Rhythmuskontrolle bei Vorhofflimmern:

State of the Art

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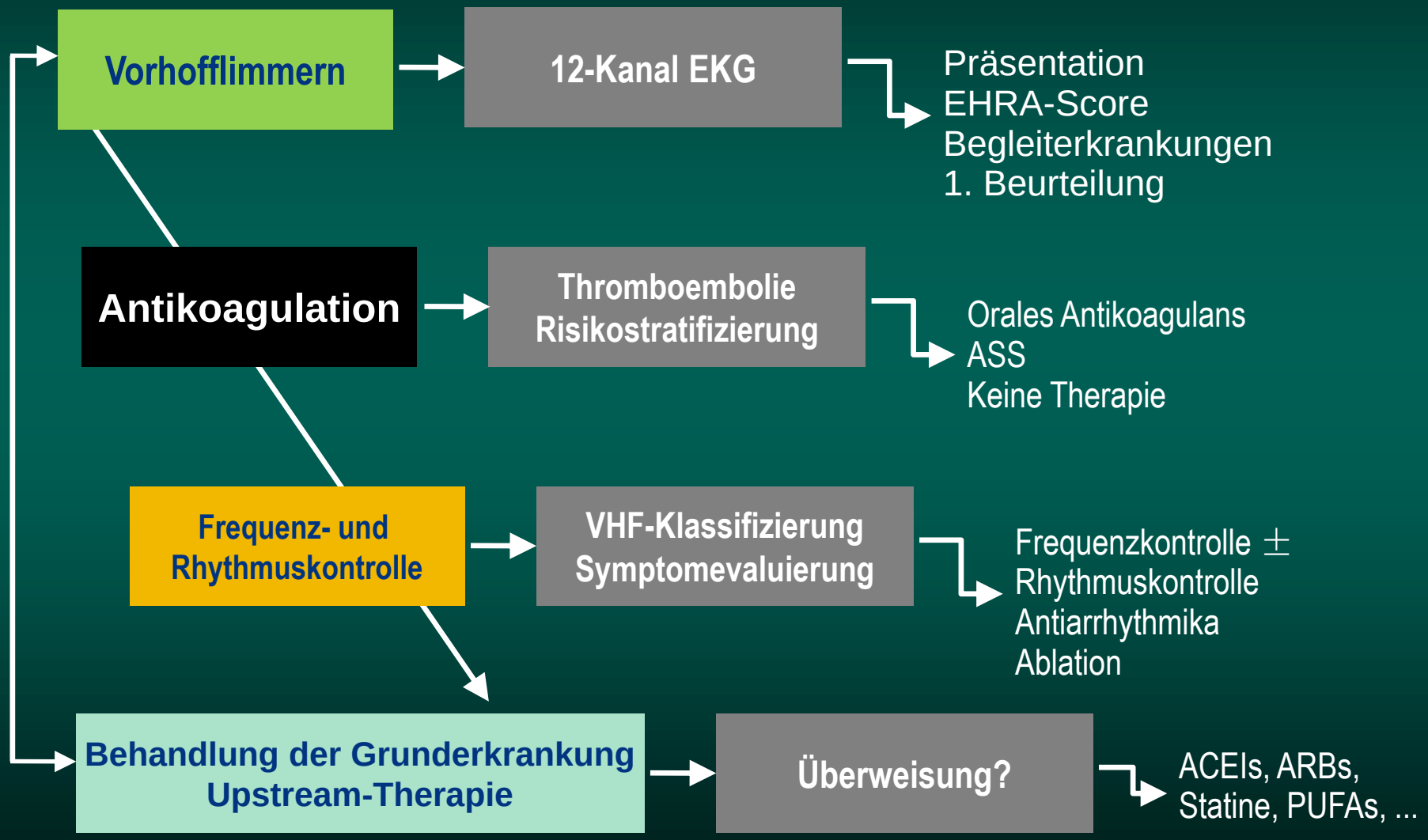
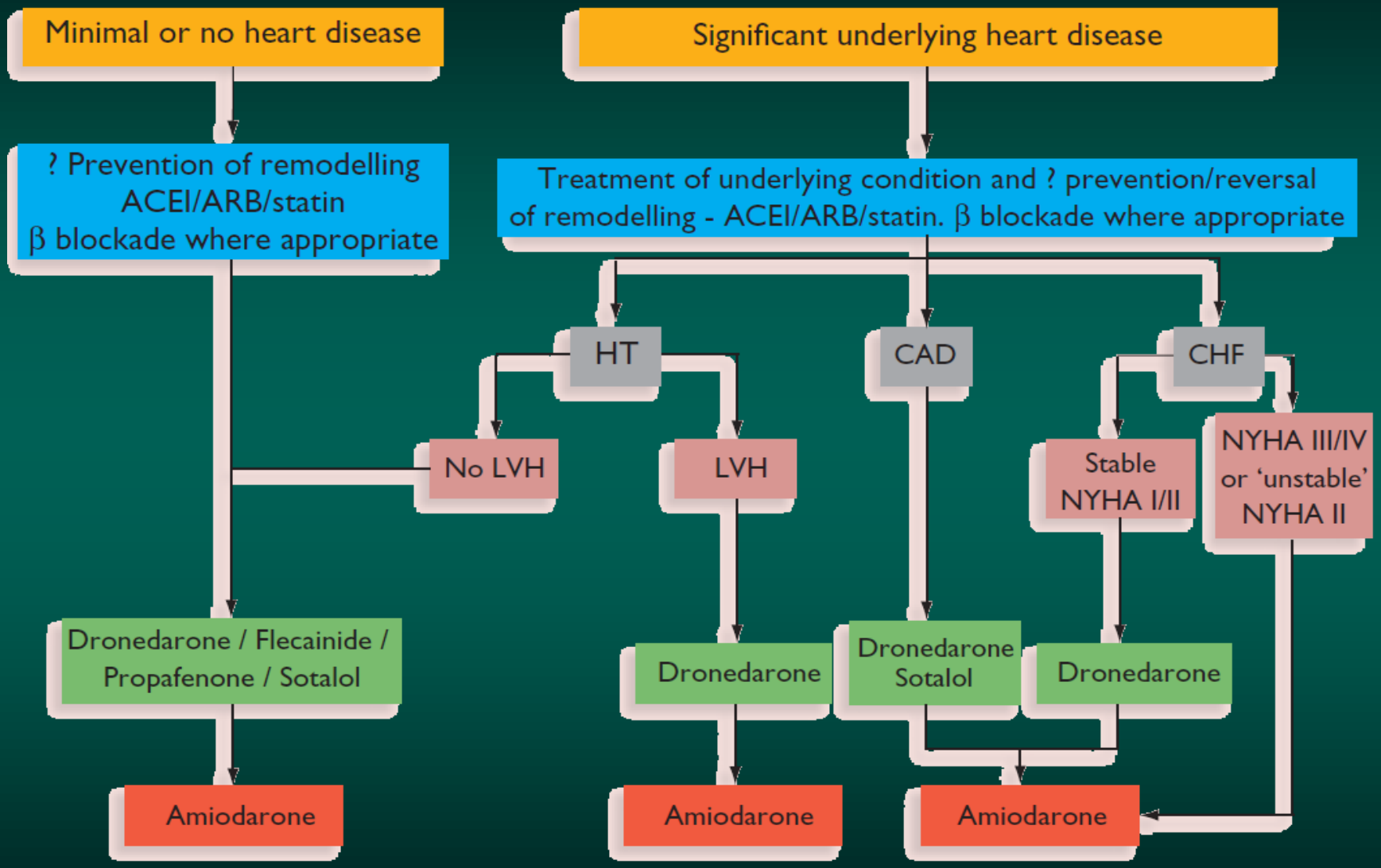
VHF – Behandlungsstrategien (ESC Leitlinien 2010)



ESC Guidelines 2010 (alt)



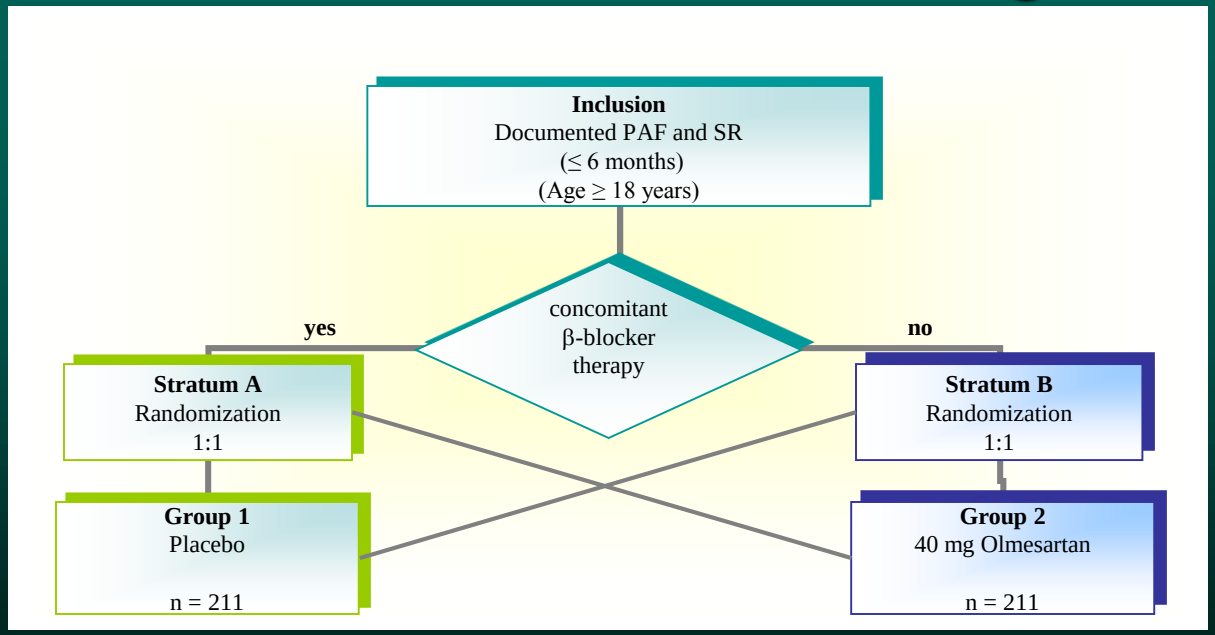
Camm AJ, et al. ESC Guidelines Afib 2010. Eur Heart J

ANTIPAF

„Angiotensin II-Antagonist in Paroxysmal Atrial Fibrillation Trial“

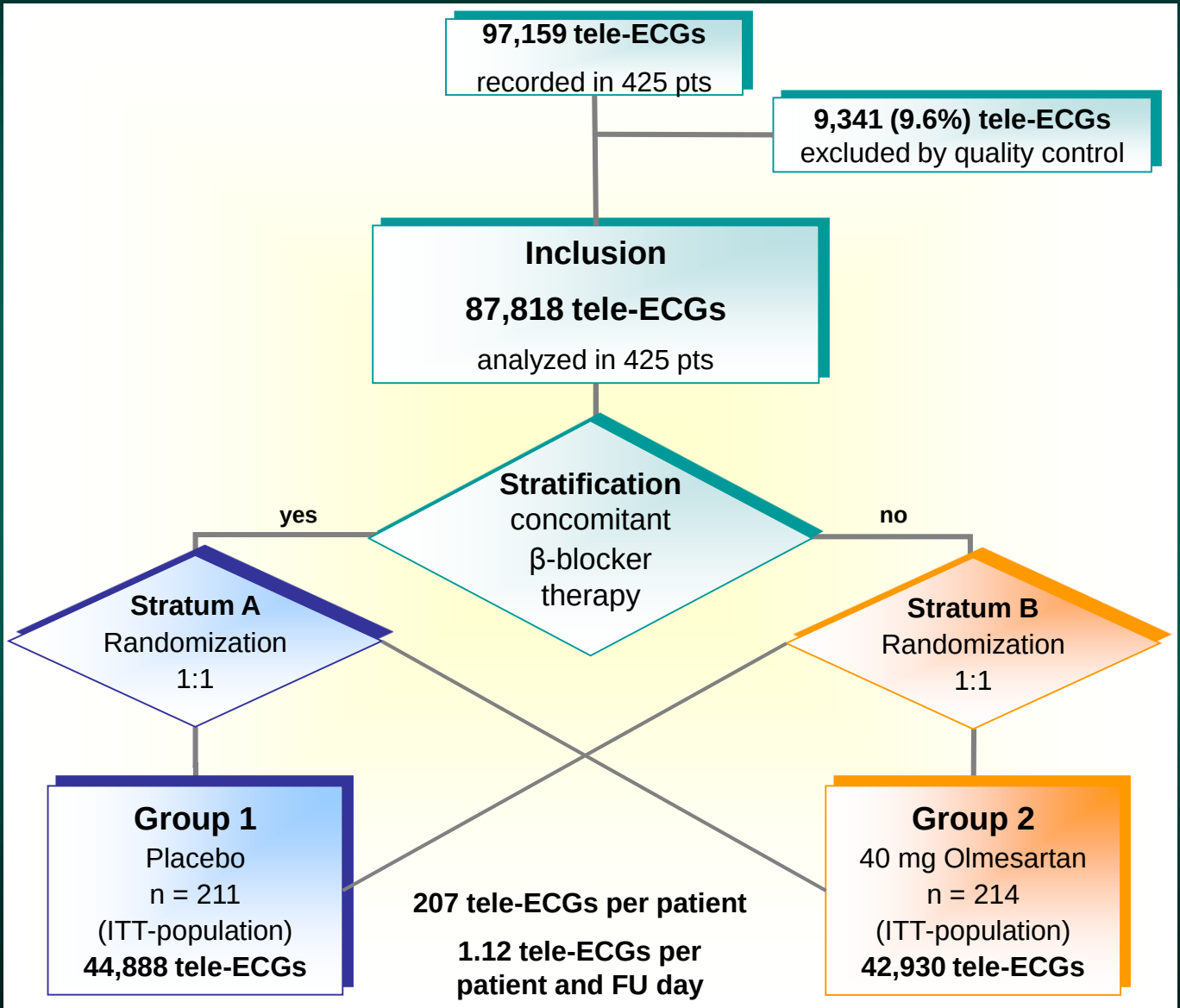
Prospektive, randomisierte, doppelblinde, multizentrische Studie

Prof. Dr. A. Goette, Magdeburg
Prof. Dr. T. Meinertz, Hamburg

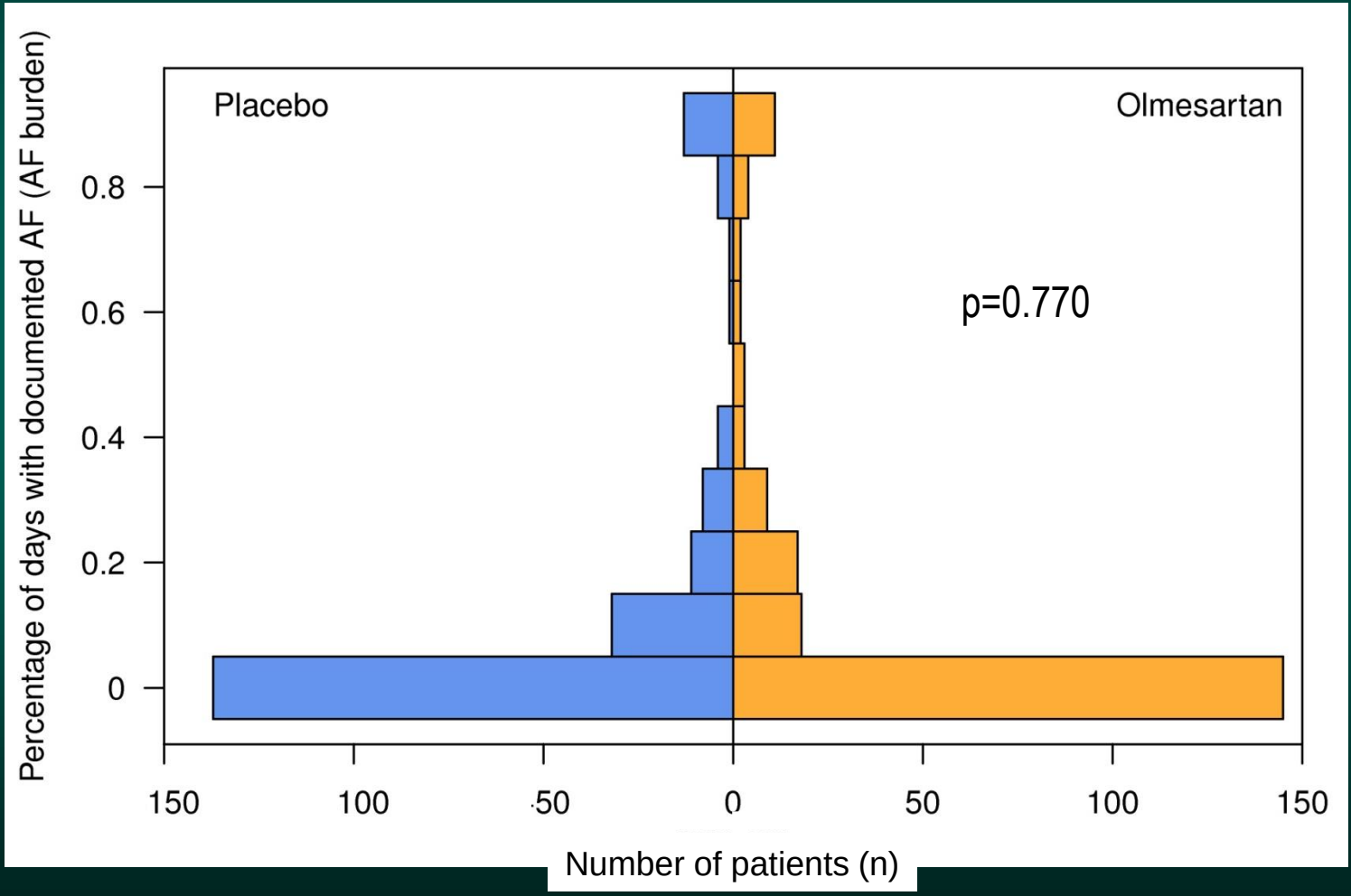


BMBF-Kompetenznetz „Vorhofflimmern“

ANTIPAF: Tele-ECG



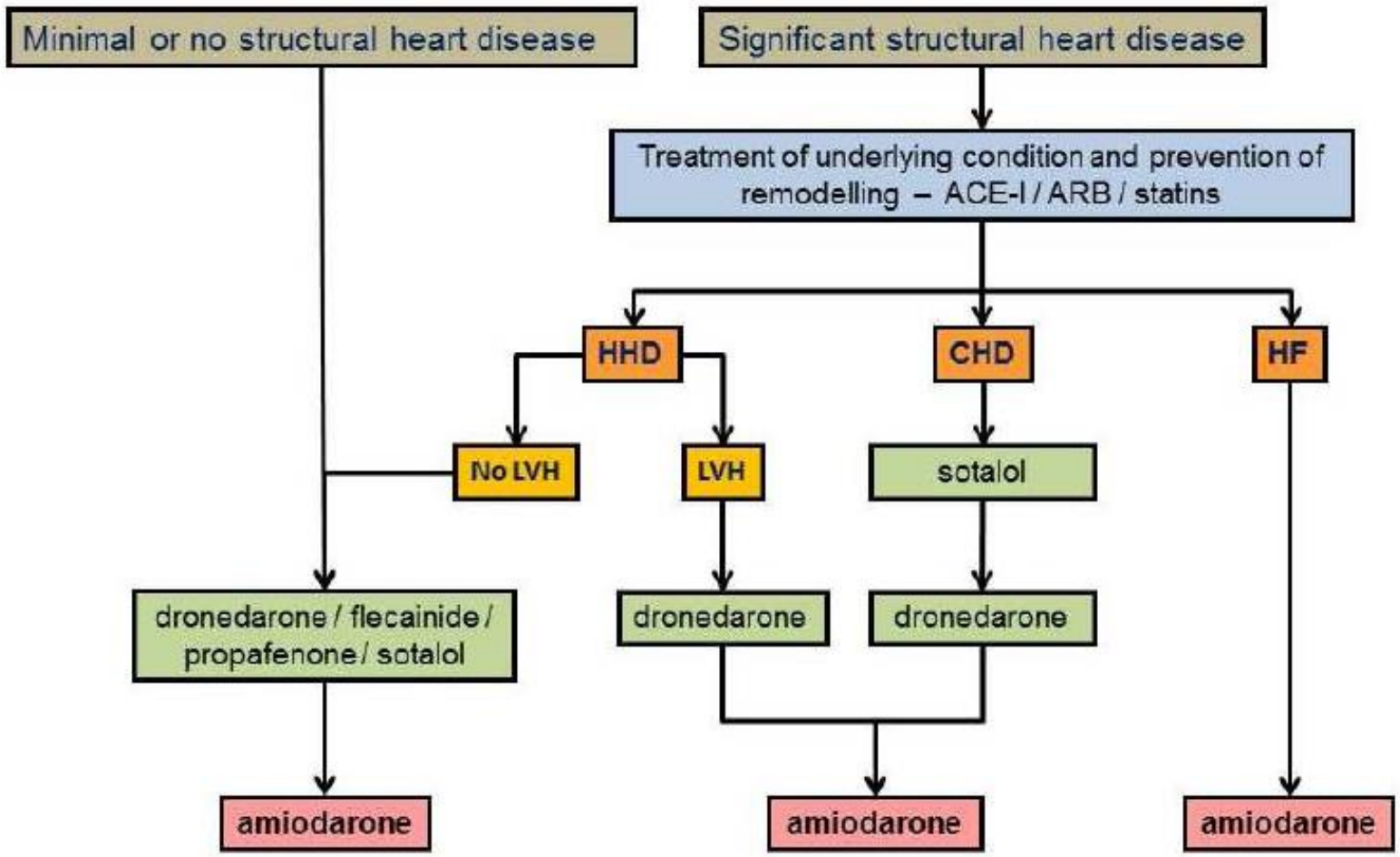
Primary Endpoint (AF burden)



Goette et al. ANTIPAF Trial. Circulation A&E 2012

Updated AF-Guideline 2012

Figure 4 Antiarrhythmic drug management of non-permanent AF



Camm et al. ESC 2012

AFFIRM Study: on-treatment analysis

TABLE 2. Covariates Significantly Associated With Survival Results With Echocardiographic Data Included

Covariate	*P*	HR	HR: 99% Confidence Limits Lower	Upper
Age at enrollment*	<0.0001	1.06	1.05	1.08
Coronary artery disease	<0.0001	1.56	1.20	2.04
Congestive heart failure	<0.0001	1.57	1.18	2.09
Diabetes	<0.0001	1.56	1.17	2.07
Stroke or transient ischemic attack	<0.0001	1.70	1.24	2.33
Smoking	<0.0001	1.78	1.25	2.53
Left ventricular dysfunction	0.0065	1.36	1.02	1.81
Mitral regurgitation	0.0043	1.36	1.03	1.80
Sinus rhythm	<0.0001	0.53	0.39	0.72
Warfarin use	<0.0001	0.50	0.37	0.69
Digoxin use	0.0007	1.42	1.09	1.86
Rhythm-control drug use	0.0005	1.49	1.11	2.01

*Per year of age.

Continuous vs Episodic Prophylactic Treatment With Amiodarone for the Prevention of Atrial Fibrillation

A Randomized Trial

Sheba Ahmed, MD
Michiel Rienstra, MD, PhD
Harry J. G. M. Crijns, MD, PhD
Thera P. Links, MD, PhD
Ans C. P. Wiesfeld, MD, PhD
Hans L. Hillege, MD, PhD
Hans A. Bosker, MD, PhD
Dirk J. A. Lok, MD
Dirk J. Van Veldhuisen, MD, PhD
Isabelle C. Van Gelder, MD, PhD
for the CONVERT Investigators

Context Amiodarone effectively suppresses atrial fibrillation but causes many adverse events.

Objective To compare major events in patients randomized to receive episodic amiodarone treatment with those who received continuous amiodarone treatment while still aiming to prevent atrial fibrillation.

Design, Setting, and Participants A randomized trial of 209 ambulatory patients with recurrent symptomatic persistent atrial fibrillation, conducted from December 2002 through March 2007 at 7 Dutch medical centers.

Intervention Patients were randomly assigned to receive either episodic or continuous amiodarone treatment after electrical cardioversion following amiodarone loading. Episodic amiodarone treatment was discontinued after a month of sinus rhythm and reinitiated if atrial fibrillation relapsed (1 month peri–electrical cardioversion). In the continuous treatment group amiodarone was maintained throughout.

Main Outcome Measures The primary end point was a composite of amiodarone and underlying heart disease–related major events. The secondary end points were all-cause mortality and cardiovascular hospitalizations.

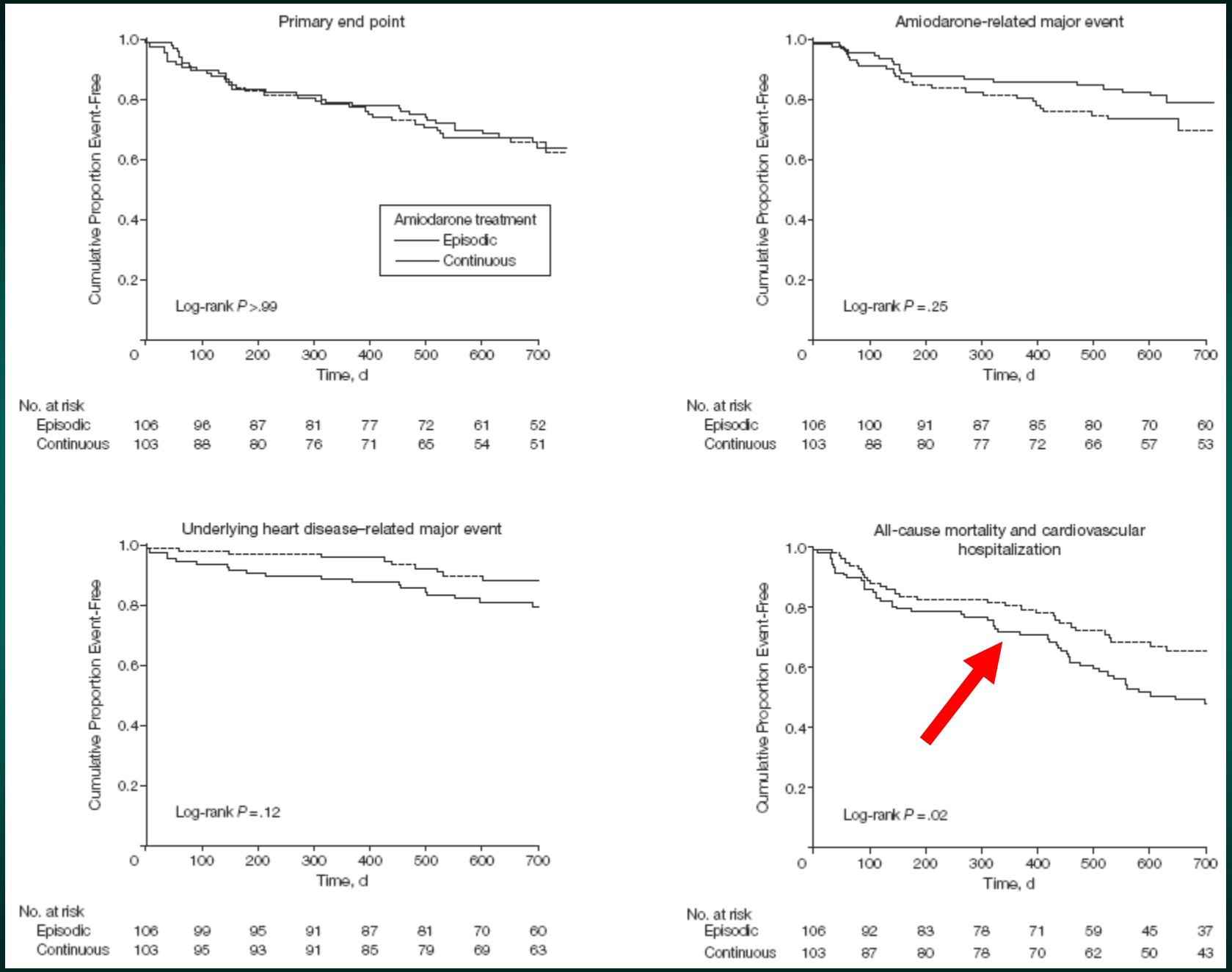
Results After a median follow-up of 2.1 years (range, 0.4-2.5 years), 51 (48%) of those receiving episodic treatment vs 64 (62%) receiving continuous treatment had sinus rhythm ($P=.05$). There were 85 atrial fibrillation recurrences (80%) among the episodic treatment group vs 56 (54%) in the continuous treatment group ($P<.001$). No significant difference existed in the incidence of the primary composite end point between each group (37 [35%] episodic vs 34 [33%] continuous; incidence rate difference, 0.2; 95% confidence interval [CI], −10.2 to 10.6). However, there were nonstatistically significant differences in the incidence of amiodarone-related major events (20 [19%] episodic vs 25 [24%] continuous; incidence rate difference, −2.0; 95% CI, −8.7 to 4.6) and underlying heart disease–related major events (17 [16%] episodic vs 9 [9%] continuous; incidence rate difference, 3.6; 95% CI, −1.6 to 8.7). All-cause mortality and cardiovascular hospitalizations were higher among those receiving episodic treatment (56 [53%] vs 35 [34%], $P=.02$).

Conclusions In this study population, there was no difference in the composite of amiodarone and cardiac major adverse events between groups. However, patients receiving episodic treatment had a significantly increased rate of atrial fibrillation recurrence and a significantly higher rate of all-cause mortality and cardiovascular hospitalizations.

Trial Registration clinicaltrials.gov Identifier: NCT00392431

JAMA. 2008;300(15):1784-1792 www.jama.com

Atrial fibrillation is not a benign disease. It may cause symptoms, heart failure, and stroke.[1] Recent studies have established that morbidity and mortality are comparable between rate- and rhythm-control therapy.[2-5] However, long-term maintenance of sinus rhythm provides a variety of benefits, including an improvement in cardiac function and quality of life.[6-8] Therefore, maintenance of sinus rhythm is still the treatment of choice in symptomatic patients, those with tachycardiomyopathy, and when adequate rate control cannot be achieved.[3] However, success of pharmacological rhythm control is rather limited.[3,9] With a serial antiarrhythmic drug approach, no more than



Ahmed et al. JAMA 2008

AAD (History)

1914 Quinidine

1950 Lidocaine

1951 Procainamide

1956 Ajmaline

1962 Disopyramide

1967 Amiodarone

1972 Mexiletine

1975 Flecainide

1976 Propafenone

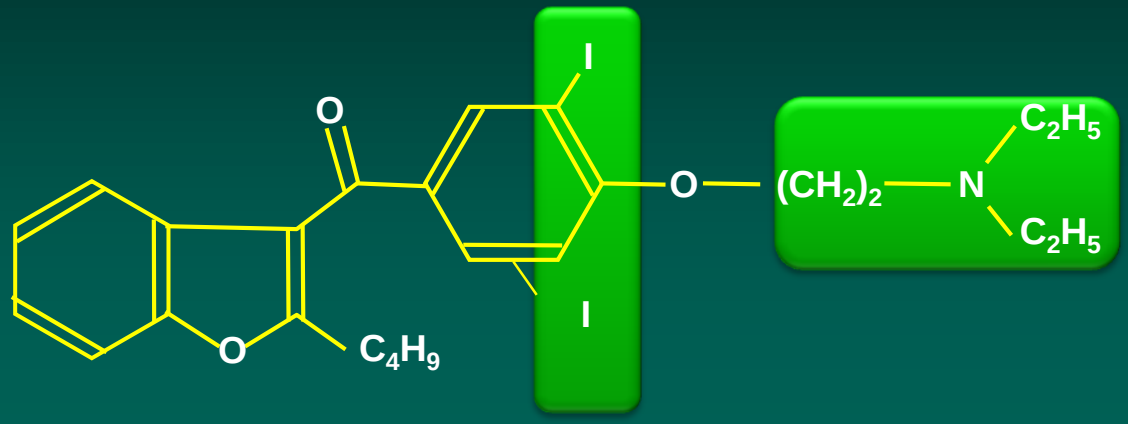
1985 Sotalol

1989 CAST

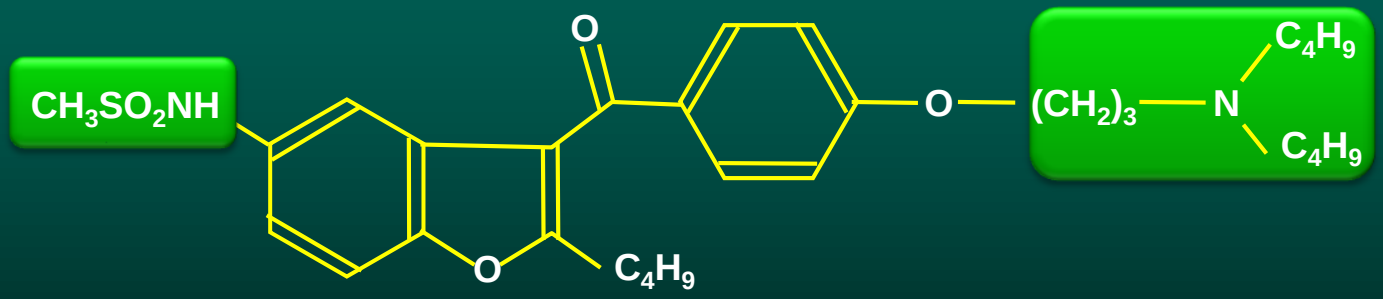
2000 Dofetilide

2009 Dronedarone

Dronedarone vs Amiodarone



Amiodaron (MW = 682)

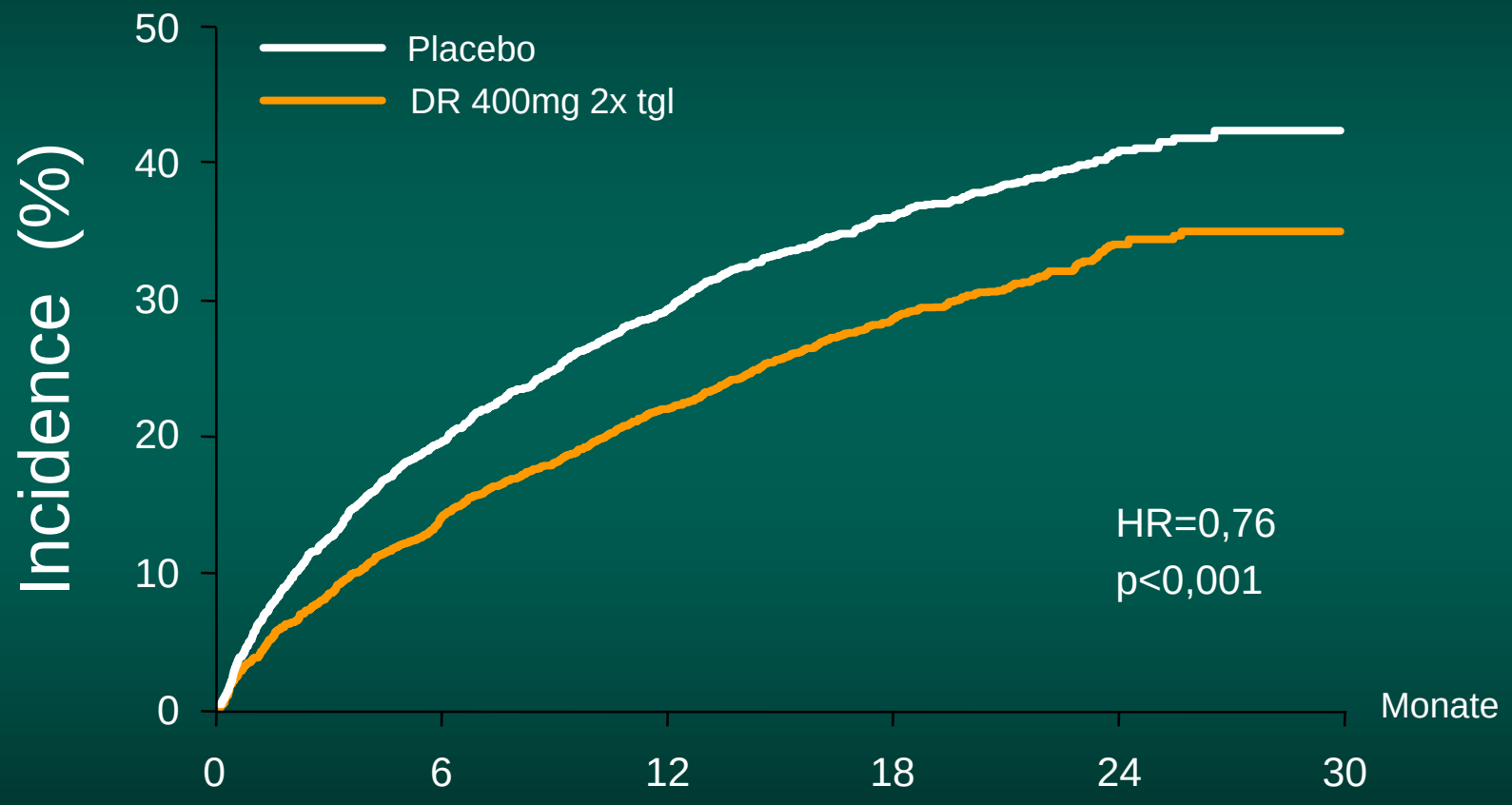


Dronedaron (MW = 593)

Sun et al. Circulation 1999;100:2276–2281

ATHENA: Primary Endpoint

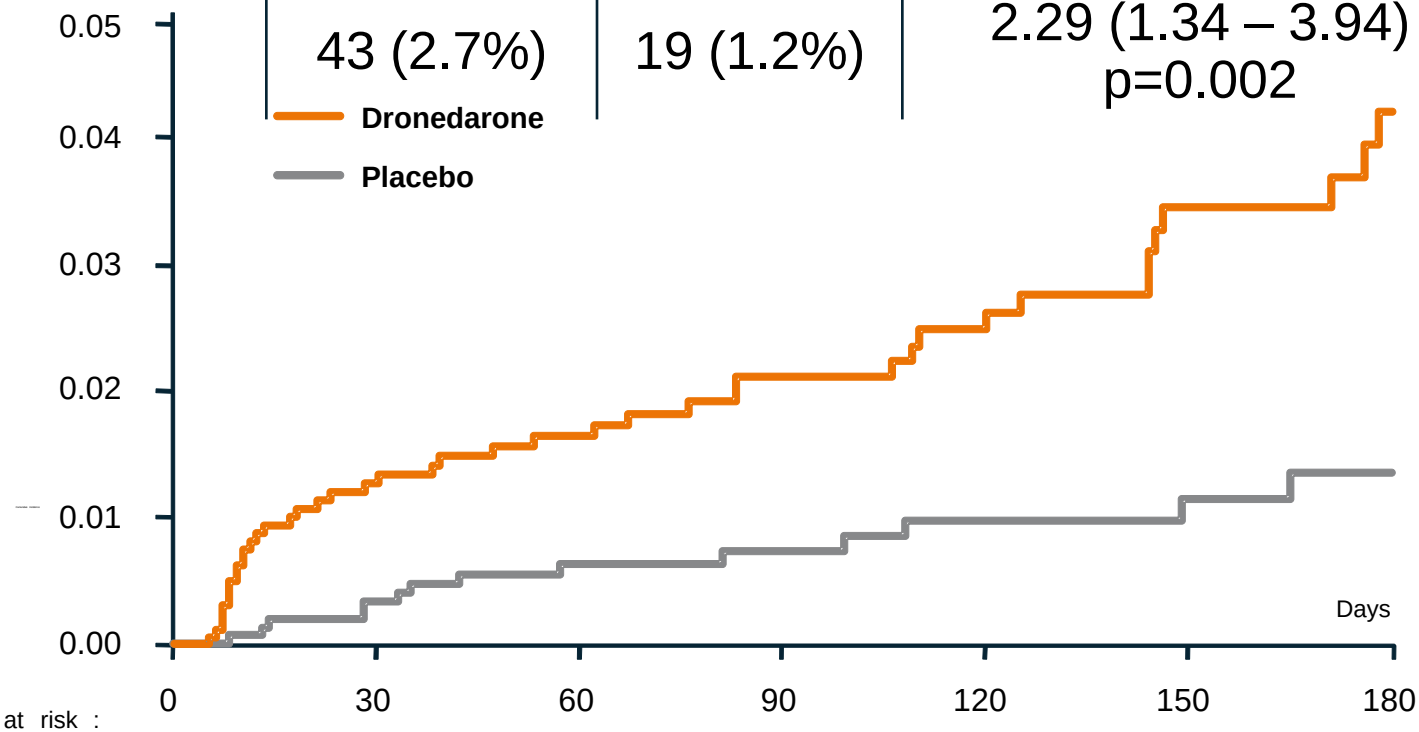
„Time to first cardiovascular hospitalization or death"



Hohnloser SH et al. N Engl J Med 2009;360:668-678

Stroke, systemic embolism, myocardial infarction or cardiovascular death

Dronedarone	Placebo	Dronedarone vs placebo HR and 95% CI
43 (2.7%)	19 (1.2%)	2.29 (1.34 – 3.94) p=0.002



Number at risk :

Dronedarone	**1619**	**1421**	**930**	**353**
Placebo	**1617**	**1445**	**908**	**377**

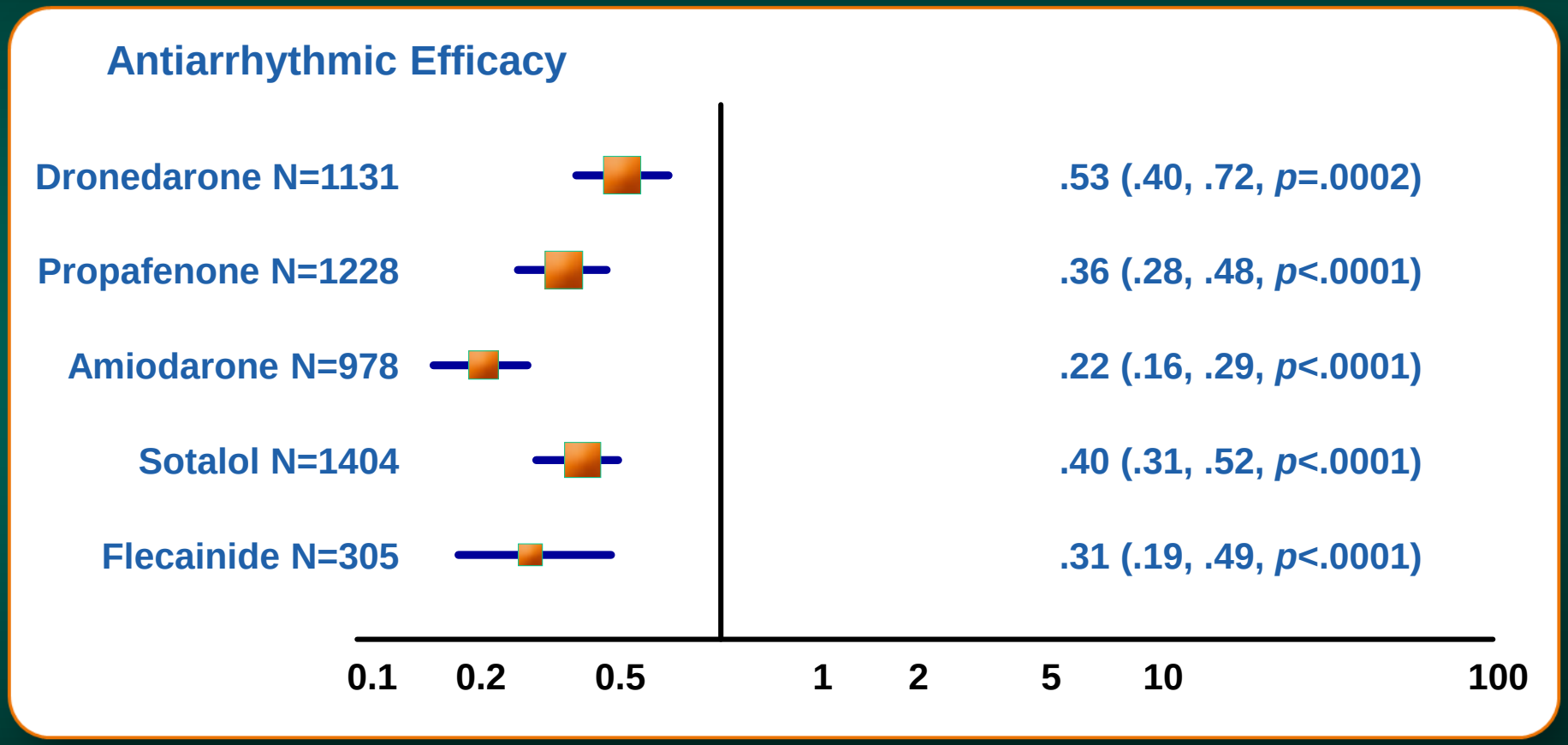
Updated AF-Guideline 2012

Recommendations	Class[a]	Level[b]	Ref.[c]
Dronedarone is moderately effective in maintaining sinus rhythm.	I	A	139
Dronedarone reduces the need for cardiovascular hospitalizations in patients with paroxysmal or persistent AF.	IIa	A	134
Short term (4 weeks) antiarrhythmic therapy after cardioversion may be considered in selected patients, e.g. patients at risk for therapy-associated complications.	IIb	B	133
Dronedarone should not be used in patients with permanent AF.	III	A	5
Dronedarone should not be used in patients with heart failure.	III	B	135 142

[a]Class of recommendation.

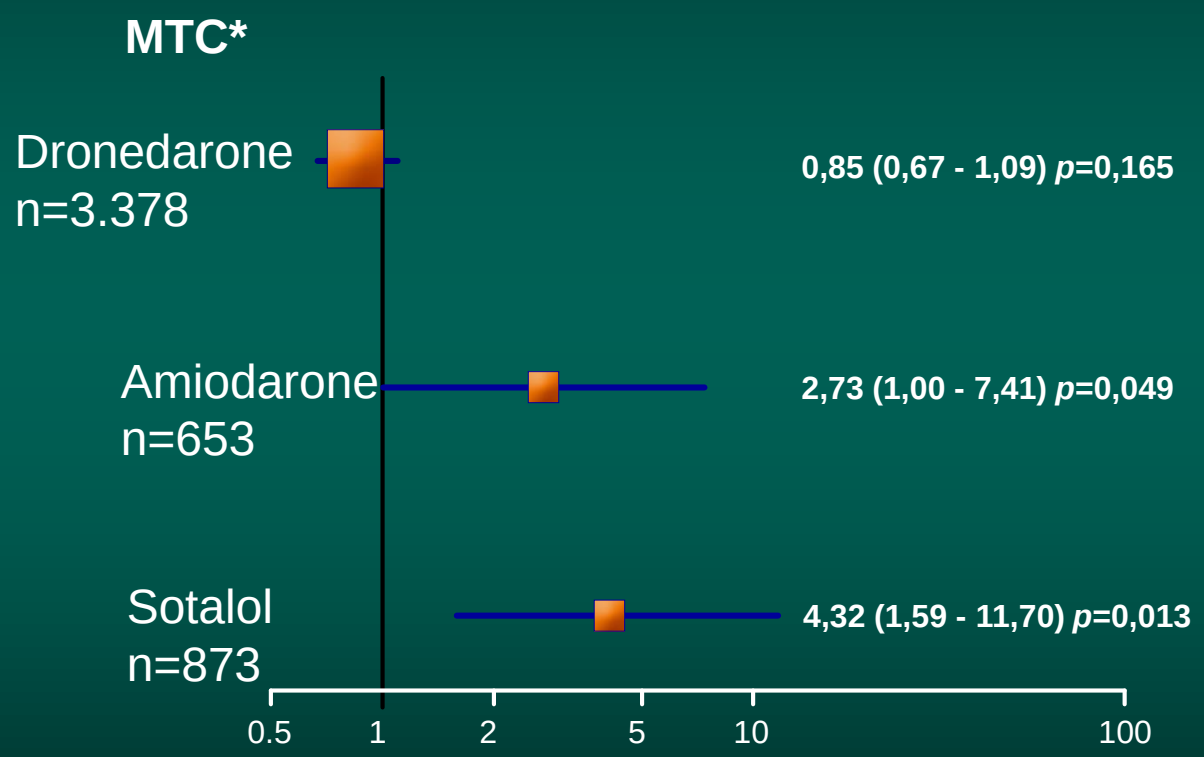
Camm et al. ESC 2012

Efficacy of AAD (Meta-Analysis of 30 Studies)



Freemantle et al. Europace. 2011 Mar;13(3):329-45

AAD & Mortality (Meta-Analysis of 30 Studies)



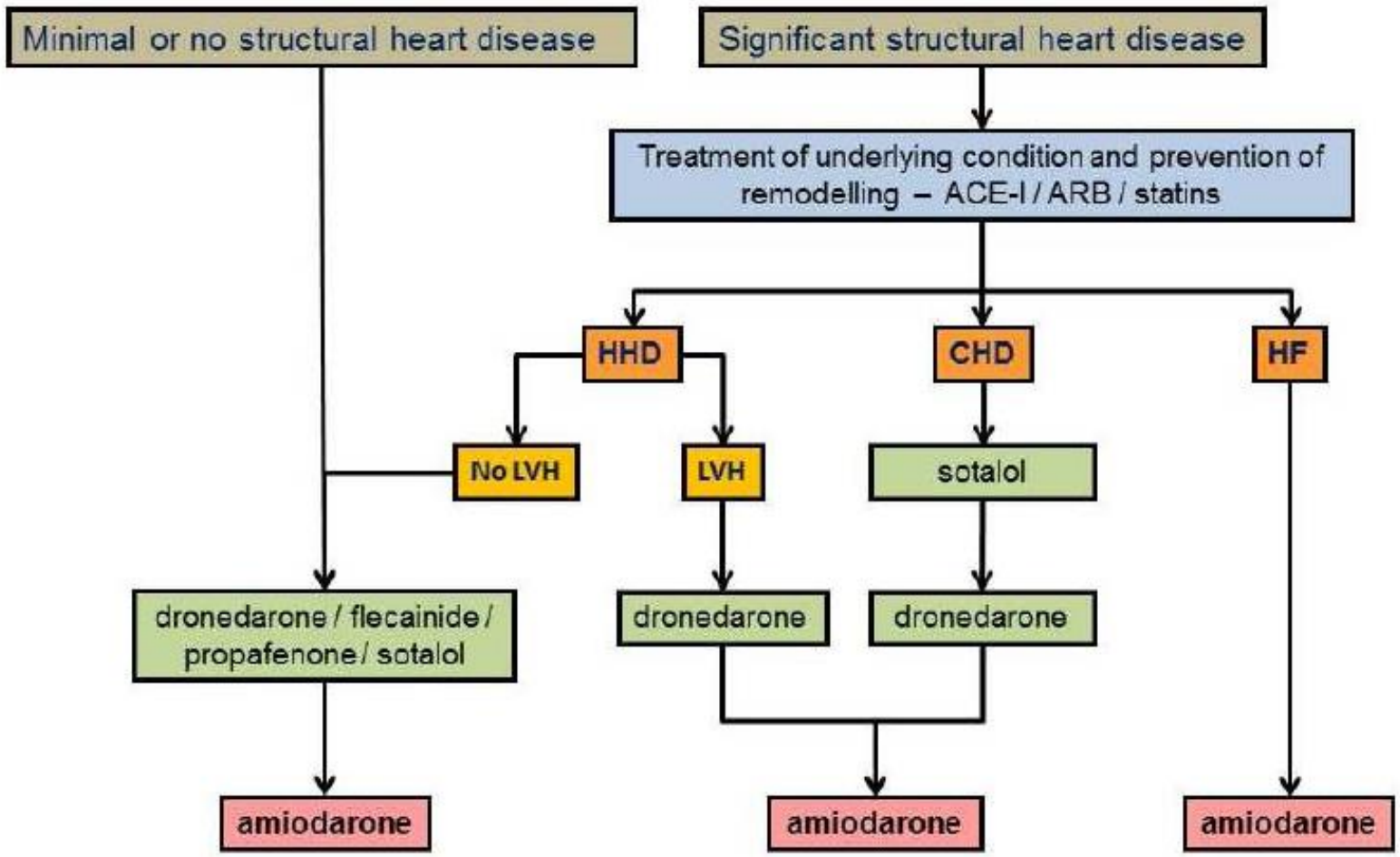
*mixed treatment comparison

Europace. 2011 Mar;13(3):329-45. Epub 2011 Jan 11

Freemantle N, et al. *Circulation* Nov 2009;**120**:S691–2:Abstract 2752.

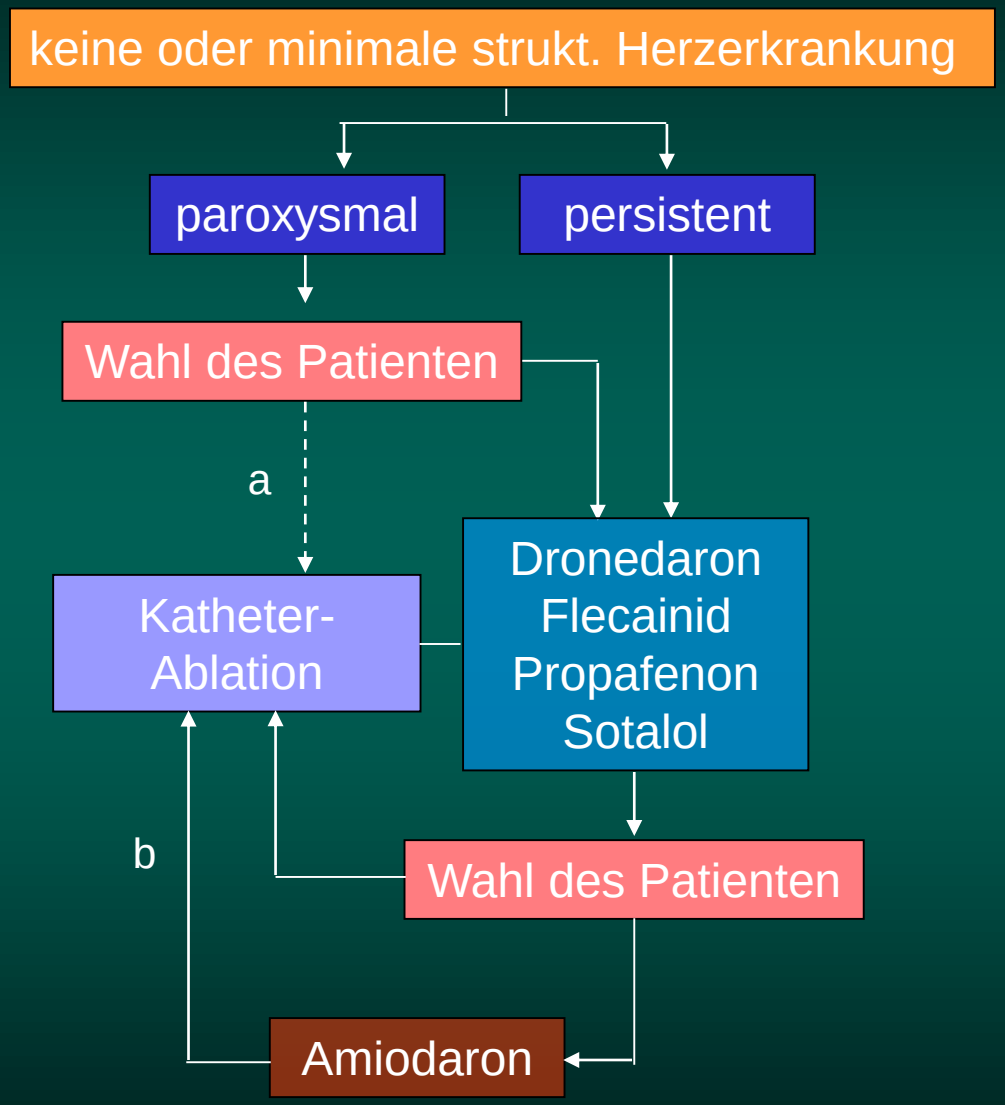
Updated AF-Guideline 2012

Figure 4 Antiarrhythmic drug management of non-permanent AF



Camm et al. ESC 2012

Antiarrhythmische Medikation und/oder linksventrikuläre Ablation zur Rhythmuskontrolle bei Vorhofflimmern

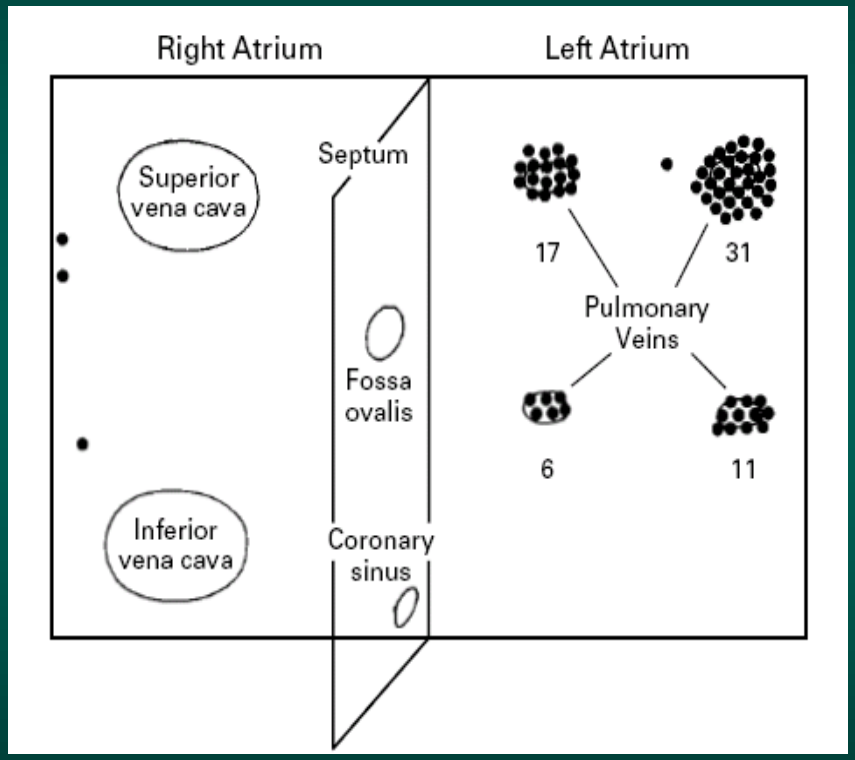


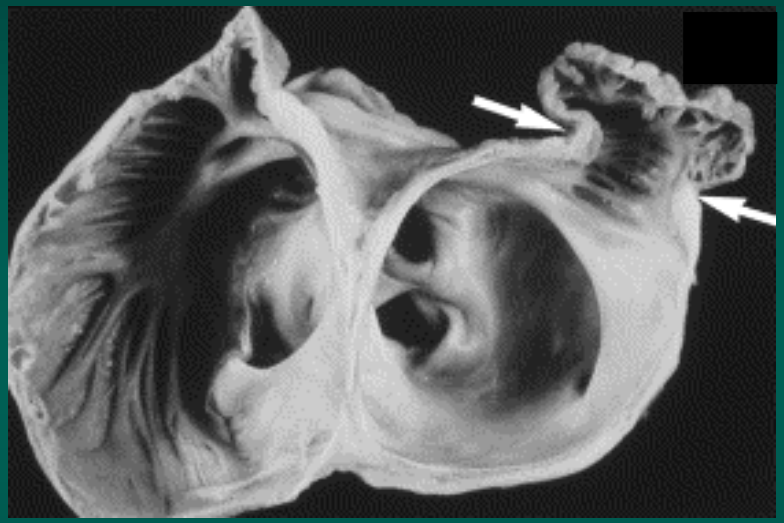
a – normalerweise Pulmonalvenen-Isolation; b – umfassendere LA ablation kann notwendig sein
c – Vorsicht bei KHK d – nicht empfohlen bei LVH

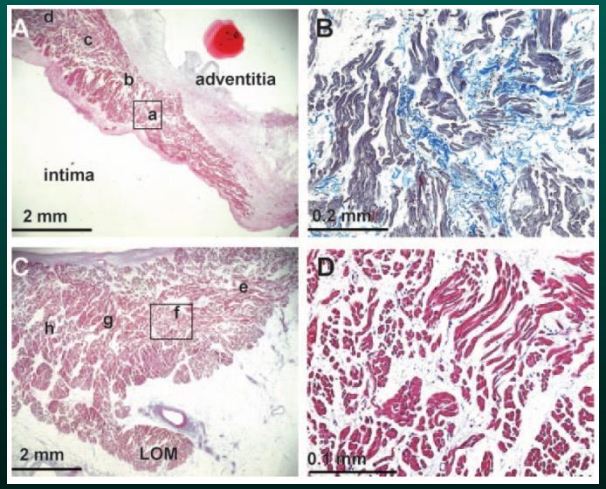
Eur Heart J doi:10.1093/eurheartj/ehs253

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.

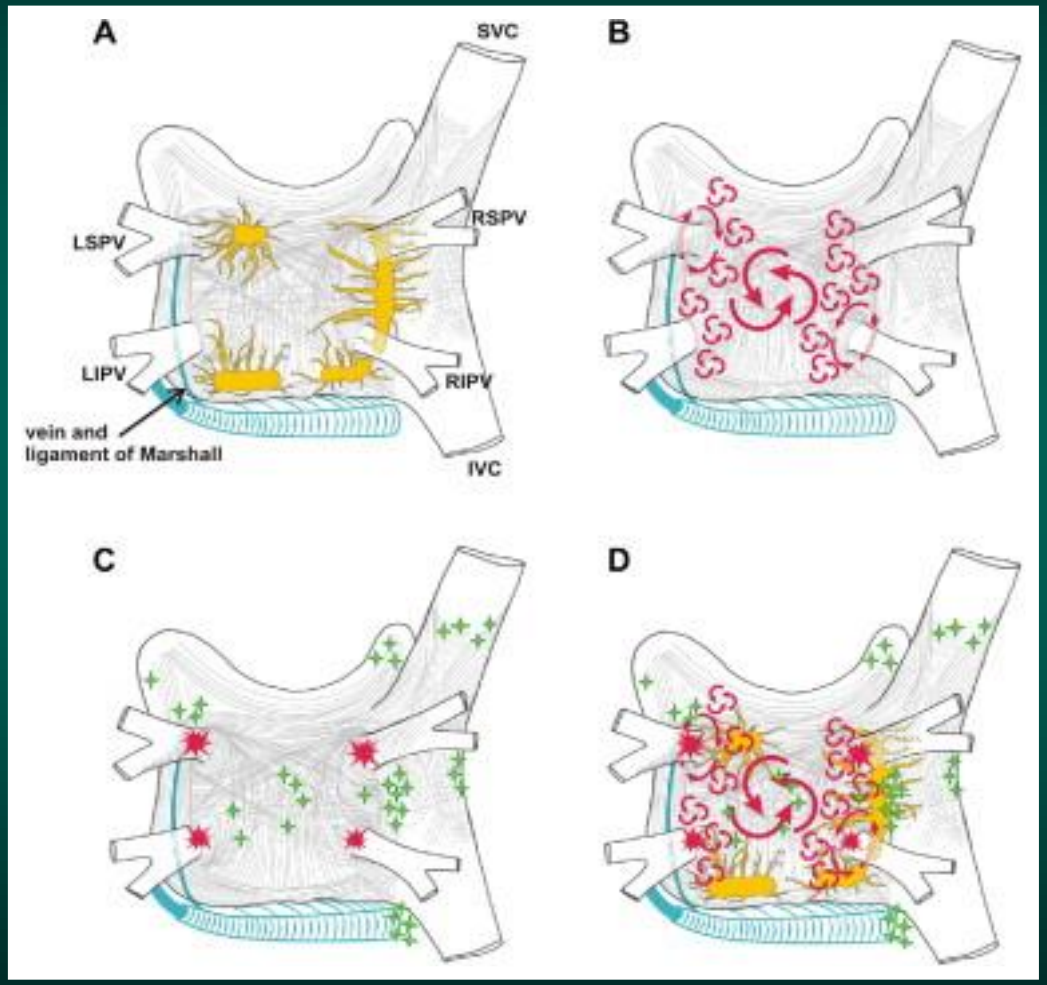






Haissaguerre et al. NEJM 1998

Complex pathophysiology of persistent AF

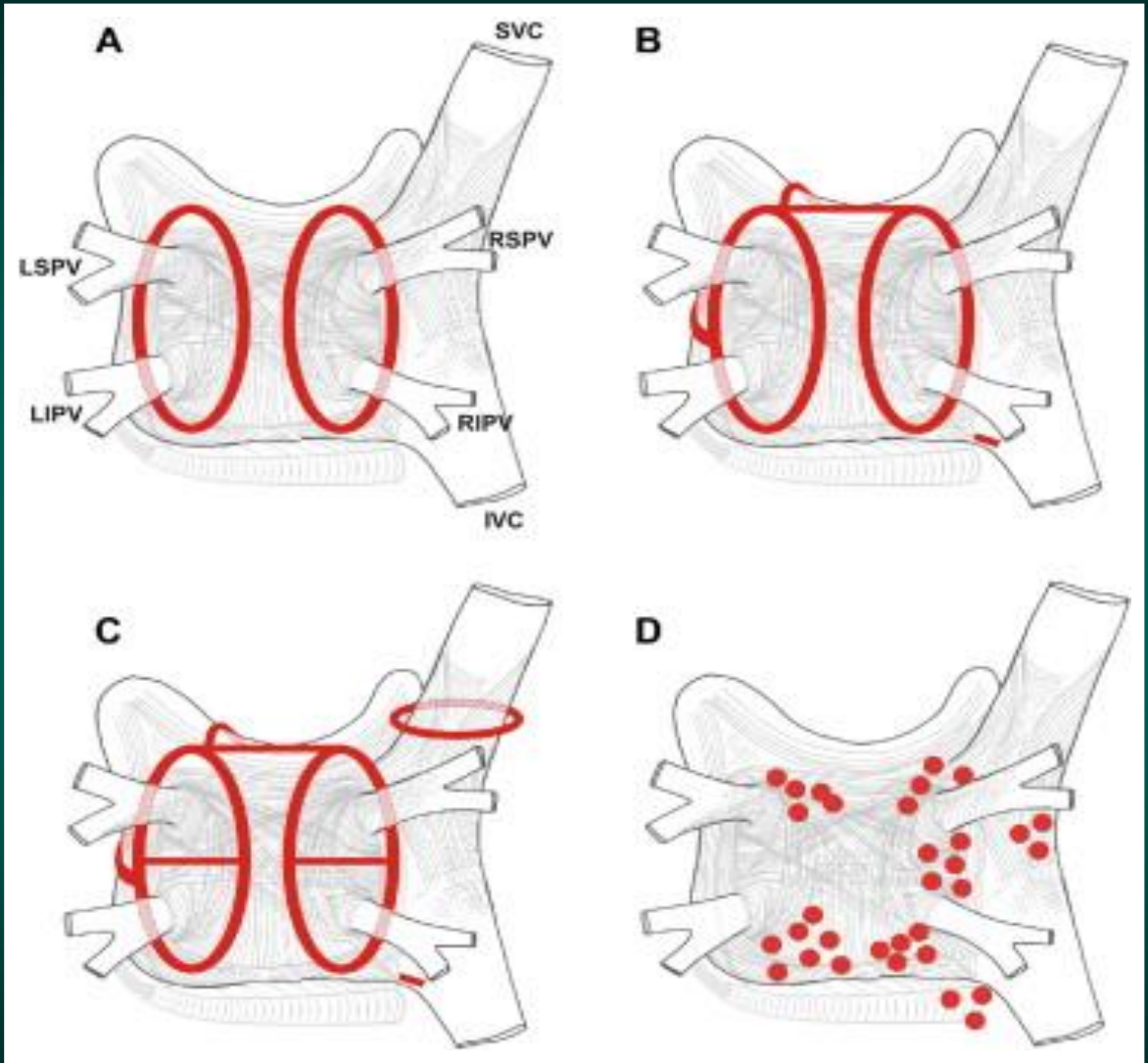


Involvement of RA in 20 – 25% of pts with persistent AF

Hocini et al; JACC 2010
Rostock et al; CircEP 2008
Haissaguerre et al, JCE2005

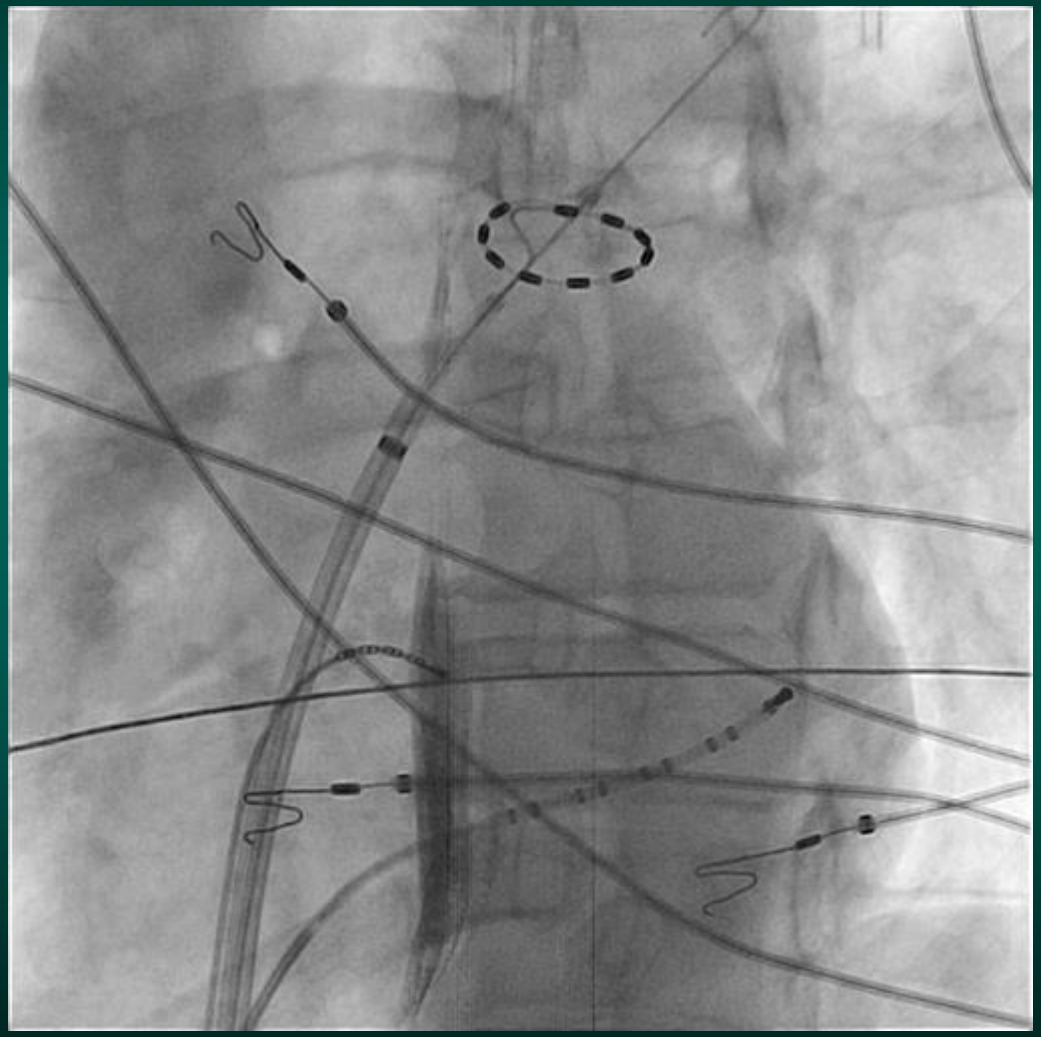
HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation. Heart Rhythm 2007; 4: 816-61.

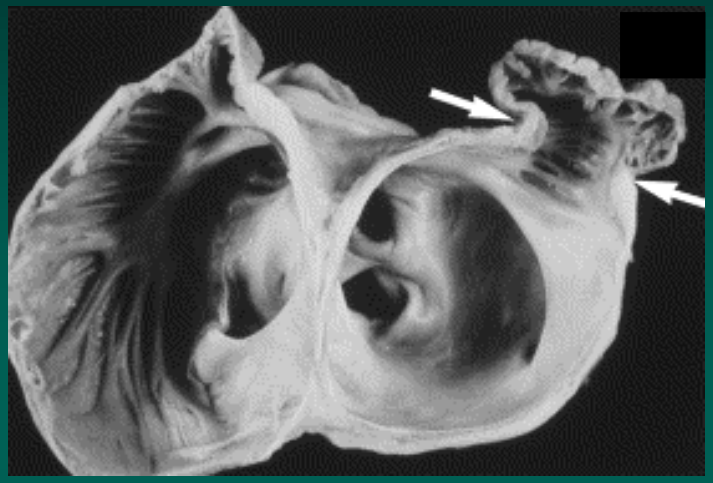
Lesion-Sets in persistent AF

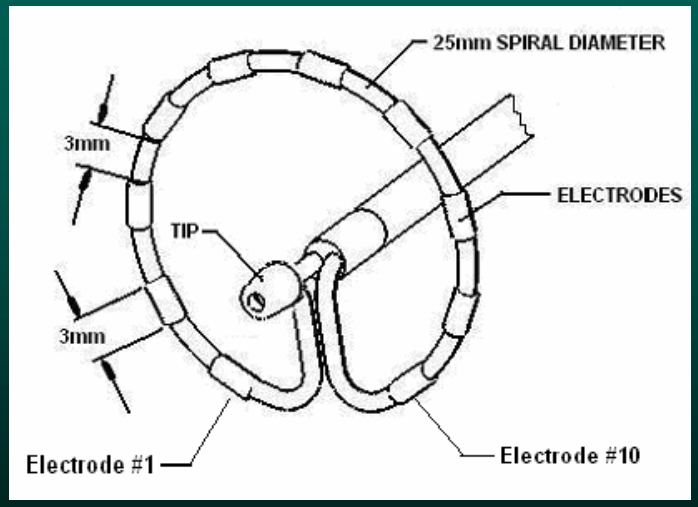


HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation. Heart Rhythm 2007; 4: 816-61.

Pulmonalvenenisolation

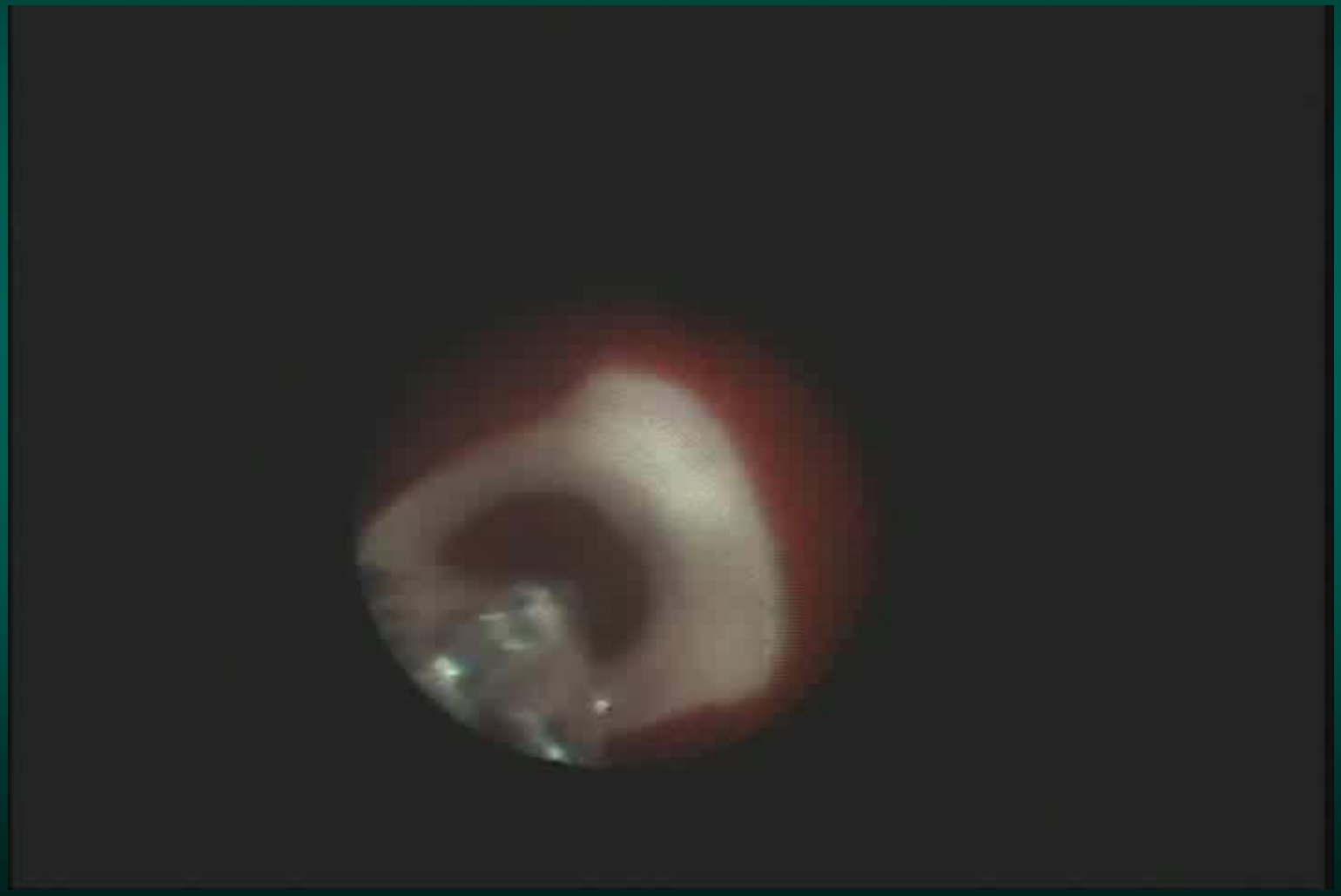




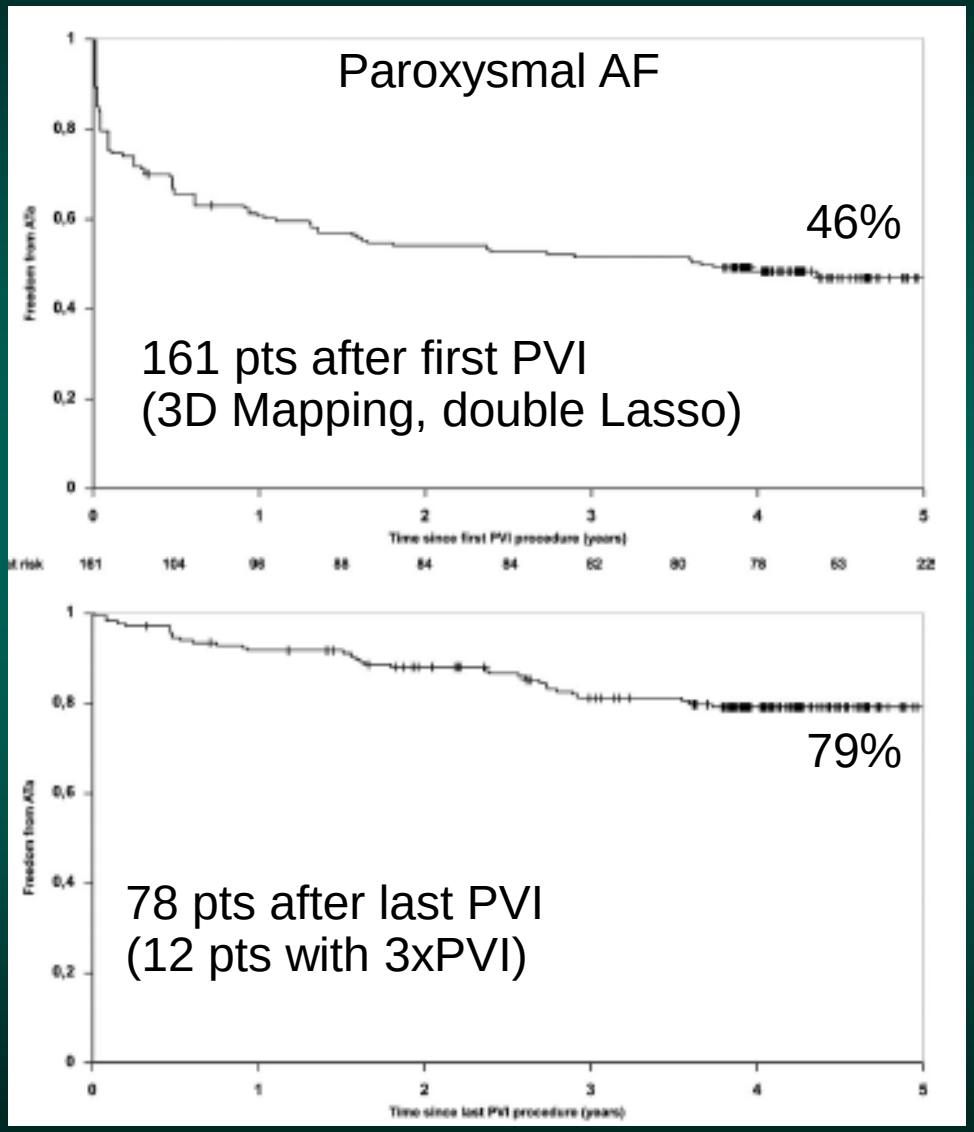


Endoskopische Laserablation

(St. Vincenz-Krankenhaus Paderborn)



Catheter ablation for atrial fibrillation: are results maintained at follow-up?



Ouyang et al. Circulation 2010

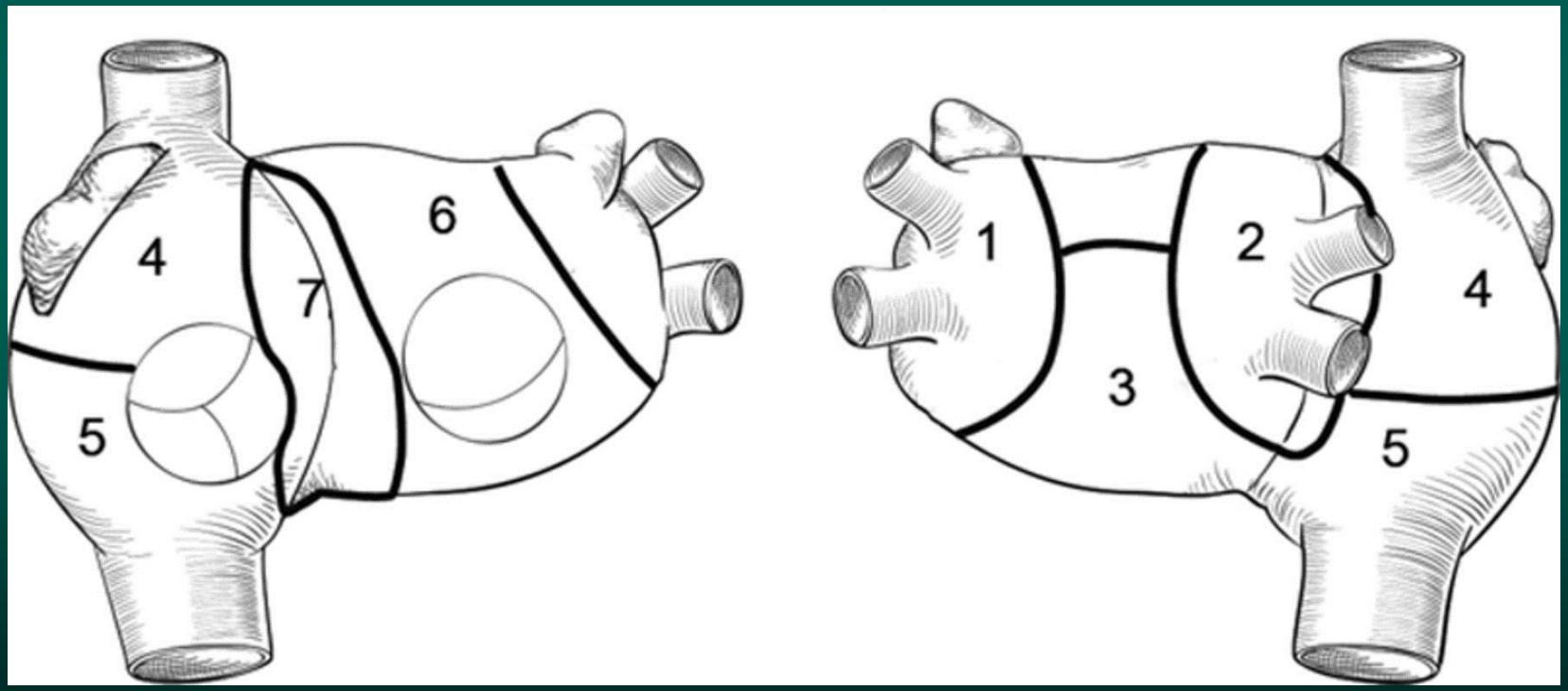
Driver Domains in Persistent Atrial Fibrillation CLINICAL PERSPECTIVE

by Michel Haissaguerre, Meleze Hocini, Arnaud Denis, Ashok J. Shah, Yuki Komatsu, Seigo Yamashita, Matthew Daly, Sana Amraoui, Stephan Zellerhoff, Marie-Quitterie Picat, Adam Quotb, Laurence Jesel, Han Lim, Sylvain Ploux, Pierre Bordachar, Guillaume Attuel, Valentin Meillet, Philippe Ritter, Nicolas Derval, Frederic Sacher, Olivier Bernus, Hubert Cochet, Pierre Jais, and Remi Dubois

Circulation
Volume 130(7):530-538
August 12, 2014

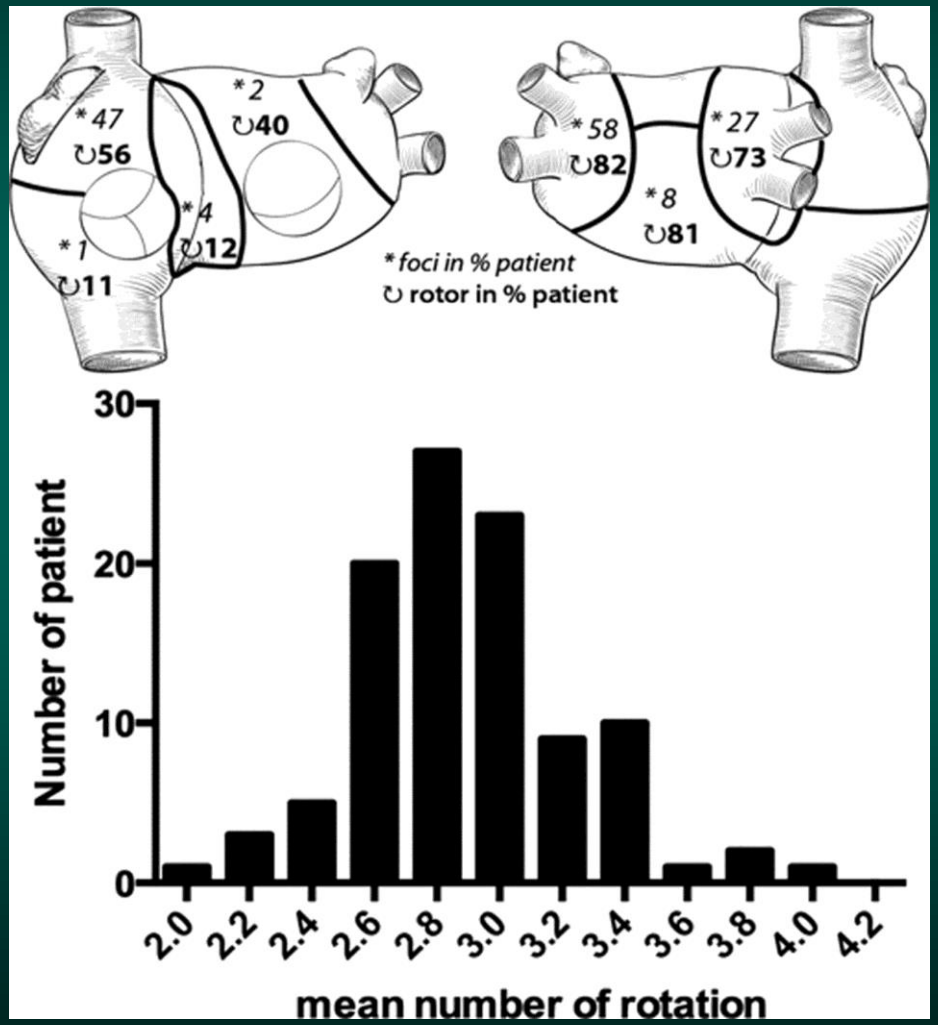
Biatrial schema is divided into 7 regions:

1. indicates the left pulmonary veins and left appendage
2. right pulmonary veins and posterior interatrial groove
3. inferior and posterior left atrium
4. upper half of right atrium and appendage
5. lower half of right atrium
6. anterior left atrium and roof
7. anterior interatrial groove).



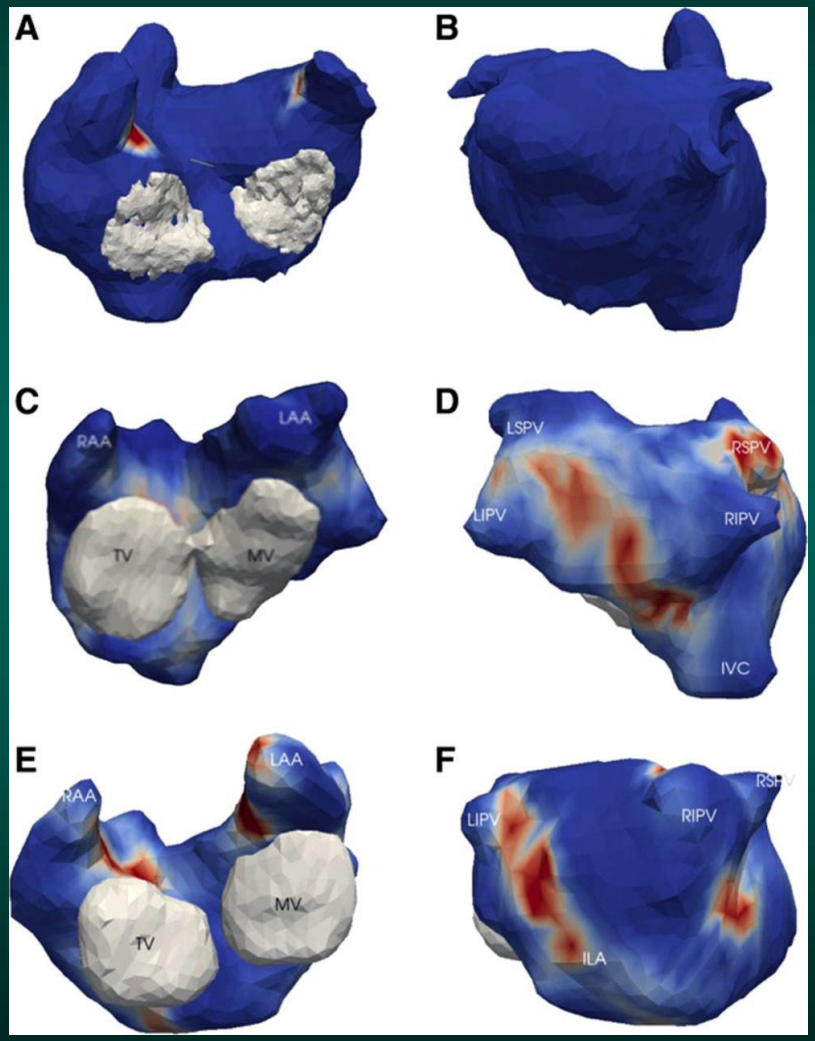
Haissaguerre M et al. Circulation. 2014;130:530-538

Distribution of drivers (focal breakthroughs, asterisk; reentry events, curved arrows) in 7 regions is reported as the percentage of patients.

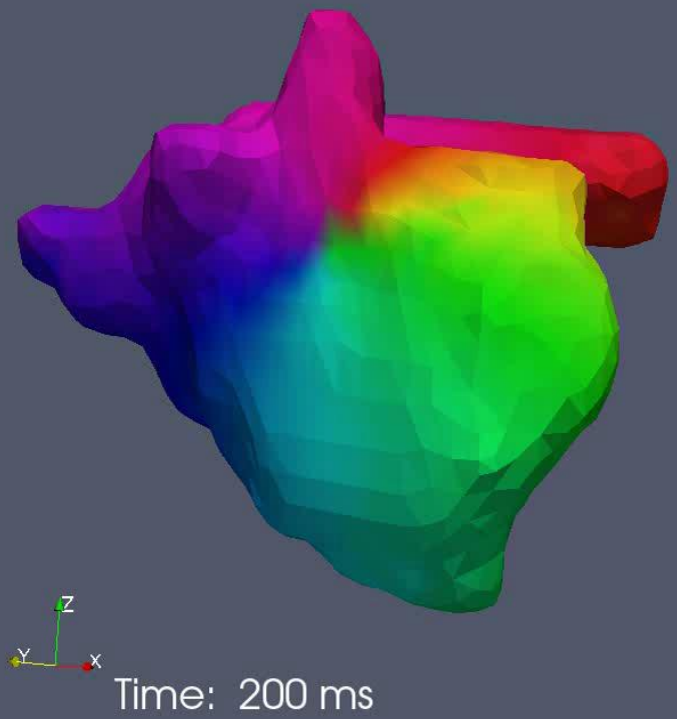


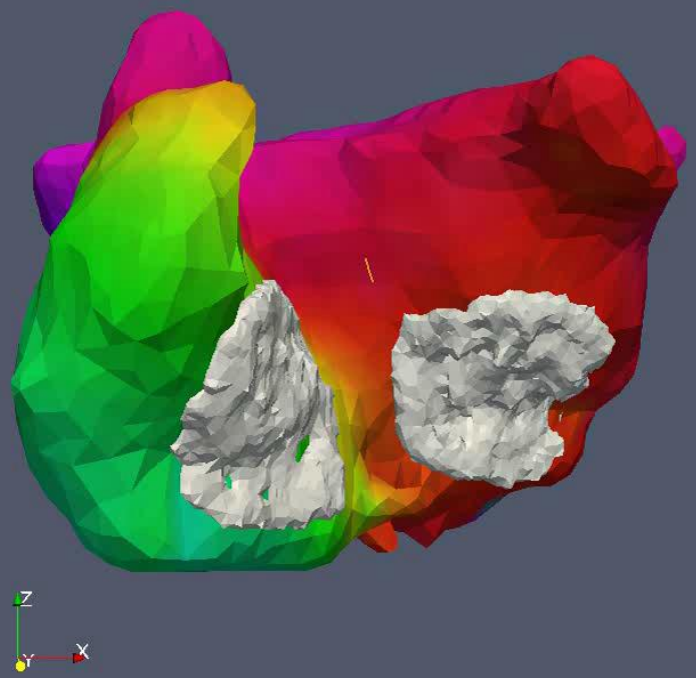
Haissaguerre M et al. Circulation. 2014;130:530-538

The arrhythmogenic driver-density maps of 3 patients showing 2-, 3-, and 5-driver regions, respectively.

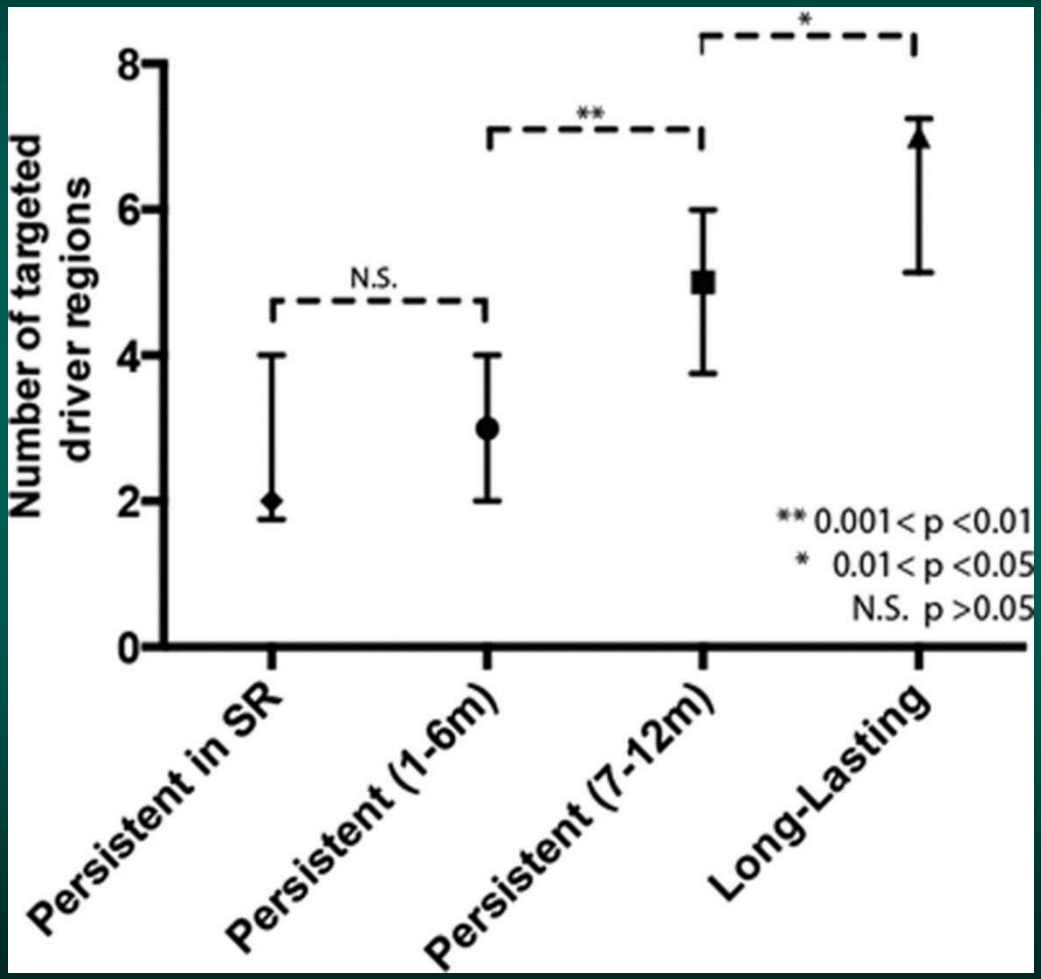


Haissaguerre M et al. Circulation. 2014;130:530-538


Z
Y
X
Time: 200 ms


Z
Y
X

The median (first and third quartiles) number of driver regions ablated to terminate AF increases with the duration of persistent AF. Two regions were targeted in patients presenting in sinus rhythm (SR).



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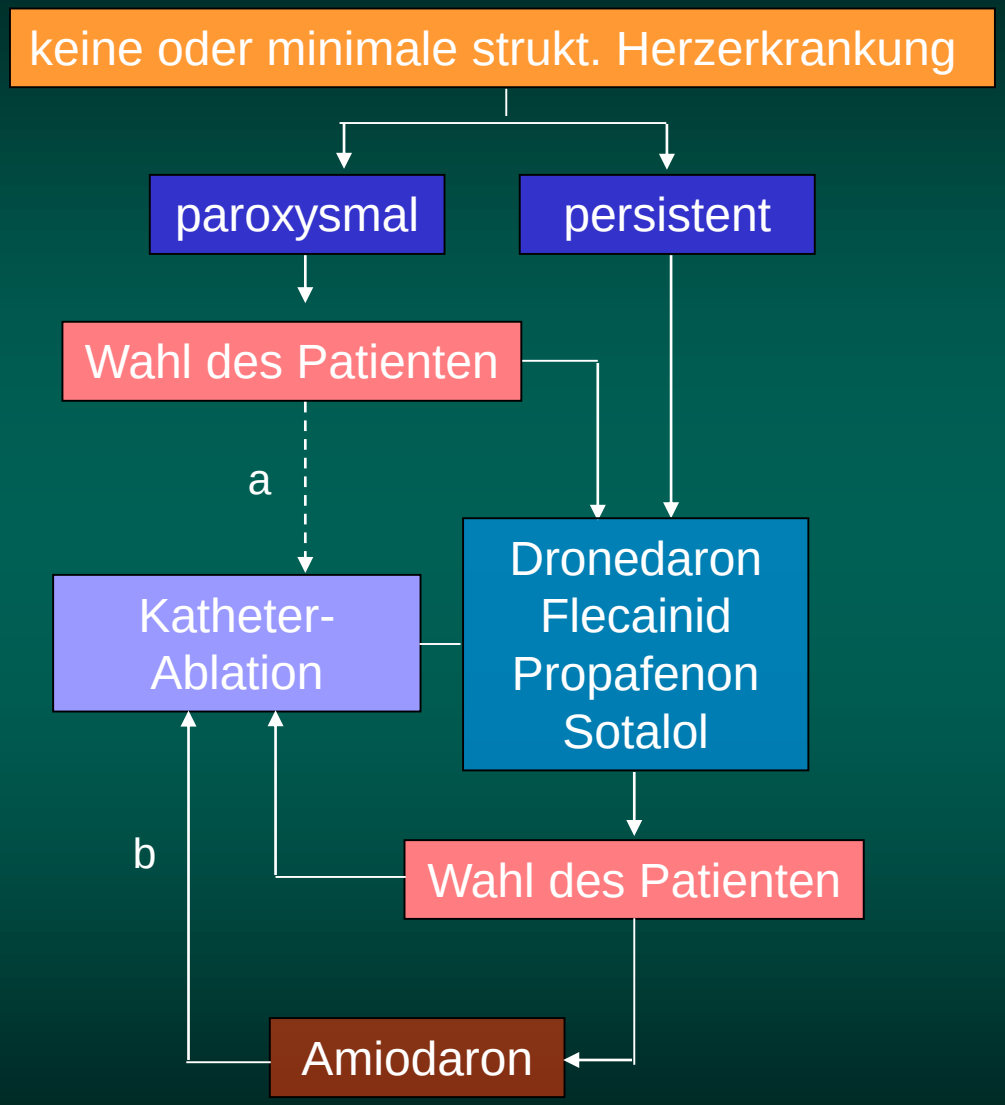
Antiarrhythmische Medikation und/oder linksventrikuläre Ablation zur Rhythmuskontrolle bei Vorhofflimmern



a – normalerweise Pulmonalvenen-Isolation; b – umfassendere LA ablation kann notwendig sein
c – Vorsicht bei KHK d – nicht empfohlen bei LVH

Eur Heart J doi:10.1093/eurheartj/ehs253

ladwig@helmholtz-muenchen.de

QUINTA: Quality-of-Live-Inventory-Tailored-for-Atrial-Fibrillation Patients

Vital exhaustion: feelings of sustained fatigue, emotional burn-out, feelings of dejection as result of prolonged exposure to various sources of life stress.

Depression, depressed mood: negative affectivity, reduced drive, endocrine and inflammatory perturbations, cognitive impairments

Ilness intrusiveness: high impact on daily living, being preoccupied by the disease condition, pessimistic outlook on the future course of disease, negative self perceived health

Well-being: components of positive mood; vitality, general interests, positive drive

Prospective Assessment of Short- and Long-Term Quality of Life After Ablation for Atrial Fibrillation

STEPHANIE FICHTNER, M.D.,* ISABEL DEISENHOFER, M.D.,*
SIBYLLE KINDSMÜLLER, M.D.,† MARIJANA DZIJAN-HORN, M.D.,*
STYLIANOS TZEIS, M.D.,* TILKO REENTS, M.D.,* JINJIN WU, M.D.,*
HEIDI LUISE ESTNER, M.D.,* CLEMENS JILEK, M.D.,* SONIA AMMAR, M.D.,*
SUSANNE KATHAN, DIPL.BIOL.,* GABRIELE HESSLING, M.D.,* and
KARL-HEINZ LADWIG, PH.D.†

Results: **QoL was improved significantly 3 months after ablation in all patients (regardless of ablation success or AF type) and stayed significantly improved after a median of 4.3±0.5 years (AFSS, AFSC, WHO, MDI, VE, PE (all P < 0.001), and SV (P = 0.007)). Patients who had a successful ablation improved significantly more than patients with an unsuccessful ablation in the AFSS, AFSC, and MDI questionnaire (delta change from baseline to long-term follow-up P = <0.001, P = <0.001, and P = 0.039, respectively).**

Quality of life questionnaires results				
N, mean (SD)	Baseline	3 months	4.3 years	p-value
Atrial fibrillation severity scale	22.3 (4.8)	17.4 (4.8)	15.6(6.2)	<0.0001
AF Symptom Checklist	14.6 (8.8)	8.8 (7.3)	8.0 (9.0)	<0.0001
Perceived impact of disease	19.6 (5.5)	18.9 (5.7)	11.8 (3.6)	<0.0001
WHO-Five Well Being Index	49.5 (24.1)	61.7 (23.6)	65.7 (24)	<0.0001
Major Depression Index	13.6 (8.6)	10.4 (8.9)	9.0 (10)	<0.0001
Sleep and vegetative exhaustion	5.9 (1.8)	6.3 (7.8)	6.5 (1.9)	<0.0001
Vital exhaustion	8.7 (3.2)	6.9 (2.7)	6.3 (3.1)	<0.0001

(J Cardiovasc Electrophysiol, Vol. 23, pp. 121-127, February 2012)

Angiotensin II-Antagonist in Paroxysmal Atrial Fibrillation (ANTIPAF) Trial

Andreas Goette, MD; Norbert Schön, MD; Paulus Kirchhof, MD; Günter Breithardt, MD; Thomas Fetsch, MD; Karl Georg Häusler, MD; Helmut U. Klein, MD; Gerhard Steinbeck, MD; Karl Wegscheider, PhD; Thomas Meinertz, MD

(*Circ Arrhythm Electrophysiol*. 2012;5:43-51.)

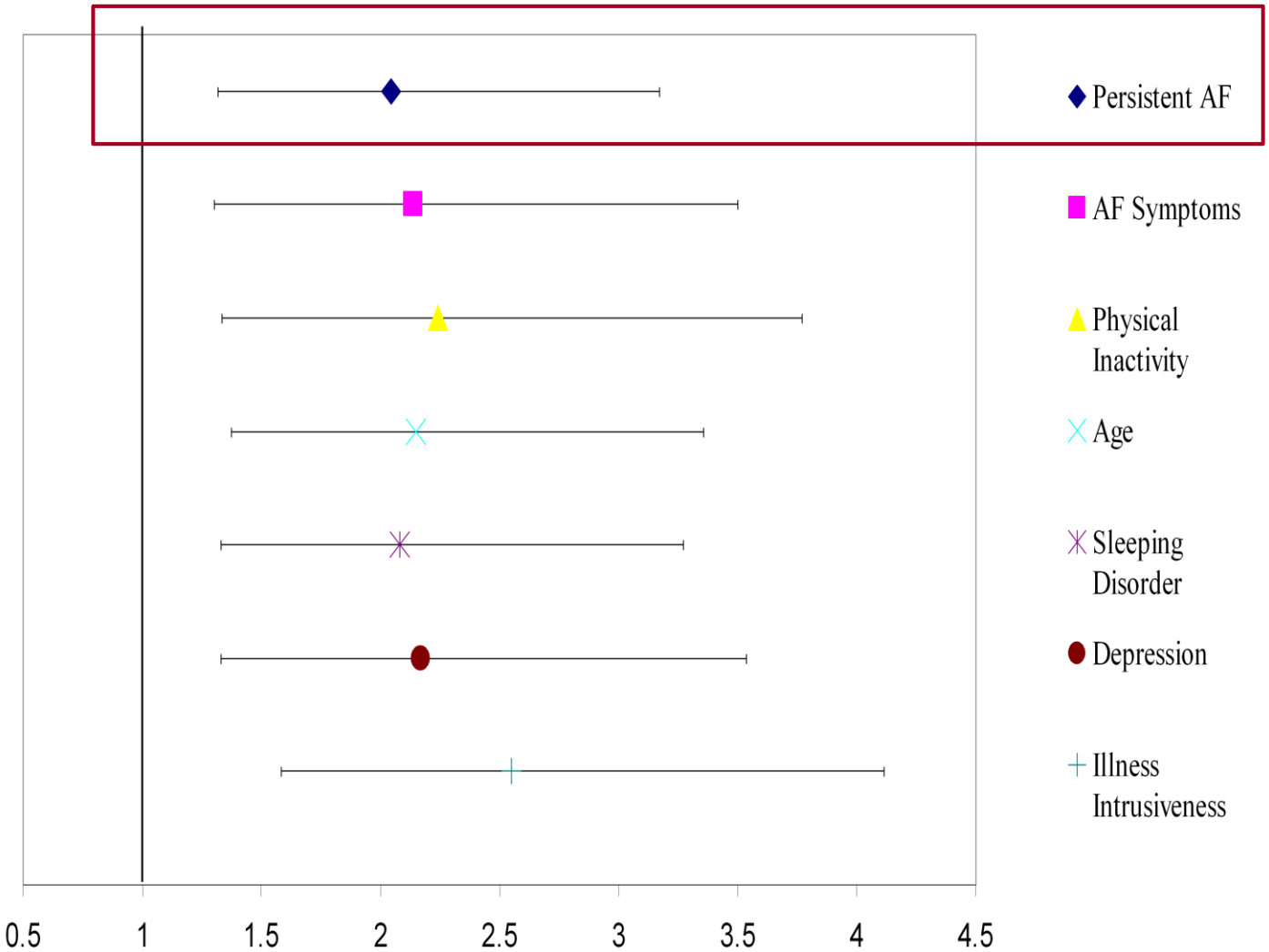
Short-term versus long-term antiarrhythmic drug treatment after cardioversion of atrial fibrillation (Flec-SL): a prospective, randomised, open-label, blinded endpoint assessment trial

Paulus Kirchhof, Dietrich Andresen, Ralph Bosch, Martin Borggrefe, Thomas Meinertz, Ulli Parade, Ursula Ravens, Alexander Samol, Gerhard Steinbeck, Andras Treszl, Karl Wegscheider, Günter Breithardt

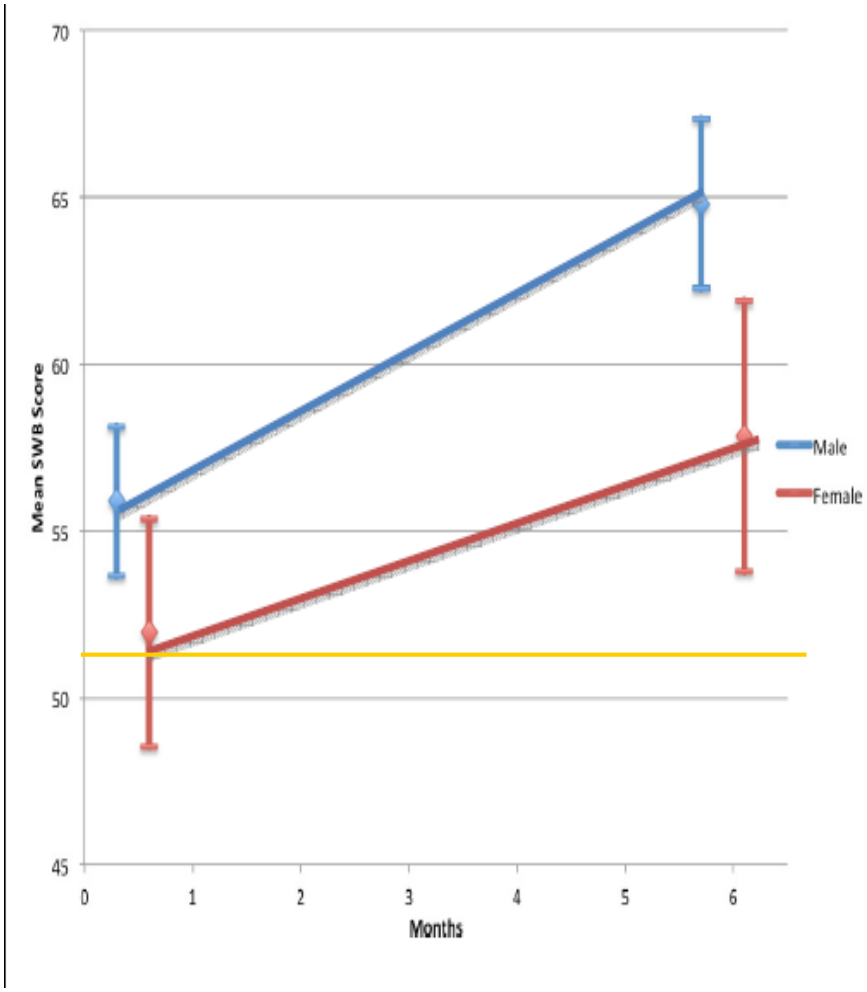
Lancet 2012; 380: 238–46

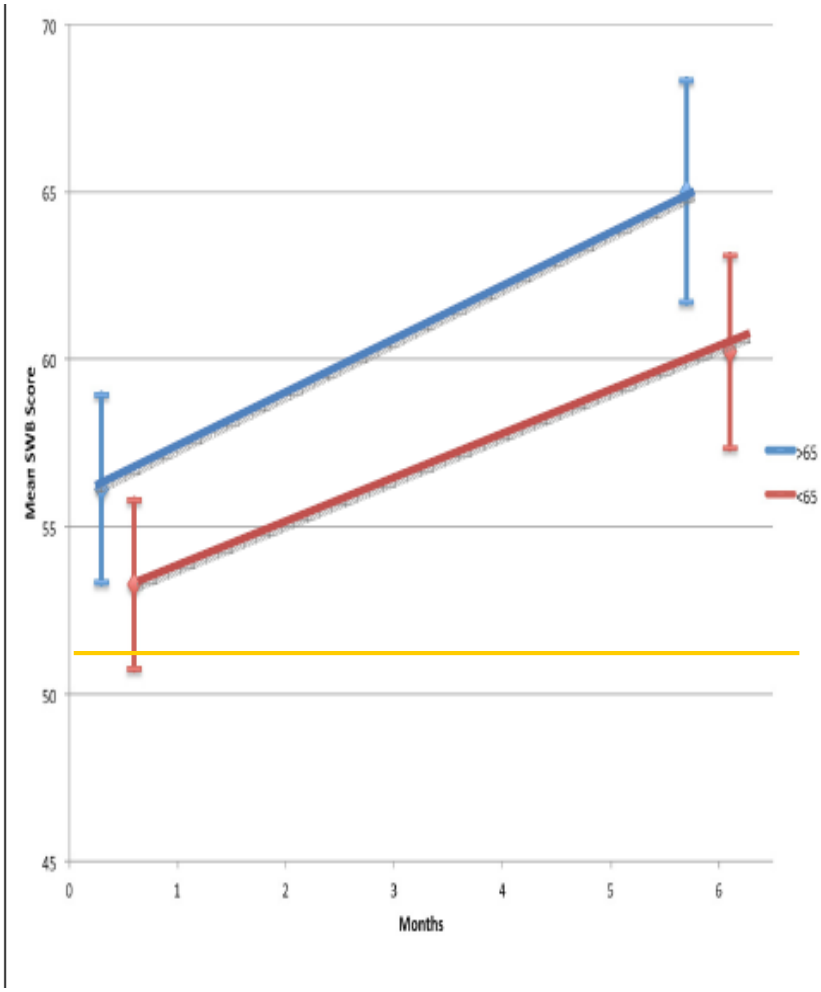
Contributors to Quality of Life (PC) in AF patients at baseline.

Findings from a multivariate regression analysis

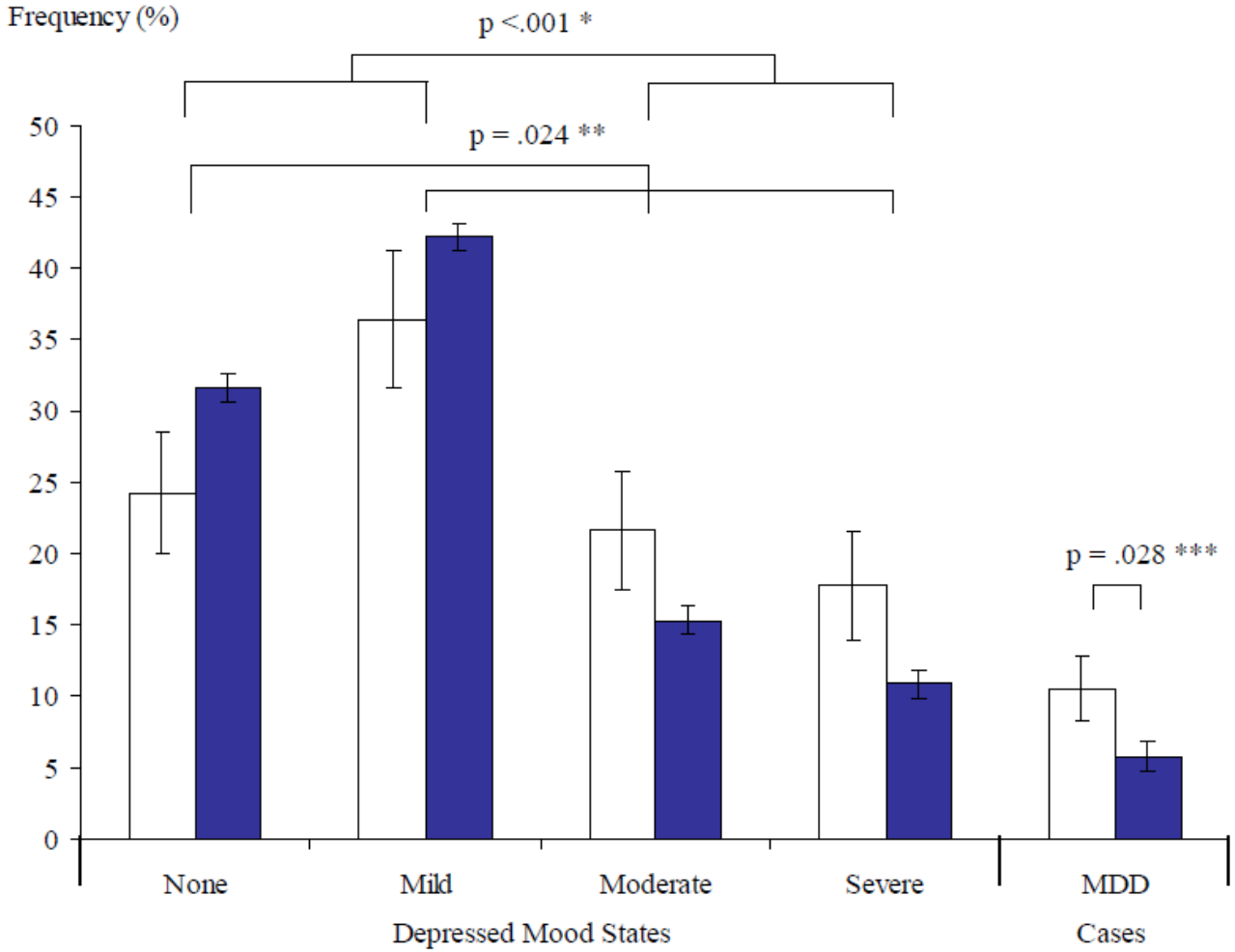


Subjective Wellbeing (SWB): Mean Scores at baseline and at 6 months follow-up, stratfied for sex and age (65 years)





Prevalence of Depressed Mood Severity and Caseness of MDD stratified for AF Type



□ Persistent
■ Paroxysmal

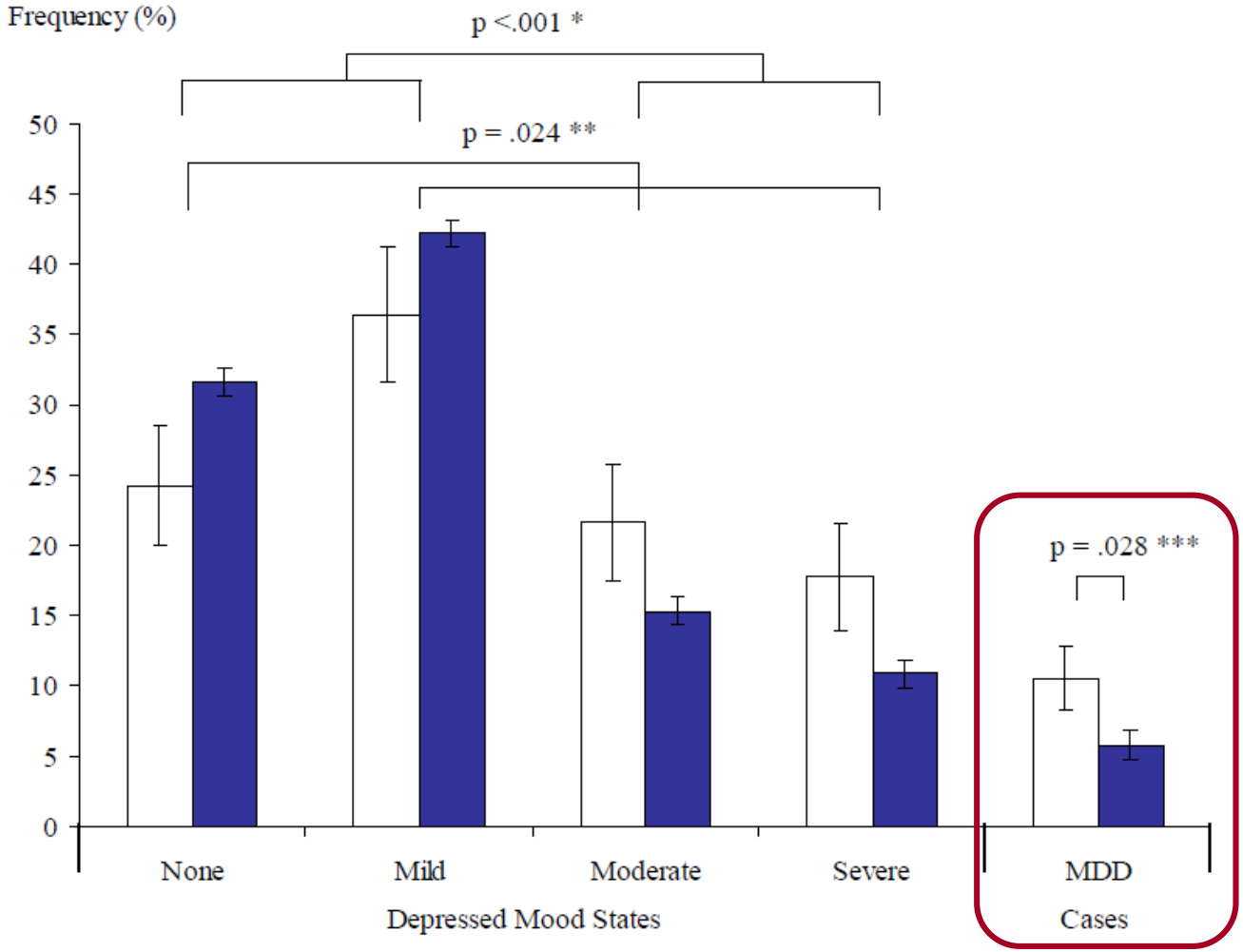
* Mantel Haenszel p value for the association between AF type and none/mild vs moderate/severe depressed mood.

** Mantel Haenszel p value for the association between AF type and none vs mild/moderate/severe depressed mood

*** Mantel Haenszel p value for the association between AF type and MDD

von Eisenhart Rothe, Goette& Ladwig EUROPACE 2014

Prevalence of Depressed Mood Severity and Caseness of MDD stratified for AF Type



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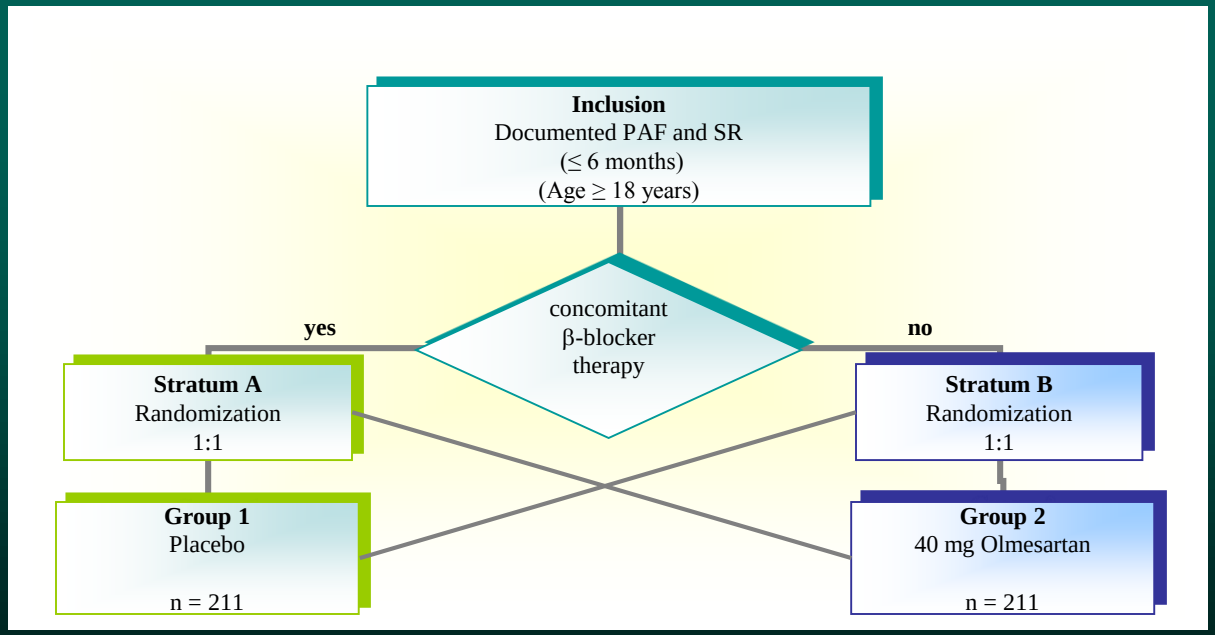
von Eisenhart Rothe, Goette& Ladwig EUROPACE 2014

ANTIPAF

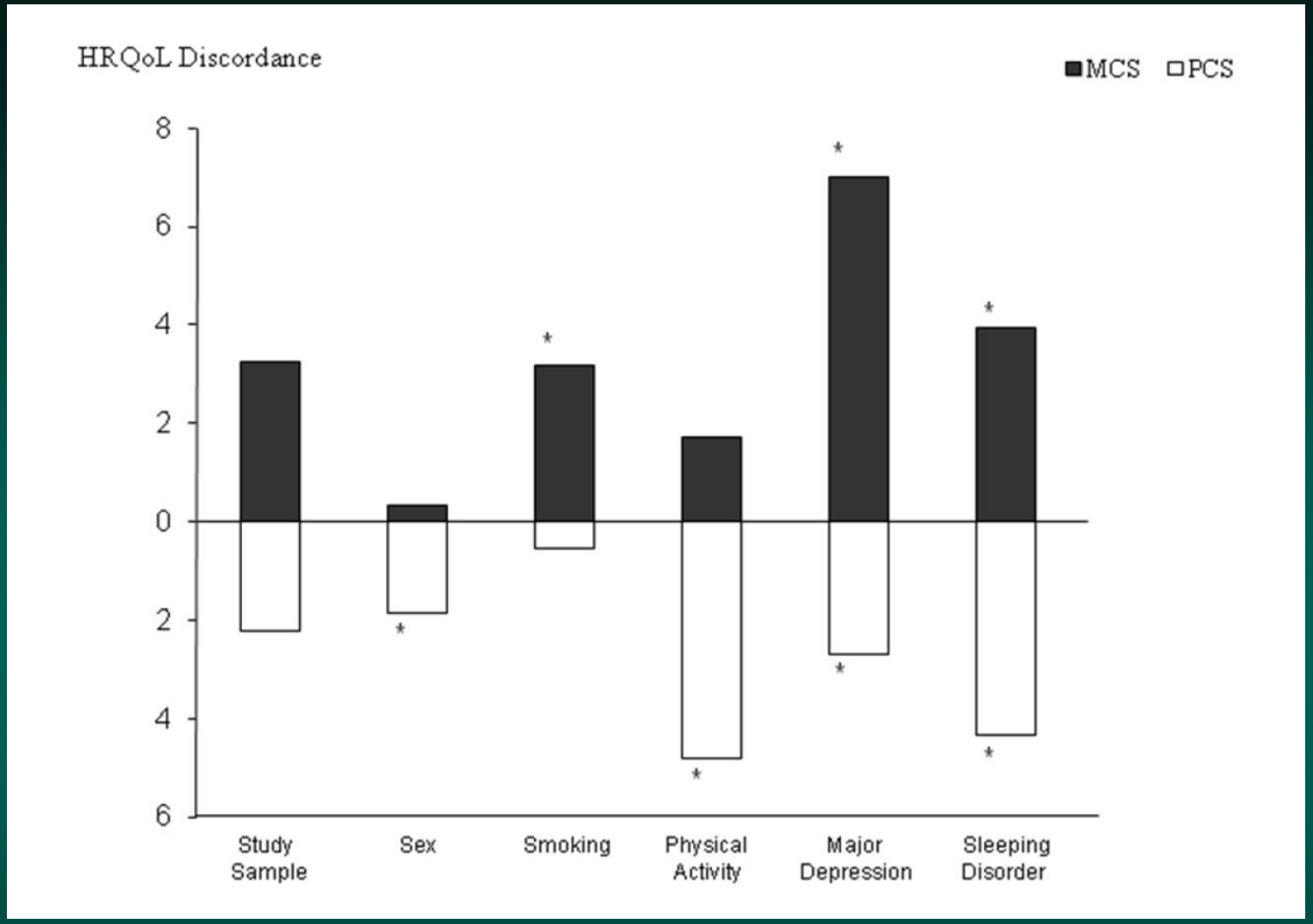
„Angiotensin II-Antagonist in Paroxysmal Atrial Fibrillation Trial“

Prospektive, randomisierte, doppelblinde, multizentrische Studie

Substudie: Kann ein Arzt die QoL seiner Patienten schätzen?



BMBF-Kompetenznetz „Vorhofflimmern“



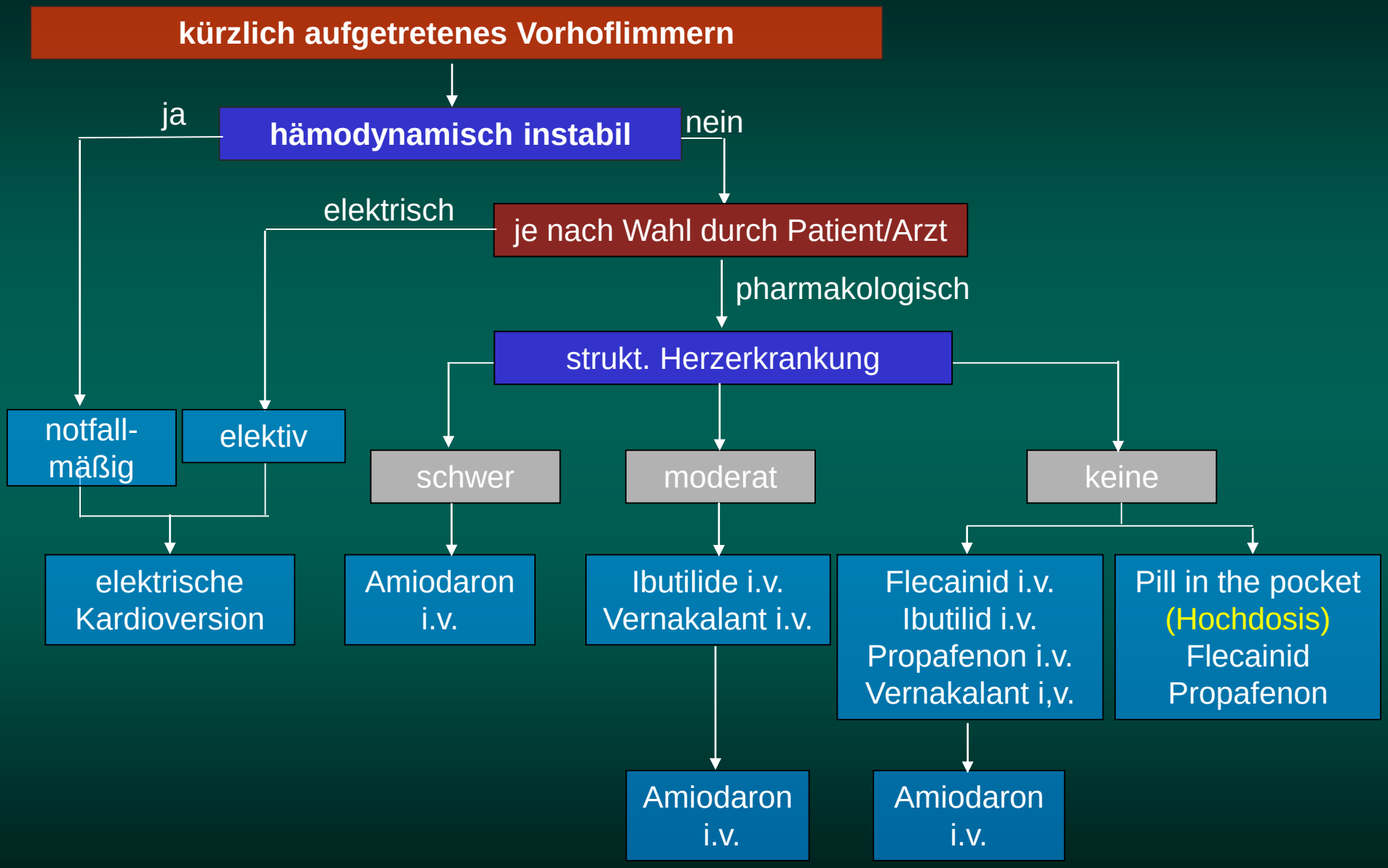
Conclusions: In patients with AF, even in the absence of significant concomitant cardiac diseases, depression, followed by sleeping disorder and physical inactivity were significantly associated with discordance. These findings should be considered by physicians when choosing treatment strategies

von Eisenhart Rothe,…, Ladwig and Goette. Am Heart J 2013; 166(3):589-96

ESC AF Guidelines 2012

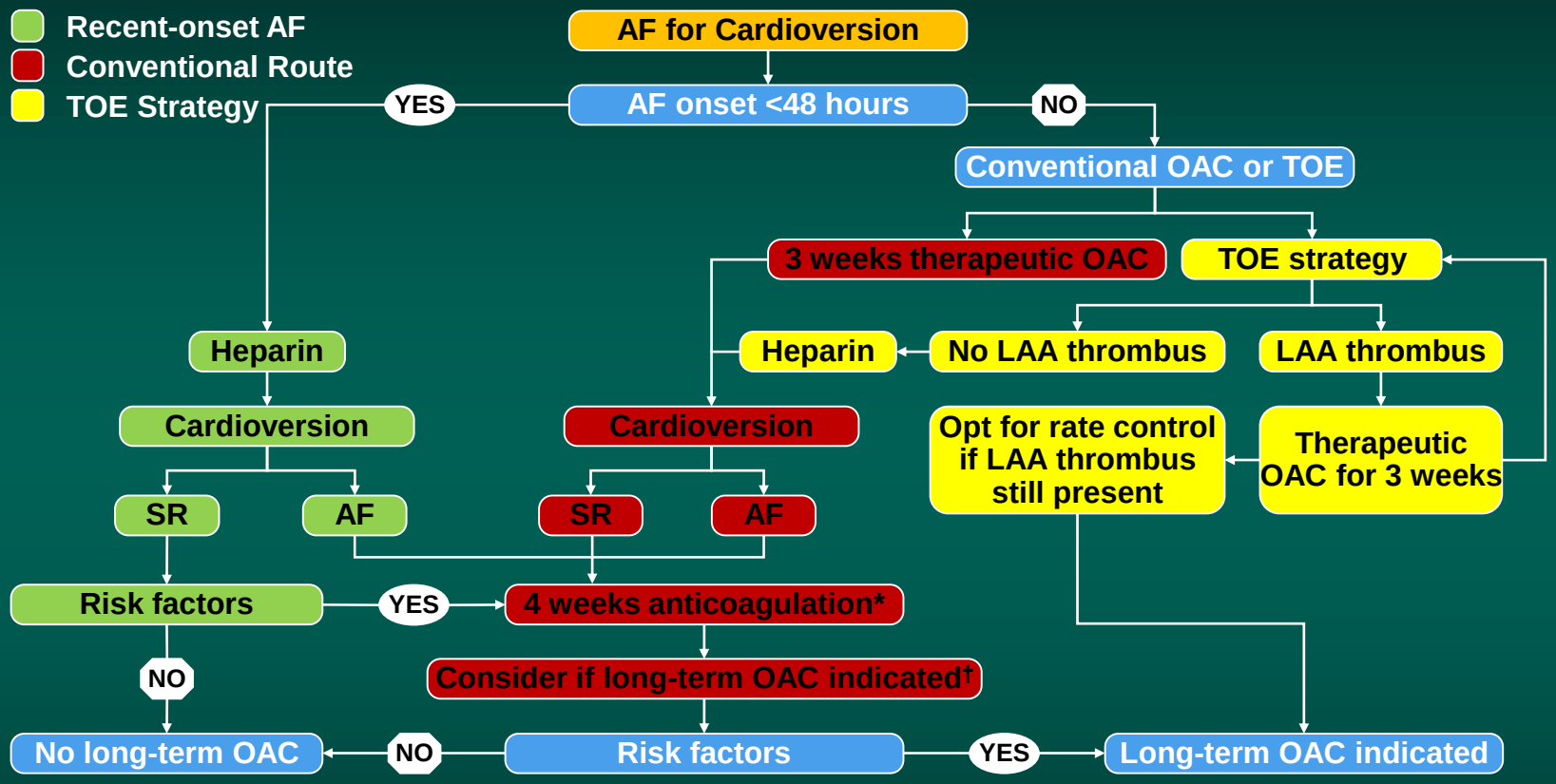
Cardioversion

Indikationen für elektrische und pharmakologische Kardioversion und Wahl des Anti-arrhythmikums zur Kardioversion bei Patienten mit kürzlich aufgetretenem Vorhofflimmern



Eur Heart J doi:10.1093/eurheartj/ehs253

Cardioversion Strategy in AF



*Anticoagulation should normally be continued for 4 weeks after a cardioversion attempt except when AF is recent onset and no risk factors are present

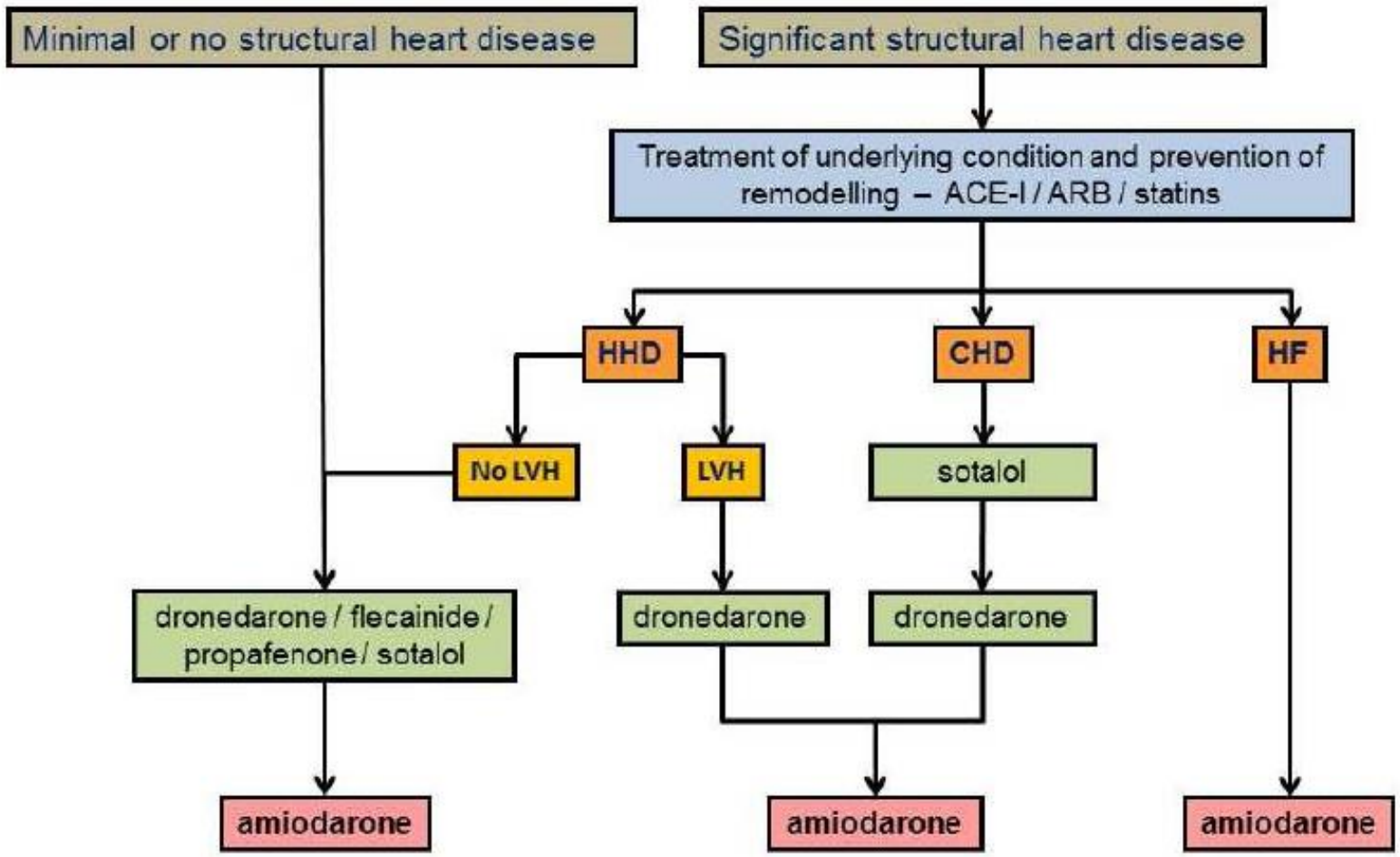
†Long-term OAC if stroke risk factors and/or risk of AF recurrence/presence of thrombus

AF=atrial fibrillation; LAA=left atrial appendage; OAC=oral anticoagulant; SR=sinus rhythm; TOE = transoesophageal echocardiography

ESC AF Guidelines. Eur Heart J 2010;31:2369–2429

Updated AF-Guideline 2012

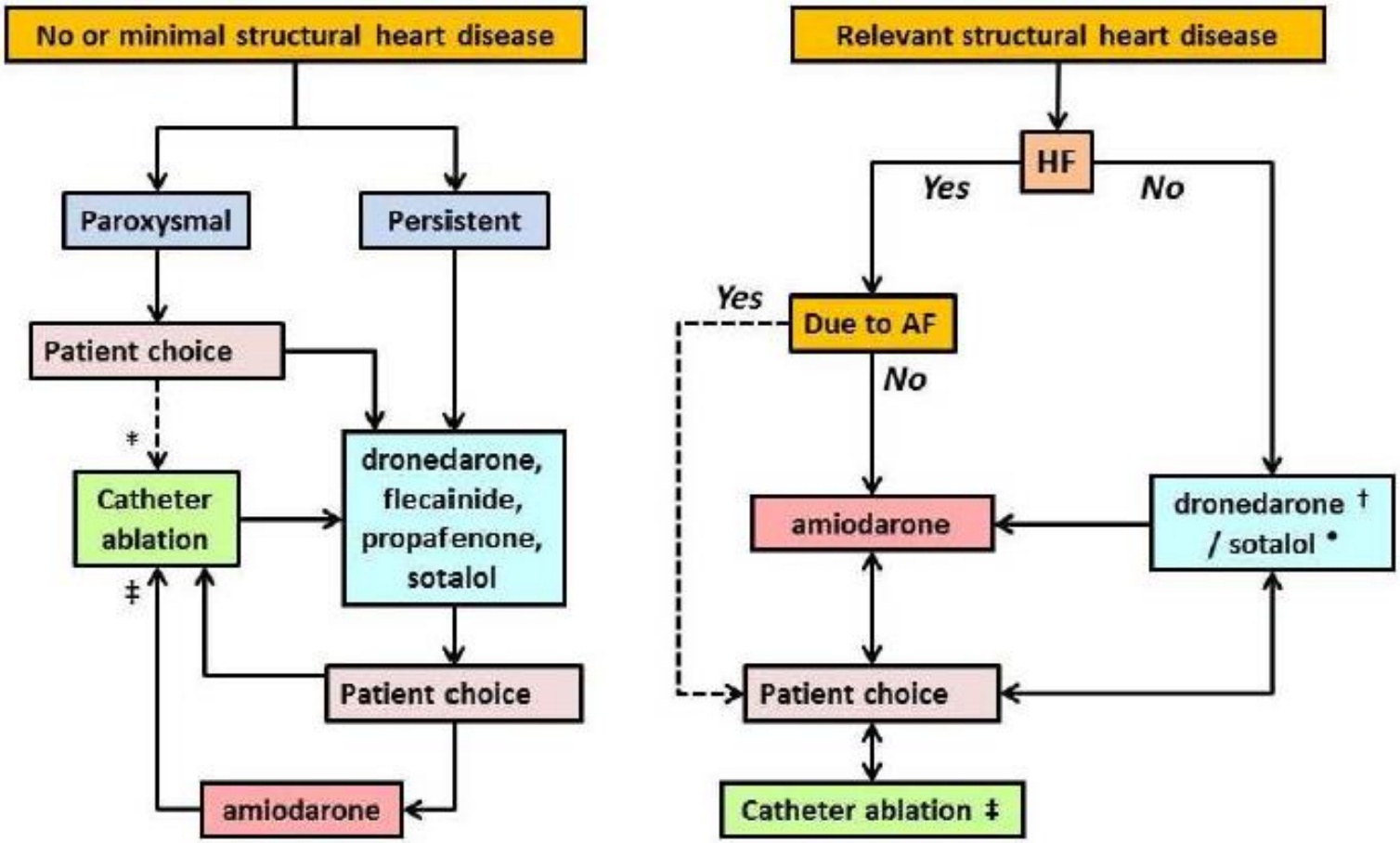
Figure 4 Antiarrhythmic drug management of non-permanent AF



Camm et al. ESC 2012

Updated AF-Guideline 2012

Figure 5 Antiarrhythmic drugs and/or left atrial ablation for rhythm control in AF



* = usually pulmonary vein isolation is appropriate ‡ = more extensive left atrial ablation may be needed;
HF = heart failure; † = caution with coronary heart disease; • = contraindicated with left ventricular hypertrophy.

Vielen Dank !

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