Καρδιακές αρρυθμίες, προβλήματα στη θεραπεία

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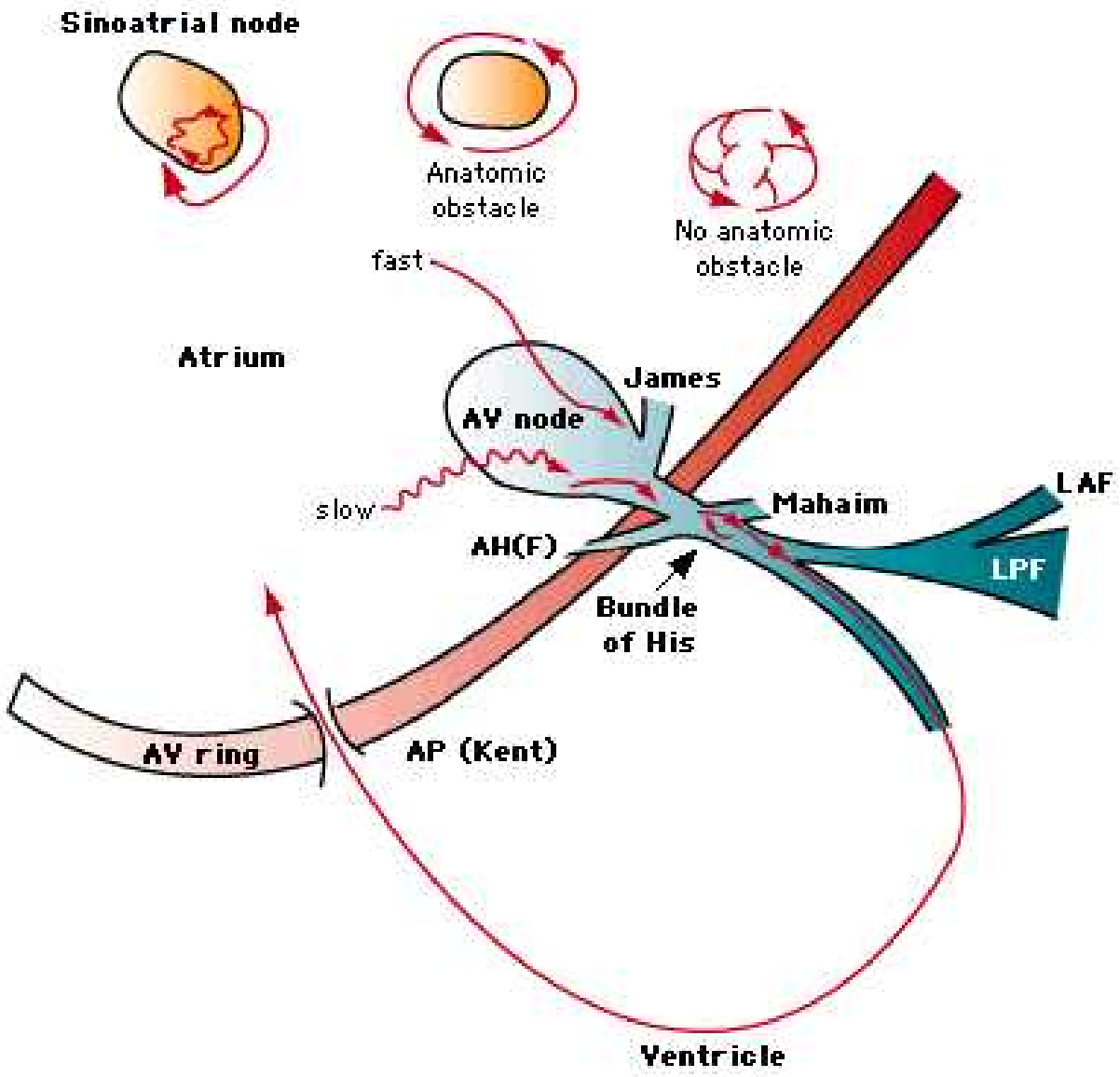
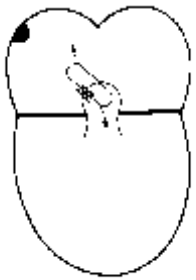
Καρδιακές αρρυθμίες

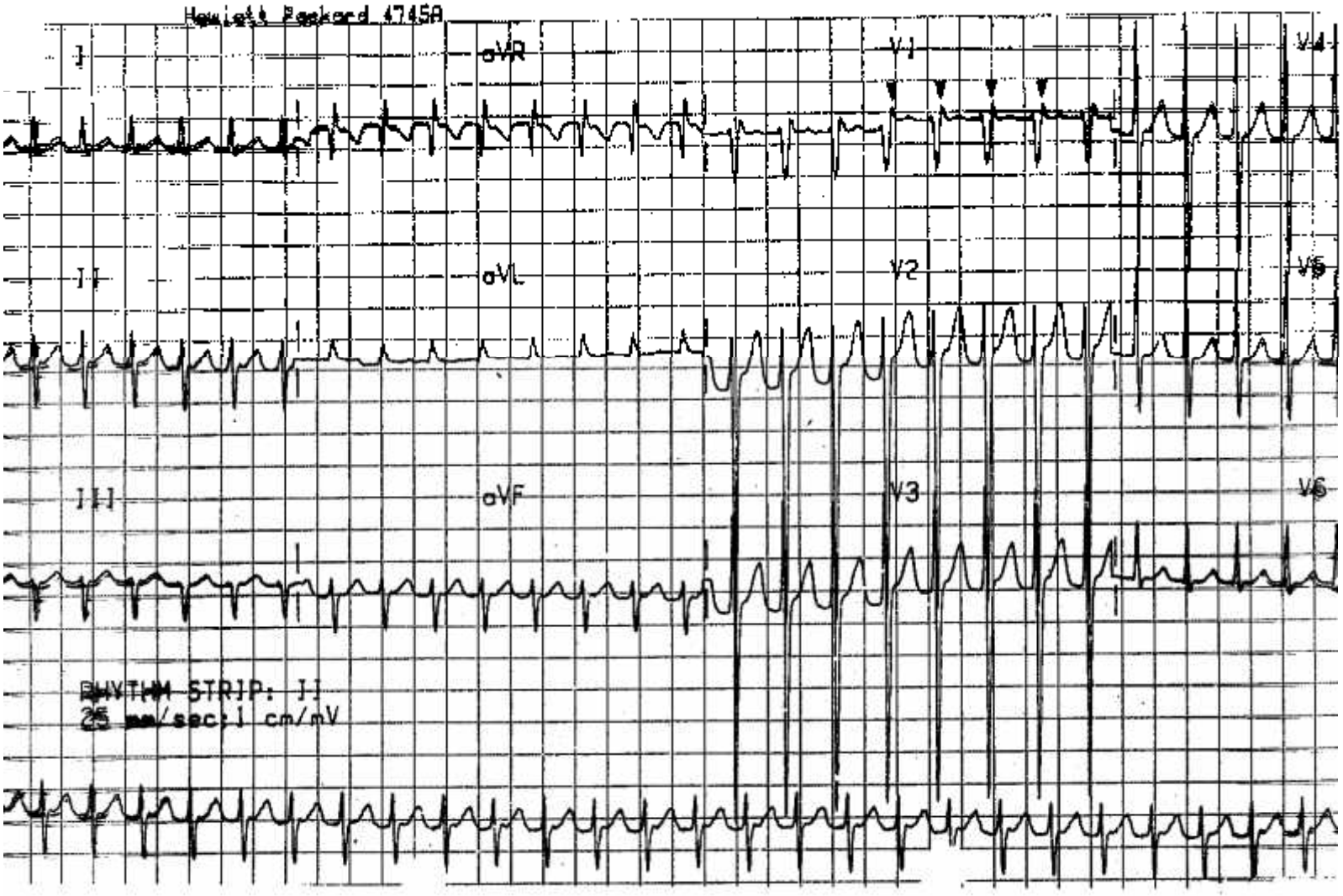
- Διαταραχές της αγωγής
- Υπερκοιλιακές
- Κοιλιακές

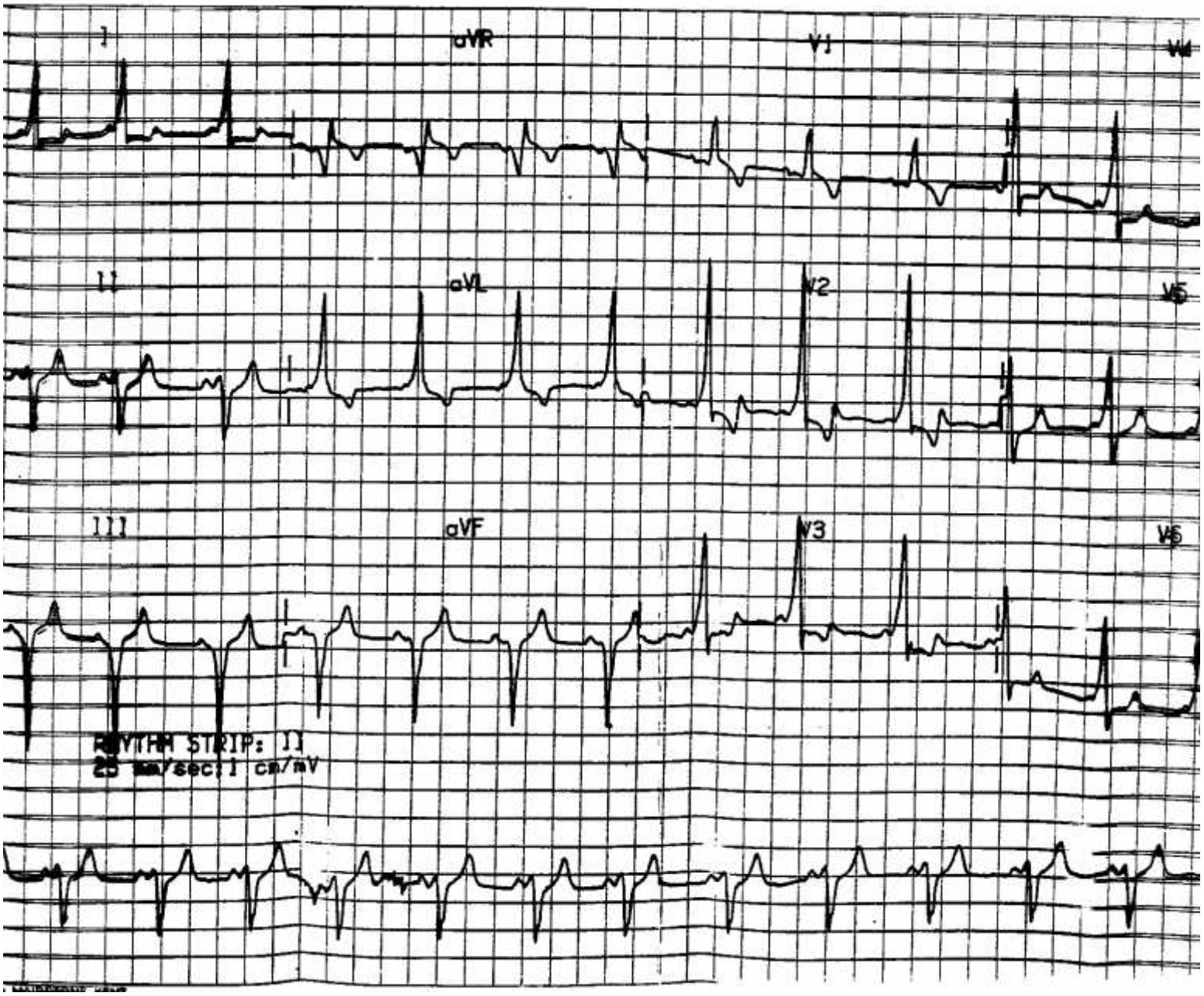

Sinoatrial node
Anatomic obstacle
No anatomic obstacle
fast
Atrium
James
AV node
slow
Mahaim
LAF
AH(F)
LPF
Bundle of His
AV ring
AP (Kent)
Ventricle

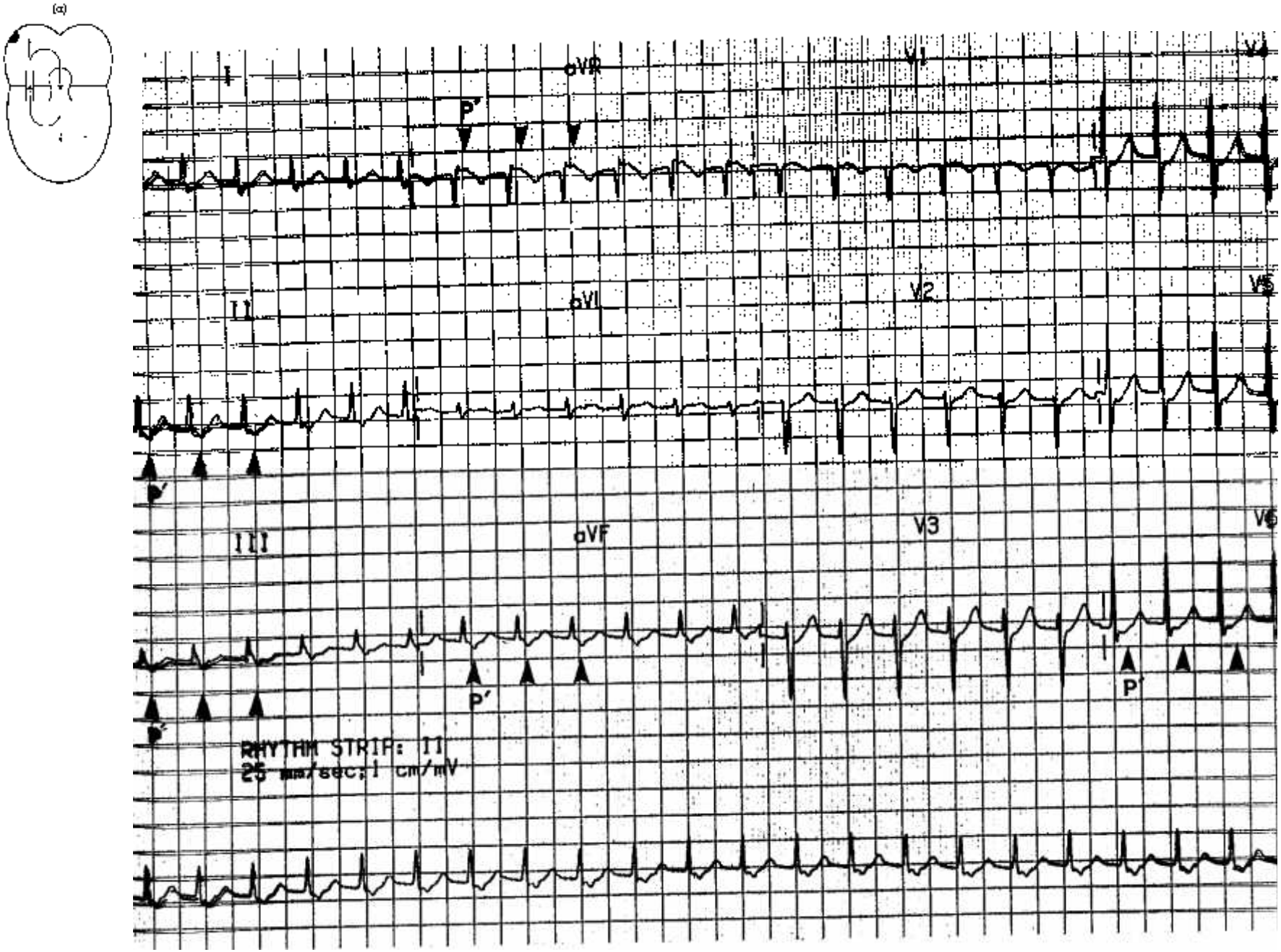
Θεραπευτική αντιμετώπιση

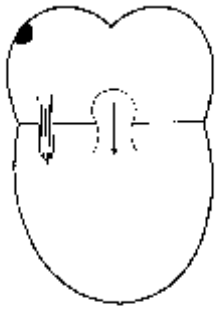
- Διακοπή του επεισοδίου
- Αντιμετώπιση υποκείμενης αιτίας
- Πρόληψη υποτροπών
- Αντιαρρυθμικά φάρμακα (Vaughan-Williams)
- Υβριδικές θεραπείες



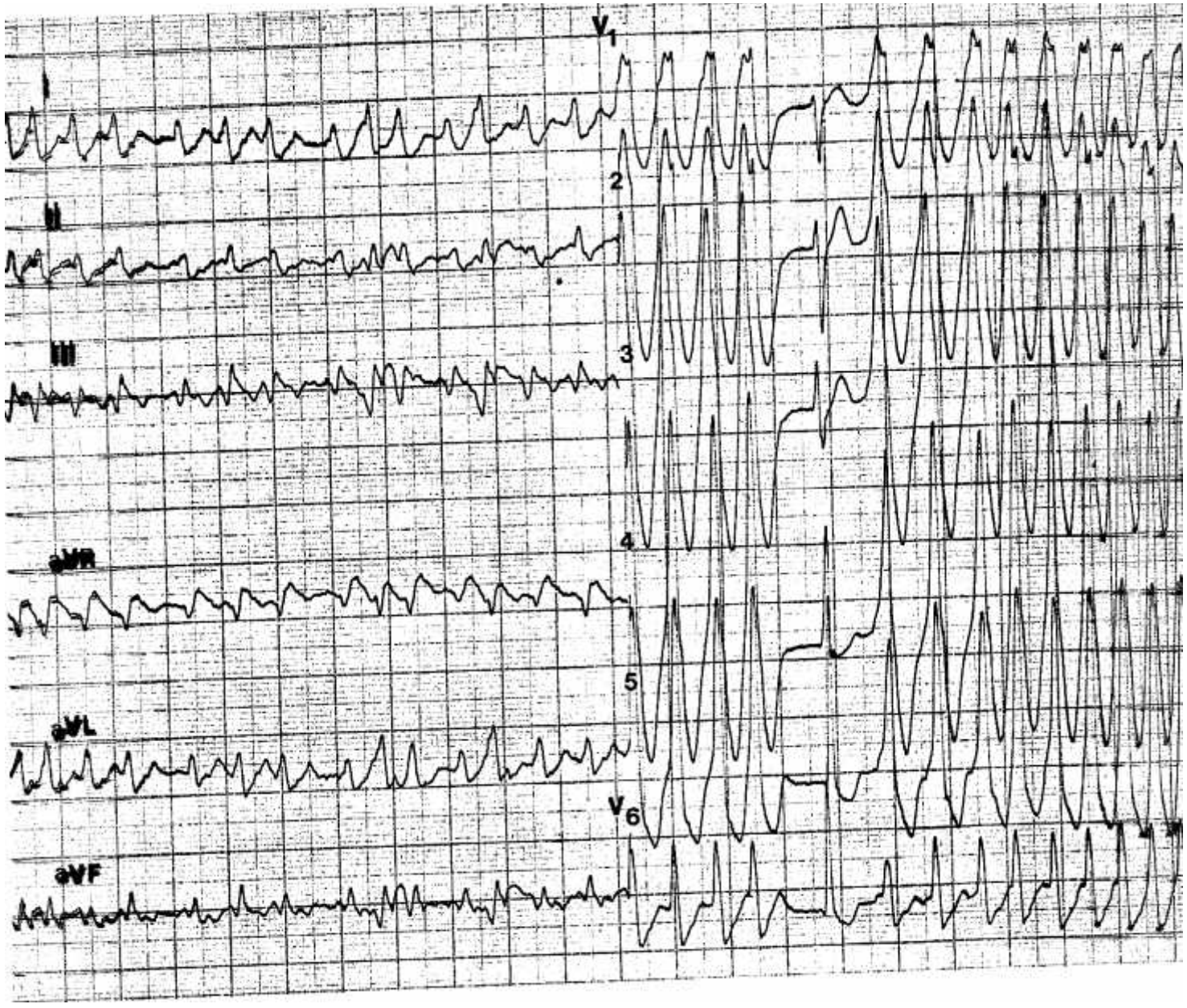

Hewlett Packard 47545A
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
RHYTHM STRIP: II
25 mm/sec; 1 cm/mV


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
RHYTHM STRIP: II
25 mm/sec; 1 cm/mV


(a)
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
P'
RHYTHM STRIP: II
25 mm/sec; 1 cm/mV

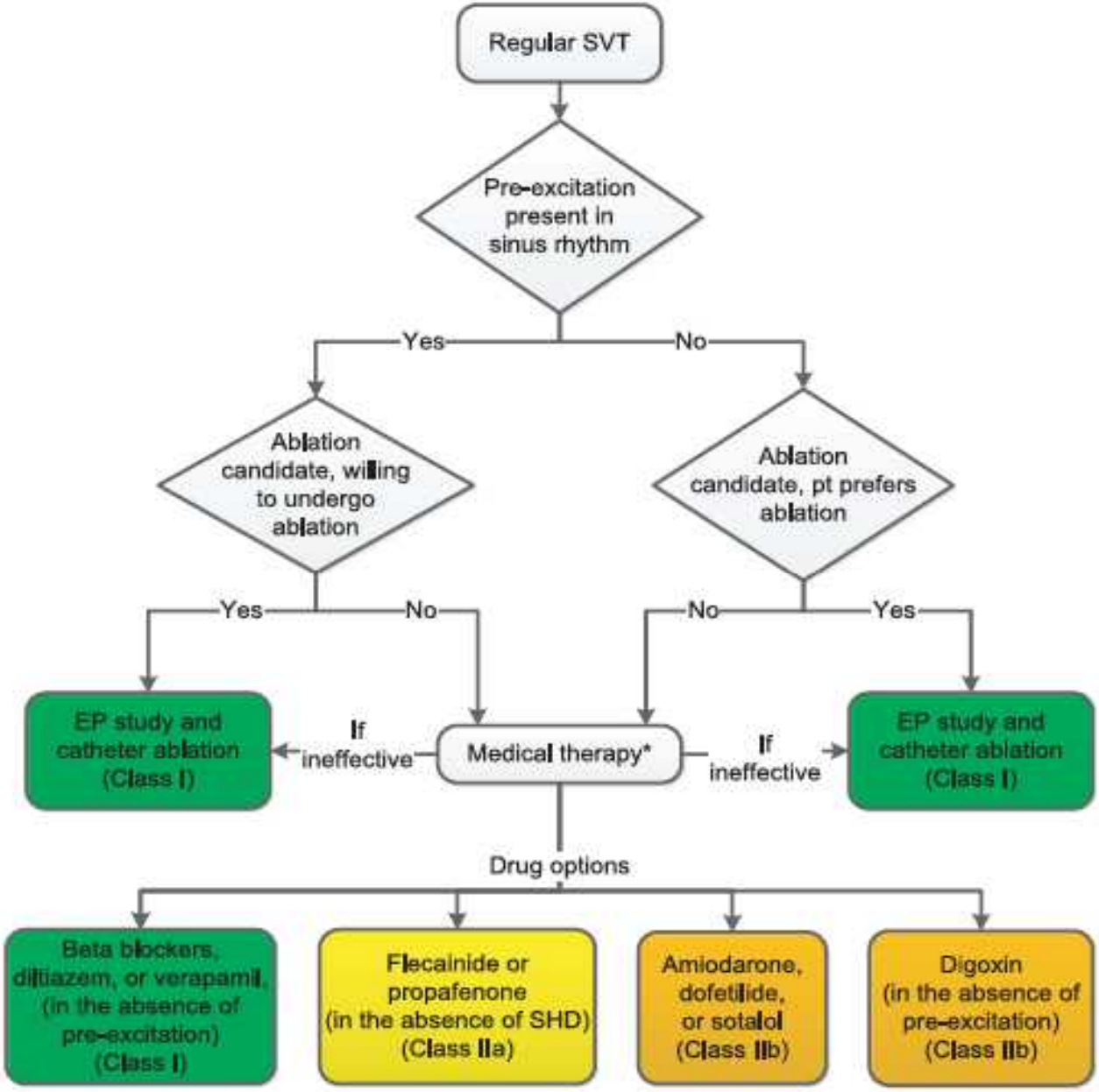


BCT



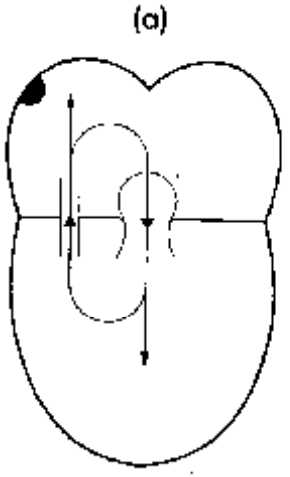
Φαρμακευτική αντιμετώπιση - προβλήματα

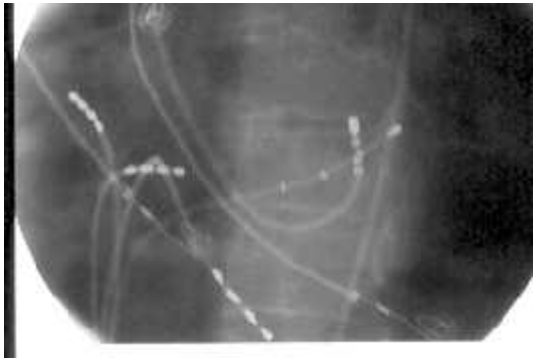
- Αποτελεσματικότητα?
- Παρενέργειες
- Επιπλοκές

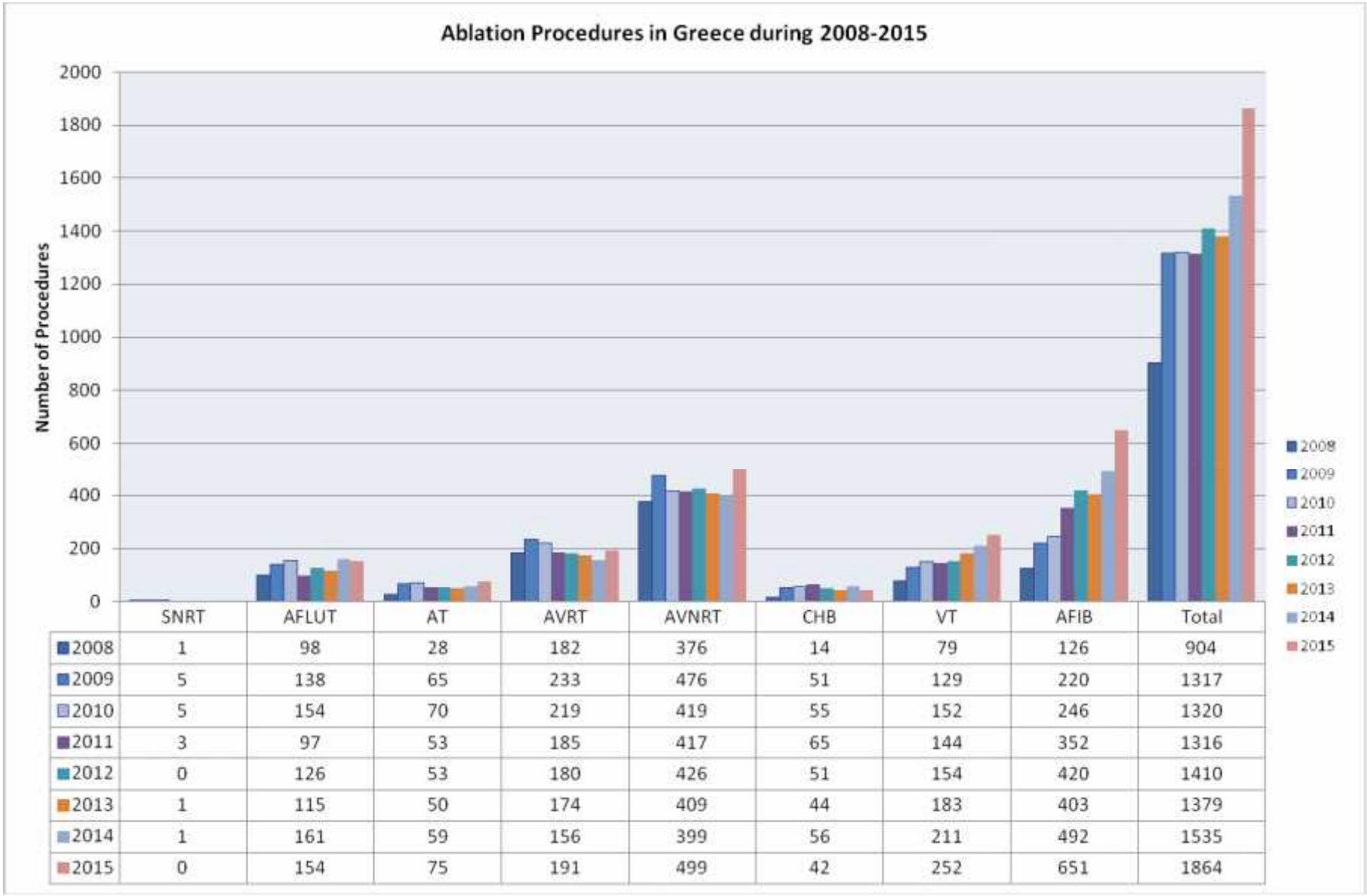


ACC Guidelines JACC 2014

Κατάλυση ταχυκαρδίας

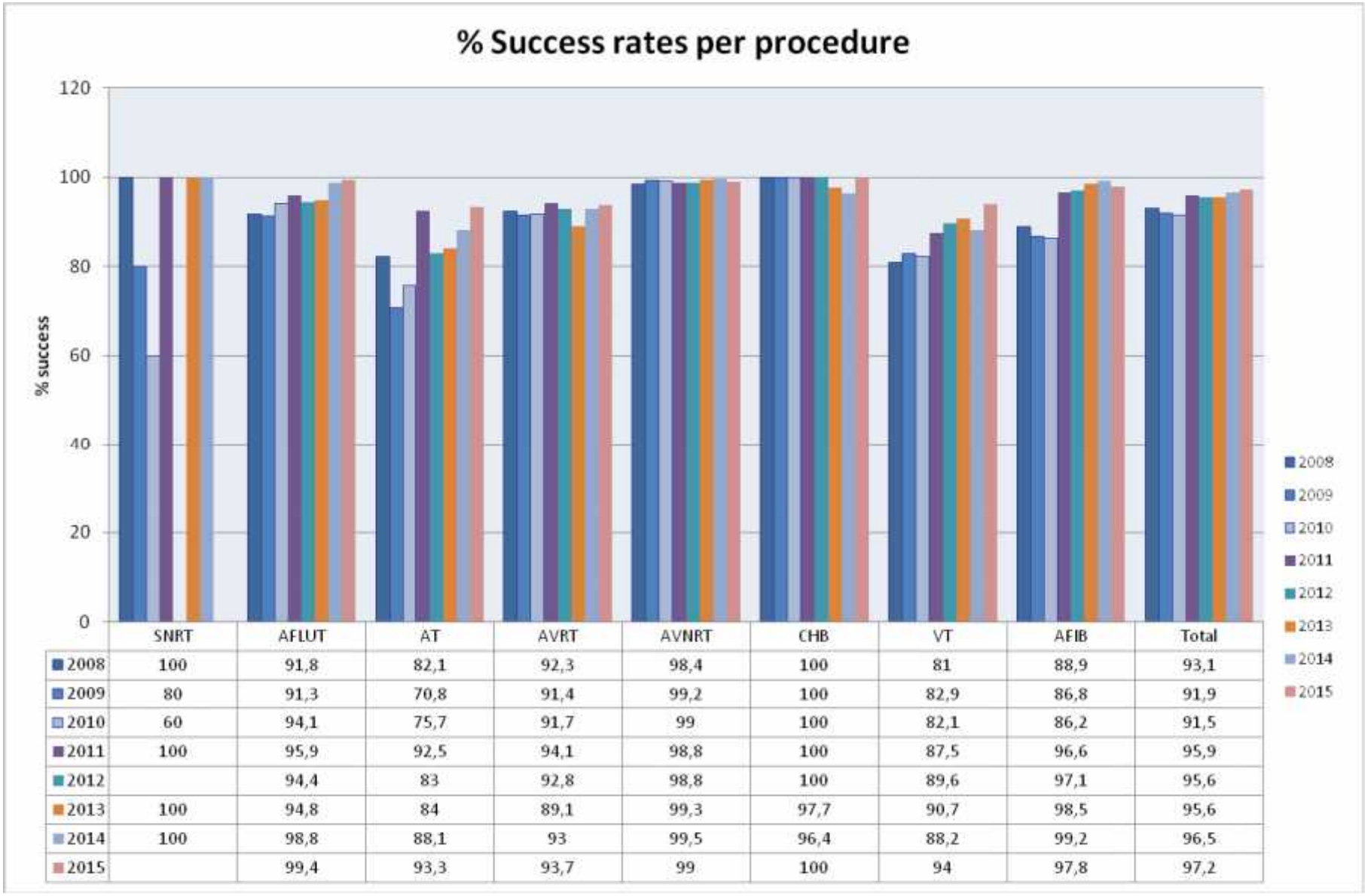






	SNRT	AFLUT	AT	AVRT	AVNRT	CHB	VT	AFIB	Total
2008	1	98	28	182	376	14	79	126	904
2009	5	138	65	233	476	51	129	220	1317
2010	5	154	70	219	419	55	152	246	1320
2011	3	97	53	185	417	65	144	352	1316
2012	0	126	53	180	426	51	154	420	1410
2013	1	115	50	174	409	44	183	403	1379
2014	1	161	59	156	399	56	211	492	1535
2015	0	154	75	191	499	42	252	651	1864

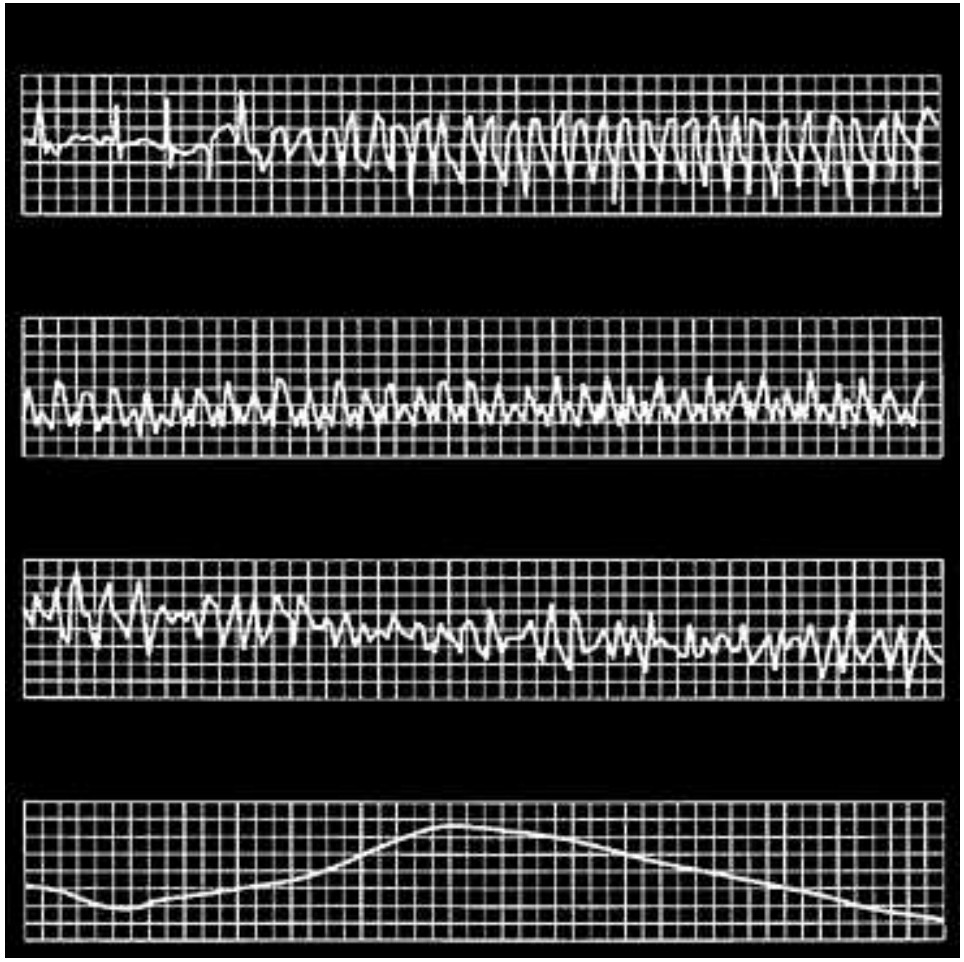
Vassilikos et al, EuroPace 2015



	SNRT	AFLUT	AT	AVRT	AVNRT	CHB	VT	AFIB	Total
2008	100	91,8	82,1	92,3	98,4	100	81	88,9	93,1
2009	80	91,3	70,8	91,4	99,2	100	82,9	86,8	91,9
2010	60	94,1	75,7	91,7	99	100	82,1	86,2	91,5
2011	100	95,9	92,5	94,1	98,8	100	87,5	96,6	95,9
2012		94,4	83	92,8	98,8	100	89,6	97,1	95,6
2013	100	94,8	84	89,1	99,3	97,7	90,7	98,5	95,6
2014	100	98,8	88,1	93	99,5	96,4	88,2	99,2	96,5
2015		99,4	93,3	93,7	99	100	94	97,8	97,2

Vassilikos et al, EuroPace 2015

Καταγραφή επεισοδίου αιφνιδίου Θανάτου



“Prediction is very difficult, especially about the future”

Niels Bohr, physicist

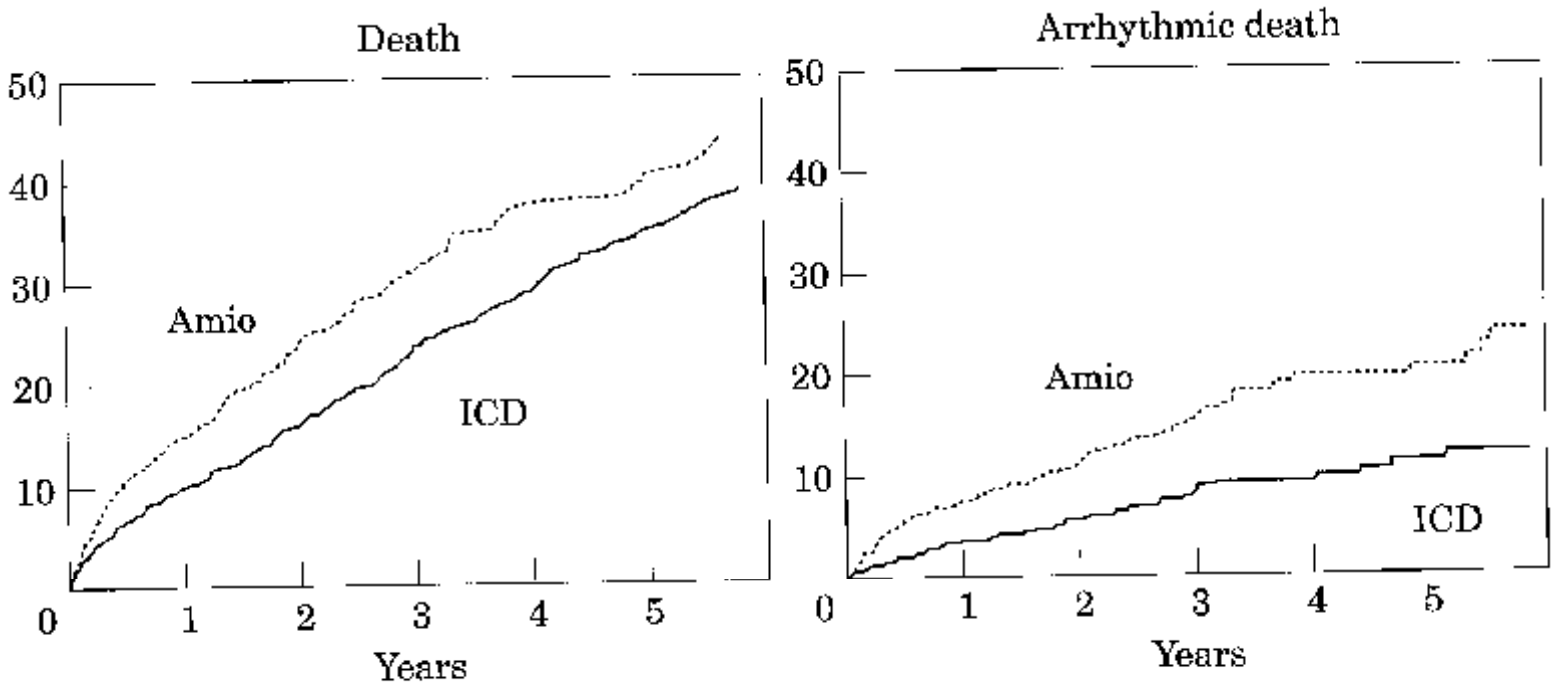
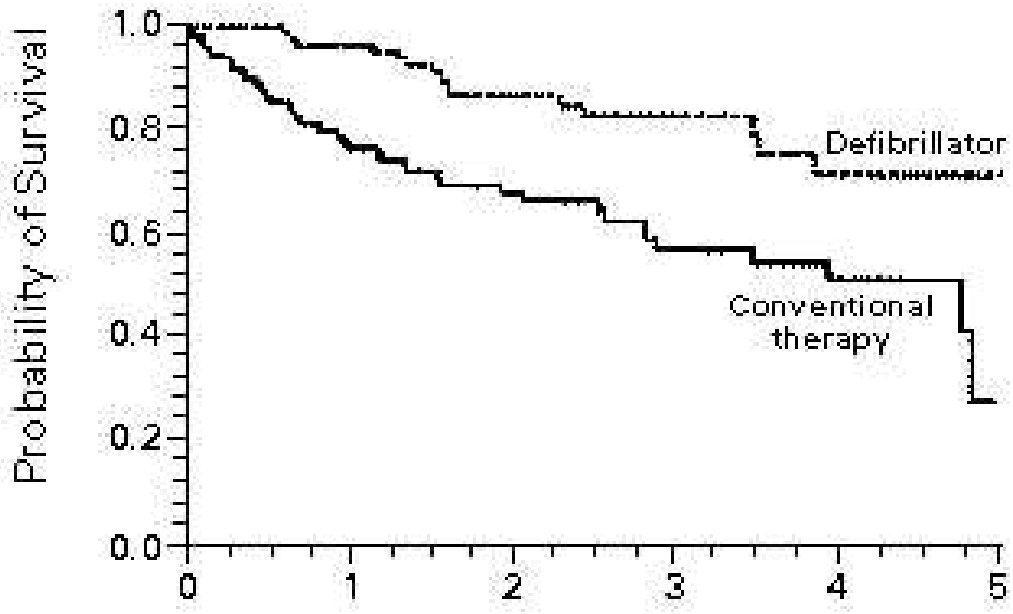


Figure 1 **Cumulative risk of fatal events or the amiodarone (. . .) and ICD (—) treatment arms.**

Eur Heart J, Vol. 21, issue 24, December 2000

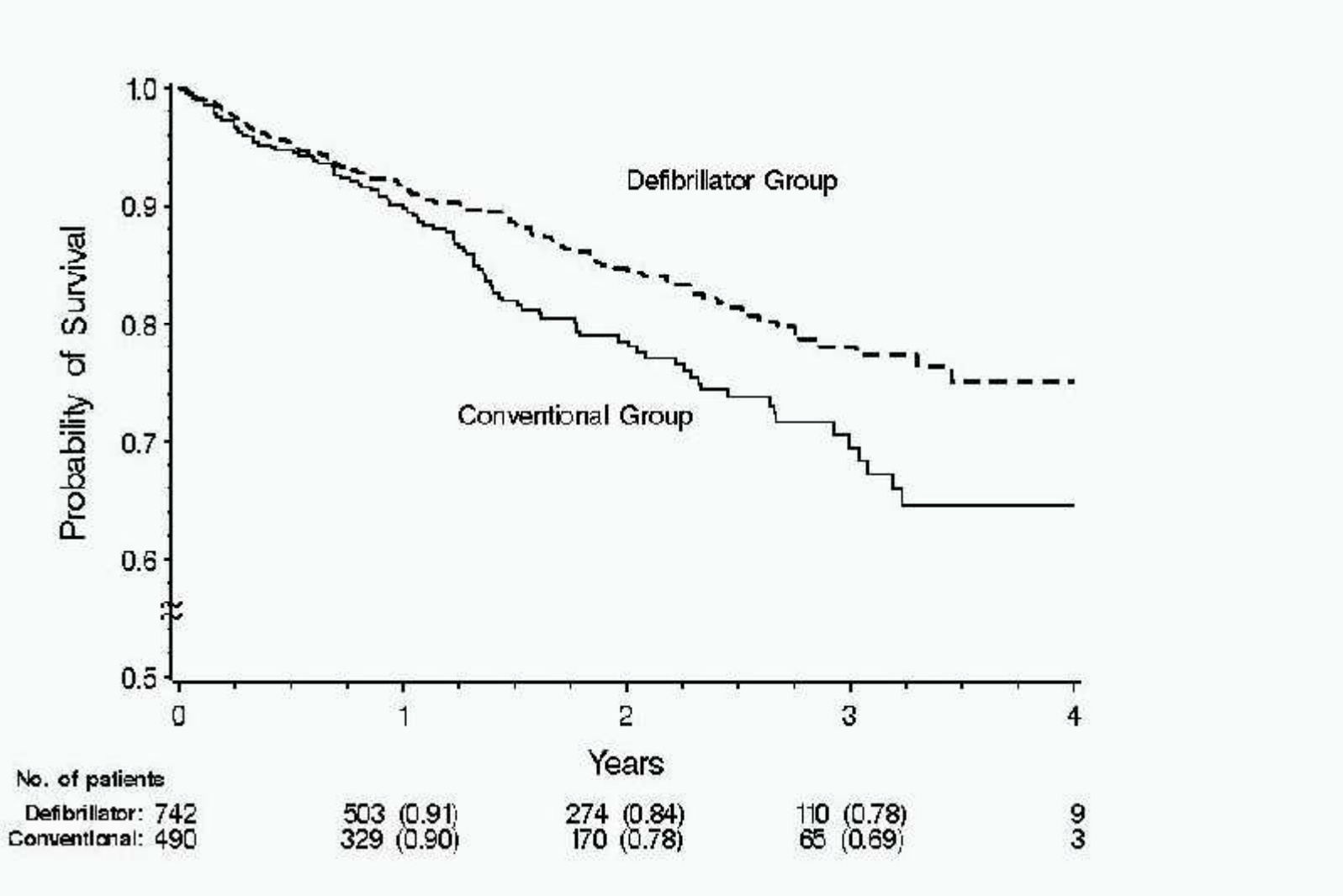
Connoly et al., Eur Heart J 2000

MADIT

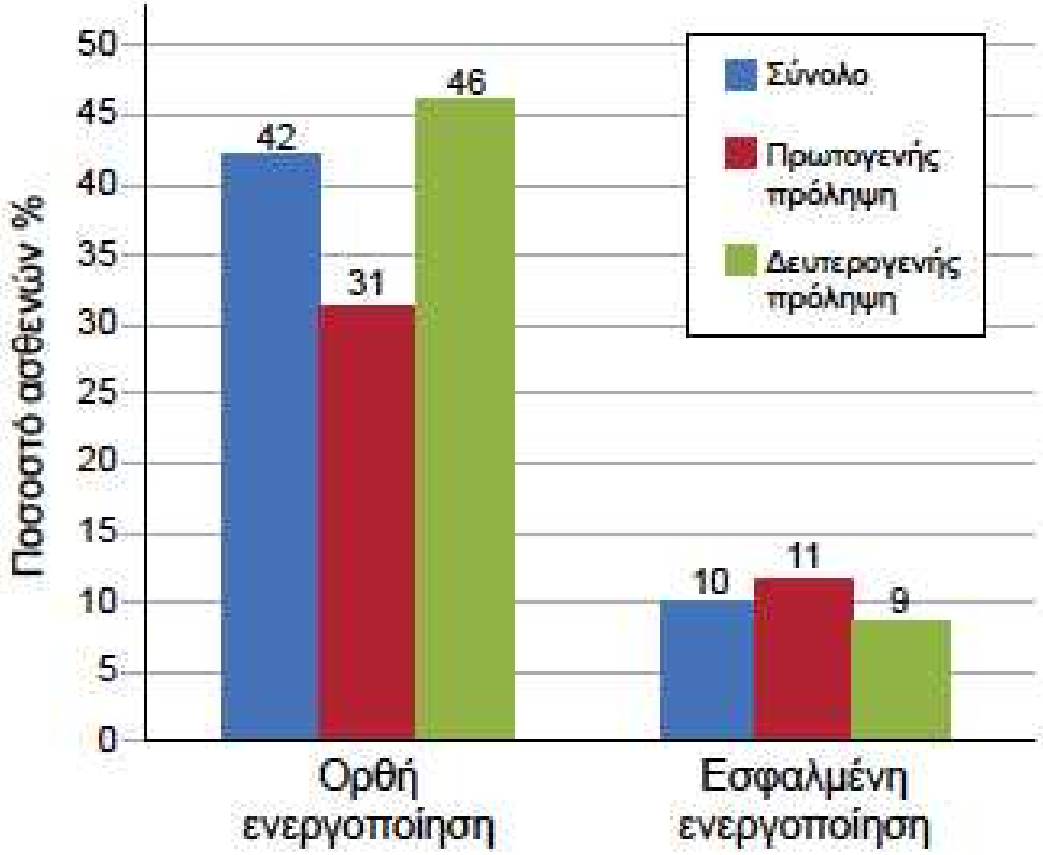


No. of Patients						
Defibrillator	95	80	53	31	17	3
Conventional therapy	101	67	48	29	17	0

MADIT II


Probability of Survival
1.0
0.9
0.8
0.7
0.6
0.5
Defibrillator Group
Conventional Group
0
1
2
3
4
Years
No. of patients
Defibrillator: 742
Conventional: 490
503 (0.91)
329 (0.90)
274 (0.84)
170 (0.78)
110 (0.78)
65 (0.69)
9
3

AHEPA experience

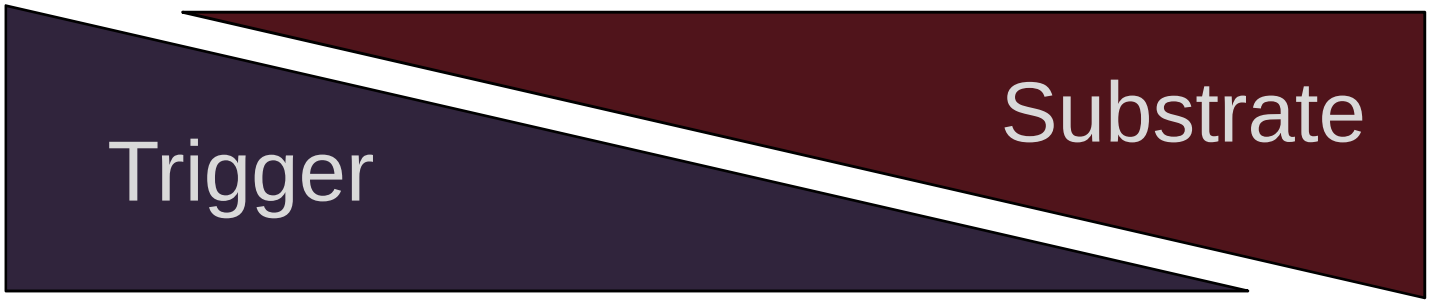


Vassilikos et al, HJC 2011

AF mechanisms

Paroxysmal AF

Persistent AF

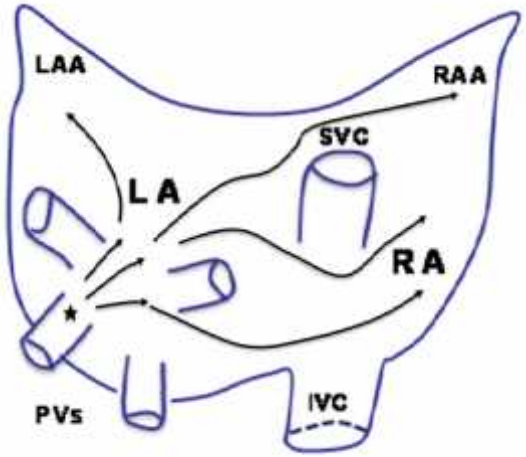


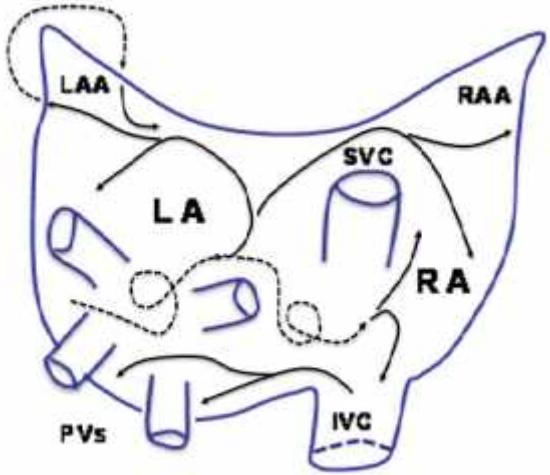
No Structural Heart Disease

Structural Heart Disease

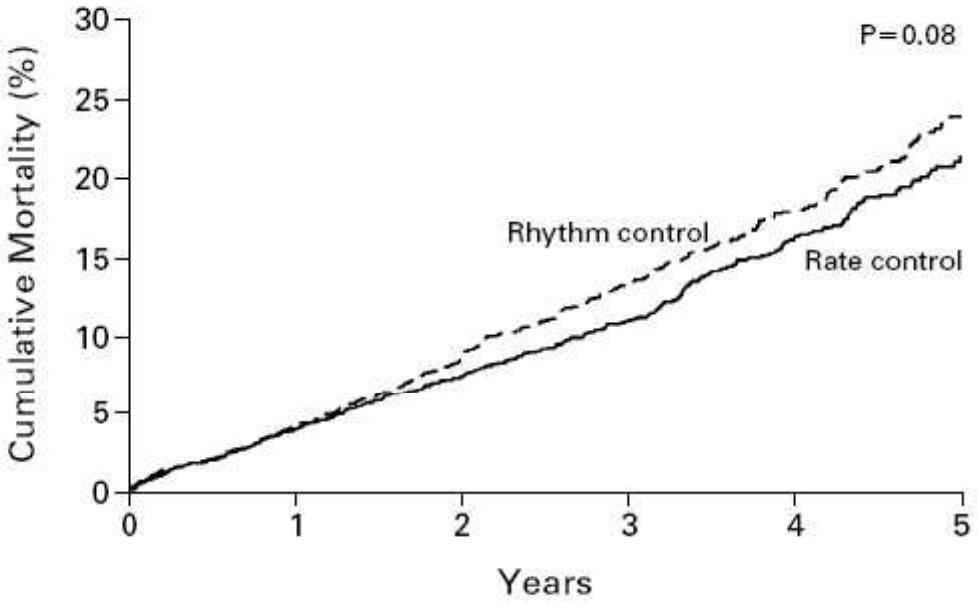
PV triggers

Multiple Wavelets, Nests, Rotors





AFFIRM Trial: Rhythm vs Rate Control

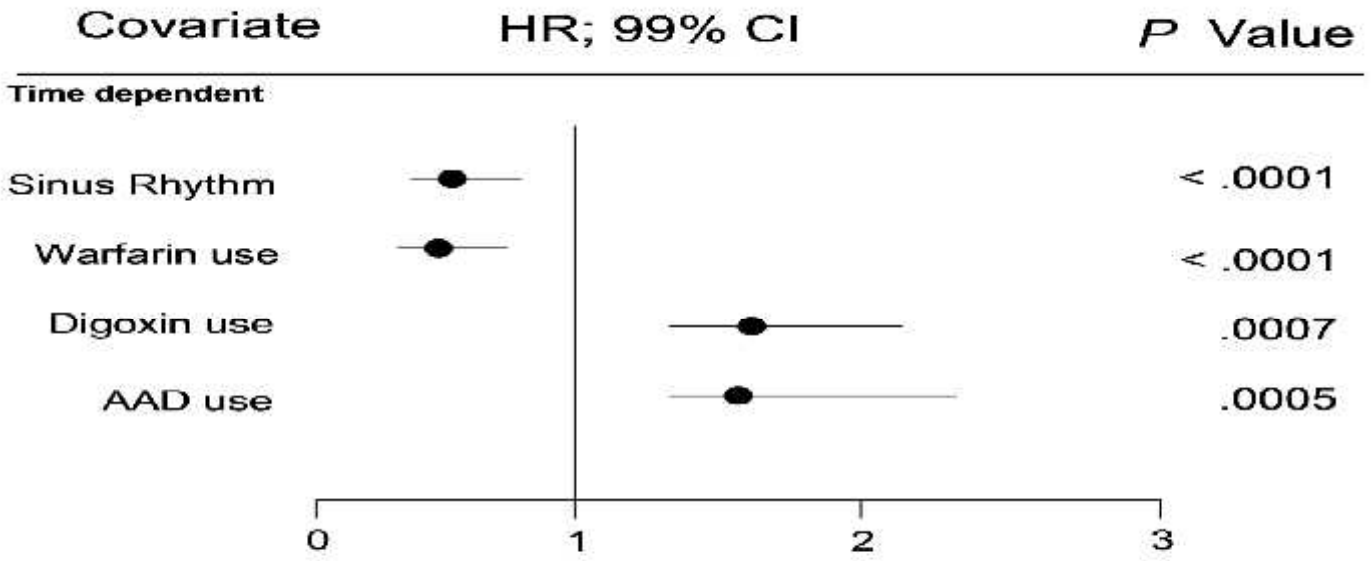


No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

- Cumulative mortality from any cause in the rhythm-control group and the rate-control group

Wyse et al. NEJM 2002;347:1825-33

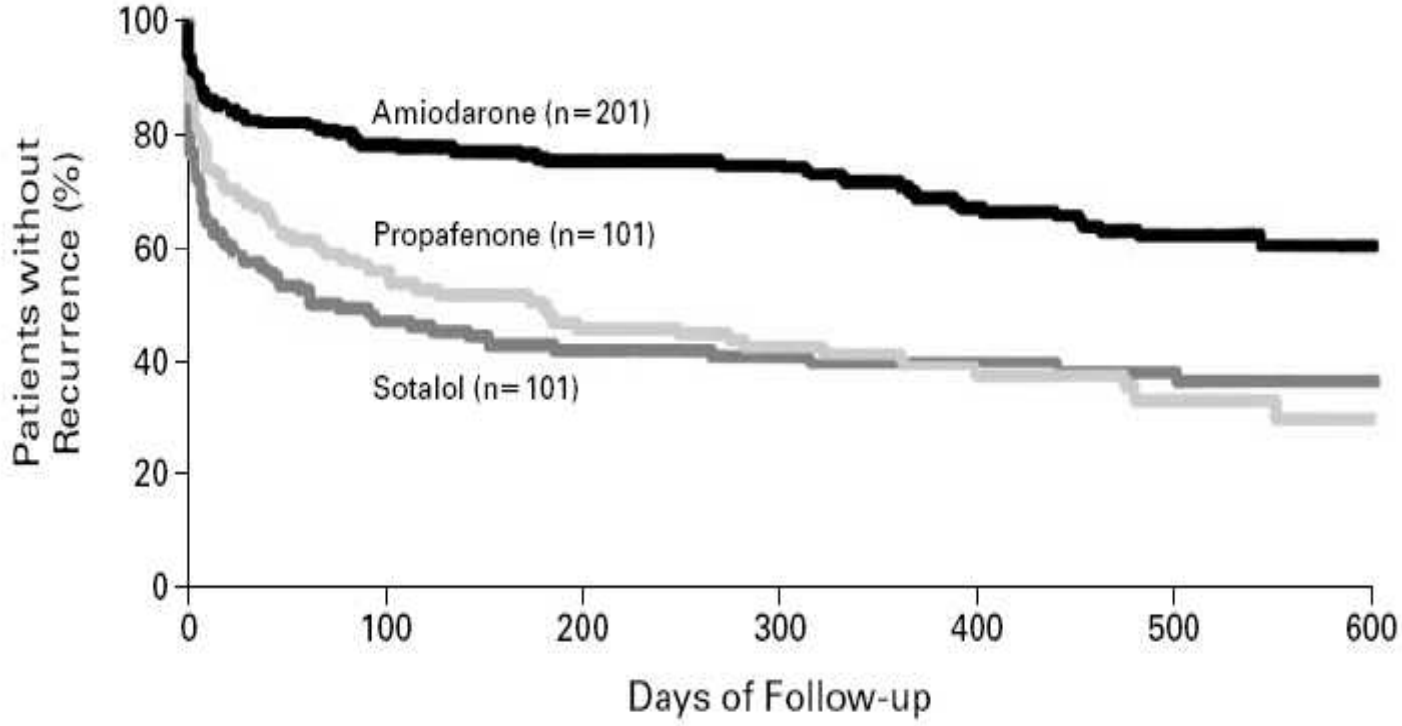
AFFIRM: Independent predictors of survival



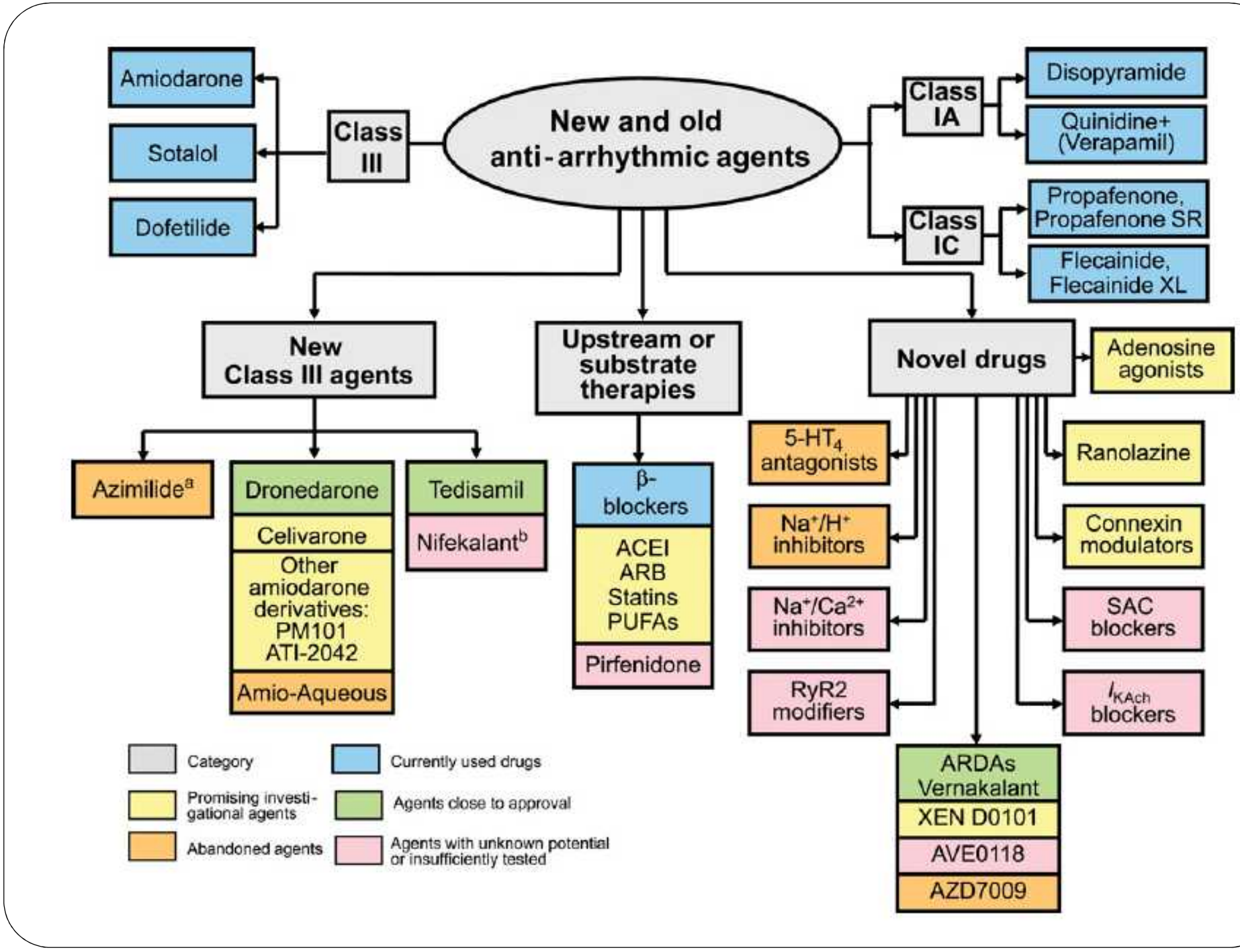
- The risks of AADs counterbalance the benefits of sinus rhythm

Corley et al. Circulation 2004;109:1509-13

Amiodarone: the most effective AA agent



*Roy et al. NEJM 2000;*342:913-20


New and old anti-arrhythmic agents
Class III
Amiodarone
Sotalol
Dofetilide
Class IA
Disopyramide
Quinidine+ (Verapamil)
Class IC
Propafenone, Propafenone SR
Flecainide, Flecainide XL
New Class III agents
Azimilide[a]
Dronedarone
Celivarone
Other amiodarone derivatives: PM101 ATI-2042
Amio-Aqueous
Tedisamil
Nifekalant[b]
Upstream or substrate therapies
β-blockers
ACEI ARB Statins PUFAs
Pirfenidone
Novel drugs
Adenosine agonists
5-HT4 antagonists
Na+/H+ inhibitors
Na+/Ca2+ inhibitors
RyR2 modifiers
Ranolazine
Connexin modulators
SAC blockers
IKAch blockers
ARDAs Vernakalant
XEN D0101
AVE0118
AZD7009
Category
Currently used drugs
Promising investigational agents
Agents close to approval
Abandoned agents
Agents with unknown potential or insufficiently tested

Europace (2014) 16, 973–979
doi:10.1093/europace/eut407

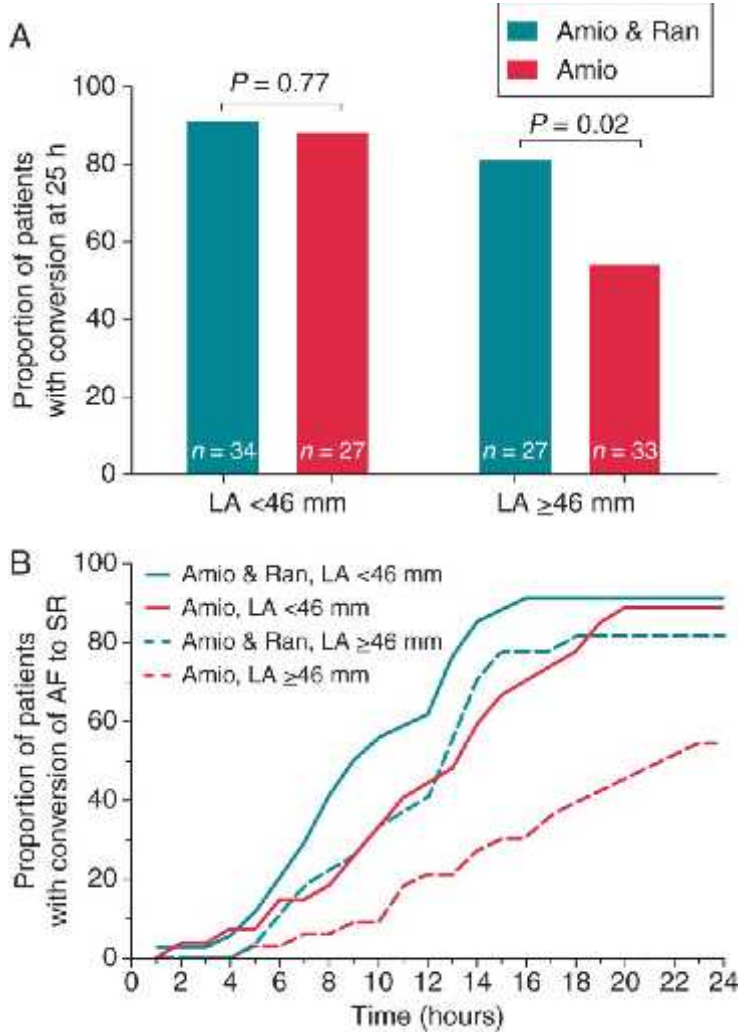
CLINICAL RESEARCH
Atrial fibrillation

Ranolazine enhances the efficacy of amiodarone for conversion of recent-onset atrial fibrillation

Konstantinos C. Koskinas[1*†], Nikolaos Fragakis[1†], Demosthenes Katritsis[2], Vassileios Skeberis[1], and Vassileios Vassilikos[1]

121 patients were randomized in a 1 : 1 ratio to either **intravenous amiodarone** (60 min loading dose of 5 mg/kg followed by maintenance infusion of 50 mg/h until conversion to SR, for a maximum of 24 h) or **intravenous amiodarone** at the same dosage and duration **plus oral ranolazine 1500 mg** given once at the time of randomization.

Conversion rate of AF to SR at 24 h in patients stratified according to LA diameter by TTE < 46 mm (left) vs. ≥46 mm (right) and according to treatment with amiodarone plus ranolazine (Amio and Ran) vs. amiodarone alone (Amio).



Koskinas K C et al. Europace 2014;16:973-979

6.2.2. Upstream Therapy: Recommendations

CLASS IIa

1. An ACE inhibitor or angiotensin-receptor blocker (ARB) is reasonable for primary prevention of new-onset AF in patients with HF with reduced LVEF (130,379,380). *(Level of Evidence: B)*

CLASS IIb

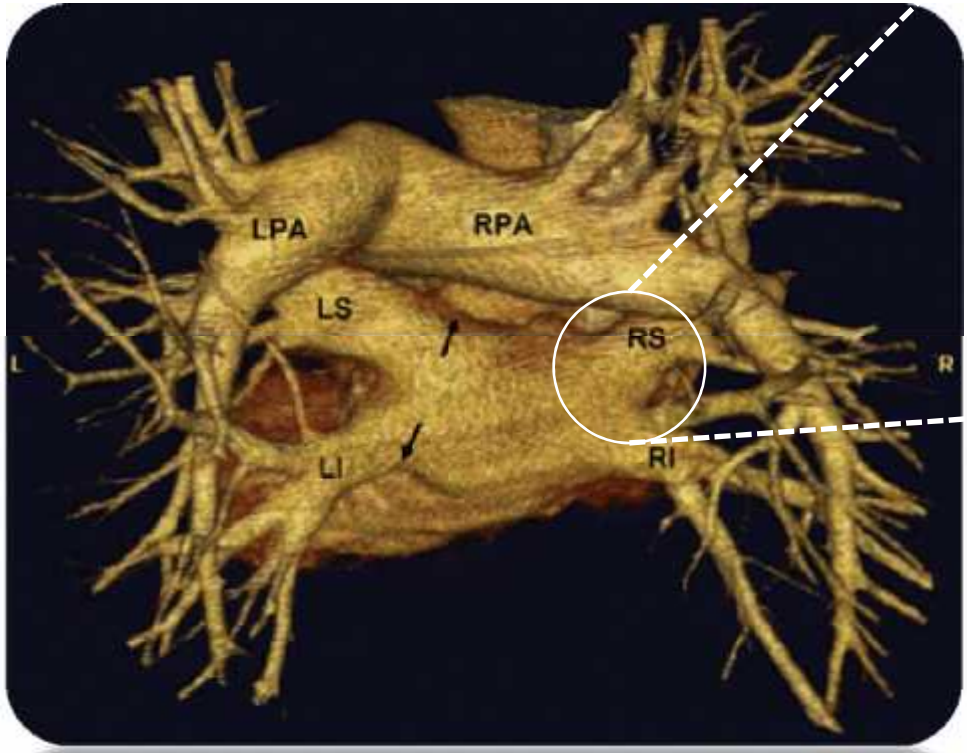
1. Therapy with an ACE inhibitor or ARB may be considered for primary prevention of new-onset AF in the setting of hypertension (381). *(Level of Evidence: B)*
2. Statin therapy may be reasonable for primary prevention of new-onset AF after coronary artery surgery (136,382). *(Level of Evidence: A)*

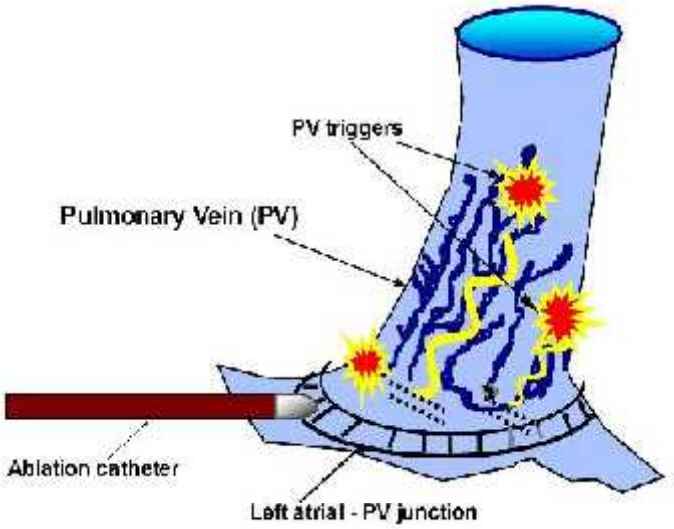
CLASS III: NO BENEFIT

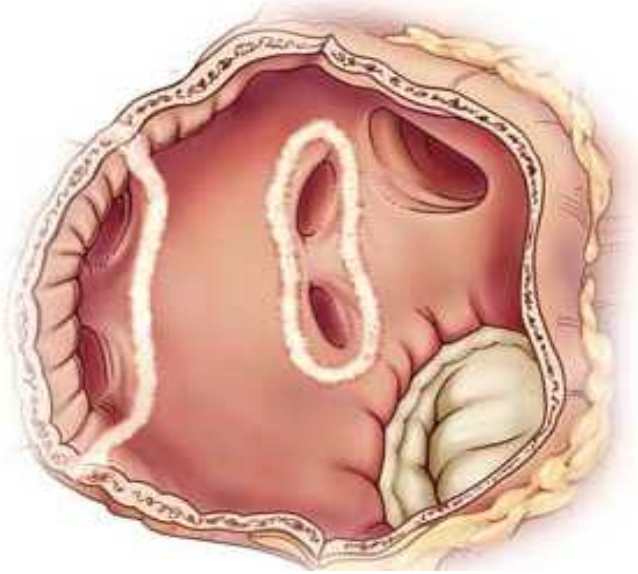
1. Therapy with an ACE inhibitor, ARB, or statin is not beneficial for primary prevention of AF in patients without cardiovascular disease (383). *(Level of Evidence: B)*

ACC Guidelines JACC 2014

Στρατηγική ελέγχου ρυθμού - Ablation





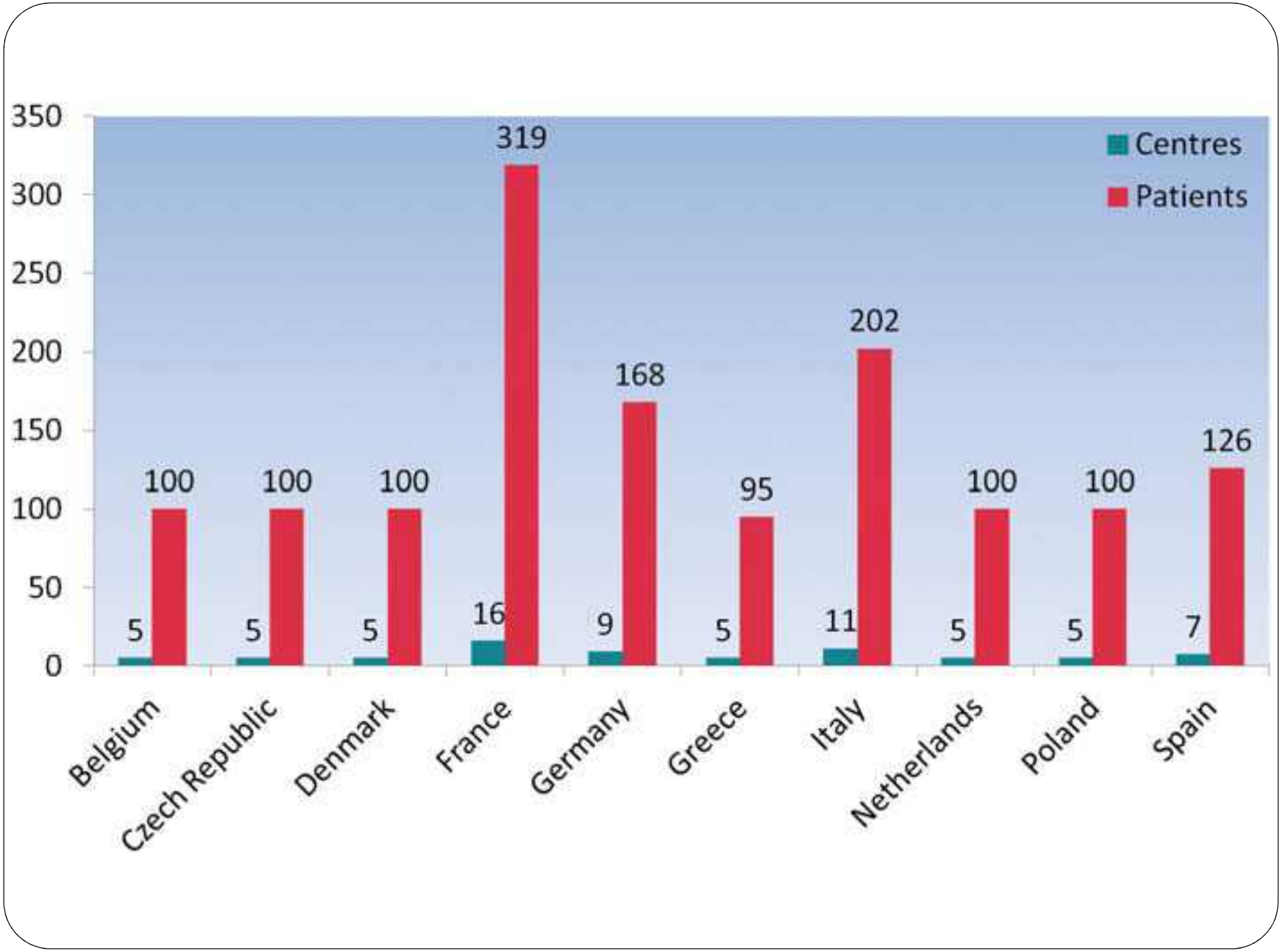


EURObservational Research Programme

Atrial Fibrillation Ablation Pilot Registry

1-year follow-up results

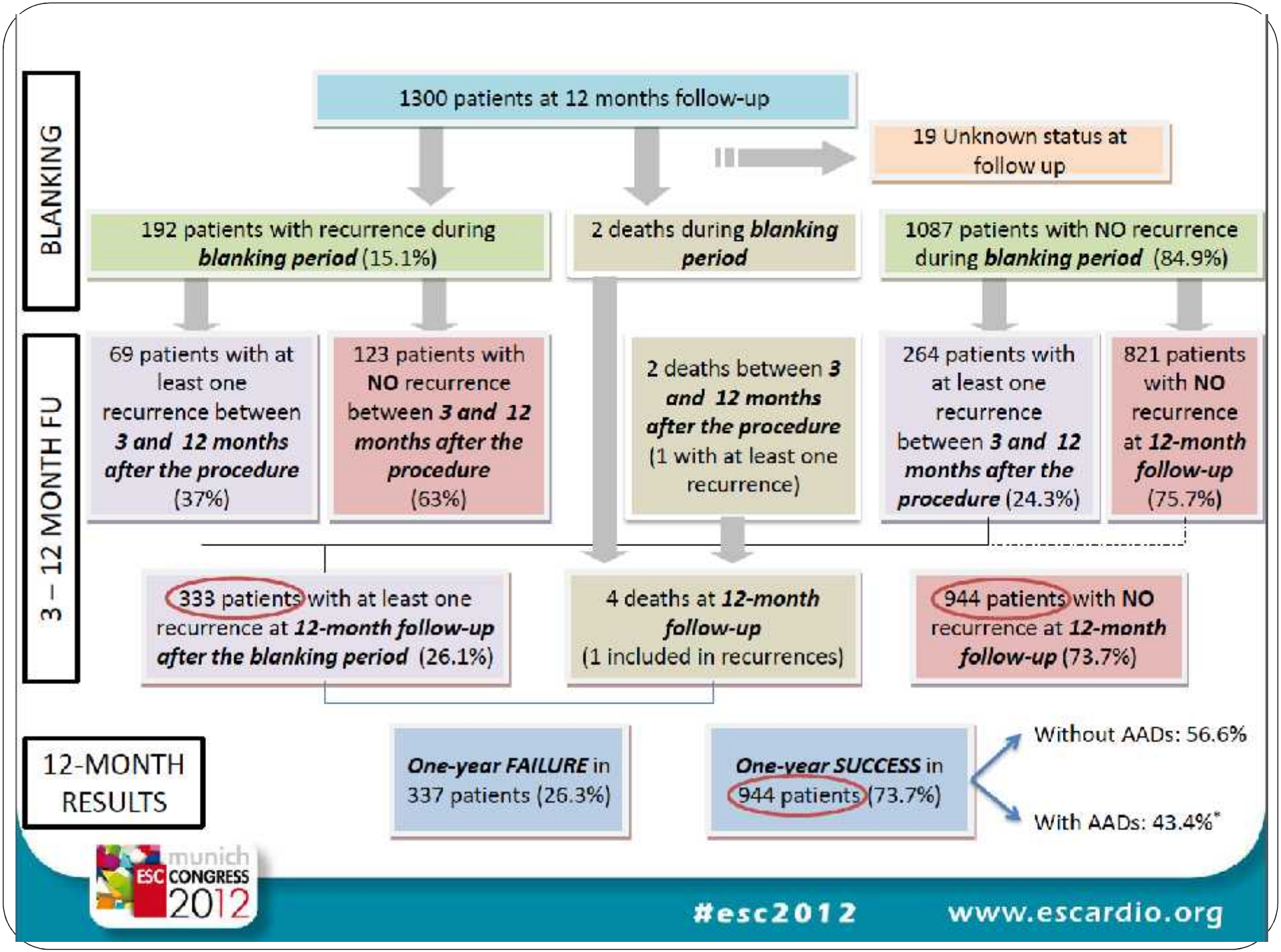
Elena Arbelo[1], Josep Brugada [1], Gerhard Hindricks[2], Aldo Maggioni[3], Luigi Tavazzi[4], Panos Vardas[5], Frédéric Anselme[6], Giuseppe Inama[7], Pierre Jais[8], Zbigniew Kalarus[9], Josef Kautzner[10], Thorsten Lewalter[11], Georges Mairesse[12], Julian Perez-Villacastin[13], Sam Riahi[14], Milos Taborsky[15], George Theodorakis[16], Serge Trines[17], on the behalf of the *Atrial Fibrillation Ablation Pilot Study Investigators**


350
300
250
200
150
100
50
0
Centres
Patients
100
100
100
319
168
95
202
100
100
126
5
5
5
16
9
5
11
5
5
7
Belgium
Czech Republic
Denmark
France
Germany
Greece
Italy
Netherlands
Poland
Spain

Indications for ablation (%)

• Symptoms	89.7
• Quality of life	73.4
• Desire for drug-free lifestyle	34.9
• Desire for sinus rhythm	39.6

Arbello et al, EuroPace 2012


BLANKING
1300 patients at 12 months follow-up
19 Unknown status at follow up
192 patients with recurrence during blanking period (15.1%)
2 deaths during blanking period
1087 patients with NO recurrence during blanking period (84.9%)
3 – 12 MONTH FU
69 patients with at least one recurrence between 3 and 12 months after the procedure (37%)
123 patients with NO recurrence between 3 and 12 months after the procedure (63%)
2 deaths between 3 and 12 months after the procedure (1 with at least one recurrence)
264 patients with at least one recurrence between 3 and 12 months after the procedure (24.3%)
821 patients with NO recurrence at 12-month follow-up (75.7%)
333 patients with at least one recurrence at 12-month follow-up after the blanking period (26.1%)
4 deaths at 12-month follow-up (1 included in recurrences)
944 patients with NO recurrence at 12-month follow-up (73.7%)
12-MONTH RESULTS
One-year FAILURE in 337 patients (26.3%)
One-year SUCCESS in 944 patients (73.7%)
Without AADs: 56.6%
With AADs: 43.4%*
munich ESC CONGRESS 2012
#esc2012
www.escardio.org

Europace (2012) 14, 528–606
doi:10.1093/europace/eus027

HRS/EHRA/ECAS EXPERT CONSENSUS STATEMENT

2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Patient Selection, Procedural Techniques, Patient Management and Follow-up, Definitions, Endpoints, and Research Trial Design

TABLE 2: CONSENSUS INDICATIONS FOR CATHETER AND SURGICAL ABLATION of AF

	CLASS	LEVEL
INDICATIONS FOR CATHETER ABLATION of AF		
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Catheter ablation is recommended*	I	A
Persistent: Catheter ablation is reasonable	IIa	B
Longstanding Persistent: Catheter ablation may be considered	IIb	B
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Catheter ablation is reasonable	IIa	B
Persistent: Catheter ablation may be considered	IIb	C
Longstanding Persistent: Catheter ablation may be considered	IIb	C

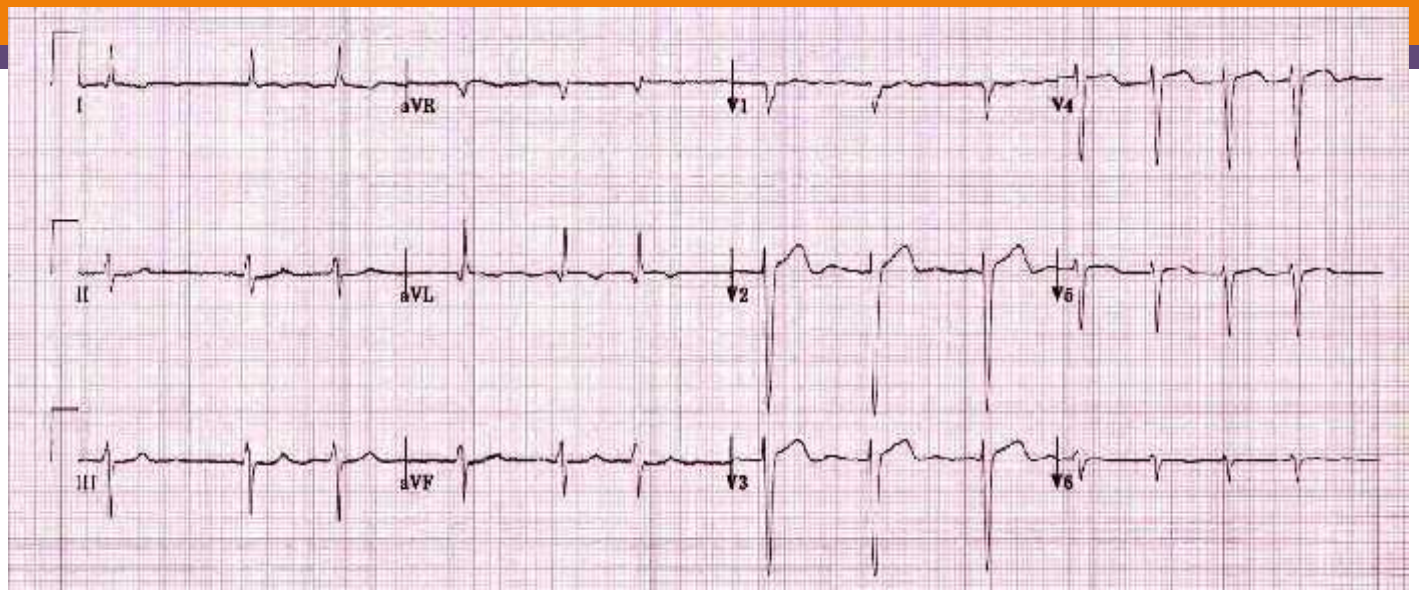
Κριτήρια εξατομίκευσης στρατηγικής

- Παρουσία συμπτωμάτων
- Τύπος κολπικής μαρμαρυγής
- Ηλικία
- Συνυπάρχουσες παθήσεις
- Διαστάσεις αριστερού κόλπου
- Προτίμηση ασθενούς

Recommendations	Class[a]	Level[b]
Rate control should be the initial approach in elderly patients with AF and minor symptoms (EHRA score 1).	I	A
Rate control should be continued throughout a rhythm control approach to ensure adequate control of the ventricular rate during recurrences of AF.	I	A
Rhythm control is recommended in patients with symptomatic (EHRA score ≥2) AF despite adequate rate control.	I	B
Rhythm control in patients with AF and AF-related heart failure should be considered for improvement of symptoms.	IIa	B
Rhythm control as an initial approach should be considered in young symptomatic patients in whom catheter ablation treatment has not been ruled out.	IIa	C
Rhythm control should be considered in patients with AF secondary to a trigger or substrate that has been corrected (e.g. ischaemia, hyperthyroidism).	IIa	C

Περίπτωση ασθενούς (1)

- **Γυναίκα, 82 ετών, υπερτασική, υπό καρβεδιλόλη**
- **Ασυμπτωματική, χωρίς αναφερόμενο περιορισμό της λειτουργικής ικανότητας**
- **Σε τυχαίο έλεγχο προ τριμήνου διαπιστώθηκε…**



- **TFTs: εφο, ΤΤΕ: ήπια συγκεντρική υπερτροφία, μέτρια ανεπάρκεια μιτροειδούς, διάταση αριστερού κόλπου (LA:47mm)**

Ασυμπτωματική – αγνώστου έναρξης AF

Καλά ελεγχόμενη κοιλιακή ανταπόκριση

Αυξημένη ηλικία – διάταση LA

Υπέρταση – μέτρια MR

Recommendations for rate and rhythm control of AF

Recommendations	Class[a]	Level[b]	Ref.[c]
Rate control should be the initial approach in elderly patients with AF and minor symptoms (EHRA score I).	I	A	86–87, 90

Προσοχή!! Ανάγκη λήψης αντιπηκτικών

CHA2DS2VASc score: 4

Περίπτωση ασθενούς (2)

- **Άνδρας 53 ετών, ελεύθερο ατομικό αναμνηστικό**
- **Πρώτο επεισόδιο συμπτωματικής κολπικής μαρμαρυγής (160 bpm)**
- **TFTs OK – Φυσιολογικό υπερηχογράφημα**

CHADSVASc = 0

- Έλεγχος συχνότητας (β-αναστολέας)
- Έλεγχος ρυθμού (pill in the pocket)
- Ελεγχος ρυθμού (Μόνιμα AAD + β-αναστολέα)
- Ελεγχος ρυθμού (ablation)

Περίπτωση ασθενούς (3)

- **Άνδρας 46 ετών, ελεύθερο ατομικό αναμνηστικό**
- **Σε τυχαίο έλεγχο: κολπική μαρμαρυγή (περίπου 110 bpm)**
- **Ασυμπτωματικός - TFTs OK**
- **TTE: μικρή διάταση LA-42mm, λοιπά κφ**

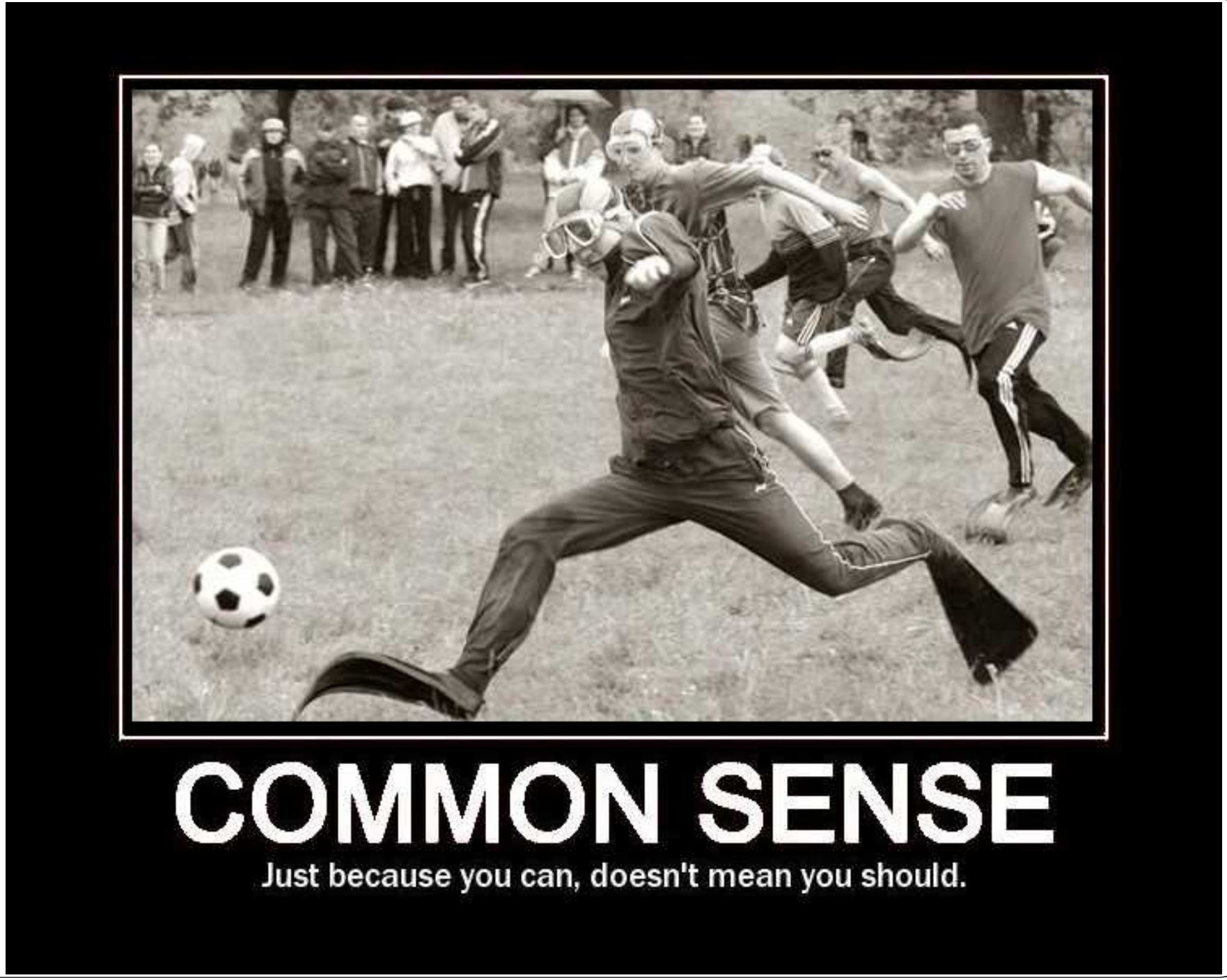
CHADSVASc = 0

- Έλεγχος συχνότητας (β-αναστολέας)
- Ανάταξη και pill in the pocket
- Ανάταξη και AAD
- Ανάταξη και ablation

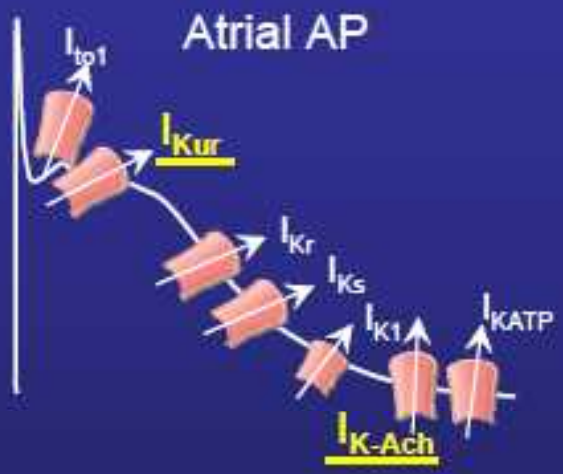
Περίπτωση ασθενούς (4)

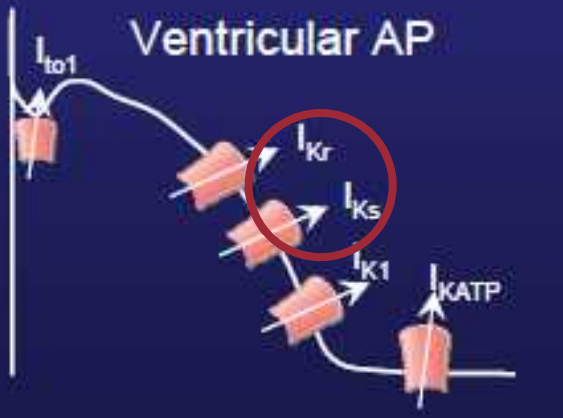
- **Γυναίκα 62 ετών, ιστορικό υπέρτασης υπό αγωγή (αΜΕΑ)**
- **Συχνοί παροξυσμοί κολπικής μαρμαρυγής από τριετίας**
- **Έντονα συμπτωματική επί παροξυσμών**
- **Φυσιολογικό υπερηχογράφημα – απουσία διάτασης αρ. κόλπου**

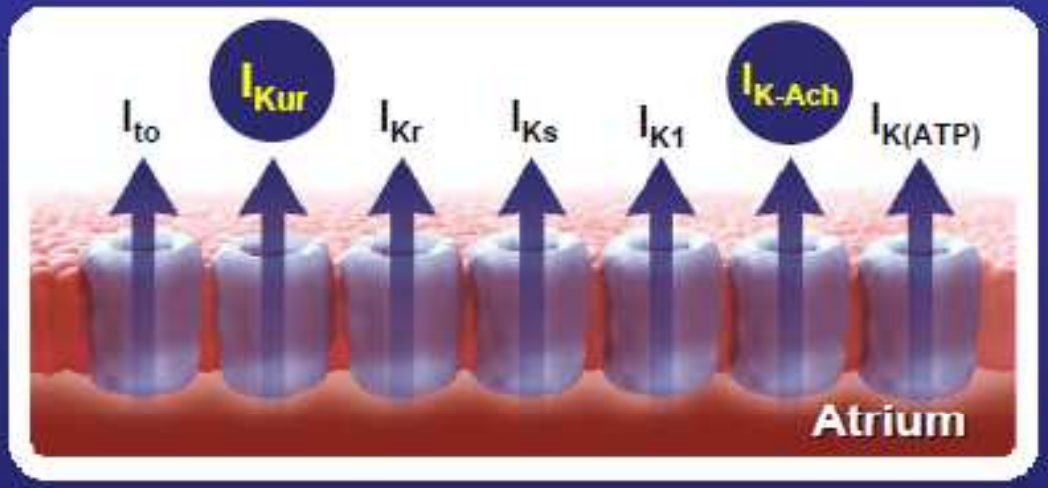
Rhythm control

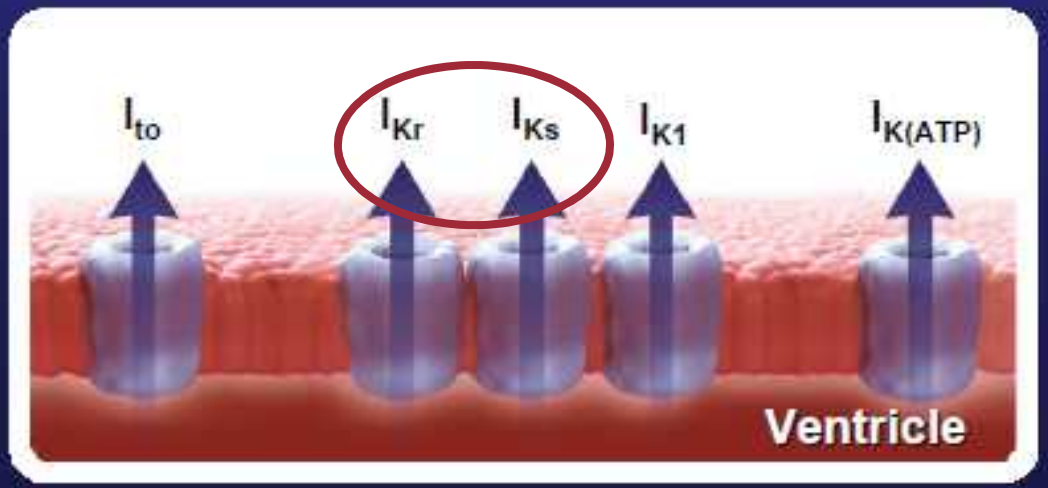

COMMON SENSE
Just because you can, doesn't mean you should.

Action Potential in the Atria and the Ventricles: Some K^+ Ion Currents Are Present Only in the Atria[1,2]









I_{to} = transient outward current; I_{Kur} = ultrarapid delayed-rectifier potassium current; I_{Kr} = rapid delayed-rectifier potassium current; I_{Ks} = slow delayed rectifier potassium current; I_{K1} = inward rectifier potassium current; I_{K-Ach} = acetylcholine-regulated potassium current; $I_{K(ATP)}$ = ATP-sensitive potassium current.

1. Ravens U et al. *Europace* 2008;10:1133–1137.

Ranolazine

- The late/sustained/persistent sodium channel current (late INa)
- The rapidly activating delayed rectifier potassium current (IKr)
- The early or peak sodium channel current (peak INa)

REVIEW

Ranolazine as a Promising Treatment Option for Atrial Fibrillation: Electrophysiologic Mechanisms, Experimental Evidence, and Clinical Implications

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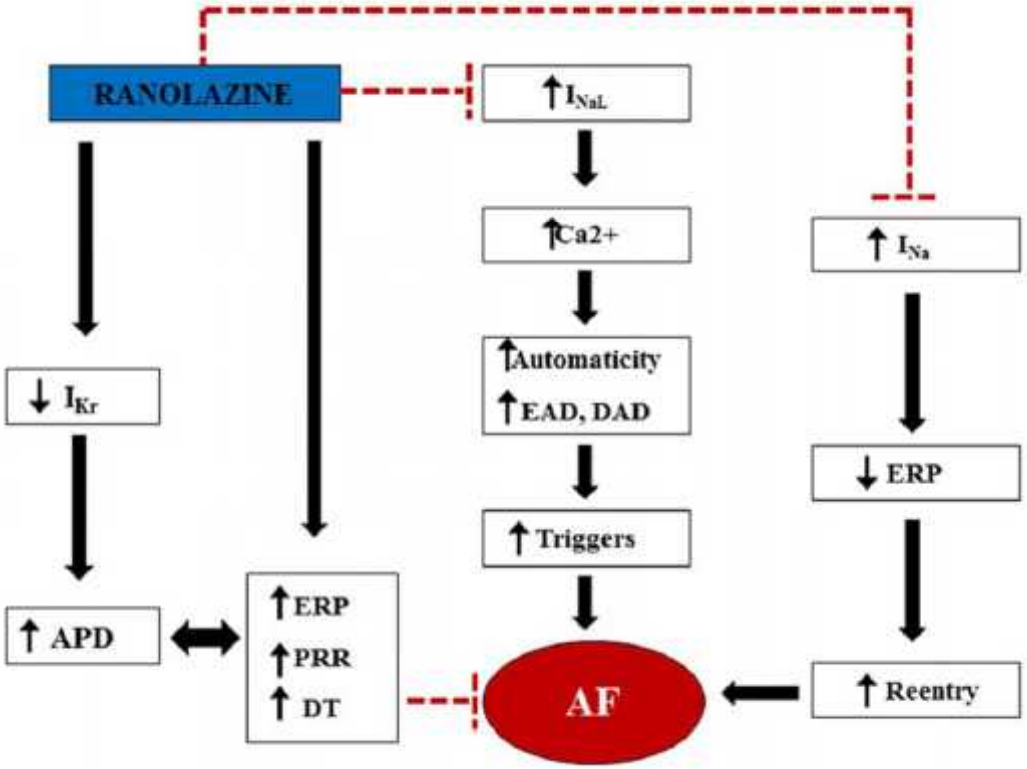

Pacing Clin Electrophysiol. 2014 Oct;37(10):1412-20.