"Ασθενείς με Κολπική Μαρμαρυγή προς καρδιοανάταξη ή κατάλυση. Δεδομένα για την Απιξαμπάνη"

Δορυφορική διάλεξη με την υποστήριξη της εταιρείας PFIZER

Παναγιώτης Ιωαννίδης

Διευθυντής Τμήματος Καρδιακής Ηλεκτροφυσιολογίας & Βηματοδότησης Βιοκλινικής Αθηνών

4ο Αρρυθμιολογικό Συνέδριο

Αθήνα, 21-22 Σεπτεμβρίου 2018

Γνωστοποιήσεις

- Ο ομιλητής έχει λάβει τιμητική αμοιβή από την Pfizer Hellas.

- ***"Οι απόψεις που εκφράζονται σε αυτή την παρουσίαση ανήκουν στον ομιλητή και δεν εκφράζουν απαραίτητα τις απόψεις της εταιρείας.***
- ***Για όλα τα φαρμακευτικά προϊόντα που αναφέρονται παρακαλείσθε να συμβουλεύεσθε τις εγκεκριμένες Περιλήψεις Χαρακτηριστικών των Προϊόντων"***

New Method for Terminating Cardiac Arrhythmias

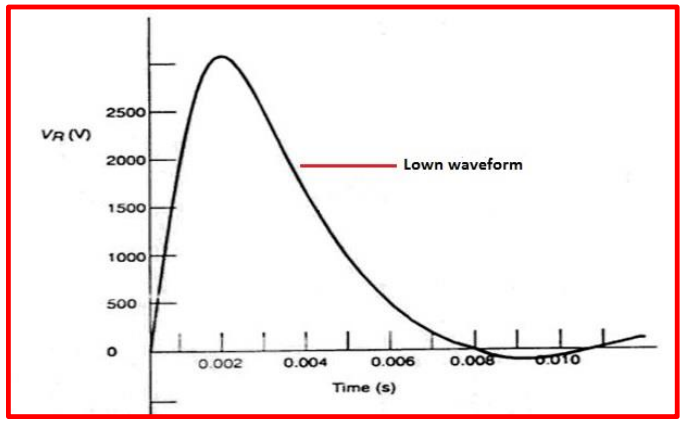
Use of Synchronized Capacitor Discharge

Bernard Lown, M.D., Raghavan Amarasingham, M.B., B.S., and Jose Neuman, M.D., Boston

THE ECTOPIC TACHYCARDIAS are currently treated by either vagal stimulation or drugs. The 3 most effective drugs are quinidine, procainamide hydrochloride, and the digitalis glycosides. When the ectopic mechanism drives the ventricles at rates above 160 per minute, cardiac output falls and coronary blood flow is compromised. This is most likely to occur with ventricular tachycardia which constitutes a serious cardiac emergency requiring immediate treatment. Frequently, how-

The requirements for an ideal method for abolishing atrial and ventricular arrhythmias can be readily spelled out. The ectopic mechanism should be controlled instantly and consistently. There should be no depression of the normal cardiac pacemakers, no prolongation of conductivity, nor impairment of myocardial contractility. Other vital structures should not be injured. Furthermore, the method should be simple in application.

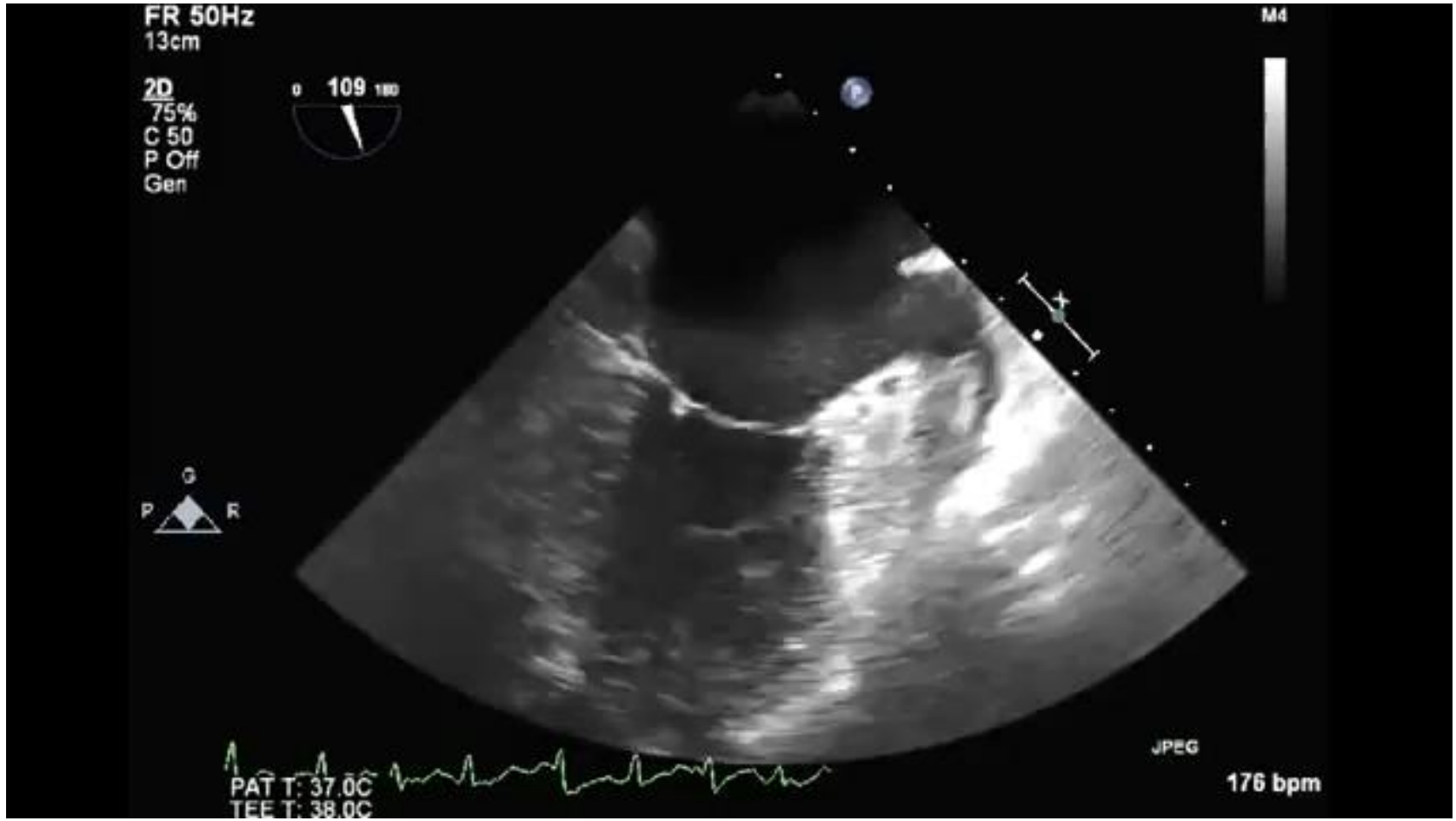
The purpose of this report is to introduce a



Bernard Lown *(1921-)*

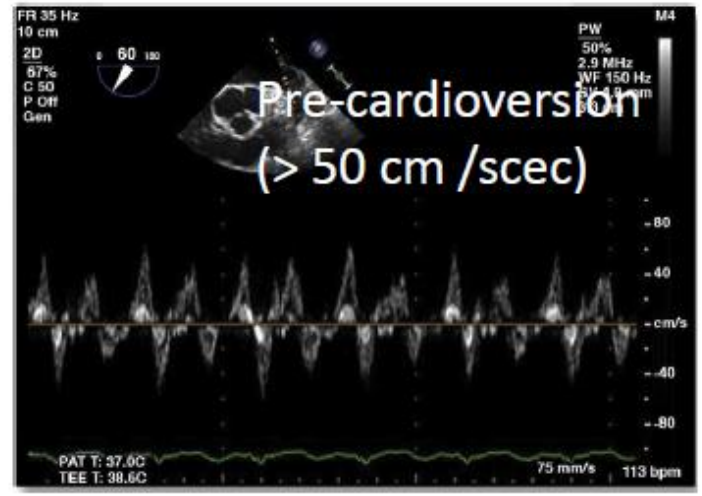
Lown B, et al. JAMA. 1962;182:548–555.
Lown B, et al. N Engl J Med. 1963;269:325–331.

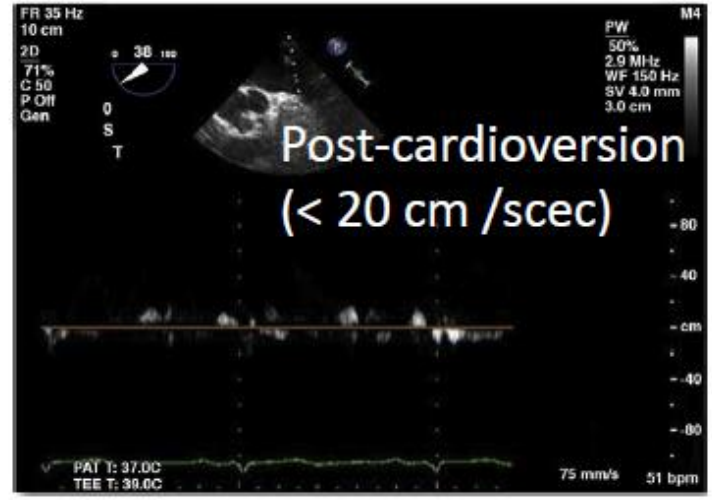
LAA thrombus



Atrial stunning after AFib cardioversion

- LAA flow velocities tend to diminish and Spontaneous Echo Contrast can develop immediately after cardioversion
- Atrial stunning has been reported with all methods of conversion of AFib to sinus rhythm:
  - Transthoracic electrical cardioversion
  - Low-energy internal electrical cardioversion
  - Pharmacological cardioversion
  - Spontaneous conversion
- Determinants of atrial stunning
  - Duration of preceding AFib
  - Atrial size
  - Structural heart disease
- Cellular mechanisms of atrial stunning
  - Tachycardia-induced atrial cardiomyopathy
  - Atrial cytosolic calcium alterations
  - Atrial fibrosis
- Full recovery of atrial stunning is achieved within 24 h in patients with brief AF (<2 weeks), within 1 week in patients with AF of moderate duration (2–6 weeks), and within 1 month in patients with prolonged AF (>6 weeks) Pre-cardioversion

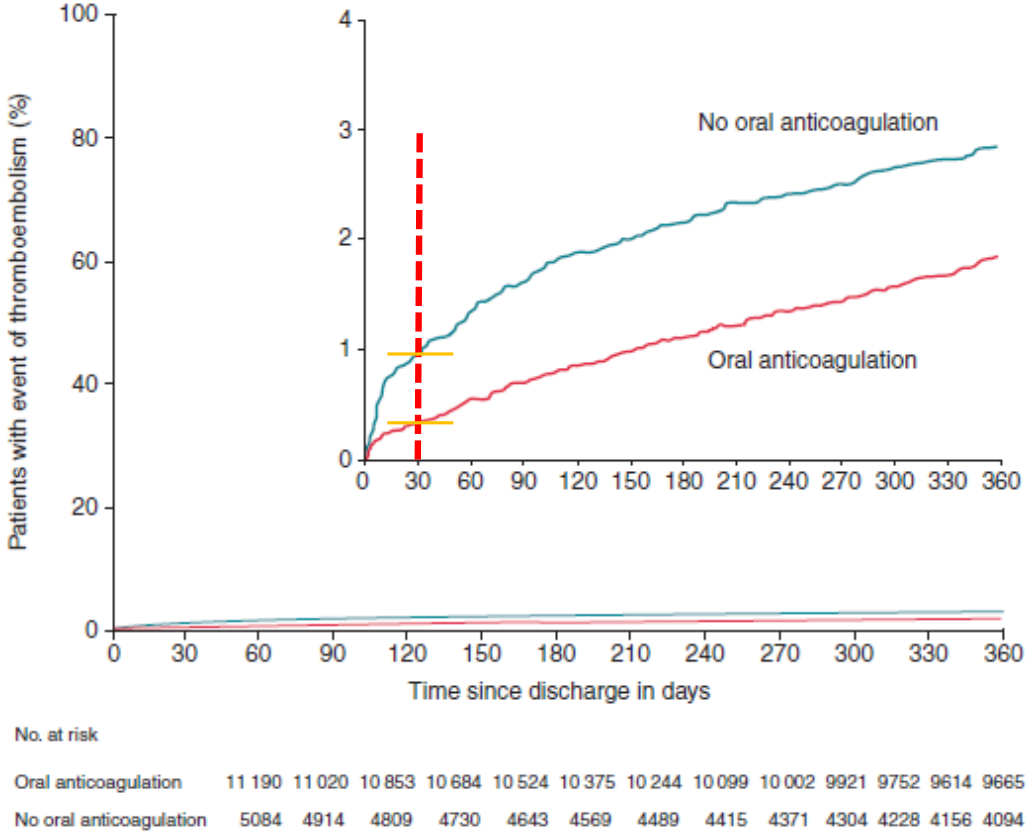




Thromboembolic risk in 16 274 atrial fibrillation patients undergoing direct current cardioversion with and without oral anticoagulant therapy

Morten Lock Hansen[1]*, Rikke Malene H.G. Jepsen[2], Jonas Bjerring Olesen[1], Martin Huth Ruwald[1], Deniz Karasoy[1], Gunnar Hilmar Gislason[1], Jim Hansen[1], Lars Køber[3], Steen Husted[4], and Christian Torp-Pedersen[5]

- 16 274 patients from the Danish National Patient Registry
- External DC cardioversion for AF from January 2000 to December 2008



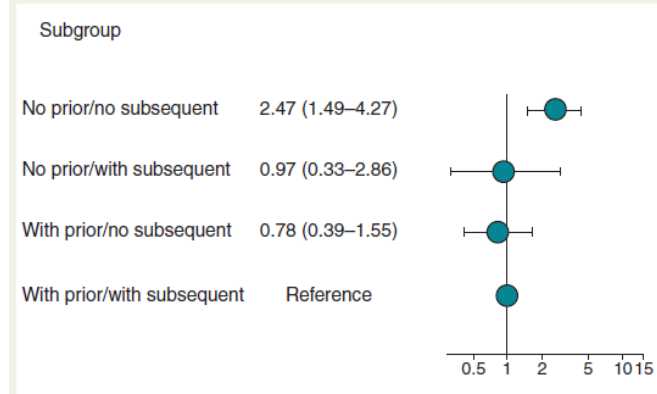


Figure 2 Risks of thromboembolism at 0–30 days of follow-up after discharge for DC cardioversion of atrial fibrillation analysed by prior and subsequent oral anticoagulant therapy.

Hansen ML, et al. Europace 2015;17:18–23

Thromboembolic risk in 16 274 atrial fibrillation patients undergoing direct current cardioversion with and without oral anticoagulant therapy

Morten Lock Hansen[1]*, Rikke Malene H.G. Jepsen[2], Jonas Bjerring Olesen[1], Martin Huth Ruwald[1], Deniz Karasoy[1], Gunnar Hilmar Gislason[1], Jim Hansen[1], Lars Køber[3], Steen Husted[4], and Christian Torp-Pedersen[5]

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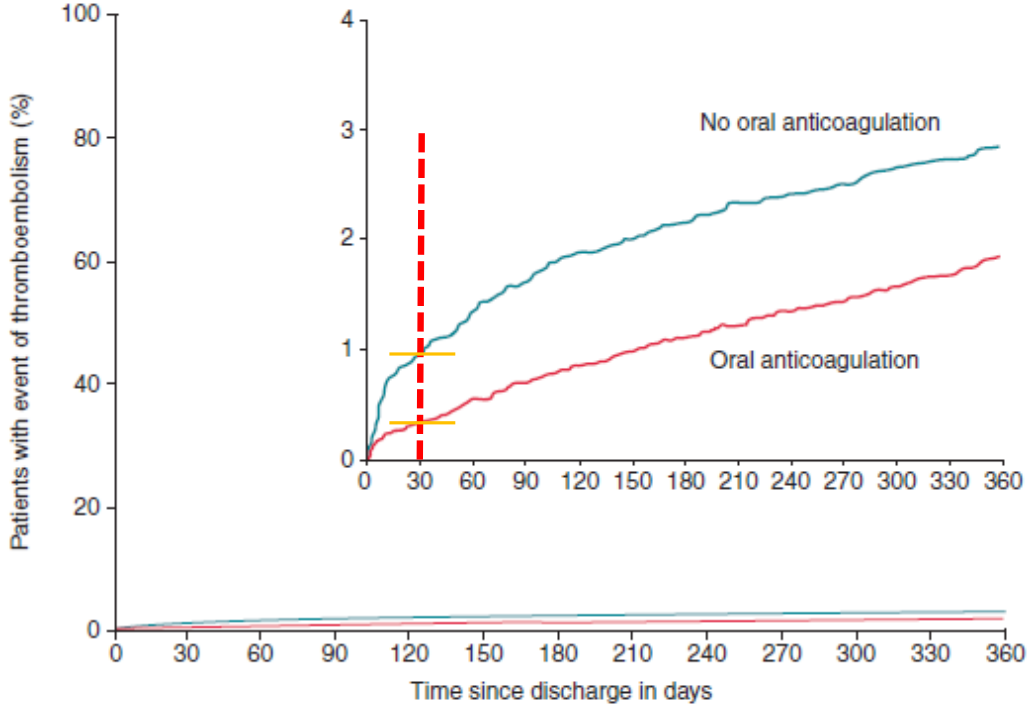

No. at risk

Oral anticoagulation	11 190	11 020	10 853	10 684	10 524	10 375	10 244	10 099	10 002	9921	9752	9614	9665
No oral anticoagulation	5084	4914	4809	4730	4643	4569	4489	4415	4371	4304	4228	4156	4094

Risk factors for thromboembolism after discharge for DC - cardioversion of atrial fibrillation

	0–30 days HR	0–360 days HR
B: CHA_2DS_2-VASc score as predictor of thromboembolism 0–30 and 0–360 days after discharge for DC cardioversion of atrial fibrillation		
CHA_2DS_2-VASc score 1[a]	1.83 (0.33–10.10)	1.57 (0.79–3.09)
CHA_2DS_2-VASc score ≥2[a]	6.86 (1.55–30.37)	4.61 (2.54–8.37)

[a]Reference: CHA_2DS_2-VASc score 0.

Hansen ML, et al. Europace 2015;17:18–23

Stroke prevention in patients undergoing cardioversion

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Recommendations	Class	Level
Stroke prevention in patients designated for cardioversion of AF		
Anticoagulation with heparin or a NOAC should be initiated as soon as possible before every cardioversion of AF or atrial flutter.	IIa	B
For cardioversion of AF/atrial flutter, effective anticoagulation is recommended for a minimum of 3 weeks before cardioversion.	I	B
Transoesophageal echocardiography (TOE) is recommended to exclude cardiac thrombus as an alternative to preprocedural anticoagulation when early cardioversion is planned.	I	B
Early cardioversion can be performed without TOE in patients with a definite duration of AF <48 hours.	IIa	B
In patients at risk for stroke, anticoagulant therapy should be continued long-term after cardioversion according to the long-term anticoagulation recommendations, irrespective of the method of cardioversion or the apparent maintenance of sinus rhythm. In patients without stroke risk factors, anticoagulation is recommended for 4 weeks after cardioversion.	I	B
In patients where thrombus is identified on TOE, effective anticoagulation is recommended for at least 3 weeks.	I	C
A repeat TOE to ensure thrombus resolution should be considered before cardioversion.	IIa	C

2016 ESC Guidelines for the management of AF. European Heart Journal 2016;37:2893-2962

Clinical outcome event rates within 30 days postcardioversion in RE-LY[1], ARISTOTLE[2], and ROCKET-AF[3], studies

	RE-LY dabigatran 150 mg	RE-LY dabigatran 110 mg	RE-LY warfarin	ARISTOTLE apixaban	ARISTOTLE warfarin	ROCKET-AF* rivaroxaban	ROCKET-AF* warfarin
Stroke† or systemic embolism	0.30	0.77	0.60	0	0	1.88	1.86
Major bleeding ‡	0.60	1.70	0.60	0.30	0.20	18.75	13.04
Death§	n/a	n/a	n/a	0.6	0.5	1.88	3.73

n/a, Not applicable
** ROCKET-AF combined event rates for cardioversion and ablation procedure.*
† Both ischemic and hemorrhagic strokes.
‡ ROCKET-AF combined major and nonmajor clinically relevant bleeding.
§ RE-LY did not report death rates within 30 days of cardioversion.

[1] Nagarakanti R, et al. Circulation 2011;123:131-6.
[2] Flaker G, et al. J Am Coll Cardiol 2014;63:1082-7.
[3] Piccini JP, et al. J Am Coll Cardiol 2013;61:1998-2006.

Rivaroxaban vs. vitamin K antagonists for cardioversion in atrial fibrillation

X-VeRT Trial

Heart Rhythm Center
www.eponline.gr

Riccardo Cappato[1†], Michael D. Ezekowitz[2†*], Allan L. Klein[3], A. John Camm[4], Chang-Sheng Ma[5], Jean-Yves Le Heuzey[6], Mario Talajic[7], Maurício Scanavacca[8], Panos E. Vardas[9], Paulus Kirchhof[10,11,12], Melanie Hemmrich[13], Vivian Lanius[14], Isabelle Ling Meng[13], Peter Wildgoose[15], Martin van Eickels[13], and Stefan H. Hohnloser[16], on behalf of the X-VeRT Investigators

Rivaroxaban in Cardioversion

- 1504 patients randomized to rivaroxaban (20 mg/day 15 mg if creatinine clearance was 30-49 mL/min Or dose-adjusted vitamin K antagonists (VKAs) in a 2:1 ratio (*parenteral anticoagulant was optional in VKAs group)
- The primary endpoint → Stroke, TIA, Peripheral Embolism, Myocardial Infarction, and Cardiovascular Death.

43% receiving ACT before the need of CV

Rivaroxaban → (978 patients) 5 (2 Strokes/SE) (0.51%) - Major bleeding in 6 pts (0.6%)

VKAs → (492 patients) 5 (3 Strokes/SE) (1.02%) - Major bleeding in 4 pts (0.8%)

- Rivaroxaban was associated with a significantly shorter time to cardioversion compared with VKAs (P<0.001).

Cappato R et al. European Heart Journal 2014;35:3346-3355

Edoxaban versus enoxaparin–warfarin in patients undergoing cardioversion of atrial fibrillation (ENSURE-AF): a randomised, open-label, phase 3b trial

ENSURE-AF Trial

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Andreas Goette*, Jose L Merino, Michael D Ezekowitz, Dmitry Zamoryakhin, Michael Melino, James Jin, Michele F Mercuri, Michael A Grosso, Victor Fernandez, Naab Al-Saady, Natalya Pelekh, Bela Merkely, Sergey Zenin, Mykola Kushnir, Jindrich Spinar, Valeriy Batushkin, Joris R de Groot, Gregory Y H Lip*, on behalf of the ENSURE-AF investigators†

Edoxaban in Cardioversion

- **Multicentre, prospective, randomised, open-label, blinded-endpoint evaluation trial**
- **2199 patients randomized 1:1 to →**
- **Edoxaban 60 mg/day* OR enoxaparin–warfarin in patients undergoing electrical cardioversion of non-valvular AF**

* *The dose of edoxaban was reduced to 30 mg per day if one or m*
[≤60 kg], or concomitant use of P-glycoprotein inhibitors)

73% receiving ACT before the need of CV

	Total by treatment			Transoesophageal echocardiography stratum			Non-transoesophageal echocardiography stratum		
	Edoxaban (n=1095)	Warfarin plus enoxaparin (n=1104)	OR (95% CI)	Edoxaban (n=589)	Warfarin plus enoxaparin (n=594)	OR (95% CI)	Edoxaban (n=506)	Warfarin plus enoxaparin (n=510)	OR (95% CI)
Primary endpoint*	5 (<1%)	11 (1%)	0·46 (0·12–1·43)	2 (<1%)	5 (1%)	0·40 (0·04–2·47)	3 (1%)	6 (1%)	0·50 (0·08–2·36)
Stroke	2 (<1%)	3 (<1%)	0·67 (0·06–5·88)	0	2 (<1%)	..	2 (<1%)	1 (<1%)	..
Intracranial haemorrhage	0	0	..	0	0	..	0	0	..
Systemic embolic event	1 (<1%)	1 (<1%)	..	1 (<1%)	1 (<1%)	..	0	0	..
Myocardial infarction	2 (<1%)	3 (<1%)	0·67 (0·06–5·88)	0	2 (<1%)	..	2 (<1%)	1 (<1%)	..
Cardiovascular death	1 (<1%)	5 (<1%)	0·20 (0–1·80)	1 (<1%)	0	..	0	5 (1%)	..

OR=odds ratio. *Primary endpoint was composite of stroke, systemic embolic event, myocardial infarction, and cardiovascular mortality.

Table 2: **Primary efficacy results in the intention-to-treat population for the overall study period**

Goette et al. Lancet 2016;388:1995-2003

Anticoagulation Naïve Patients

Initiation of warfarin in patients with atrial fibrillation: early effects on ischaemic strokes

Laurent Azoulay[1,2], Sophie Dell'Aniello[1], Teresa A. Simon[3], Christel Renoux[1,4], and Samy Suissa[1,5]*

Table 2 Timing of warfarin initiation and the risk of ischaemic stroke

Current use of warfarin monotherapy	Cases (n = 5519)	Controls[a] (n = 55 022)	Crude RR	Adjusted RR (95% CI)[b]
No use of any antithrombotic therapy for at least 1 year, n (%)	1513 (27.4)	15 499 (28.2)	1.00	1.00 (reference)
Time since initiation of warfarin, n (%)				
≤30 days	117 (2.1)	732 (1.3)	1.74	1.71 (1.39–2.12)
31–90 days	27 (0.5)	544 (1.0)	0.52	0.50 (0.34–0.75)
≥90 days	610 (11.1)	10 145 (18.4)	0.57	0.55 (0.49–0.61)

RR, rate ratio; CI, confidence interval.

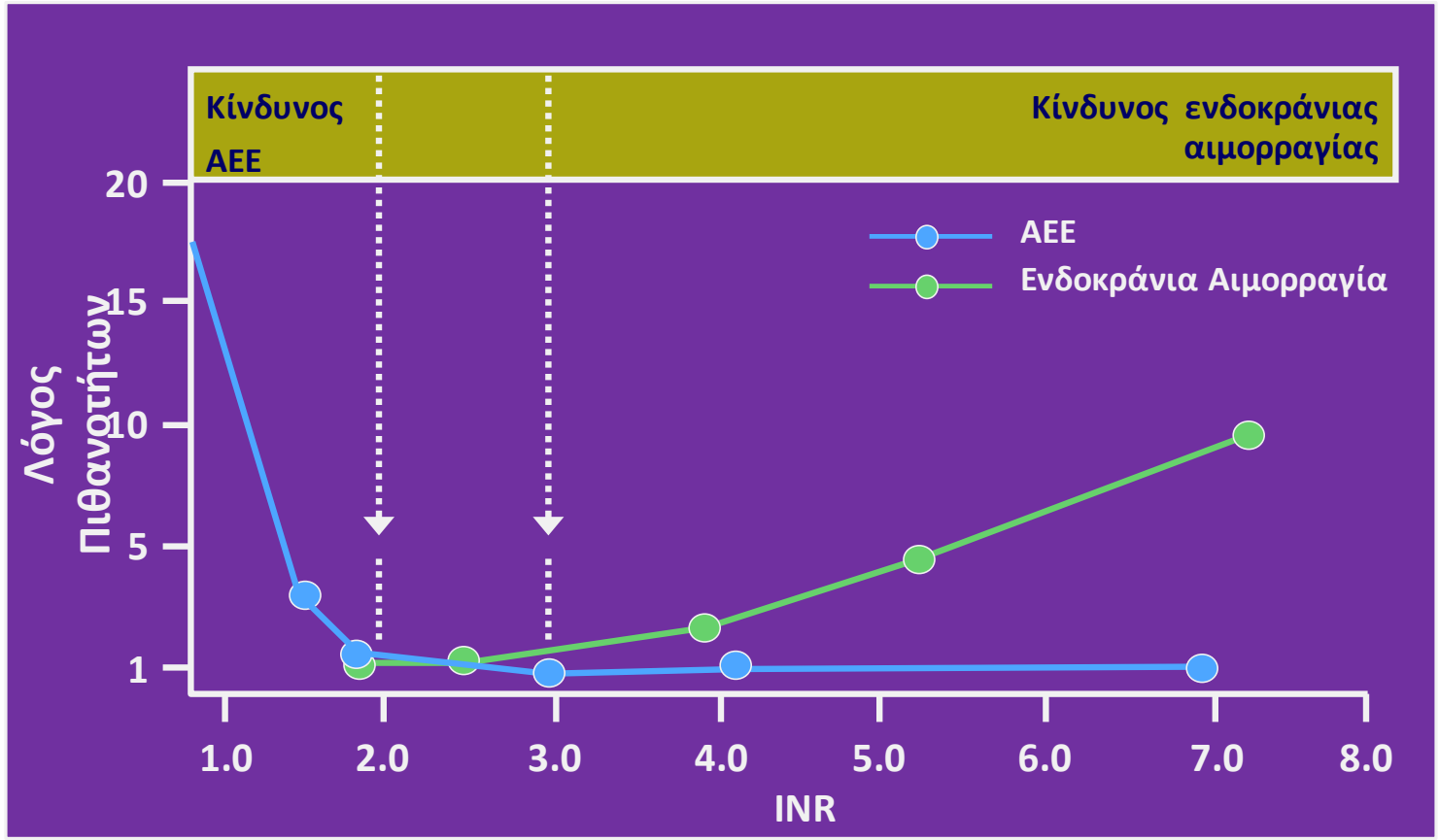
Current users of warfarin monotherapy who had used aspirin and/or clopidogrel in the year prior to index date, current users of aspirin or clopidogrel monotherapy, current users of antithrombotic combinations (including warfarin), and past users of any of these drugs in the year before index date are not displayed in the table, but were considered in the regression model for proper estimation of treatment effects (representing 3252 cases and 28 102 controls).

[a]Cases and controls were matched on age, sex, and date of atrial fibrillation diagnosis, and time since atrial fibrillation diagnosis.

[b]Adjusted for excessive alcohol use, smoking status, obesity, $CHADS_2$ score, peripheral artery disease, myocardial infarction, previous cancer, prior bleeds, venous thromboembolism, valvular disease, and use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, antidepressants, antipsychotics, non-steroidal anti-inflammatory drugs, and statins.

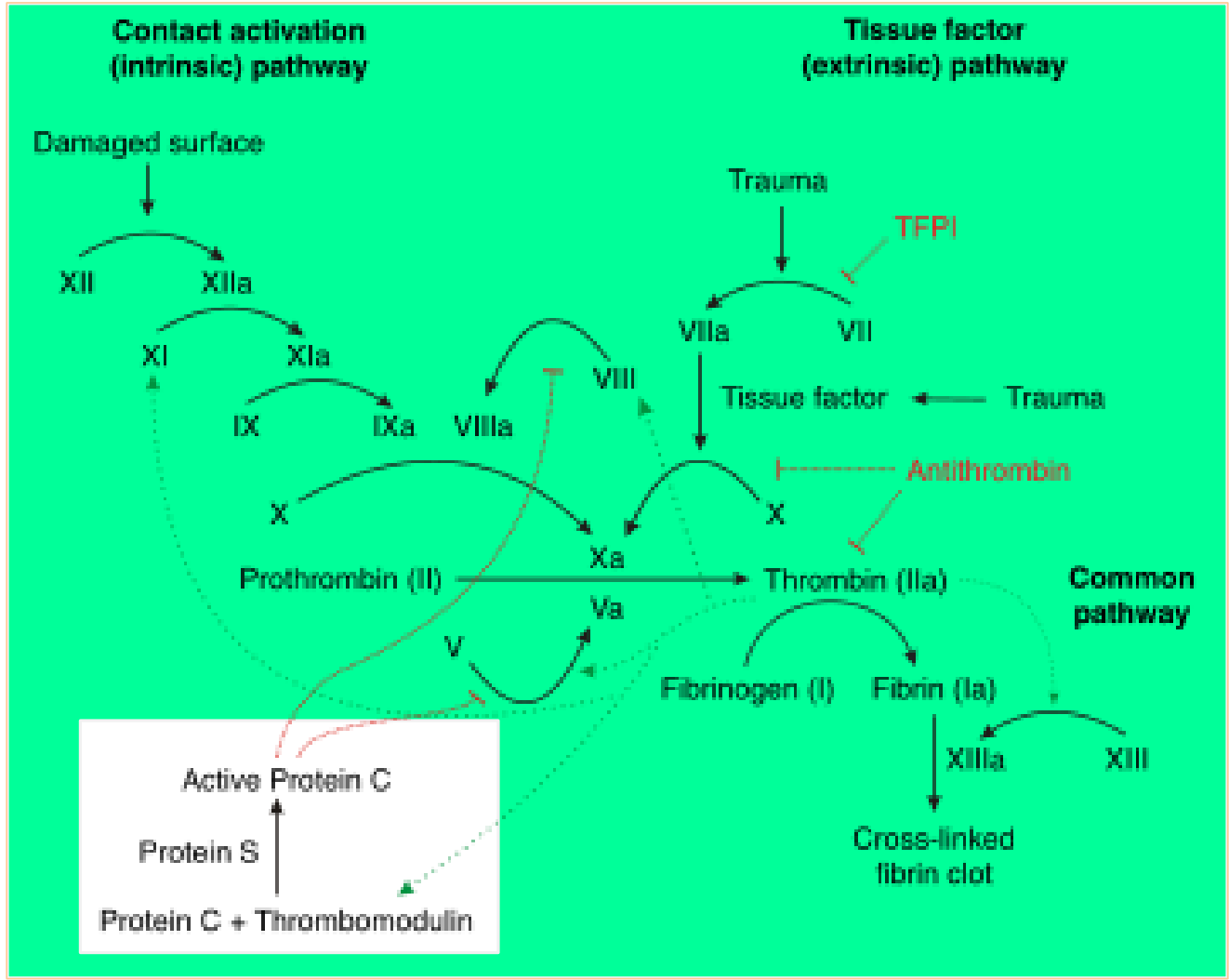
Azoulay et al. European Heart Journal 2014;35:1881-87

Οι περιορισμοί στη θεραπεία με ανταγωνιστές βιταμίνης Κ



1. Fuster V et al. *J Am Coll Cardiol* 2001;38:1231–1265
2. Hylek E and Singer D *Ann Intern Med* 1994;120:897–902
3. Hylek E et al. *N Eng J Med* 1996;335:540–546

Procoagulant Effect of Early Doses of Warfarin ?



EMANATE Study

Key Eligibility Criteria

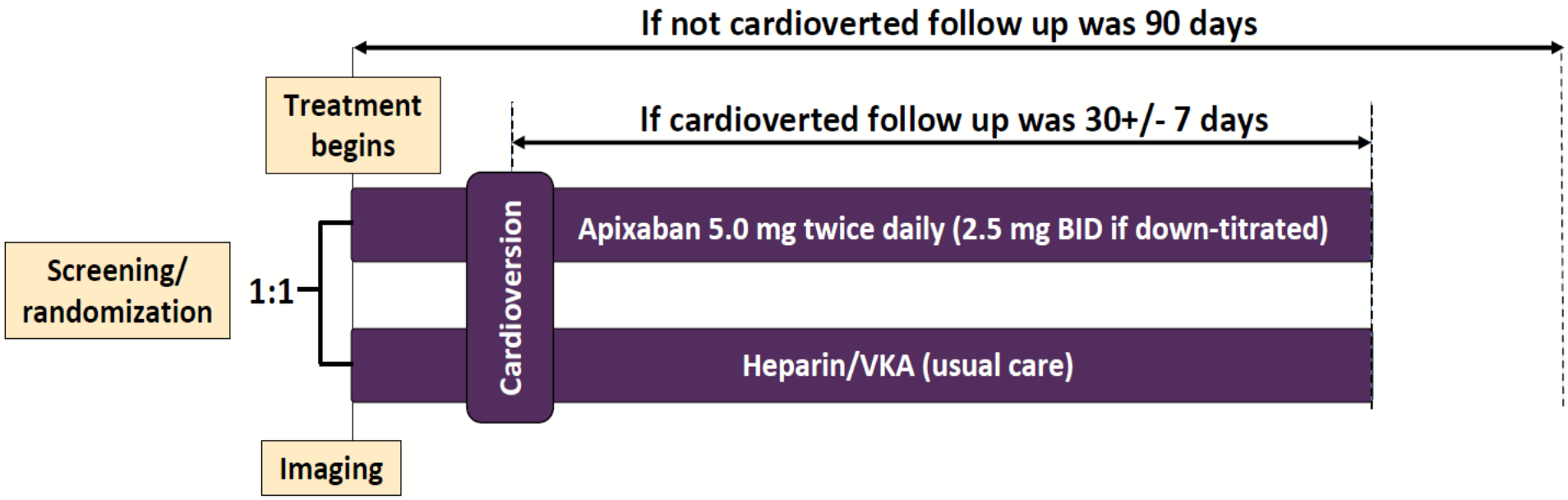
Key Inclusion Criteria	Key Exclusion Criteria
▪ Anticoagulation-naïve patients with AF (<48 hours of parenteral and/or oral anticoagulation) indicated for cardioversion.	▪ Contraindications to apixaban or heparin/VKA ▪ Mitral stenosis or previous valve surgery ▪ Other conditions requiring anticoagulation ▪ Dual antiplatelet therapy

62% never in ACT
38% receiving ACT in less than 48h

Ezekowitz et al. European Heart Journal 2018;00:1–13

EMANATE Study

Study Design



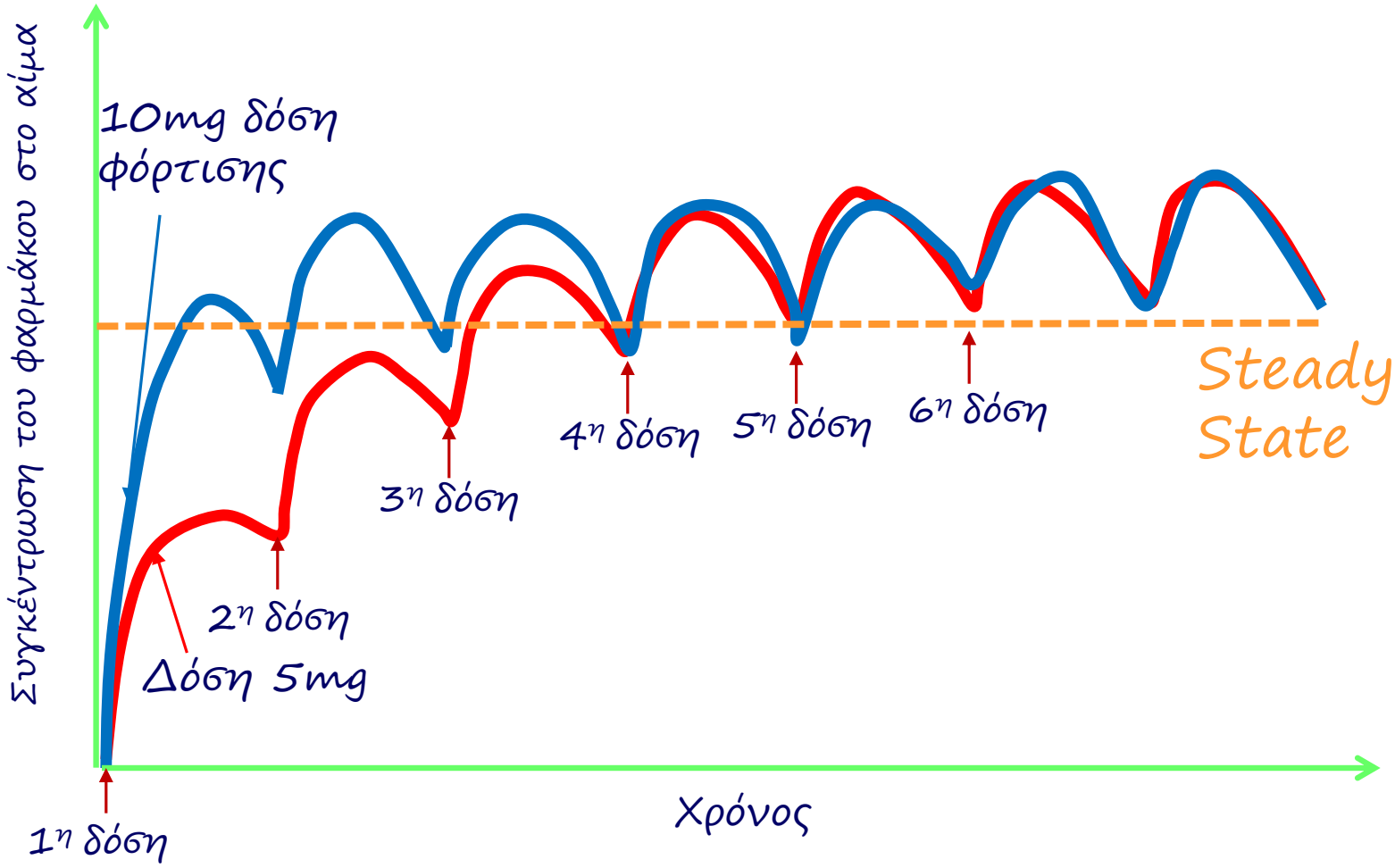
Ezekowitz et al. European Heart Journal 2018;00:1–13

Apixaban Loading Dose Option

- In patients randomized to apixaban, cardioversion could be performed 2 hours after a loading dose of 10 mg (reduced to 5 mg if 2 of the following present: age ≥ 80, weight ≤ 60 kg, serum creatinine ≥ 1.5 mg/dl [133 micromol/L).

Ezekowitz et al. European Heart Journal 2018;00:1–13

Διακύμανση της συγκέντρωσης της απιξαμπάνης στο αίμα



EMANATE Study
Patient disposition (ITT population)

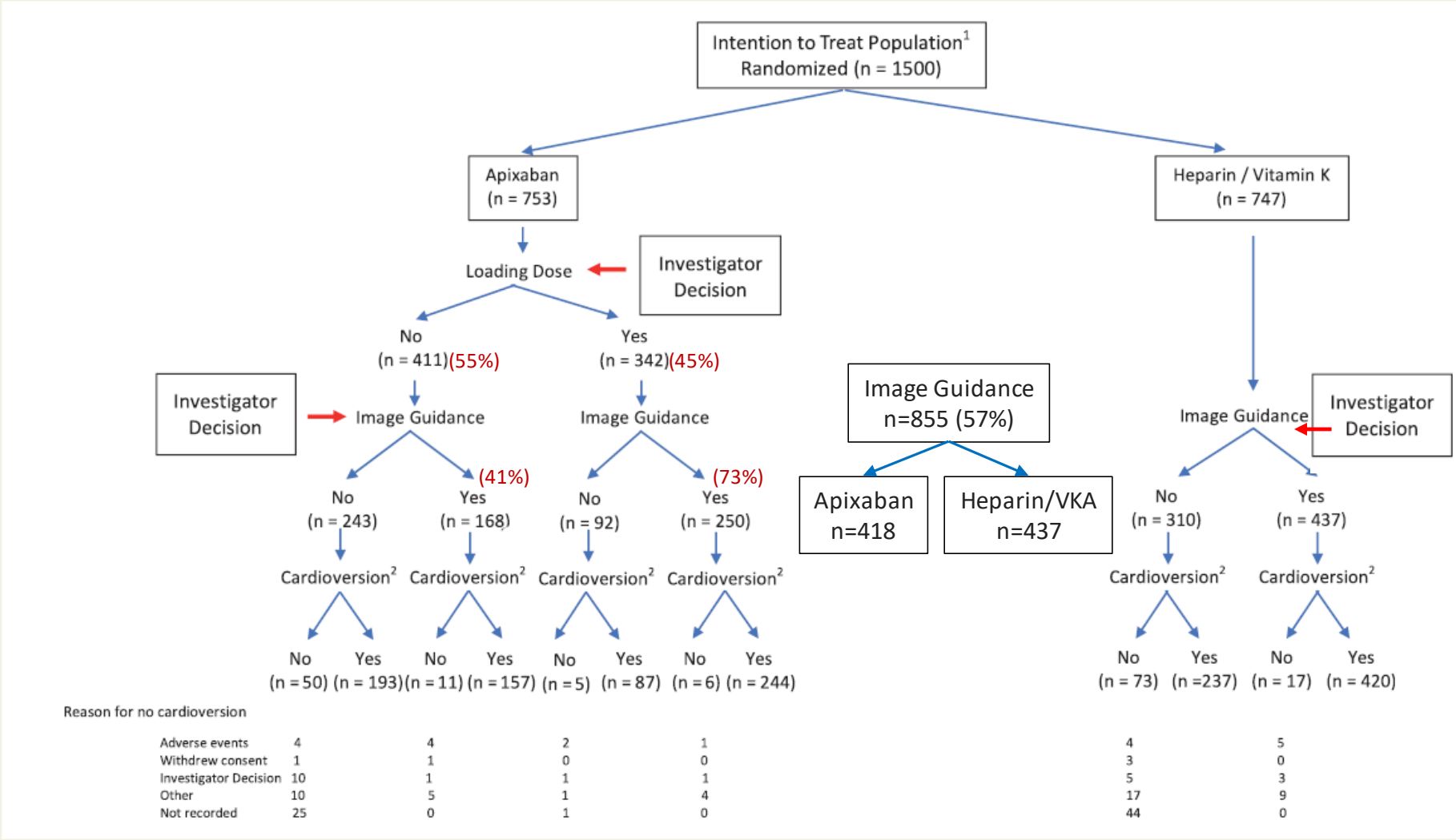


Figure 2 Patient disposition (ITT population). [1]≤48 h of anticoagulation for current episode of atrial fibrillation. [2]Includes active and first spontaneous cardioversions.

Ezekowitz et al. European Heart Journal 2018;00:1–13

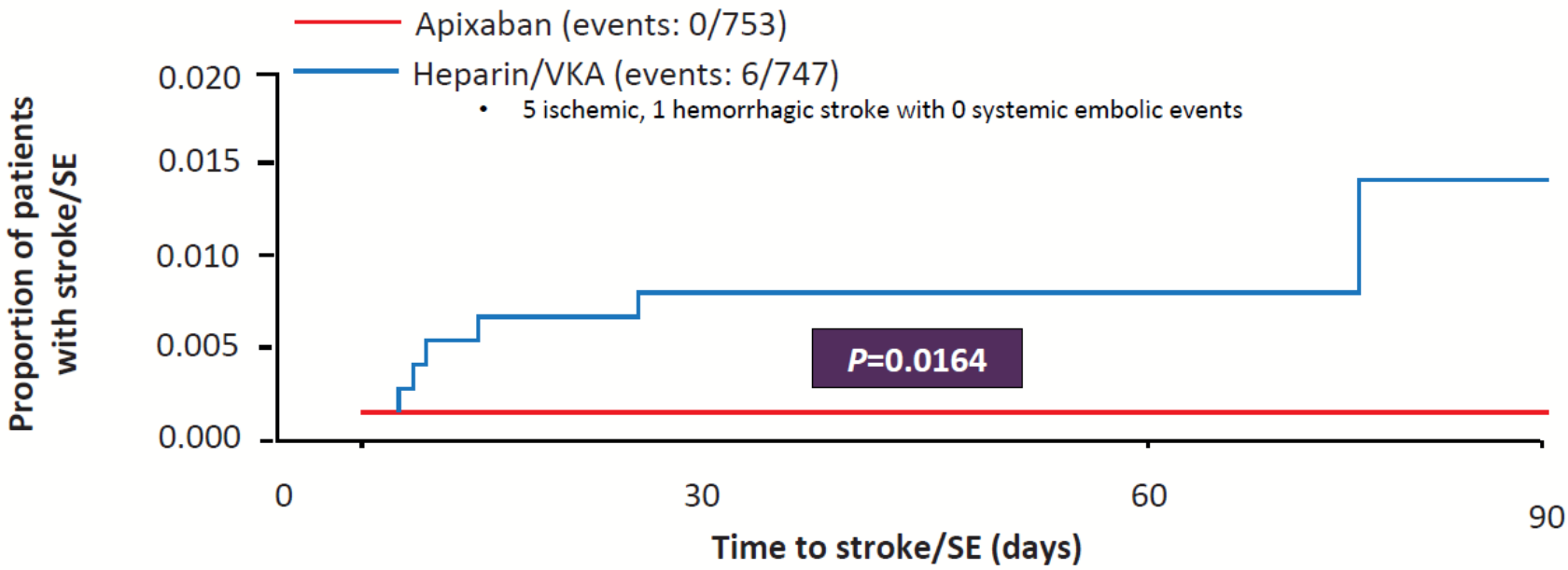
Apixaban compared to heparin/vitamin K antagonist in patients with atrial fibrillation scheduled for cardioversion: the EMANATE trial

Michael D. Ezekowitz[1,2,3]*, Charles V. Pollack Jr[4], Jonathan L. Halperin[5], Richard D. England[6], Sandra VanPelt Nguyen[6], Judith Spahr[4], Maria Sudworth[7], Nilo B. Cater[8], Andrei Breazna[8], Jonas Oldgren[9], and Paulus Kirchhof[10]

Table 2 Time from first dose to active cardioversion (days)

	Apixaban						Heparin/vitamin K antagonist		
	Loaded dose			Non-loaded dose					
	With image guidance	Without image guidance	Overall	With image guidance	Without image guidance	Overall	With image guidance	Without image guidance	Overall
n	238	34	272	155	92	247	407	111	518
Mean	3.3	4.1	3.4	21.7	32.5	25.7	11.5	40.7	17.8
(95% CI)	(2.2–4.4)	(0.8–7.4)	(2.3–4.4)	(18.3–25.0)	(29.4–35.5)	(23.2–28.2)	(9.6–13.5)	(35.6–45.7)	(15.7–19.9)
Median	1	1	1	15	30	27	2	43	2
Standard deviation	8.76	9.52	8.84	21.15	14.61	19.65	19.94	26.78	24.66
Difference (95% CI) *P*-value[a]	0.8 (2.4–3.9) $P = 0.6214$			10.8 (5.9–15.7) $P < 0.0001$			29.1 (24.6–33.7) $P < 0.0001$		
Difference (95% CI) *P*-value[b]	-22.3 (-24.9 to 19.7) $P < 0.0001$								

EMANATE Study
Stroke/Systemic Embolic Outcomes



Number at risk

Apixaban	752	6145	199	55
Heparin/VKA	747	65	231	88

One patient's adjudicated stroke date was one day prior to randomization; thus at Day 0, only 1499 were at risk for stroke. No patients had SE.
ITT population. SE = systemic embolism

Ezekowitz et al. European Heart Journal 2018;00:1–13

EMANATE Study

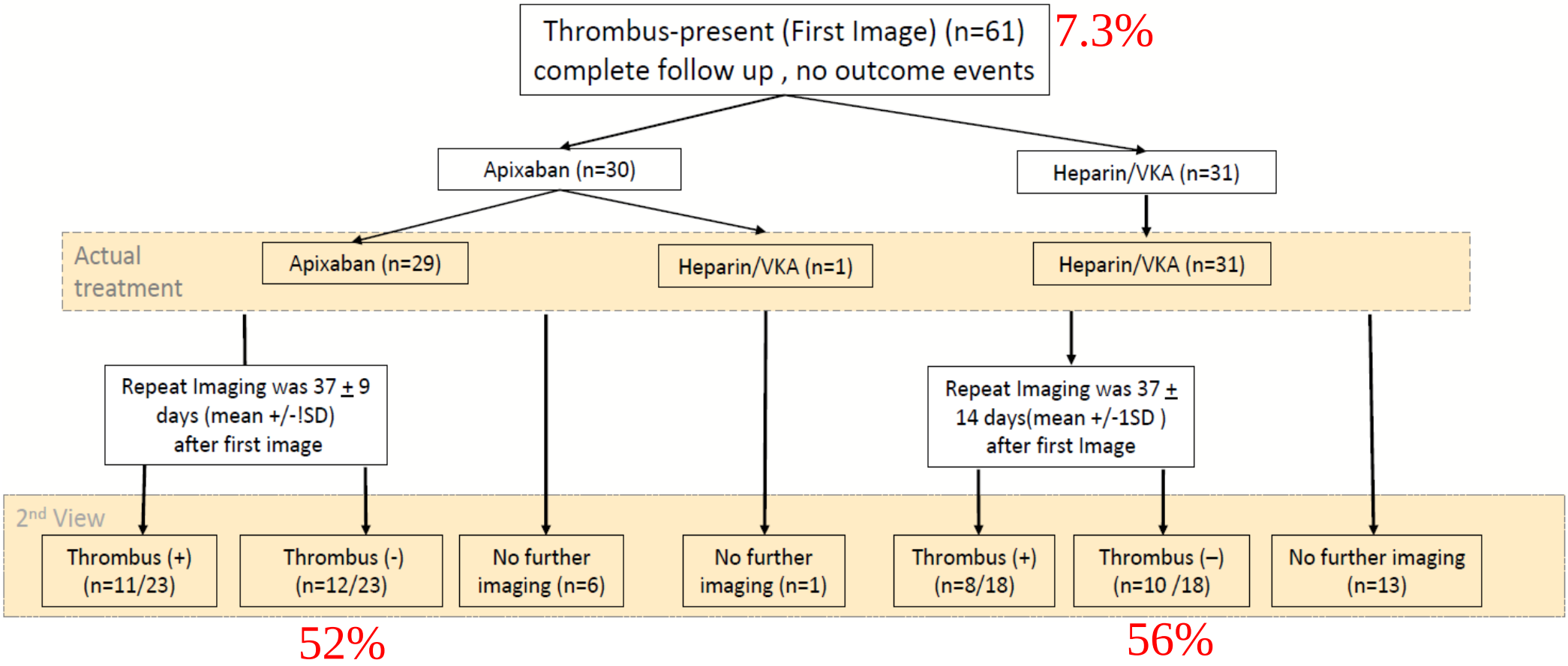
Safety Outcomes (Safety Population*, N=1456)

	Apixaban Total (n=735)	Apixaban Loading Dose Subset (n=342)	Heparin/VKA Total (n=721)
Major bleeds	3	(1)	6
Clinically relevant non-major bleeds	11	(4)	13

*Randomized and received ≥ 1 dose of study medication (by treatment received).

Ezekowitz et al. European Heart Journal 2018;00:1–13

Image-Guided Strategy (n=840)



Ezekowitz et al. European Heart Journal 2018;00:1–13

LAA Thrombus Resolution with Anticoagulant Therapy

Study	Anticoagulant Therapy	Type of AF	Thrombus resolution
Bernhardt et al. [1]	Unfractionated heparin - Phenprocoumon	Permanent 100%	16% at 1 month, 42% at 3 months, 49% at 6 months, 56% at 12 months
X-TRA [2]	Rivaroxaban	76.6% Persistent / Long-standing persistent/ Permanent	41.5% 6-8 weeks
EMENATE [3]	Apixaban	New onset 67.1%	52% at mean 37 days
EMENATE [3]	Heparin / VKA	New onset 67.5%	56% at mean 37 days
RE-LATED AF [4]	Dabigatran (150 mg bid) vs Phenprocoumon (INR 2-3)	Not known	Ongoing trial

[1] Bernhardt et al. Am J Cardiol 2004;94:801-804
[2] Lip et al. Am Heart J 2016;178:126–134.
[3] Ezekowitz et al. European Heart Journal 2018;00:1-13
[4] Ferner et al. Clin Res Cardiol 2016;105:29-36

1998: The Beginning of AF Ablation History

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SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS

MICHEL HAÏSSAGUERRE, M.D., PIERRE JAÏS, M.D., DIPEN C. SHAH, M.D., ATSUSHI TAKAHASHI, M.D., MÉLÈZE HOCINI, M.D., GILLES QUINIOU, M.D., STÉPHANE GARRIGUE, M.D., ALAIN LE MOUROUX, M.D., PHILIPPE LE MÉTAYER, M.D., AND JACQUES CLÉMENTY, M.D.

ABSTRACT

Background Atrial fibrillation, the most common sustained cardiac arrhythmia and a major cause of stroke, results from simultaneous reentrant wavelets. Its spontaneous initiation has not been studied.

Methods We studied 45 patients with frequent episodes of atrial fibrillation (mean [±SD] duration, 344±326 minutes per 24 hours) refractory to drug therapy. The spontaneous initiation of atrial fibrillation was mapped with the use of multielectrode catheters designed to record the earliest electrical activity preceding the onset of atrial fibrillation and associated atrial ectopic beats. The accuracy of the mapping was confirmed by the abrupt disappearance of triggering atrial ectopic beats after ablation with local radio-frequency energy.

Results A single point of origin of atrial ectopic beats was identified in 29 patients, two points of origin were identified in 9 patients, and three or four points of origin were identified in 7 patients, for a total of 69 ectopic foci. Three foci were in the right atrium, 1 in the posterior left atrium, and 65 (94 percent) in the pulmonary veins (31 in the left superior, 17 in the right superior, 11 in the left inferior, and 6 in the right inferior pulmonary vein). The earliest activation was found to have occurred 2 to 4 cm inside the veins, marked by a local depolarization preceding the atrial ectopic beats on the surface electrocardiogram by 106±24 msec. Atrial fibrillation was initiated by a sudden burst of rapid depolarizations (340 per minute). A local depolarization could also be recognized during sinus rhythm and abolished by radio-frequency ablation. During a follow-up period of 8±6 months after ablation, 28 patients (62 percent) had no recurrence of atrial fibrillation.

Conclusions The pulmonary veins are an important source of ectopic beats, initiating frequent paroxysms of atrial fibrillation. These foci respond to treatment with radio-frequency ablation. (N Engl J Med 1998;339:659-66.)

ATRIAL fibrillation is the most common of all sustained cardiac arrhythmias, with the prevalence increasing with age to up to 5 percent in persons more than 65 years of age, and it is a major cause of stroke.[1-3] Experimental studies and human surgical mapping studies have shown that atrial fibrillation is perpetuated by reentrant wavelets propagating in an abnormal atrial-tissue substrate.[4-8] Complex approaches have been developed to interrupt wavelets, including extensive surgical or, recently, catheter-mediated atriotomy.[9-21] There are, however, no data about the spontaneous initiation of atrial fibrillation. The triggers of atrial fibrillation may be focal targets for ablative therapy. We investigated the mode of initiation of spontaneous paroxysms of human atrial fibrillation by atrial ectopic beats, the characteristics of these triggering beats, and the effects of local ablation with radio-frequency energy.

METHODS

Characteristics of the Patients

The study population consisted of 45 patients enrolled consecutively (Table 1) who met the following criteria: the patient had to have atrial fibrillation resistant to more than two drugs, there had to be at least one episode of atrial fibrillation every two days, the patient had to be receiving anticoagulant treatment, the patient had to have frequent isolated atrial ectopic beats (more than 700 per 24 hours), and the patient had to provide informed consent. The protocol was approved by the hospital's safety committee. Antiarrhythmic drugs were discontinued two to five days before hospitalization; amiodarone was being taken by nine patients.

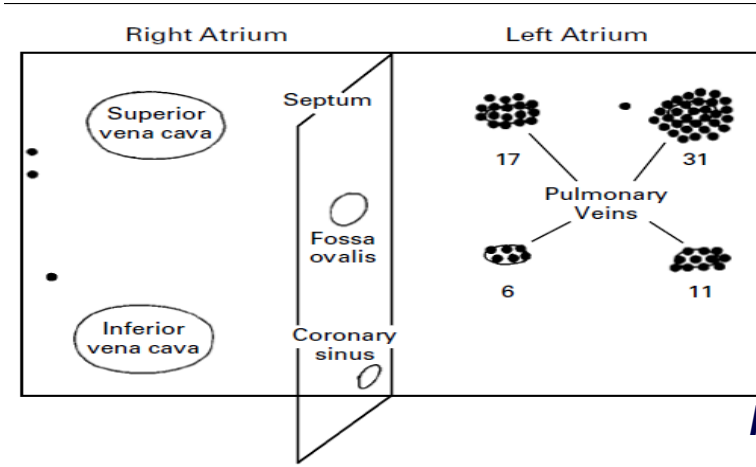
The patients were monitored by telemetry throughout their hospital stays. Before ablation, atrial fibrillation occurred daily in 39 patients and every two days in the other 6 patients, with a mean (±SD) duration of 344±326 minutes per 24 hours. Twelve-lead electrocardiographic recordings were obtained to document the morphologic features of the ectopic beats. In 37 patients, at least one instance of initiation of sustained atrial fibrillation lasting more than one minute was documented: the ectopic beat initiating atrial fibrillation had a short coupling interval (a P-on-T pattern) and morphologic features similar to those of isolated ectopic beats. Their identical origin was confirmed later by intracardiac mapping data.

Electrophysiologic Study

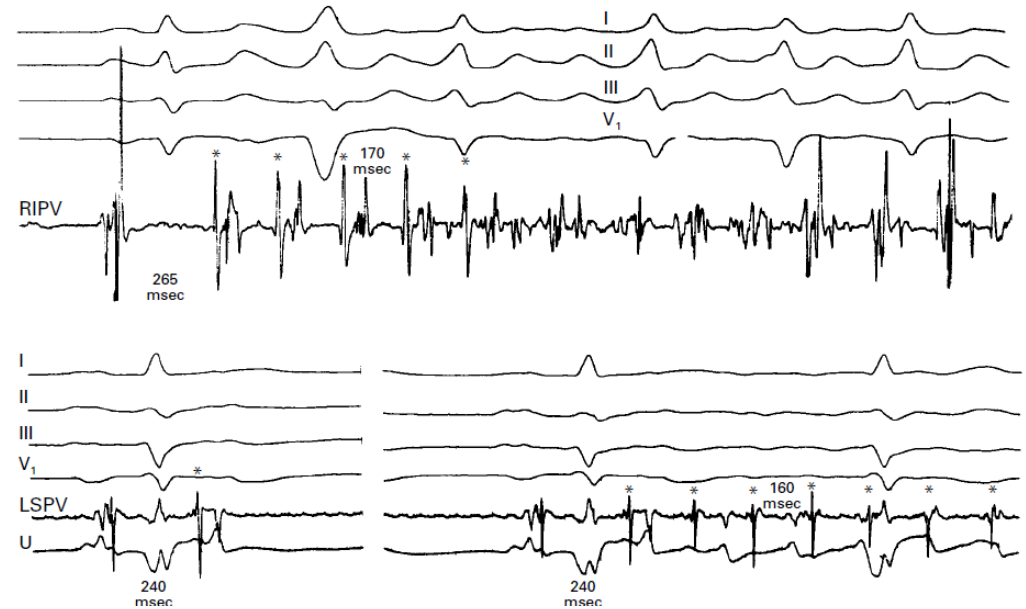
Oral anticoagulants were replaced on admission by either subcutaneous or intravenous heparin to maintain a partial-thromboplastin time of 60 to 90 seconds (control, 30 seconds). Heparin was stopped four to six hours before ablation, since transseptal catheterization was sometimes required.

Three multielectrode catheters were introduced percutaneously through the femoral veins: one quadripolar roving ablation catheter with a thermocouple and a 4-mm tip, one catheter in the right atrial appendage (for right atrial and right-pulmonary-vein foci) or coronary sinus (for left-pulmonary-vein foci) to provide stable reference electrograms during mapping, and one catheter for stimulation.[22,23] In three patients, two roving catheters were

From the Hôpital Cardiologique du Haut-Lévêque, Ave. de Magellan, 33604 Bordeaux-Pessac, France, where reprint requests should be addressed to Dr. Haïssaguerre.



Michel Haïssaguerre



Haissaguerre M., N Engl J Med 1998;339:659

Complications of Catheter Ablation of Atrial Fibrillation

A Systematic Review

Aakriti Gupta; Tharani Perera; Anand Ganesan, MBBS, PhD; Thomas Sullivan, BMa&CompS; Dennis H. Lau, MBBS, PhD; Kurt C. Roberts-Thomson, MBBS, PhD; Anthony G. Brooks, PhD; Prashanthan Sanders, MBBS, PhD

Background—Atrial fibrillation ablation is an established therapy; however, limited data are available on associated complications. This systematic review determines the incidence and potential predictors of acute complications.

Methods and Results—Electronic searches were conducted in MEDLINE and EMBASE for English scientific literature up to the 18th June 2012. A total of 2065 references were retrieved and evaluated for relevance. Reference lists of retrieved studies and review articles were examined to ensure all relevant studies were included. Data were extracted from 192 studies, total of 83 236 patients. The incidence of periprocedural complications for catheter ablation of atrial fibrillation was 2.9% (95% confidence interval, 2.6–3.2). There was a significant decrease in the acute complication rate in 2007 to 2012 compared with 2000 to 2006 (2.6% versus 4.0%; P=0.003). The complication rates reported were higher in prospective studies compared with those that retrospectively described complications (3.5% versus 2.7%; P=0.03). There were no significant associations among procedure duration, ablation time or ablation strategy, and acute complication rate.

Conclusions—Catheter ablation of atrial fibrillation has a low incidence of periprocedural complications. The acute complication rate has decreased significantly in recent years. This may reflect improved catheter technology and experience. The use of different strategies across centers worldwide seems to be safe with no established relationship between procedural variables and complication rate. (*Circ Arrhythm Electrophysiol.* 2013;6:1082-1088.)

Table 2. Major Complications

	No. of Studies	% Pooled Complication Rate (95% CI)	I^2 Statistic
Acute complication rate	183	2.9 (2.60–3.22)	83.8
Type of complication			
Death	58	0.06 (0.03–0.09)	0.0
Atrioesophageal fistula	67	0.08 (0.05–0.11)	0.0
Pulmonary vein stenosis*	118	0.5 (0.34–0.60)	79.6
Vascular complications†	117	1.4 (1.02–1.79)	94.1
Arteriovenous fistula	45	0.40 (0.28–0.55)	45.5
Femoral pseudoaneurysm	49	0.5 (0.34–0.60)	41.2
Stroke/TIA‡	155	0.6 (0.50—0.67)	46.8
Stroke	111	0.4 (0.30–0.44)	34.3
TIA	94	0.4 (0.28–0.47)	37.9
Tamponade	131	1.0 (0.83–1.14)	68.5
Pericardial effusion	67	0.7 (0.56–0.88)	55.0
Phrenic nerve injury	48	0.4 (0.22–0.54)	70.2
Diaphragmatic paralysis	21	0.3 (0.15–0.43)	0.0
DVT/PE	33	0.15 (0.09–0.21)	0.0
Pneumothorax	22	0.2 (0.08–0.29)	0.0
Hemothorax	25	0.2 (0.10–0.28)	0.0
Sepsis, abscesses, or endocarditis	20	0.1 (0.06–0.24)	0.0
Valve damage	26	0.2 (0.08–0.25)	0.0

CI indicates confidence interval; DVT, deep vein thrombosis; PE, pulmonary embolism; and TIA, transient ischemic attack.

*Pulmonary vein stenosis defined as >50% stenosis and requiring intervention.

†Vascular complications included bleeding, hematoma, arteriovenous fistula, and femoral pseudoaneurysm.

Gupta et al. Circ Arrhythm Electrophysiol. 2013;61082-88

Periprocedural Stroke and Bleeding Complications in Patients Undergoing Catheter Ablation of Atrial Fibrillation With Different Anticoagulation Management

Results From the Role of Coumadin in Preventing Thromboembolism in Atrial Fibrillation (AF) Patients Undergoing Catheter Ablation (COMPARE) Randomized Trial

Table 2. Thromboembolic Events According to AF Type

	Group 1 (Off Warfarin; n=790), n (%)	Group 2 (On Warfarin; n=794), n (%)	*P* Value
Stroke/TIA combined	39 (4.9)	2 (0.25)	<0.001
Paroxysmal	2 (0.87)	0 (0.0)	0.25
Persistent	4 (2.3)	0 (0.0)	0.06
LSP	33 (8.5)	2 (0.49)	<0.001
Stroke	29 (3.7)	2 (0.25)	<0.001
Paroxysmal	1 (0.44)	0 (0.0)	0.47
Persistent	2 (1.15)	0 (0.0)	0.25
LSP AF	26 (6.7)	2 (0.49)	<0.001
TIA	10 (1.27)	0 (0.0)	<0.001
Paroxysmal	1 (0.44)	0 (0.0)	1.00
Persistent	2 (1.15)	0 (0.0)	0.50
LSP	7 (1.81)	0 (0.0)	0.016

AF indicates atrial fibrillation; LSP, long-standing persistent; and TIA, transient ischemic attack.

Di Biase et al. Circulation. 2014;129:2638-2644

Uninterrupted NOAC vs. Uninterrupted VKA in AF Ablation. Randomized Trials

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Study	VENTURE-AF [1]		RE-CIRCUIT [2]		AXAFA – AFNET 5 [3]		ELIMINATE-AF [4]
Comparison	Uninterrupted Rivaroxaban vs. Uninterrupted VKA		Uninterrupted Dabigatran vs. Uninterrupted VKA		Uninterrupted Apixaban vs. Uninterrupted VKA		Uninterrupted Edoxaban vs. Uninterrupted VKA
NOAC Dose	20mg X 1		150mg X 2		5mg X 2 #		60mg X 1≠
No of Patients (total[a])	n=248		n=704		n=674		n=560 (planned)@
Follow up	1 month after ablation		2 months after ablation		4 months after ablation		3 months after ablation
Age (mean)	59.6 years		59.2 years		64.6 years		Ongoing Study
CHA_2DS_2-VASc (mean)	1.6		2.1		2.4		Ongoing Study
Type of AF (Paroxysmal)	Paroxysmal 73.4 %		Paroxysmal 68 %		Paroxysmal 58 %		Ongoing Study
Stroke / Systemic embolism / TIA	NOAC 0 (0%)	VKA 2 (1.6%)	NOAC 0 (0%)	VKA 0 (0%)	NOAC 2 (0.6%)	VKA 0 (0%)	Ongoing Study
Death	NOAC 0 (0%)	VKA 1 (0.8%)	NOAC 0 (0%)	VKA 0 (0%)	NOAC 1 (0.3%)	VKA 1 (0.3%)	Ongoing Study
Tamponade / Pericardial Effusion	NOAC 0 (0%)	VKA 0 (0%)	NOAC 2 (0.6%)	VKA 6 (1.9%)	NOAC 2 (0.6%)	VKA 5 (1.6%)	Ongoing Study
ISTH major bleeding	NOAC 0 (0%)	VKA 1 (0.8%)	NOAC 5 (1.5%)	VKA 23 (7.2%)	NOAC 10 (3.1%)	VKA 14 (4.4%)	Ongoing Study
Puncture site haematoma	NOAC 8 (6.5%)	VKA 10 (8%)	NOAC* 2 (0.6%)	VKA* 10 (2.9%)	NOAC 12 (3.8%)	VKA 15 (4.8%)	Ongoing Study

** ISTH major bleeding*
@ 2:1 Randomization Uninterrupted Edoxaban vs. Uninterrupted VKA
 # 2.5 mg b.i.d. if two or more of the following characteristics were present: age ≥80 years, body weight ≤60 kg, or serum creatinine level ≥1.5mg/dL
≠ 30 mg in patients indicated for a dose reduction

1 Cappato et al. European Heart Journal. 2015;36: 1805-1811
2 Calkins et al. N Engl J Med 2017; 376:1627-1636
3 Kirchhof et al. European Heart Journal. 2018;39:2942-2955
4 Hohnloser et al. Clin Cardiol. 2018;41:440-449

Apixaban in patients at risk of stroke undergoing atrial fibrillation ablation

AXAFA - AFNET 5 Study

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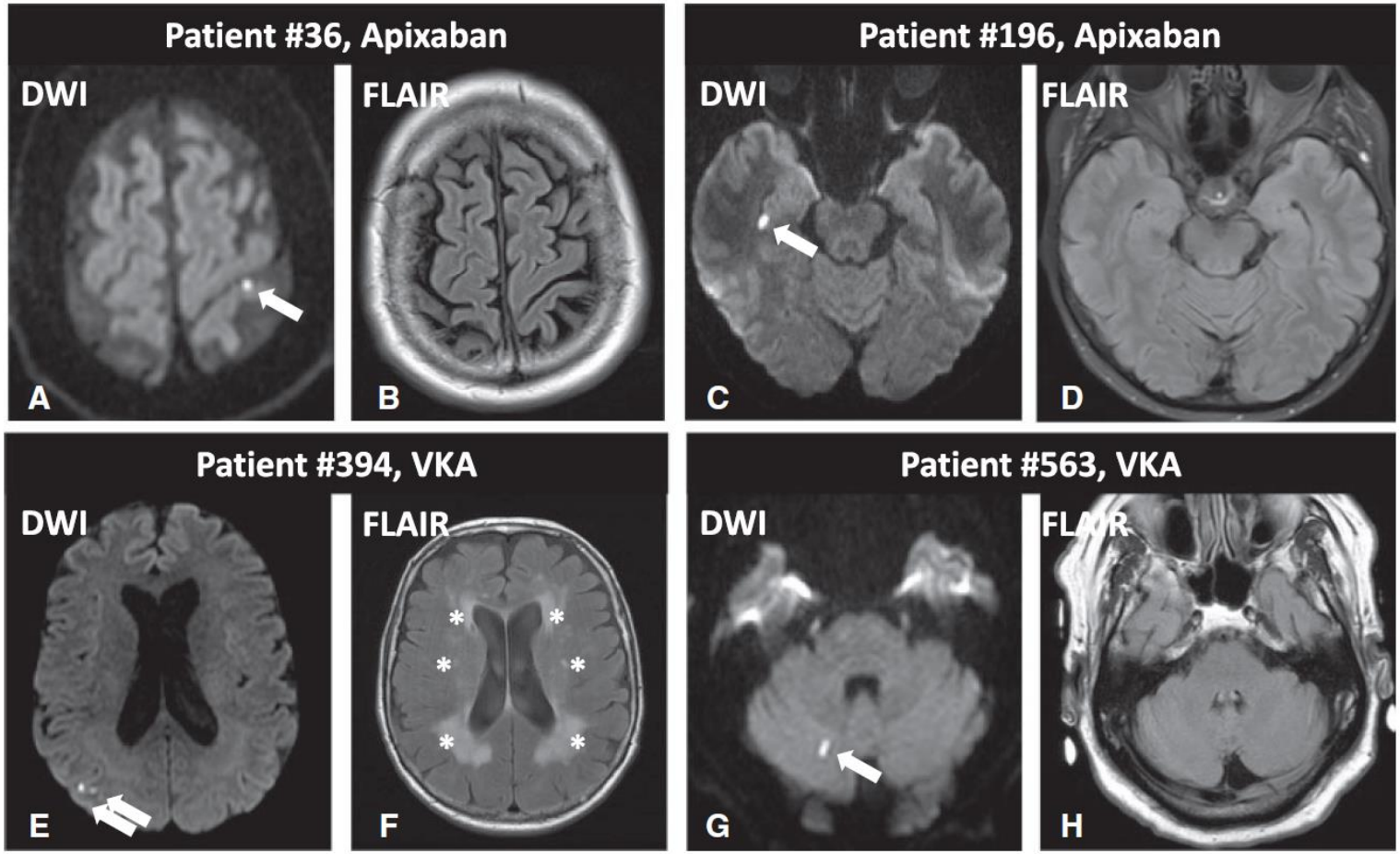
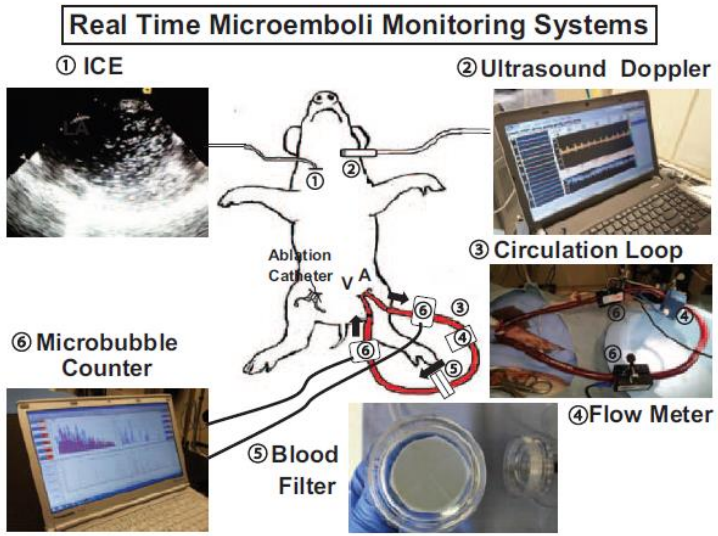
- MRI Sub-study undertook 335/674 (49.7%) patients

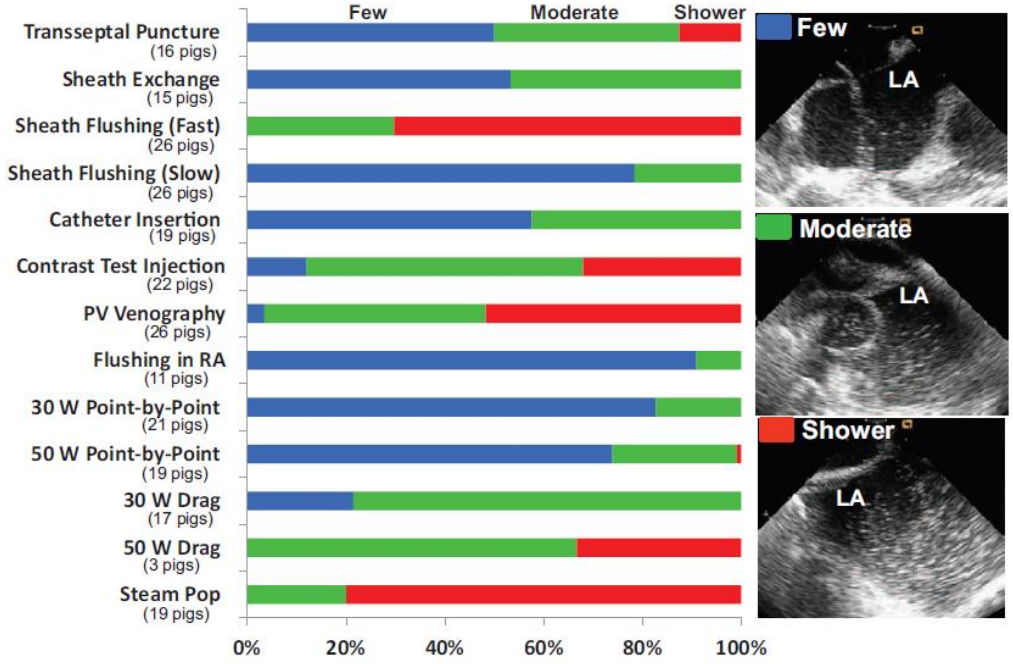


- Acute small brain lesions were found in a similar number of patients in each arm [apixaban 44/162 (27.2%); VKA 40/161 (24.8%); P = 0.64].
- Cognitive function increased at the end of follow-up (median 1 MoCA unit; P = 0.005) without differences between study groups.

Kirchhof et al. European Heart Journal. 2018;39:2942-2955

Microemboli during catheter ablation





Effect of Left Atrial Ablation Process and Strategy on Microemboli Formation During Irrigated Radiofrequency Catheter Ablation in an In Vivo Model

Mitsuru Takami, MD; H. Immo Lehmann, MD; Kay D. Parker, CVT; Kirk M. Welker, MD; Susan B. Johnson, BS; Douglas L. Packer, MD

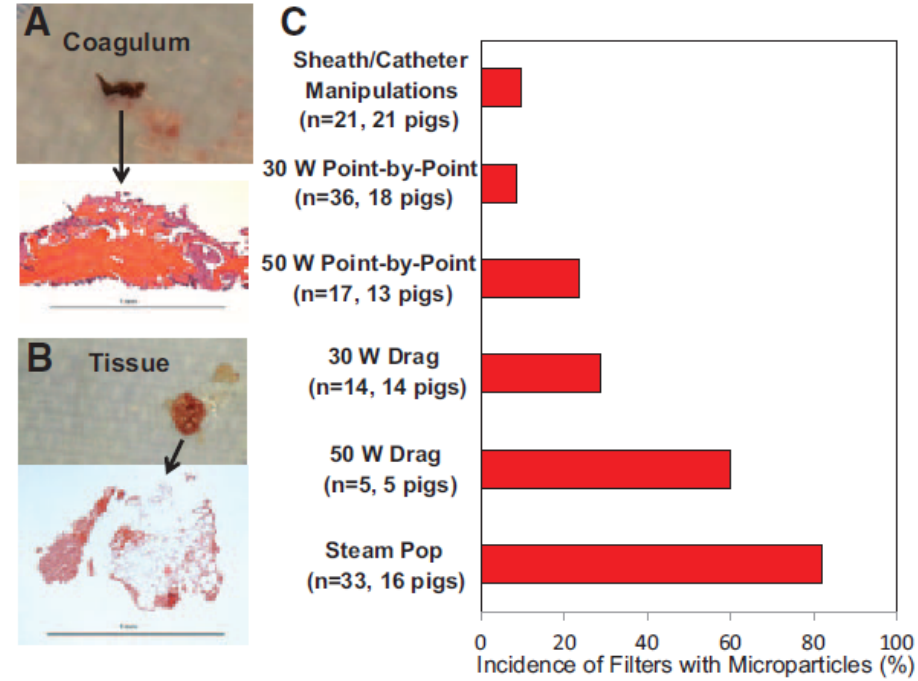


Figure 4. Microparticles in the blood filter. **A**, Coagulum on filter after 50-W point-by-point ablation. **B**, Tissue piece on filter after 50-W drag ablation with steam pop. **C**, Incidence of the filters with microparticles in each interventional step.

Takami et al. Circ Arrhythm Electrophysiol. 2016 Jan;9(1):e003226

Τι κάνω με την πρωινή δόση την ημέρα της κατάλυσης;

RE-CIRCUIT (Dabigatran)

Uninterrupted Dabigatran versus Warfarin for Ablation in Atrial Fibrillation

Hugh Calkins, M.D., Stephan Willems, M.D., Edward P. Gerstenfeld, M.D., Atul Verma, M.D., Richard Schilling, M.D., Stefan H. Hohnloser, M.D., Ken Okumura, M.D., Ph.D., Harvey Serota, M.D., Matias Nordaby, M.D., Kelly Guiver, M.Sc., Branislav Biss, M.D., Marc A. Brouwer, M.D., Ph.D., and Massimo Grimaldi, M.D., Ph.D., for the RE-CIRCUIT Investigators*

- 41,3 % των ασθενών έλαβε την τελευταία δόση <4 ώρες από την διαφραγματοστομία
- 36,6% των ασθενών ασθενών έλαβε την τελευταία δόση 4-8 ώρες από την διαφραγματοστομία
- 19,6% των ασθενών ασθενών έλαβε την τελευταία δόση >8 ώρες από την διαφραγματοστομία

AXAFA - AFNET 5 (Apixaban)

Apixaban in patients at risk of stroke undergoing atrial fibrillation ablation

Paulus Kirchhof[1,2,3,4]*, Karl Georg Haeusler[4,5], Benjamin Blank[4], Joseph De Bono[1,3], David Callans[6], Arif Elvan[7], Thomas Fetsch[8], Isabelle C. Van Gelder[9], Philip Gentlesk[10], Massimo Grimaldi[11], Jim Hansen[12], Gerhard Hindricks[13], Hussein R. Al-Khalidi[14], Tyler Massaro[15], Lluis Mont[16], Jens Cosedis Nielsen[17], Georg Nölker[18], Jonathan P. Piccini[15,19], Tom De Potter[20], Daniel Scherr[21], Ulrich Schotten[4,22], Sakis Themistoclakis[23], Derick Todd[24], Johan Vijgen[25], and Luigi Di Biase[26,27]

- Δόθηκε η πρωινή δόση βάσει πρωτοκόλλου

Pre-transseptal puncture heparin administration is safer in terms of thrombogenesis

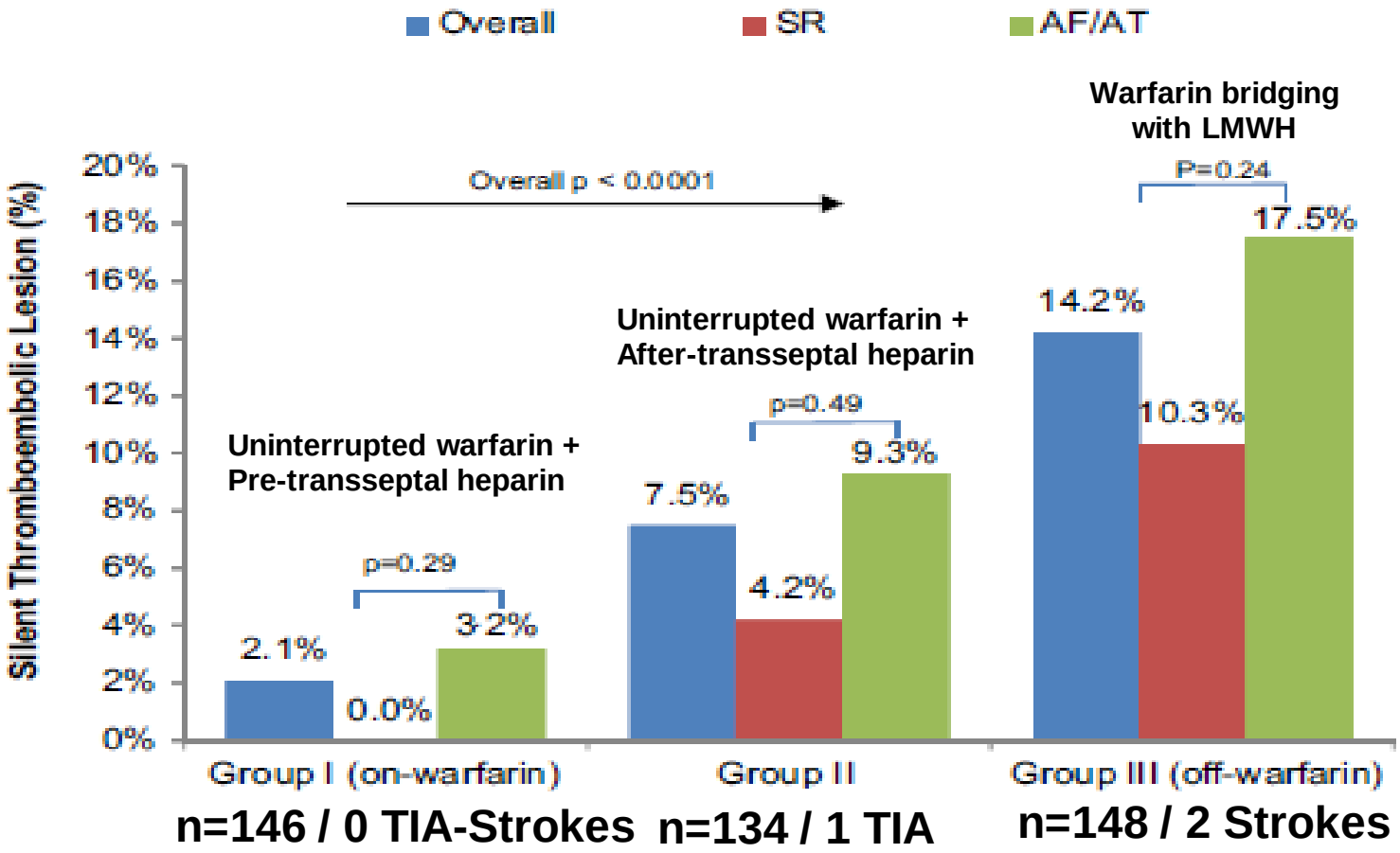
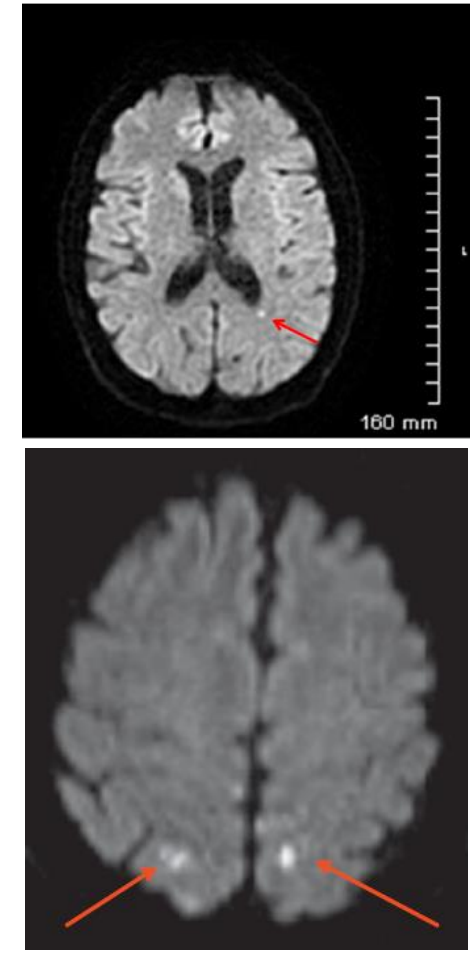
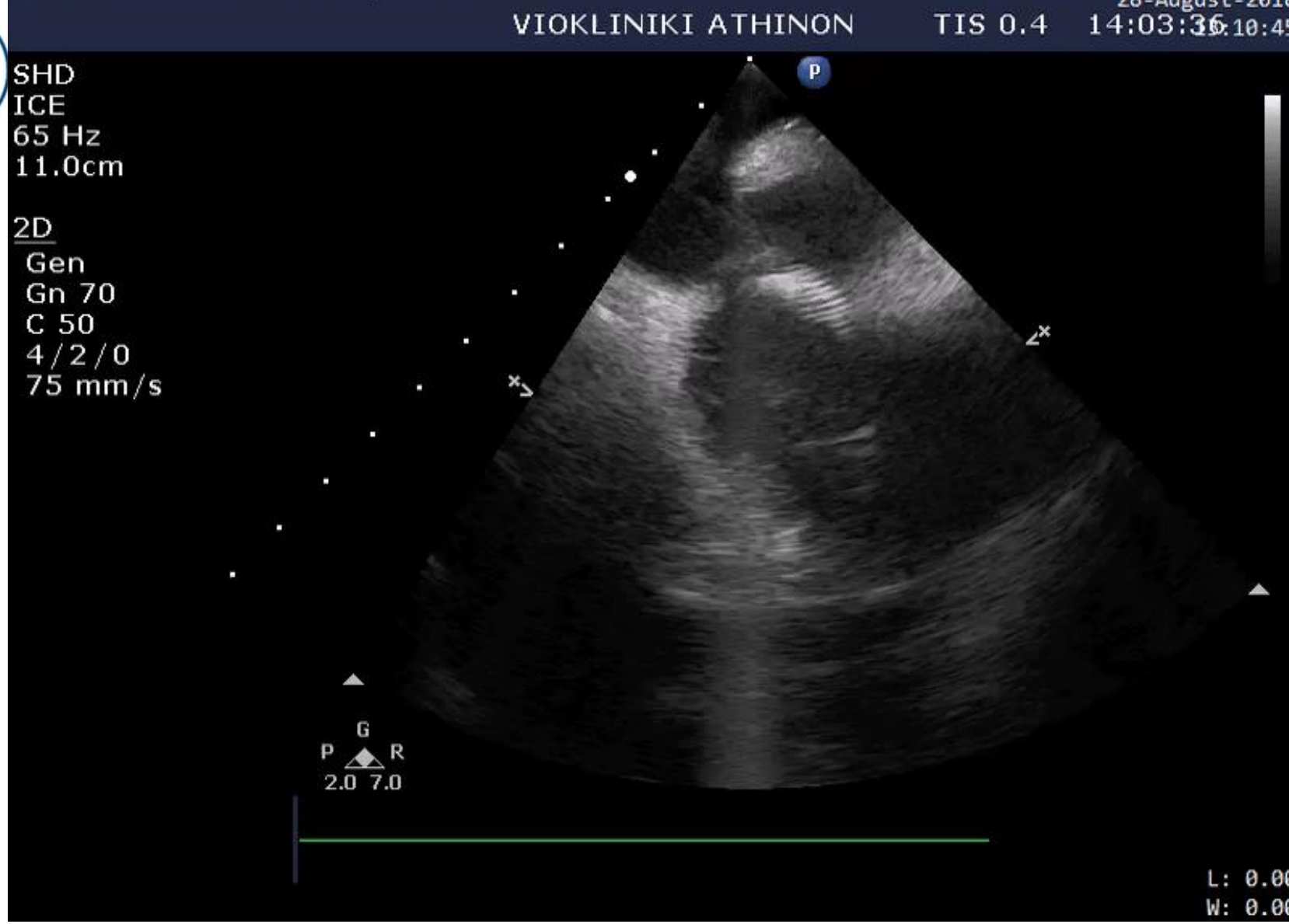


Figure 1 Incidence of silent cerebral ischemia in the 3 groups sorted by rhythm on the day of the procedure. AF = atrial fibrillation; AT = atrial tachycardia; SR = sinus rhythm.

Postablation MRI



Di Biase et al Heart Rhythm 2014;11:791-798



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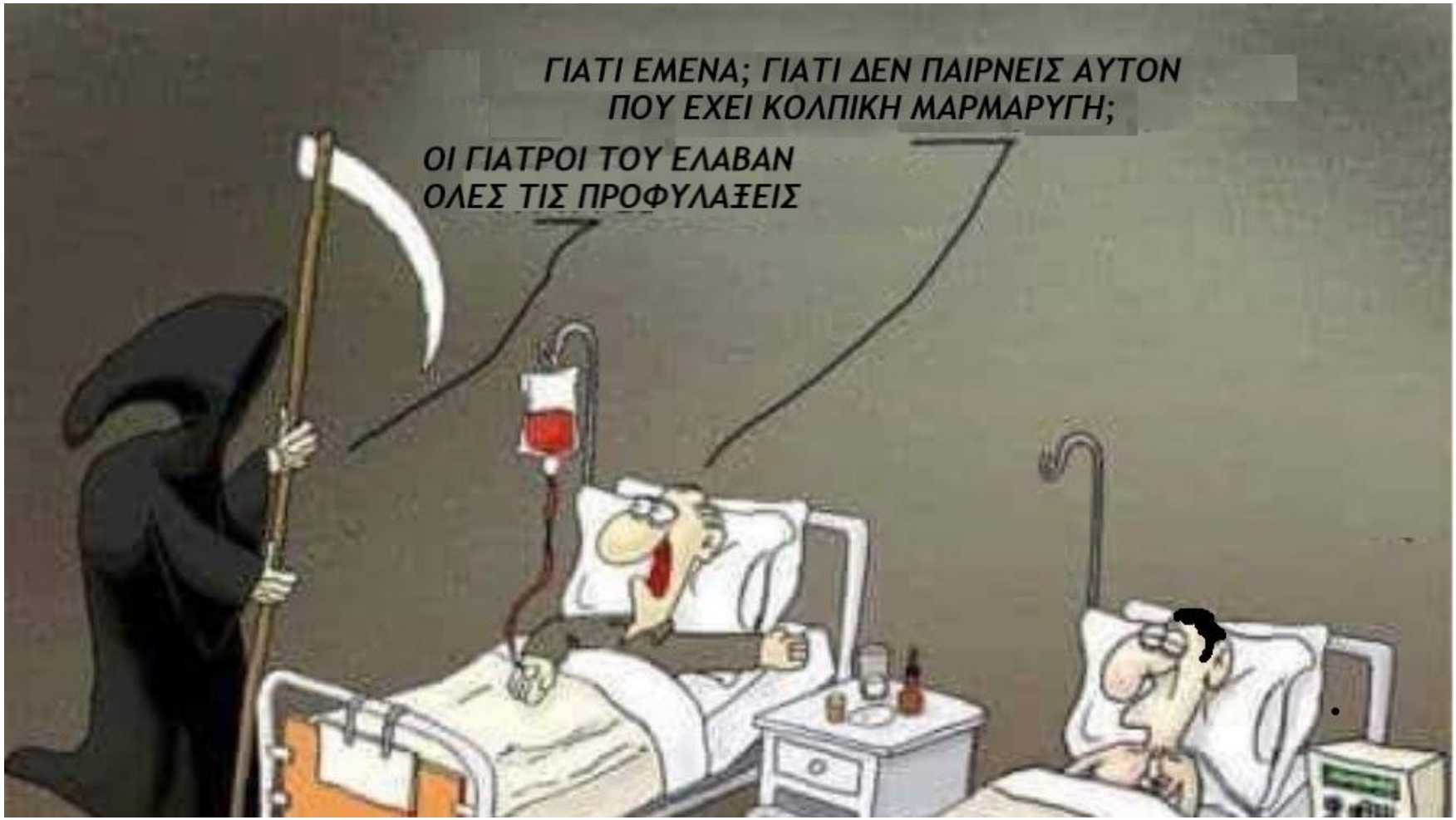
AXAFA - AFNET 5 Study

Cognitive function increased at the end of follow-up, after ablation, (median 1 MoCA unit; P = 0.005) without differences between study groups.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ΠΟΥ ΕΧΕΙ ΚΟΛΠΙΚΗ ΜΑΡΜΑΡΥΓΗ;
ΟΙ ΓΙΑΤΡΟΙ ΤΟΥ ΕΛΑΒΑΝ
ΟΛΕΣ ΤΙΣ ΠΡΟΦΥΛΑΞΕΙΣ