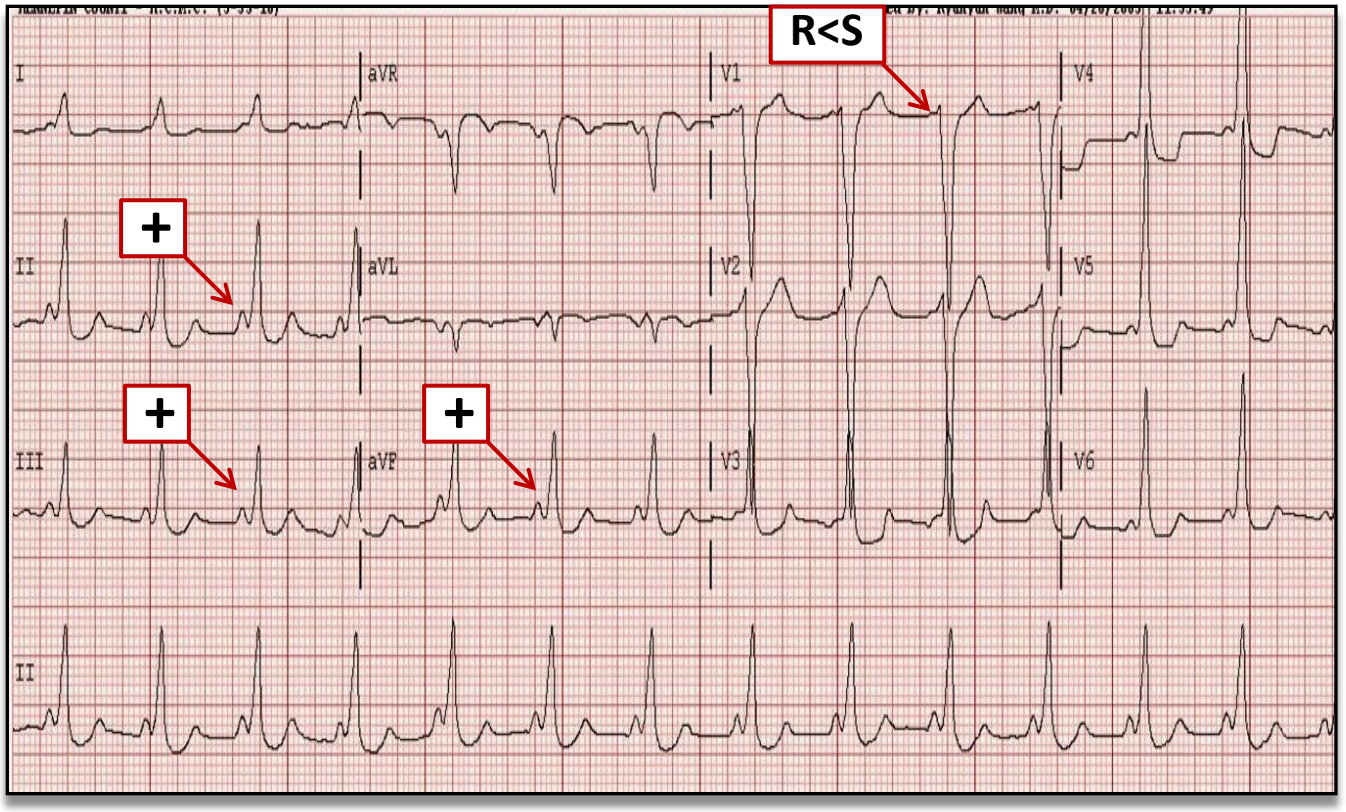
- *Beta-blokatori, verapamil……blokatori AV-čvora*
- ***Kateterska-ablacija……invazivna, uspešna***
- *III klasa (amiodaron, sotalol)……toksičnost !*
- ***IC klasa (flekainid, propafenon)…..supresija AP***

Pacijent 3°

- <u>WPW sindrom</u>

  Analiza 12-kanalnog EKG-a: vektor delta talasa

  Najverovatnije se radi o “para-Hisnom” akcesornom putu



Pacijent 3°

- WPW sindrom

Kateterska ablacija

- *Povišen rizik od AV bloka (para-Hisni AP)*

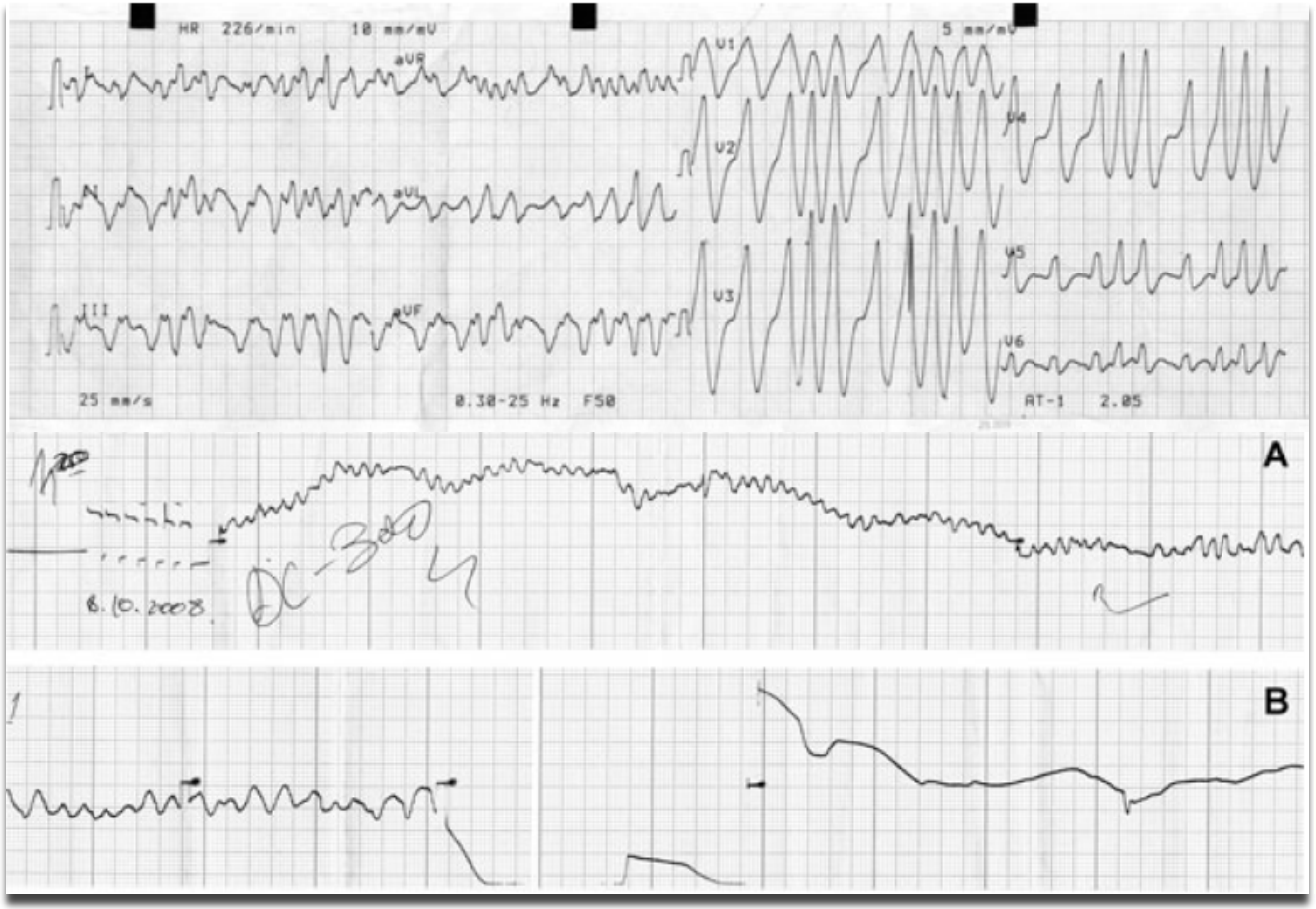
IC klasa (flekainid > propafenon)

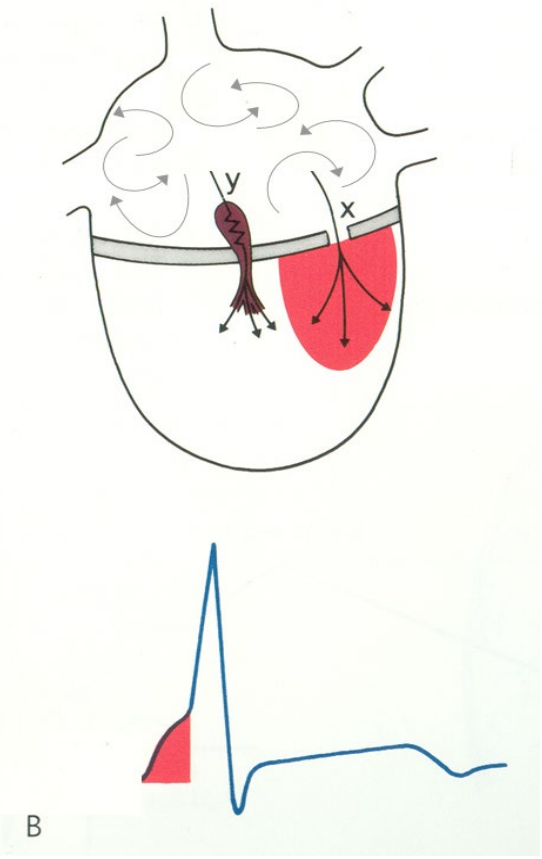
- *Flekainid blokira isključivo akcesorni put*
- *Propafen blokira oba, i AP i AV-čvor*

Pacijent 3°

- <u>WPW sindrom</u>

AF sa preekcitacijom, poguban efekat blokade AV-čvora:





Pacijent 3°

- <u>WPW sindrom</u>

  …..uveden je **Flekainid 200 mg/dnevno**

  - bez paroks.tahikardija
  - kontrolni Holter-EKG: intermitentni gubitak preekscitacije