DIU HTA

Fibrillation Auriculaire et Hypertension Artérielle

Vendredi 25 Janvier 2019

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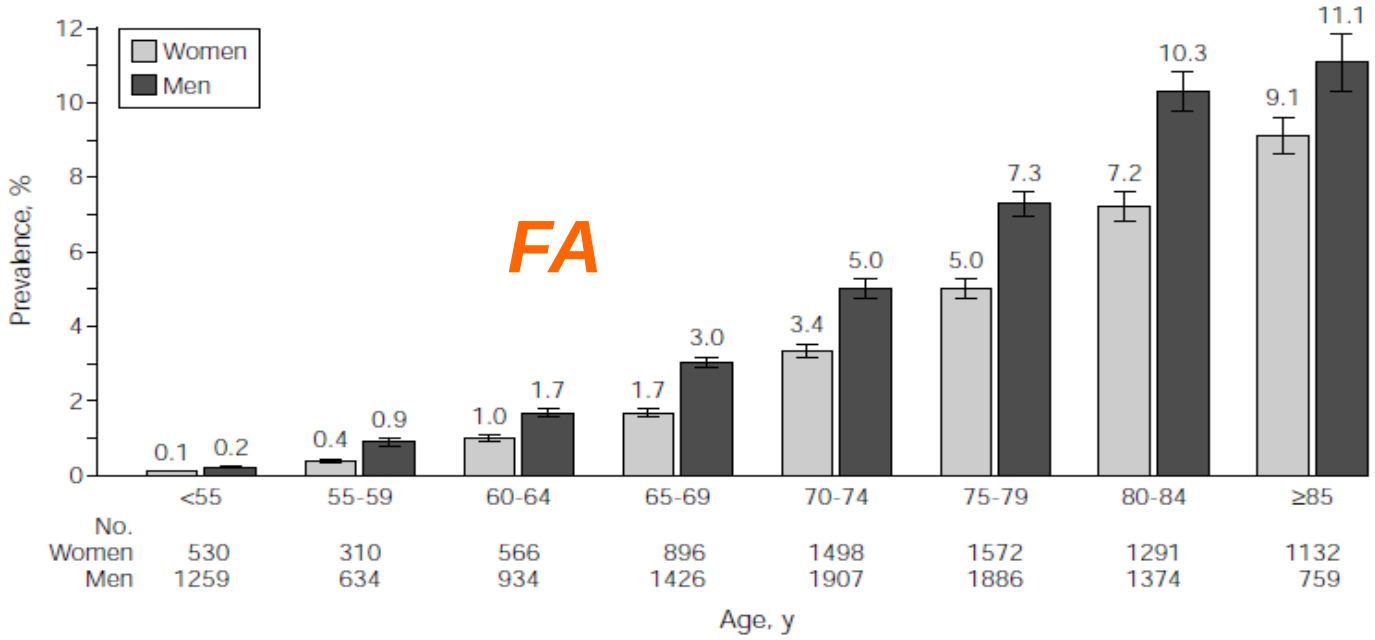
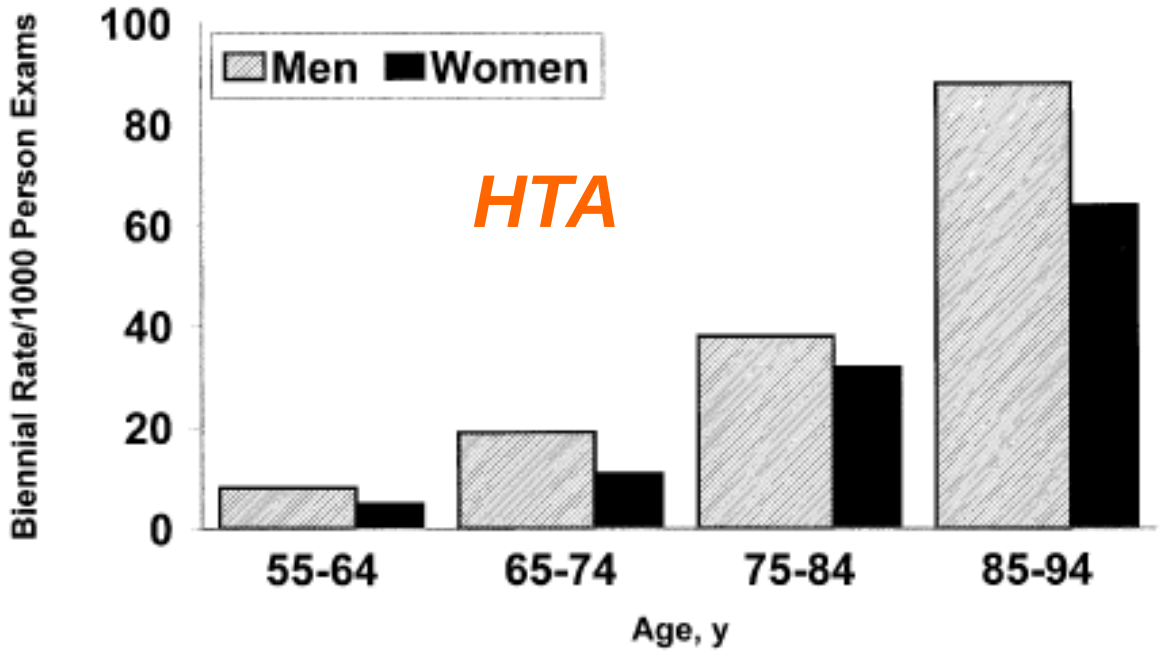
CHU GRENOBLE ALPES



Go et al, JAMA 2001



Kannel et al,
Am J Cardiol 1998

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Risk factors for Atrial fibrillation (Framingham Heart study)

CHU GRENOBLE ALPES

Risk Factors	Age-Adjusted OR		Risk Factor–Adjusted OR	
	Men	Women	Men	Women
Cigarettes	1.0	1.4†	1.1	1.4
Diabetes	1.7‡	2.1§	1.4†	1.6‡
ECG–LVH	3.0§	3.8§	1.4	1.3
Hypertension	1.8§	1.7§	1.5‡	1.4†
BMI	1.03	1.02	—	—
Alcohol	1.01	0.95	—	—

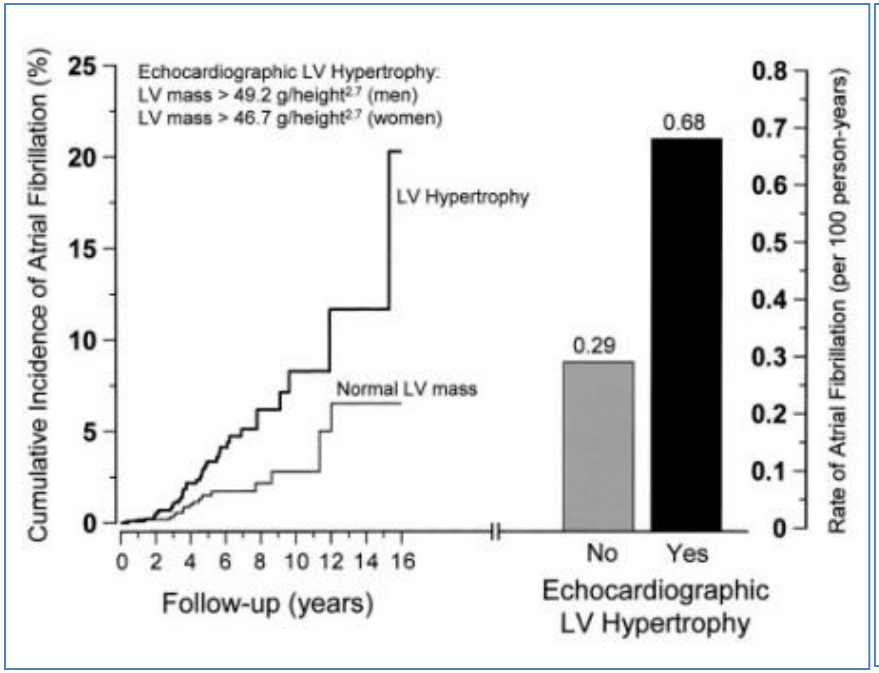
BMI = body mass index; ECG–LVH = echocardiographic left ventricular hypertrophy; OR = odds ratio.

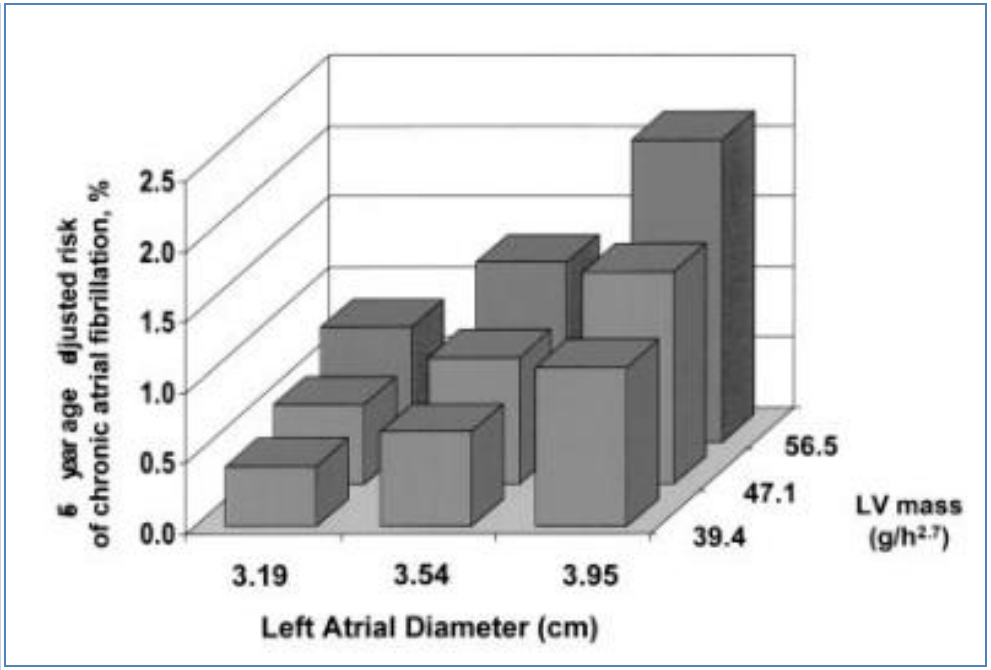
*2-year pooled logistic regression; †$p < 0.05$; ‡$p < 0.01$; §$p < 0.001$.

Adapted from *JAMA*.[7]

Kannel et al, Am J Cardiol 1998

2482 hypertendus en rythme sinusal → suivi 16 ans max





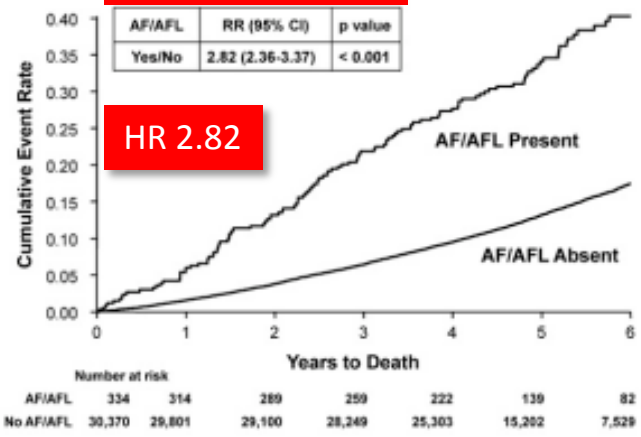
Nouvelle FA
0,46 / 100 année-patients

Verdecchia et al, Hypertension 2003

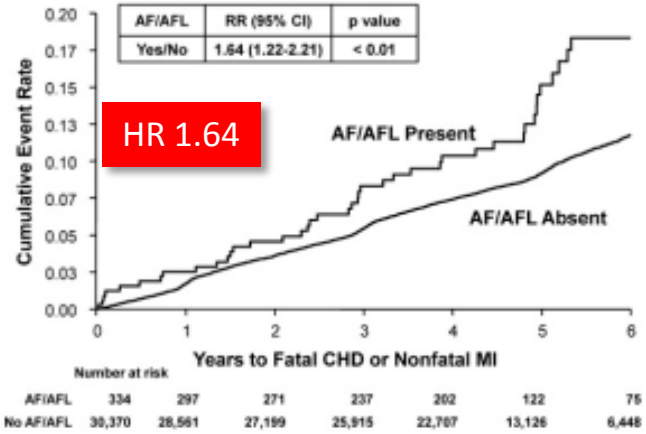
Etude ALLHAT

(N=39056 pts / FA = 1.1% à l'entrée)

Mortalité globale

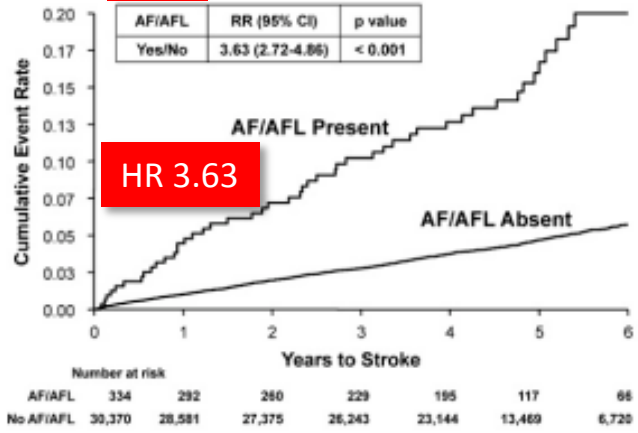


Mort par coronaropathie / IDM

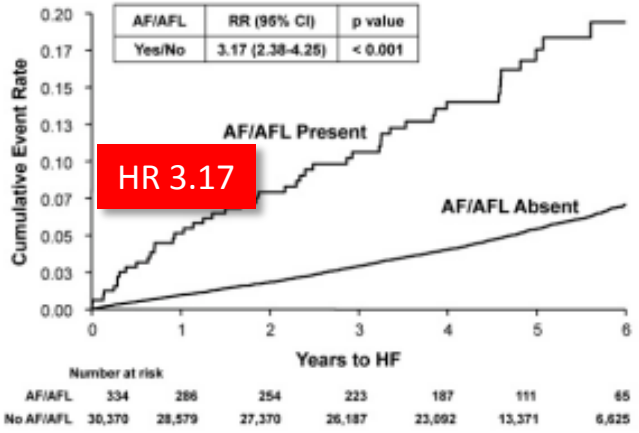


Mortalité x 2.5 FA à l'entrée ou en cours d'étude

AVC



Ins cardiaque



Haywood et al, JACC 2009

$CHADS_2$		
	Risk Factor	Points
C	Congestive heart failure	1
H	**Hypertension**	**1**
A	**Age ≥75 years**	**1**
D	Diabetes mellitus	1
S_2	**Previous stroke or TIA**	**2**

CHA_2DS_2-VASc		
	Risk Factor	Points
C	Congestive heart failure	1
H	**Hypertension**	**1**
A_2	**Age ≥75 years**	**2**
D	Diabetes Mellitus	1
S_2	**Previous stroke or TIA**	**2**
V	Vascular disease	1
A	**Age 65-74 years**	**1**
Sc	Sex (female gender)	1

HAS-BLED		
	Risk Factor	Points
H	**Hypertension**	**1**
A	Abnormal liver and renal function (1 point each)	1 or 2
S	**Stroke**	**1**
B	Bleeding	1
L	Labile INR	1
E	**Elderly (age >65)**	**1**
D	Drugs or alcohol (1 point each)	1 or 2

High risk if > 3

CHADS2, CHA2DS2-VASc and HAS-BLED scores for ischemic stroke and bleeding risk stratification:

European Heart Journal Advance Access published August 27, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw210

ESC GUIDELINES

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

Endorsed by the European Stroke Organisation (ESO)

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Qui anticoaguler?
Score CHA_2DS_2-VASc... Toujours d'actualité

CHA_2DS_2-VASc risk factor	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left-ventricular ejection fraction	1
Hypertension Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment	1
Age 75 years or older	2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin	1
Previous stroke, transient ischaemic attack, or thromboembolism	2
Vascular disease Previous myocardial infarction, peripheral artery disease, or aortic plaque	1
Age 65–74 years	1
Sex category (female)	1

ESC 2016

Maximum score : 9

Evaluer le risque hémorragique

Modifiable bleeding risk factors:
Hypertension (especially when systolic blood pressure is >160 mmHg)
Labile INR or time in therapeutic range <60% in patients on vitamin K antagonists
Medication predisposing to bleeding, such as antiplatelet drugs and non-steroidal anti-inflammatory drugs
Excess alcohol (≥8 drinks/week)
Potentially modifiable bleeding risk factors:
Anaemia
Impaired renal function
Impaired liver function
Reduced platelet count or function

Non-modifiable bleeding risk factors:
Age (>65 years) (≥75 years)
History of major bleeding
Previous stroke
Dialysis-dependent kidney disease or renal transplant
Cirrhotic liver disease
Malignancy
Genetic factors
Biomarker-based bleeding risk factors:
High-sensitivity troponin
Growth differentiation factor-15
Serum creatinine/estimated CrCl

Les scores à la trappe…

ESC 2016

Types de FA

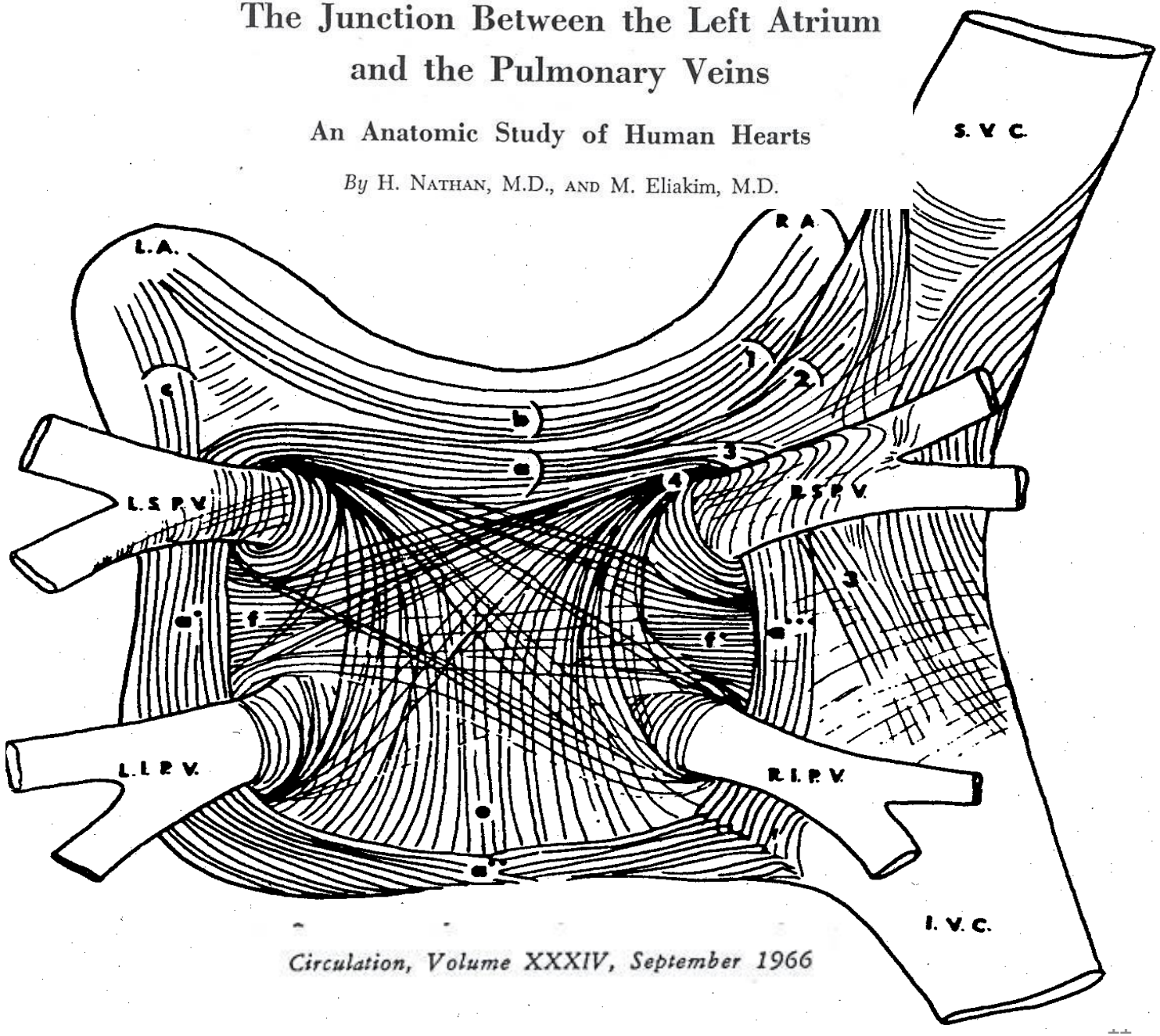
AF pattern	Definition
First diagnosed AF	AF that has not been diagnosed before, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms.
Paroxysmal AF	Self-terminating, in most cases within 48 hours. Some AF paroxysms may continue for up to 7 days. AF episodes that are cardioverted within 7 days should be considered paroxysmal.
Persistent AF	AF that lasts longer than 7 days, including episodes that are terminated by cardioversion, either with drugs or by direct current cardioversion, after 7 days or more.
Long-standing persistent AF	Continuous AF lasting for ≥1 year when it is decided to adopt a rhythm control strategy.
Permanent AF	AF that is accepted by the patient (and physician). Hence, rhythm control interventions are, by definition, not pursued in patients with permanent AF. Should a rhythm control strategy be adopted, the arrhythmia would be re-classified as 'long-standing persistent AF'.

ESC 2016

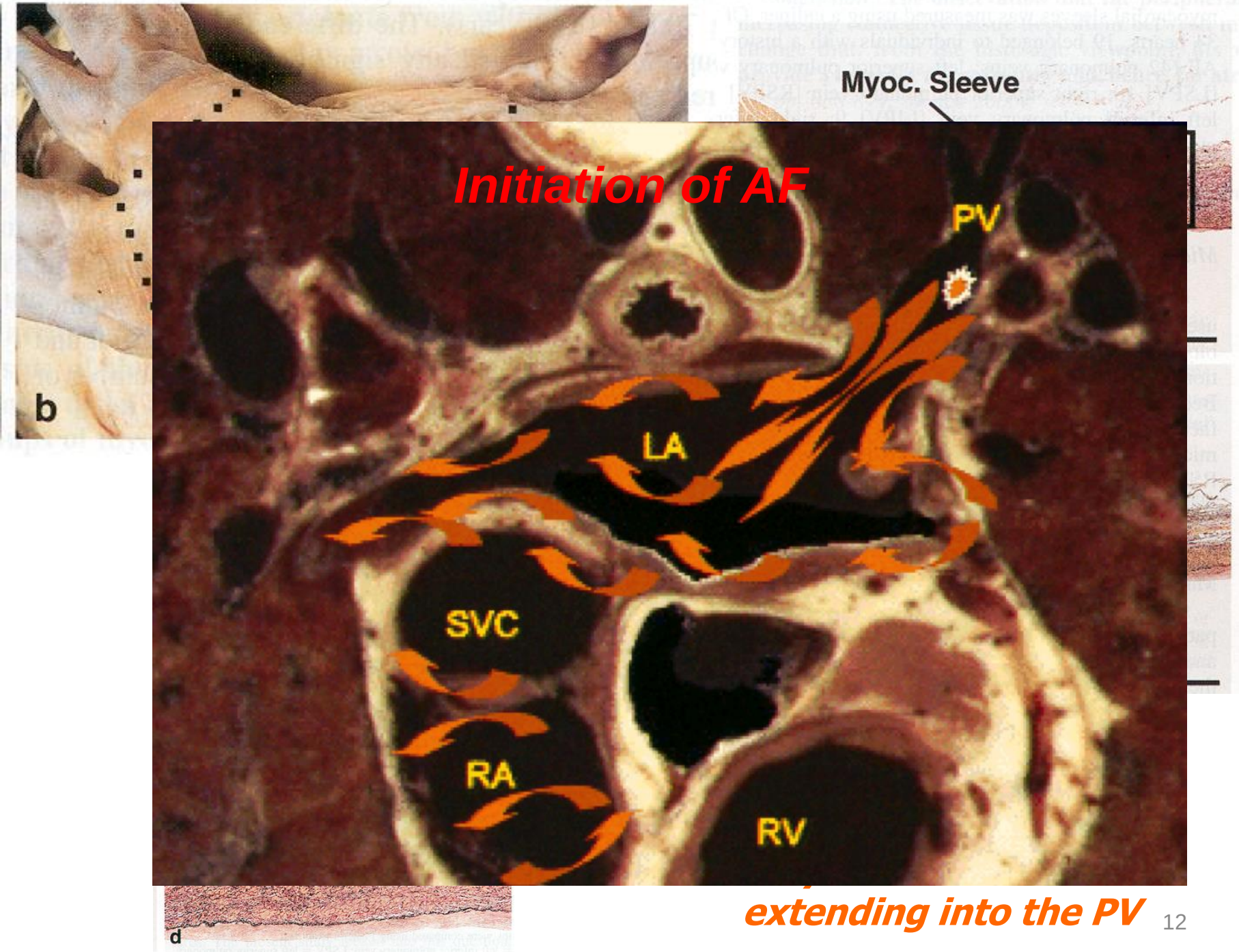
The Junction Between the Left Atrium and the Pulmonary Veins

An Anatomic Study of Human Hearts

By H. NATHAN, M.D., AND M. Eliakim, M.D.

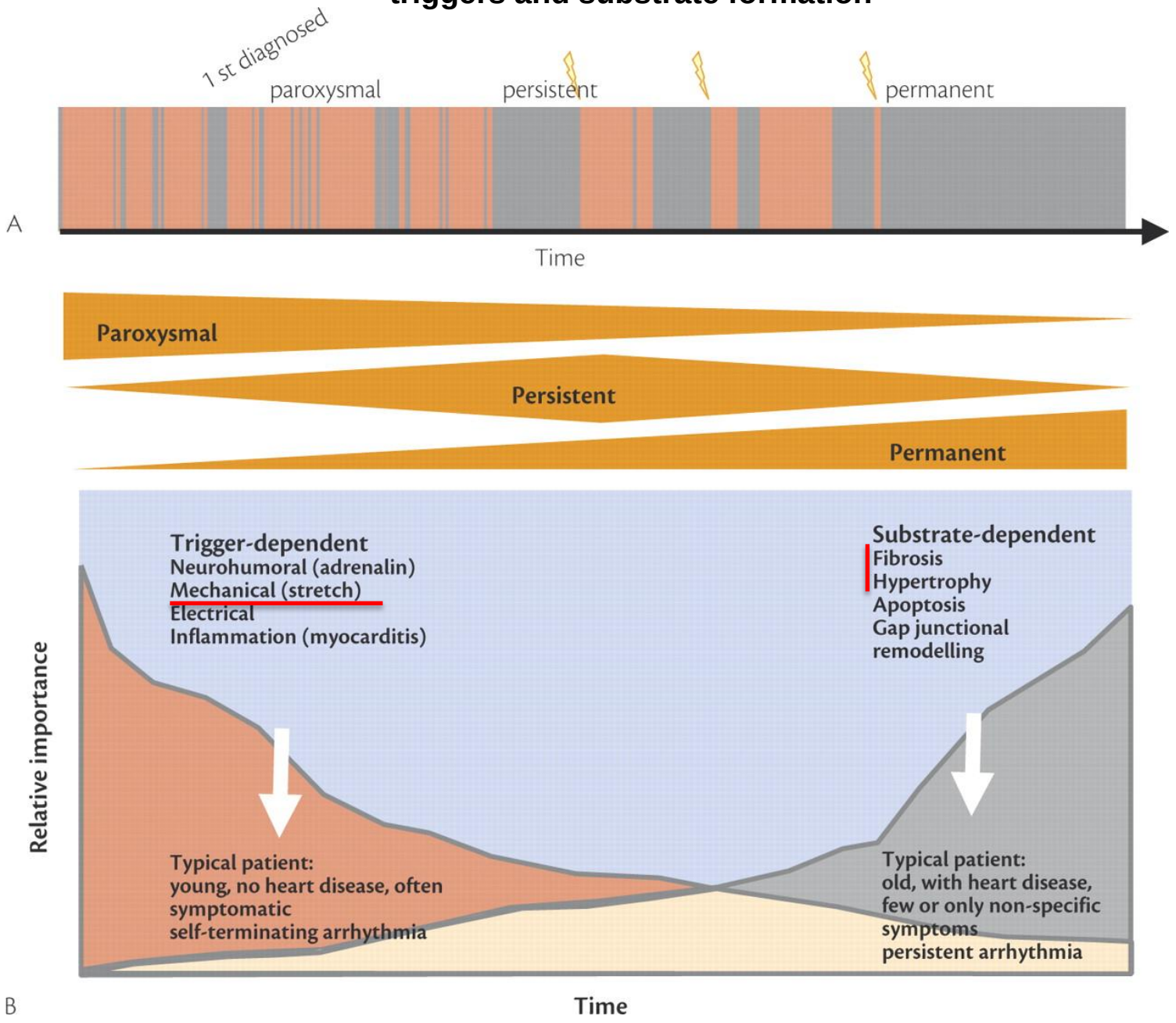


Circulation, Volume XXXIV, September 1966

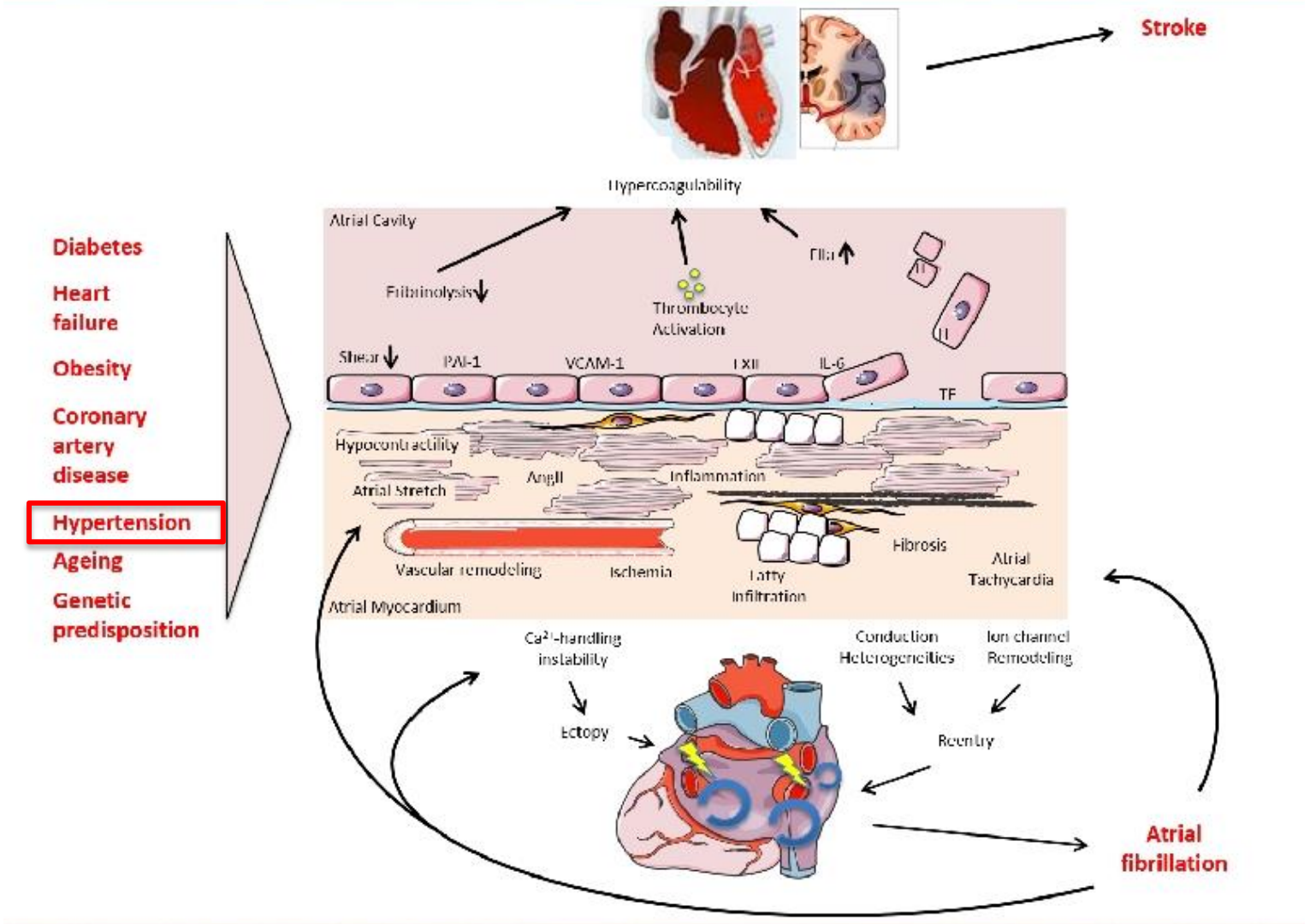


extending into the PV

Progression of atrial fibrillation from paroxysmal to permanent and the importance of specific triggers and substrate formation



Major mechanisms causing AF to consider when deciding on management



AngII = angiotensin II; TF = tissue factor; FXII = factor XII; IL-6 = interleukin 6; PAI-1 = plasminogen activator inhibitor 1; VCAM-1 = vascular cell adhesion molecule 1

Cardiovascular and other conditions independently associated with AF

Characteristic/comorbidity	Association with AF
Genetic predisposition (based on multiple common gene variants associated with AF)	HR range 0.4–3.2
Older age 50-59 years 60-69 years 70-79 years 80-89 years	HR: 1.00 (reference) 4.98 (95% CI 3.49–7.10) 7.35 (95% CI 5.28–10.2) 9.33 (95% CI 6.68–13.0)
Hypertension (treated) vs. none	HR 1.32 (95% CI 1.08–1.60)
Heart failure vs. none	HR 1.43 (95% CI 0.85–2.40)
Valvular heart disease vs. none	RR 2.42 (95% CI 1.62–3.60)
Myocardial infarction vs. none	HR 1.46 (95% CI 1.07–1.98)
Thyroid dysfunction Hypothyroidism Subclinical hyperthyroidism Overt hyperthyroidism	(reference: euthyroid) HR 1.23 (95% CI 0.77–1.97) RR 1.31 (95% CI 1.19–1.44) RR 1.42 (95% CI 1.22–1.63)
Obesity (body mass index) None (<25 kg/m²) Overweight (25–30 kg/m²) Obese (≥31 kg/m²)	HR: 1.00 (reference) 1.13 (95% CI 0.87–1.46) 1.37 (95% CI 1.05–1.78)
Diabetes mellitus vs. none	HR 1.25 (95% CI 0.98–1.60)

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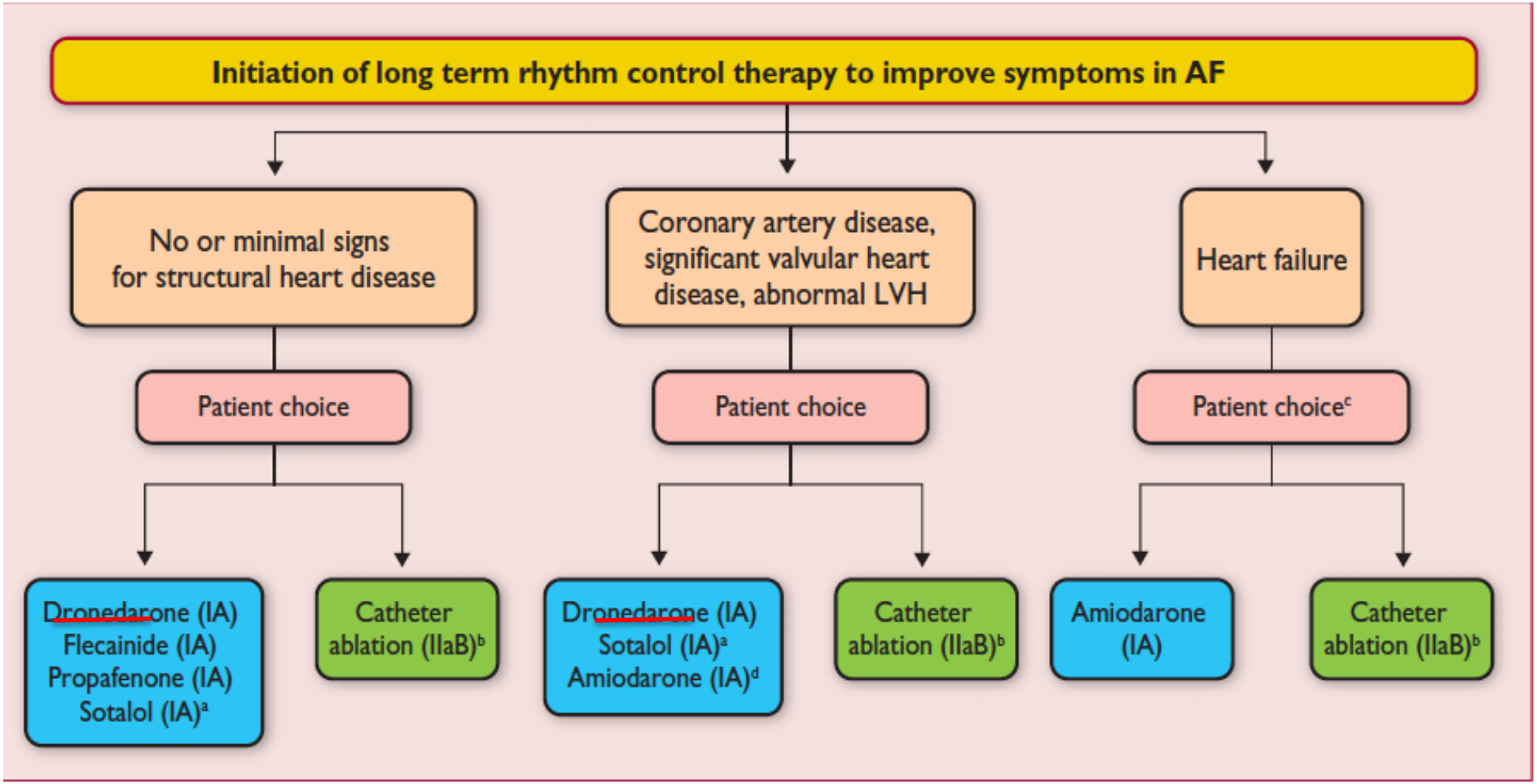


AF = atrial fibrillation; HF = heart failure; LVH = left ventricular hypertrophy;
[a]Sotalol requires careful evaluation of proarrhythmic risk.
[b]Catheter ablation should isolate pulmonary veins and can be performed using radiofrequency or cryoballoon catheters.
[c]Catheter ablation as a first-line therapy is usually reserved for heart failure patients with tachycardiomyopathy.
[d]Amiodarone is a second-choice therapy in many patients because of its extracardiac side-effects.

Initiation of long term rhythm control therapy in symptomatic patients with AF

European Heart Journal 2016

Catheter ablation of atrial fibrillation (1)

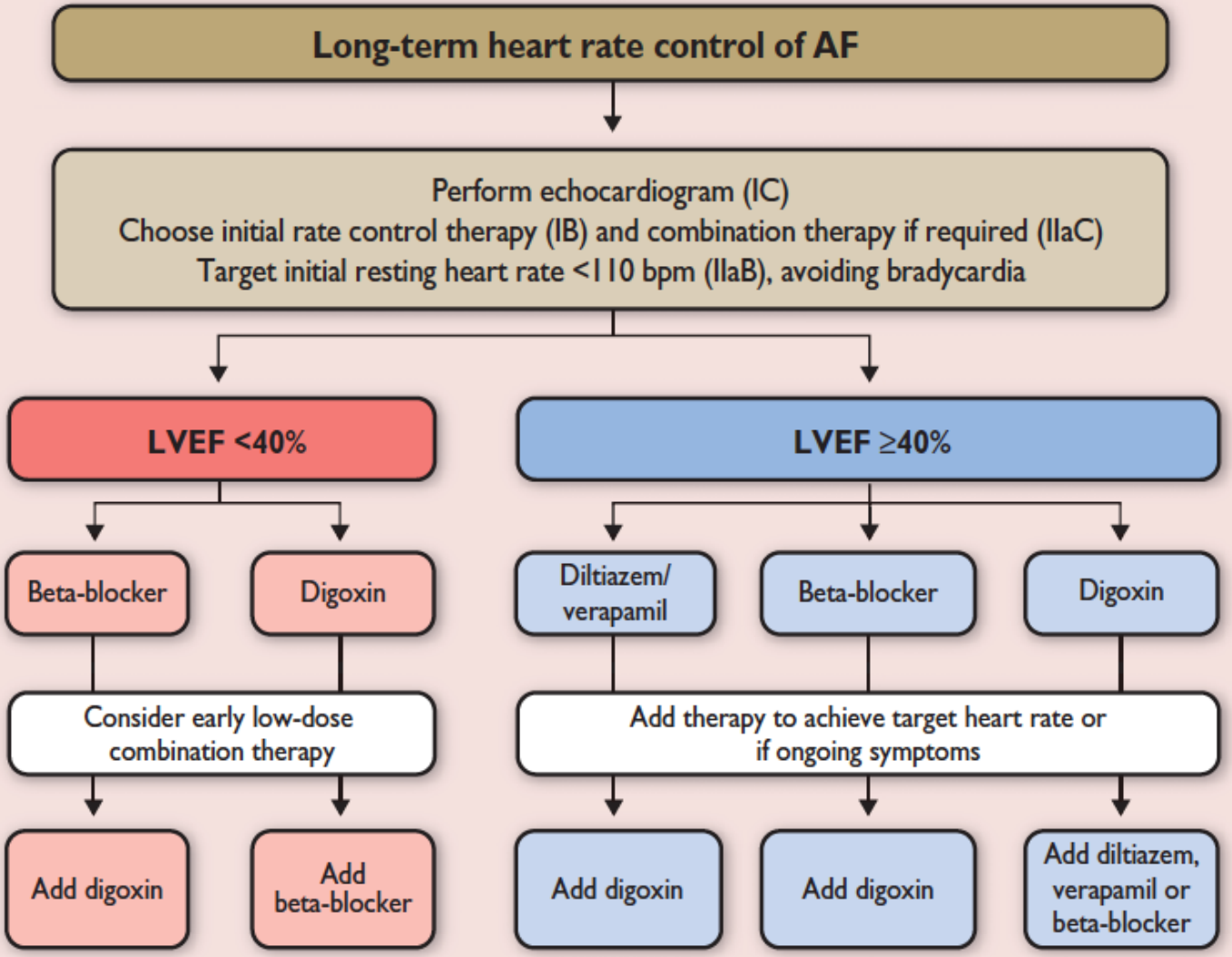
Recommendations	Class	Level
Catheter ablation of symptomatic paroxysmal AF is recommended to improve AF symptoms in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.	I	A
Ablation of common atrial flutter should be considered to prevent recurrent flutter as part of an AF ablation procedure if flutter has been documented or occurs during the AF ablation.	IIa	B
Catheter ablation of AF should be considered as first-line therapy to prevent recurrent AF and to improve symptoms in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.	IIa	B
All patients should receive oral anticoagulation for at least 8 weeks after catheter (IIaB) or surgical (IIaC) ablation.	IIa	B C
Anticoagulation for stroke prevention should be continued indefinitely after apparently successful catheter or surgical ablation of AF in patients at high-risk of stroke.	IIa	C
When catheter ablation of AF is planned, continuation of oral anticoagulation with a VKA (IIaB) or NOAC (IIaC) should be considered during the procedure, maintaining effective anticoagulation.	IIb	B C
Catheter ablation should target isolation of the pulmonary veins using radiofrequency ablation or cryothermy balloon catheters.	IIa	B

European Heart Journal 2016

Catheter ablation of atrial fibrillation (2)

Recommendations	Class	Level
AF ablation should be considered in symptomatic patients with AF and heart failure with reduced ejection fraction to improve symptoms and cardiac function when tachycardiomyopathy is suspected.	IIa	C
AF ablation should be considered as a strategy to avoid pacemaker implantation in patients with AF-related bradycardia.	IIa	C
Catheter or surgical ablation should be considered in patients with symptomatic persistent or long-standing persistent AF refractory to AAD therapy to improve symptoms, considering patient choice, benefit and risk, supported by an AF Heart Team.	IIa	C

European Heart Journal 2016



Long-term heart rate control in patients with atrial fibrillation

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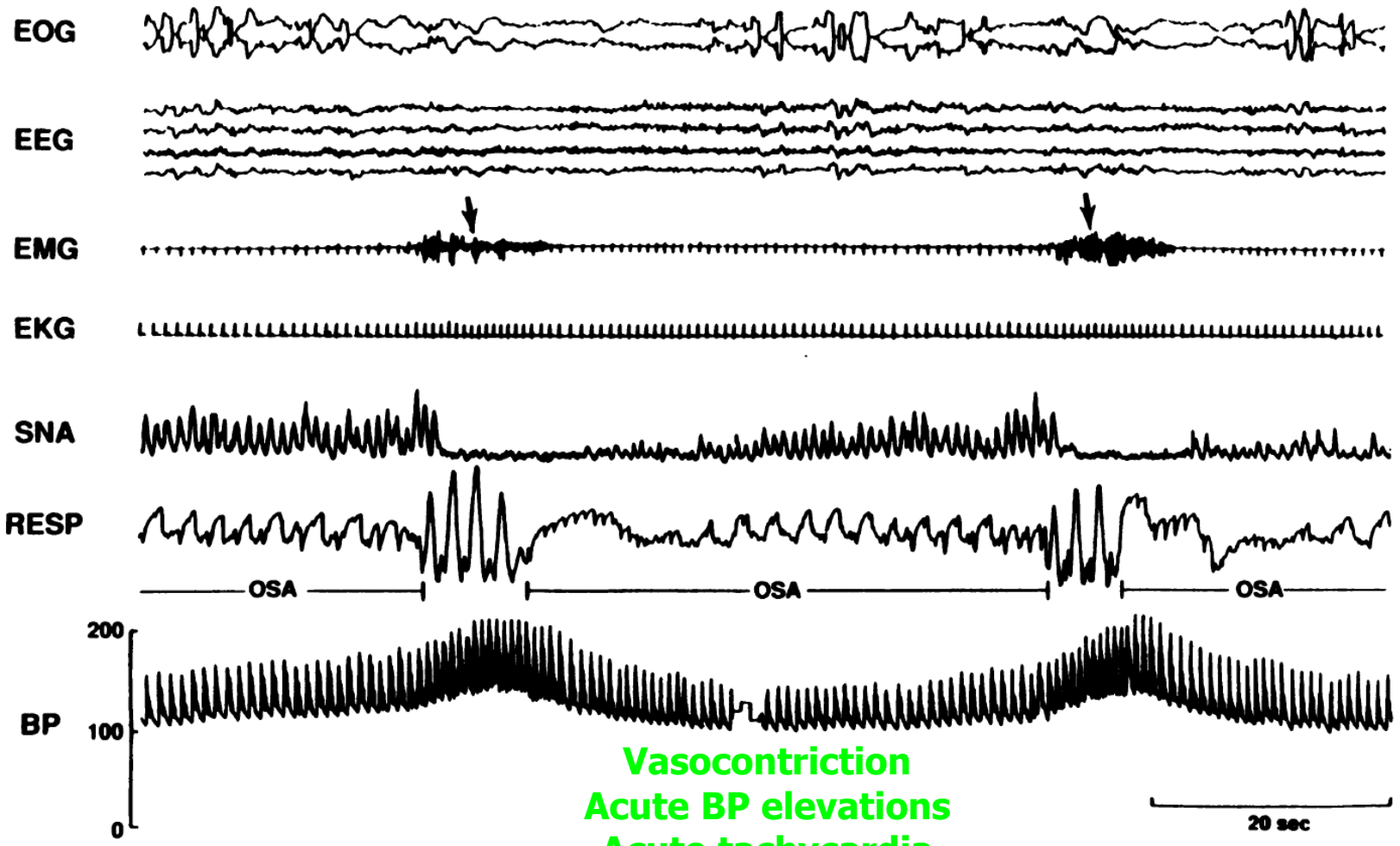
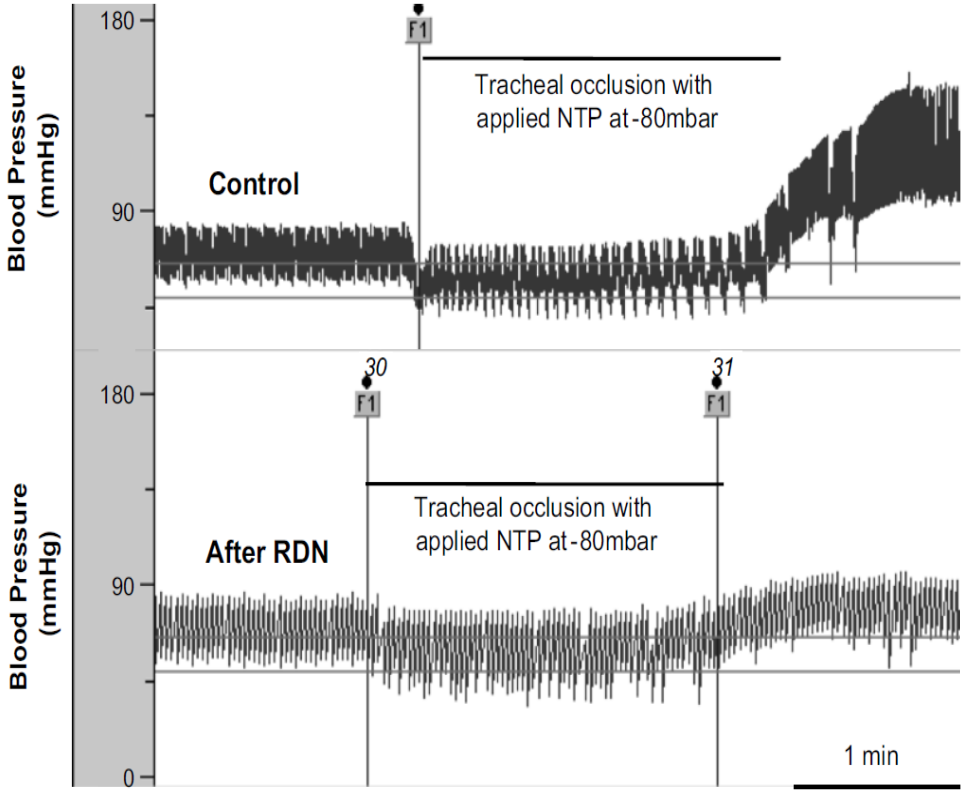
Mechanisms of arrhythmias in OSA



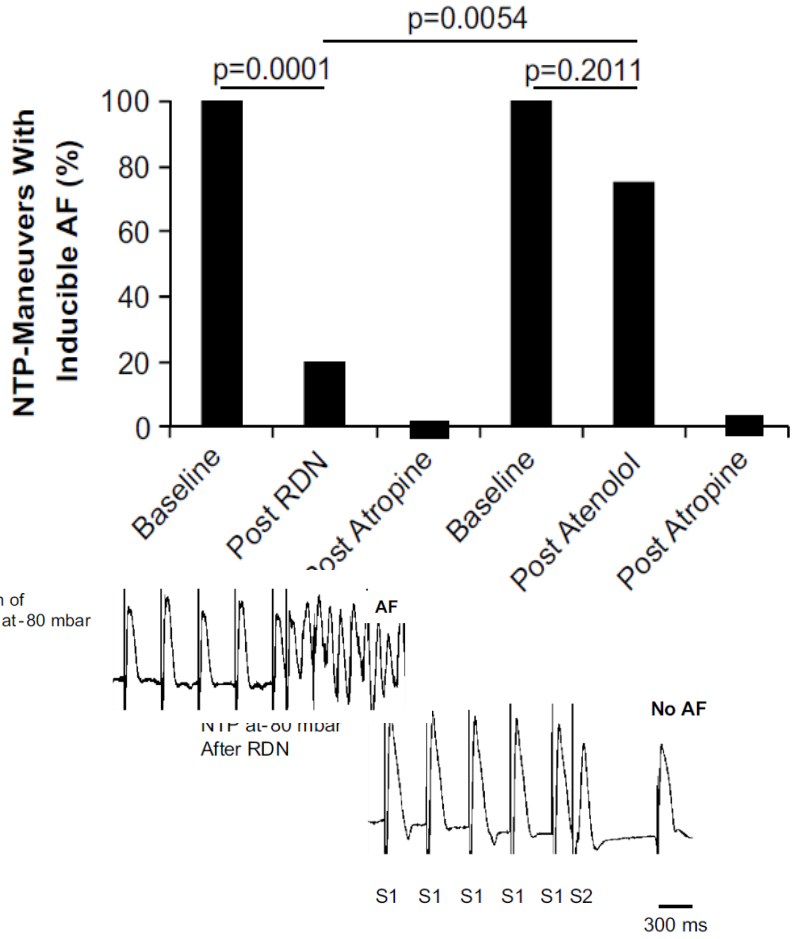
Vasocontriction
Acute BP elevations
Acute tachycardia

Somers V *J Clin Invest 1995;96:1897-1904*

Renal Sympathetic Denervation (RDN) Suppresses Postapneic Blood Pressure Rises and Atrial Fibrillation in a Model for OSA



RDN reduced NTP-induced AF-inducibility and inhibited post apneic BP rise

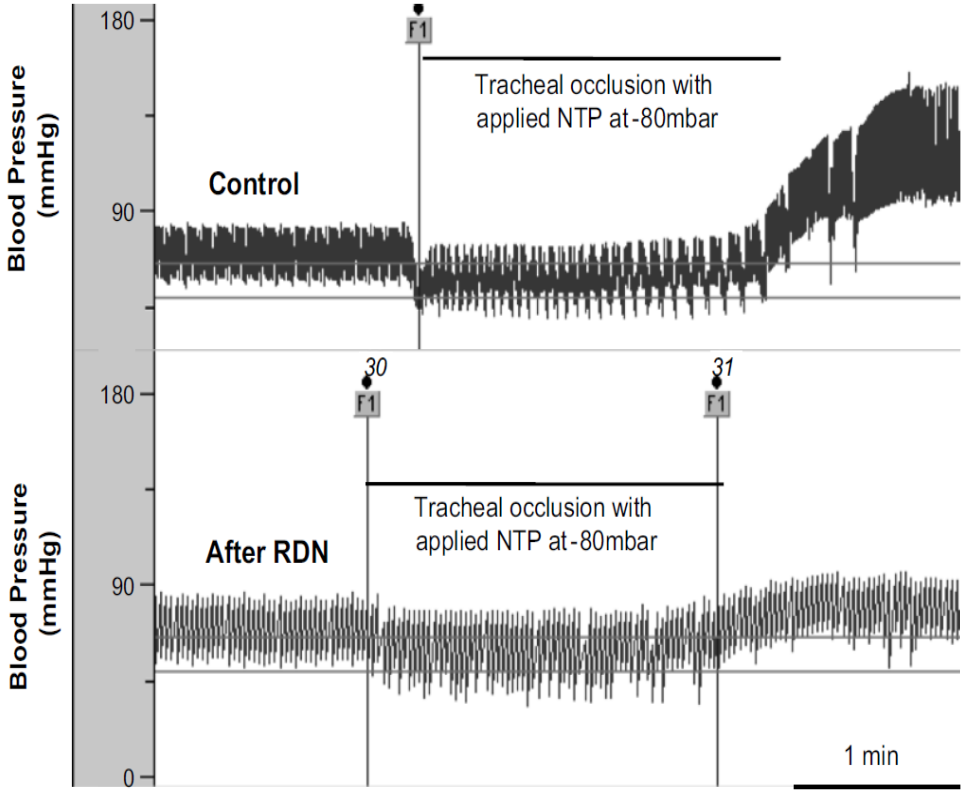


Tracheal occlusion with applied negative tracheal pressure (NTP; at 80 mbar) increased AF inducibility

Effects of RDN on AF inducibility and BP increase during obstructive events (20 anesthetized pigs)

Linz D Hypertension 2012;96:1897-1904

Renal Sympathetic Denervation (RDN) Suppresses Postapneic Blood Pressure Rises and Atrial Fibrillation in a Model for OSA



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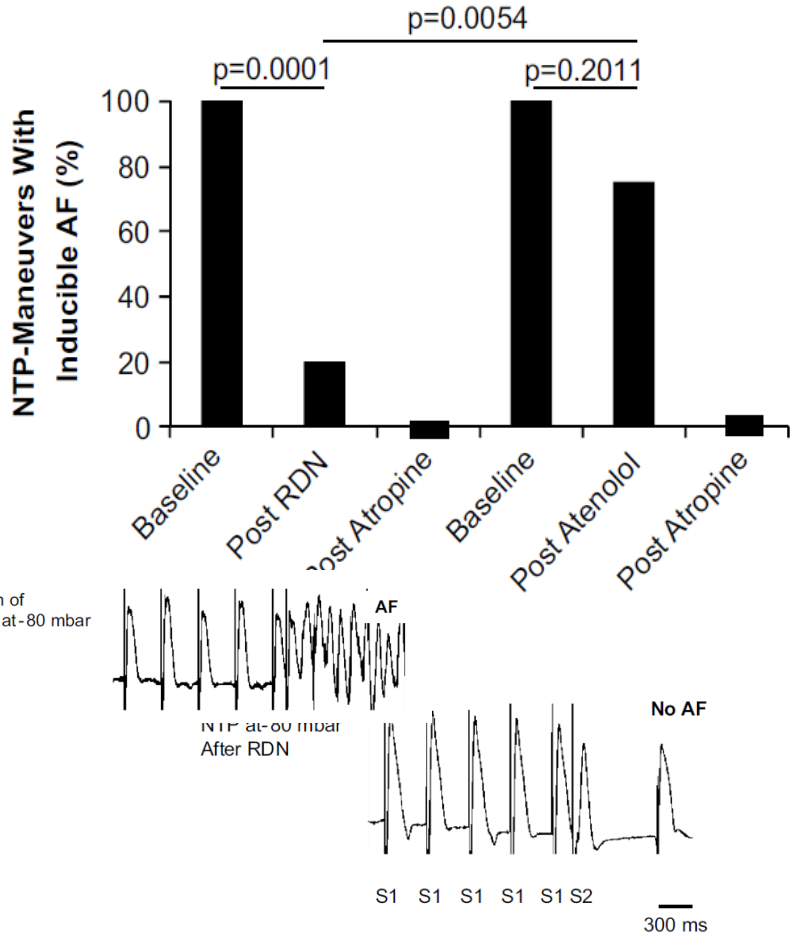

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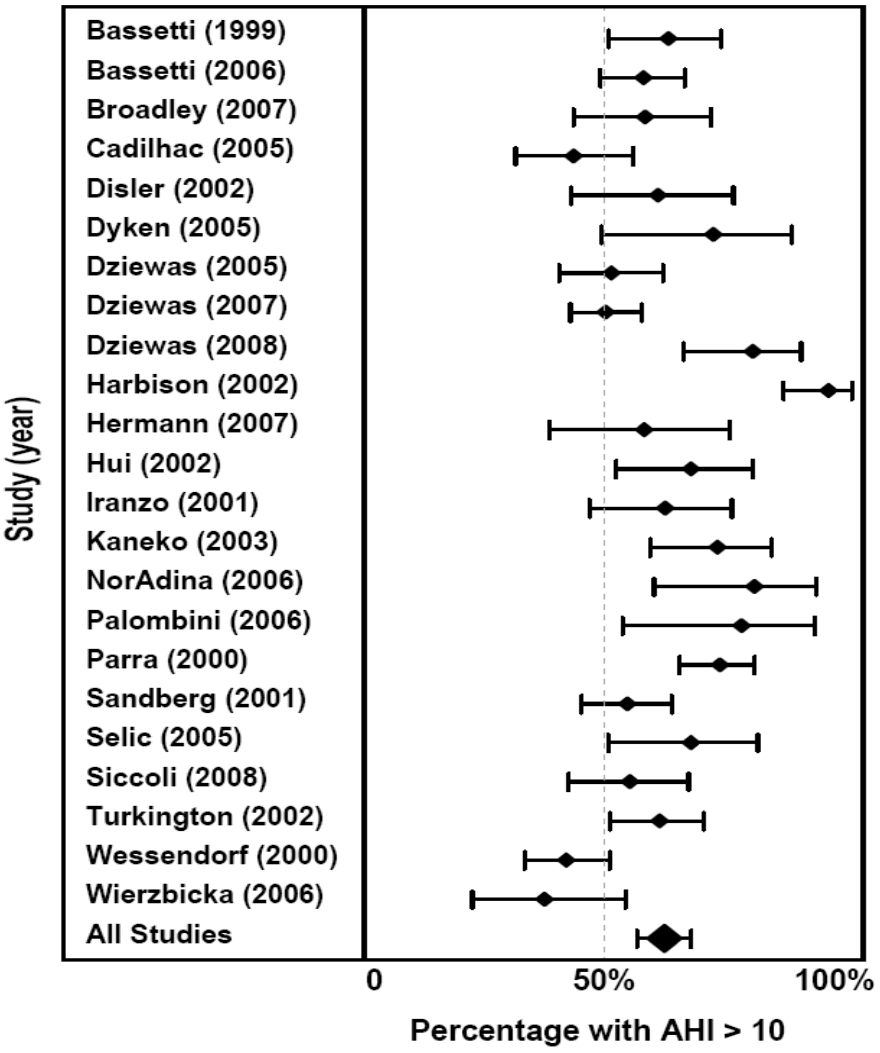
Effects of RDN on AF inducibility and BP increase during obstructive events (20 anesthetized pigs)

Linz D Hypertension 2012;96:1897-1904

OSA prevalence in stroke patients

Study & Year, Country	N (% female)	Stroke Type (% recurrent)	% of Eligible	Location
Bassetti 1999, USA	80 (38)	I, T (11)	63%	Stroke Unit
Bassetti 2006, Switzerland	152 (32)	I (-)	-	Stroke Unit
Broadley 2007, Australia	55 (42)	I, H (-)	68%	Stroke Unit
Brown 2008, USA	30 (33)	I (27)	-	Stroke & Rehab
Cadhilac 2005, Australia	78 (32)	I, H (19)	29%	Home
Disler 2002, Australia	38 (-)	I, H (-)	-	Rehab Unit
Dyken 1996, USA	24 (46)	I, H (-)	56%	Stroke Unit
Dziewas 2005, Germany	102 (33)	I (25)	-	Stroke Unit
Dziewas 2007, Germany	214 (34)	I (0)	-	Stroke Unit
Dziewas 2008, Germany	55 (24)	I (0)	-	Stroke Unit
Harbison 2003, UK	78 (49)	I, H (18)	-	Stroke Unit
Hermann 2007, Switzerland	31 (36)	I (0)	-	Stroke Unit
Hsu 2006, UK	66 (32)	I, H (9)	10%	Stroke Unit
Hui 2002, China	51 (45)	I (-)	80%	Stroke Unit
Iranzo 2002, Spain	50 (40)	I (0)	-	Stroke Unit
Kaneko 2003, Canada	60 (39)	I, H (18)	98%	Rehab Unit
Martinez 2005, Spain	95 (-)	I, T (-)	68%	Rehab Unit
Mohsenin 1995, USA	10 (20)	I (-)	59%	Rehab Unit
Nachtmann 2003, Germany	235 (30)	I (25)	59%	Rehab Unit
NorAdina 2006, Malaysia	28 (29)	I (11)	31%	Stroke Unit
Palombini 2006, USA	21 (-)	I (-)	42%	Stroke Unit
Parra 2000, Spain	161 (49)	I, T, H (0)	-	Stroke Unit
Rola 2007, Poland	70 (14)	I, T (-)	-	Stroke Unit
Sandberg 2001, Sweden	133 (59)	I, H (39)	88%	Rehab Unit
Selic 2005, Switzerland	41 (20)	I (-)	91%	Stroke Unit
Siccolli 2008, Switzerland	74 (34)	I (0)	-	Stroke Unit
Turkington 2002, UK	120 (58)	I (27)	82%	Stroke Unit
Wessendorf 2000, Germany	147 (35)	I (0)	86%	Rehab Unit
Wierzbicka 2006, Poland	43 (19)	I, T (-)	-	Stroke Unit



Johnson KG et al. J Clin Sleep Med 2010; 6:131-7

Incident stroke and sleep apnea

Covariate	Unadjusted	Adjusted	
		Age -Adjusted	Fully Adjusted[§]
	Hazard Ratio (95% Confidence Interval for Ratio of Hazards)		
OAHI			
IV quartile (19.13 – 164.5)	3.91 (1.55, 9.86)	3.05 (1.21, 7.72)	2.86 (1.10, 7.39)
III quartile (9.50 – <19.13)	2.35 (0.89, 6.20)	1.97 (0.74, 5.21)	1.86 (0.70, 4.95)
II quartile (4.05 - <9.50)	1.96 (0.71, 5.40)	1.86 (0.68, 5.13)	1.86 (0.67, 5.12)
I quartile (0 – <4.05)	1.0	1.0	1.0

In the mild to moderate range (OAHI 5 to 25),
one unit increase in OAHI in men was estimated to increase stroke risk by 6%

5422 participants followed median 8.7 years
193 incident ischemic strokes observed

Redline S et al. *AJRCCM 2010;182:269-77*

Association between atrial fibrillation and stroke in OSA: A population-based case-control study

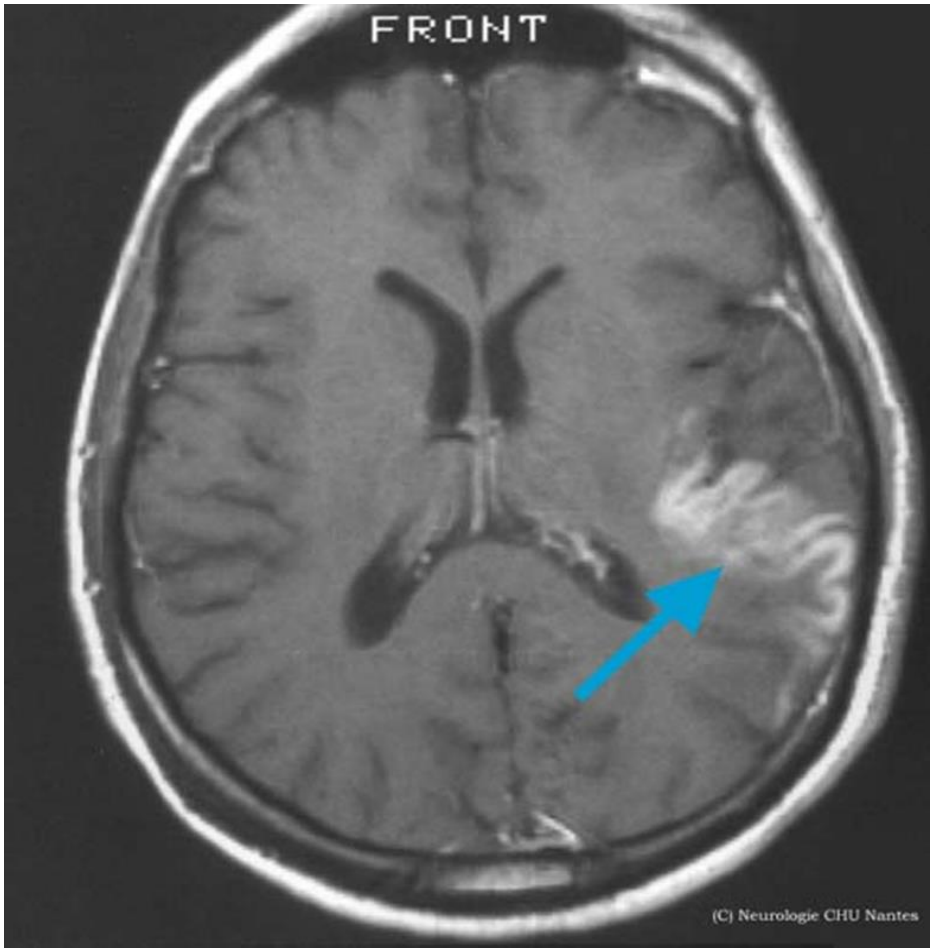
Characteristic	Corrected odds ratio	Upper confidence interval	Lower confidence interval	*p* Value
Atrial fibrillation	5.34	17.29	1.79	0.0099
Smoking status	2.81	9.03	0.98	0.0558
Hypertension	0.81	2.66	0.24	0.7242
Coronary artery disease	1.90	5.89	0.61	0.5267

Patients with OSA who had a stroke had higher rates of AF even after accounting for potential confounders

Mansukhani MP et al. Sleep Med 2013;14:243–246

Hazard ratio of each variable of the CHA_2DS_2 Vasc score to predict stroke is similar or lower to the hazard ratio of OSA (with the exception of prior stroke)

CHA_2DS_2-VASc risk factor	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left-ventricular ejection fraction	+1
Hypertension Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment	+1
Age 75 years or older	+2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin	+1
Previous stroke, transient ischaemic attack, or thromboembolism	+2
Vascular disease Previous myocardial infarction, peripheral artery disease, or aortic plaque	+1
Age 65–74 years	+1
Sex category (female)	+1



Modify CHA_2DS_2 Vasc score by adding one extra "S" at the end (CHA_2DS_3 Vasc)?

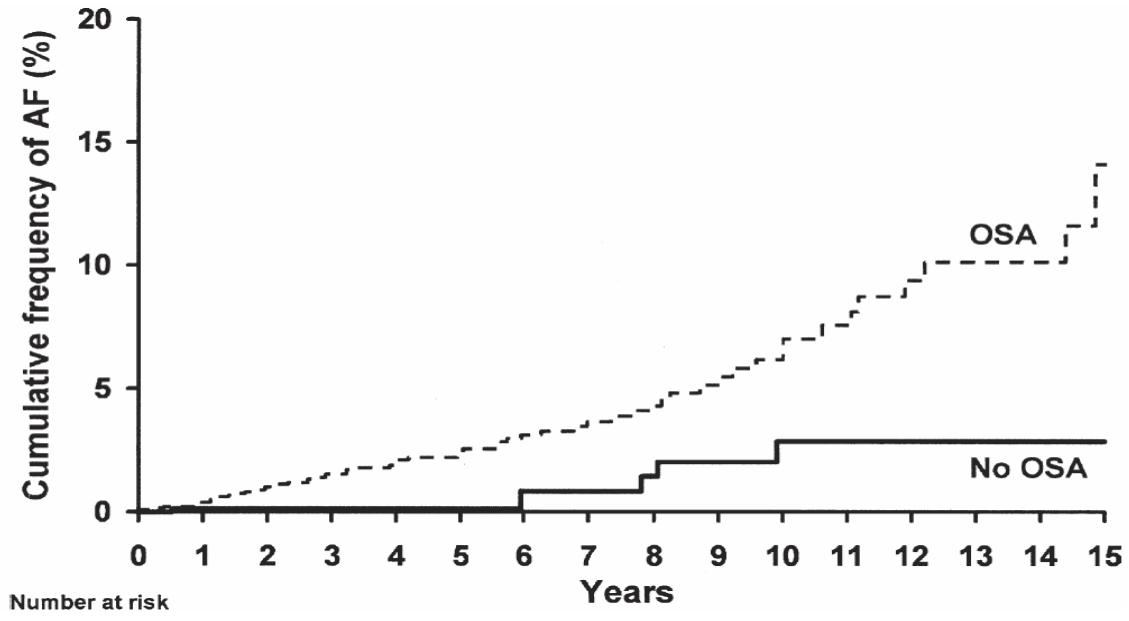
Barone DA Curr Atheroscler Rep. 2013;15:334

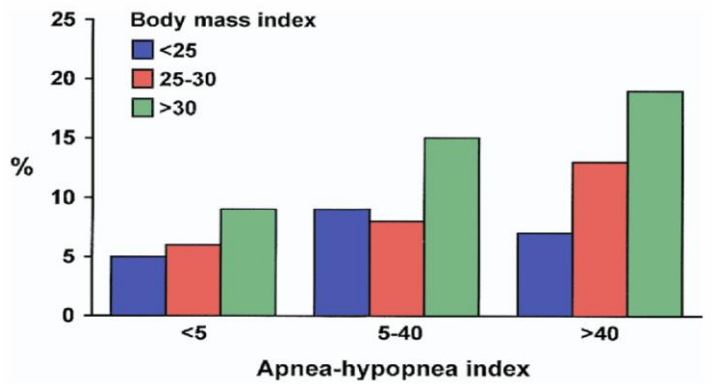
OSA, obesity and the risk of atrial fibrillation

Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation

Apoor S. Gami, MD,*† Dave O. Hodge, MS,‡ Regina M. Herges, BS,‡ Eric J. Olson, MD,†§ Jiri Nykodym, BS,*† Tomas Kara, MD,*† Virend K. Somers, MD, PHD, FACC*†‖

	HR	95% CI	p Value
<65 yrs old			
Age (per 10 yrs)	2.04	1.48–2.80	<0.001
Male gender	2.66	1.33–5.30	0.006
Coronary artery disease	2.66	1.46–4.83	0.001
Body mass index (per 1 kg/m^2)	1.07	1.05–1.10	<0.001
Decrease in nocturnal oxygen saturation (per −1%)*	3.29	1.35–8.04	0.009
≥65 yrs old			
Heart failure	7.68	4.32–13.66	<0.001





3,542 subjects, Obstructive sleep apnea in 2,626 subjects (74%)

Gami et al, J Am Coll Cardiol 2007;49:565–71

UFR de Médecine

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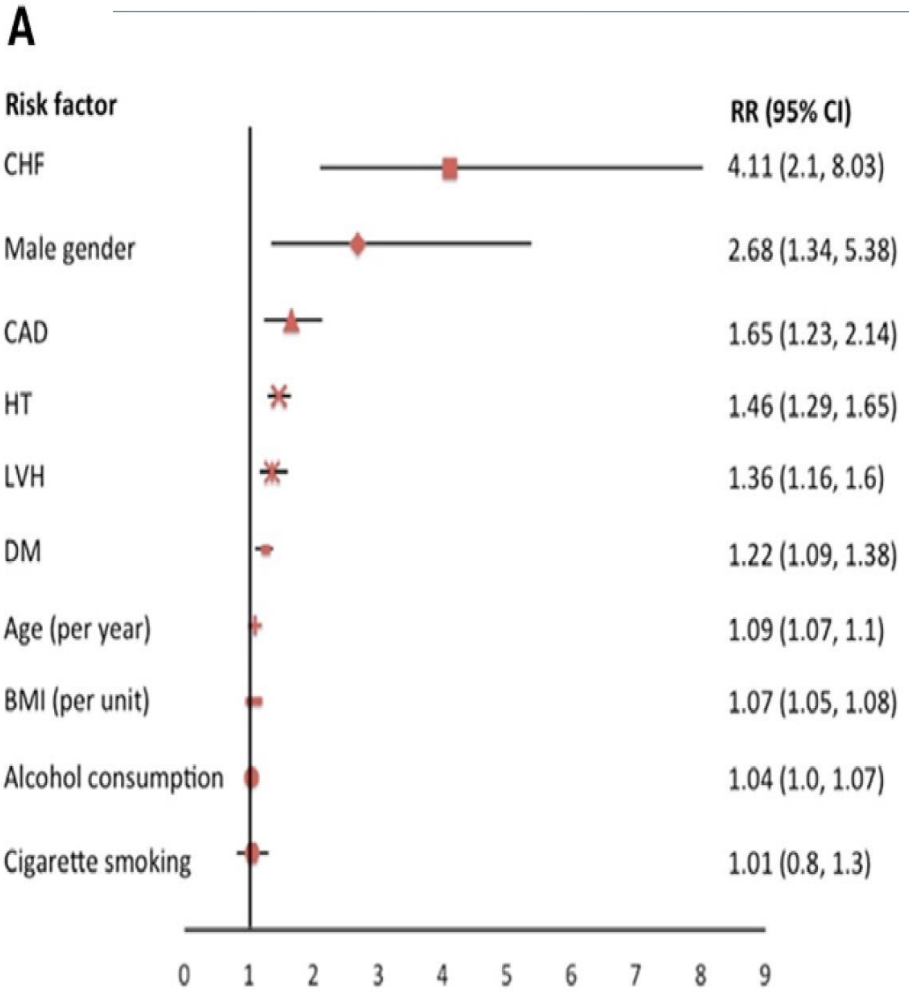
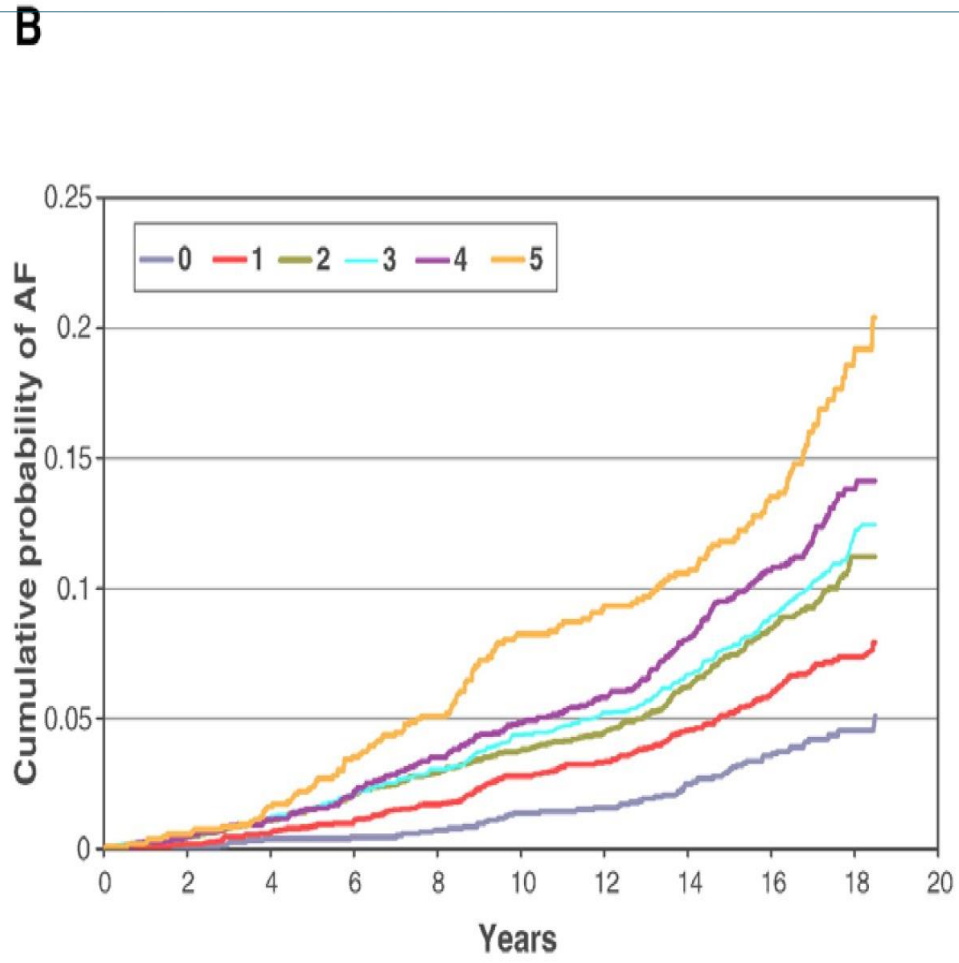
Association of risk factors with AF development.





Chamberlain AM, et al. Metabolic syndrome and incidence of atrial fibrillation among blacks and whites in the Atherosclerosis Risk in Communities (ARIC) Study. Am Heart J. 2010;159:850–856.

Stroke Risk Factors Beyond the CHA_2DS_2-VASc Score: Can We Improve Our Identification of "High Stroke Risk" Patients With Atrial Fibrillation?

Filip M. Szymanski, MD[a,*], Gregory Y.H. Lip, MD[b,c], Krzysztof J. Filipiak, MD[a], Anna E. Platek, MD[a], Anna Hrynkiewicz-Szymanska, MD[d], and Grzegorz Opolski, MD[a]

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UNIVERSITÉ Grenoble Alpes
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Some of the factors associated with an increased thromboembolic risk that are not issued in the CHA_2DS_2-VASc score

Factors associated with an increased thromboembolic risk, that are not issued in the CHA_2DS_2-VASc score

- Chronic kidney disease
- Obstructive sleep apnea
- Left atrial enlargement
- Left atrial strain
- Atrial mechanical discordance, electromechanical delay or increased orifice size
- Decreased flow velocity of left atrial appendage
- Echocardiographic spontaneous contrast, smoke, sludge, or thrombus
- Troponin
- NT-proBNP
- Adiponectine
- D-dimer
- Smoking

Am J Cardiol 2015;116:1781-1788

Stroke Risk Factors Beyond the CHA_2DS_2-VASc Score: Can We Improve Our Identification of "High Stroke Risk" Patients With Atrial Fibrillation?

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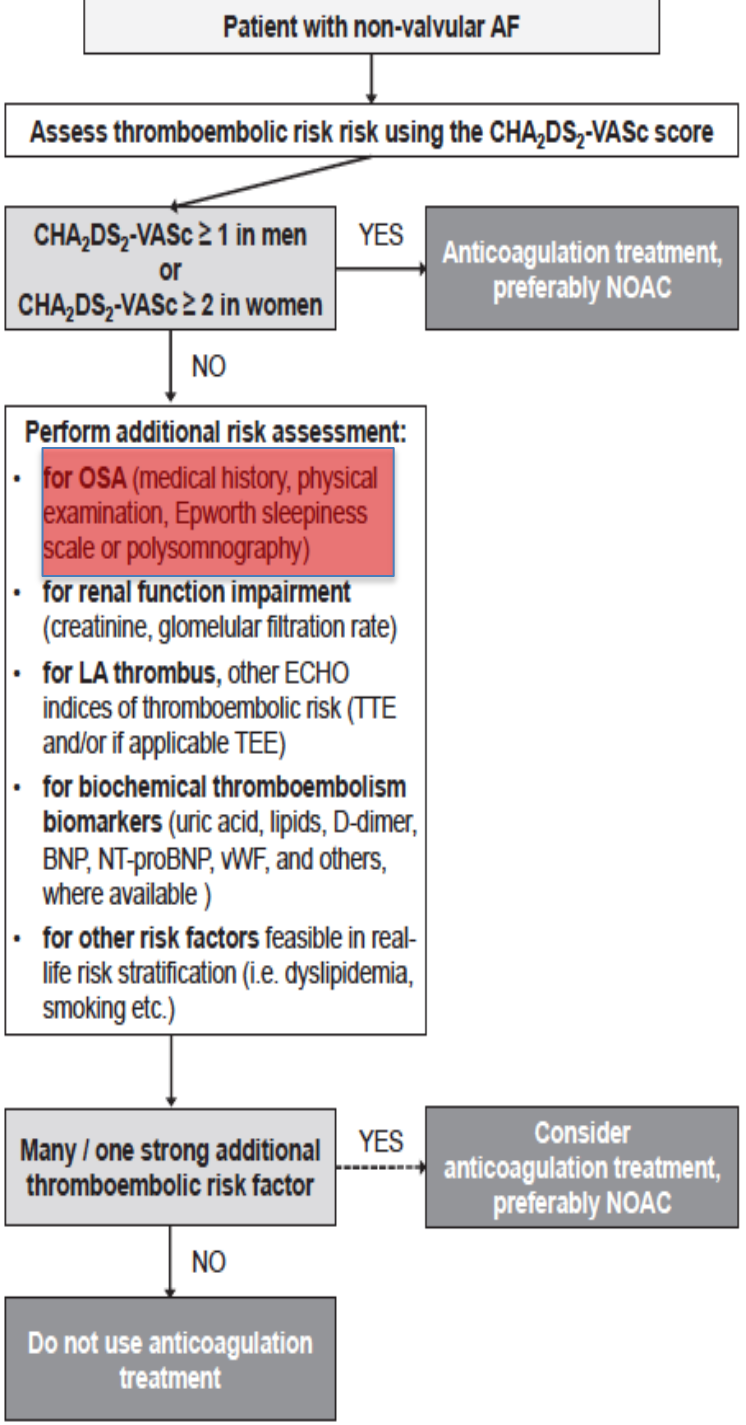
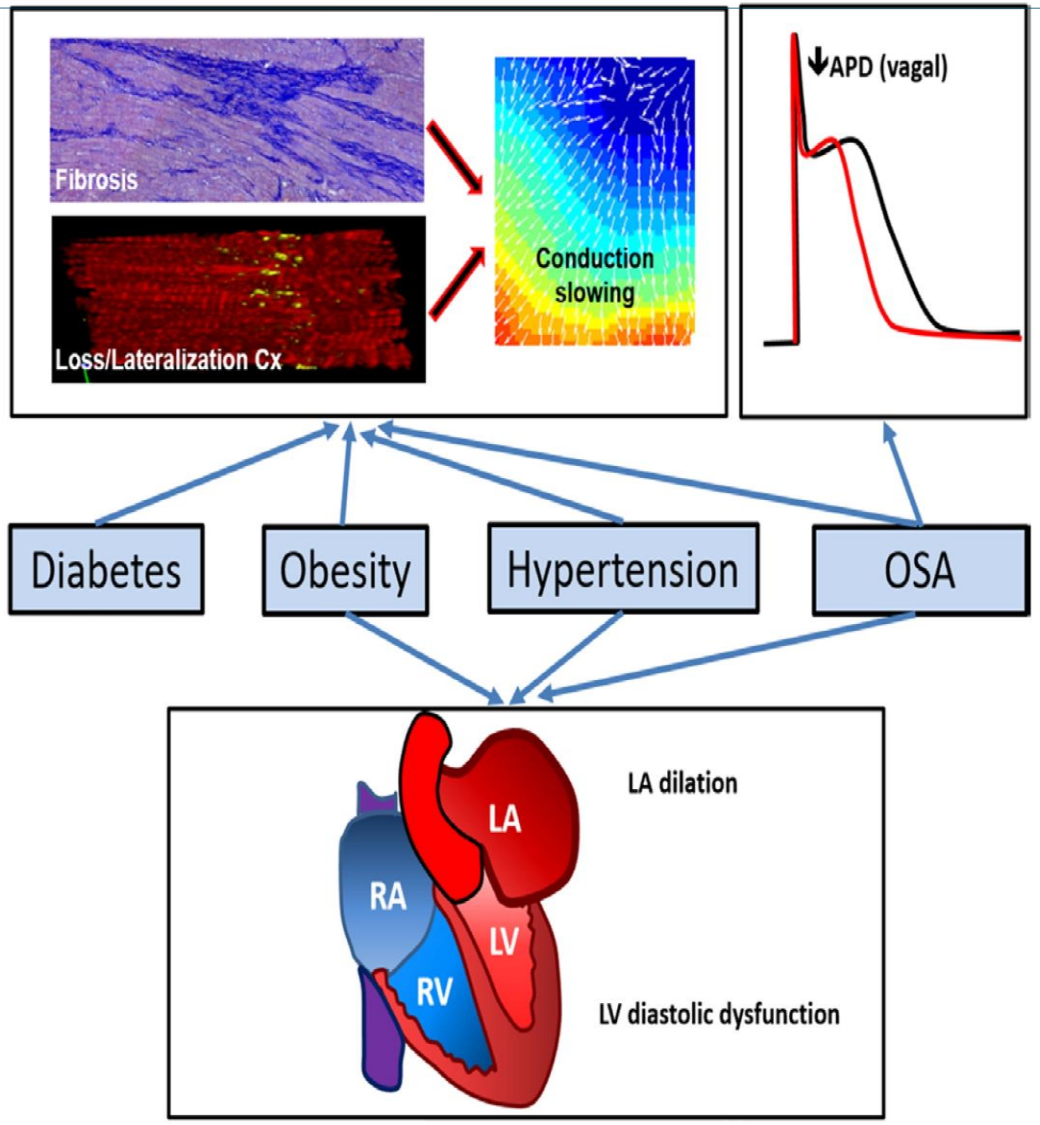


Am J Cardiol 2015;116:1781-1788

Modifiable Risk Factors and Atrial Fibrillation

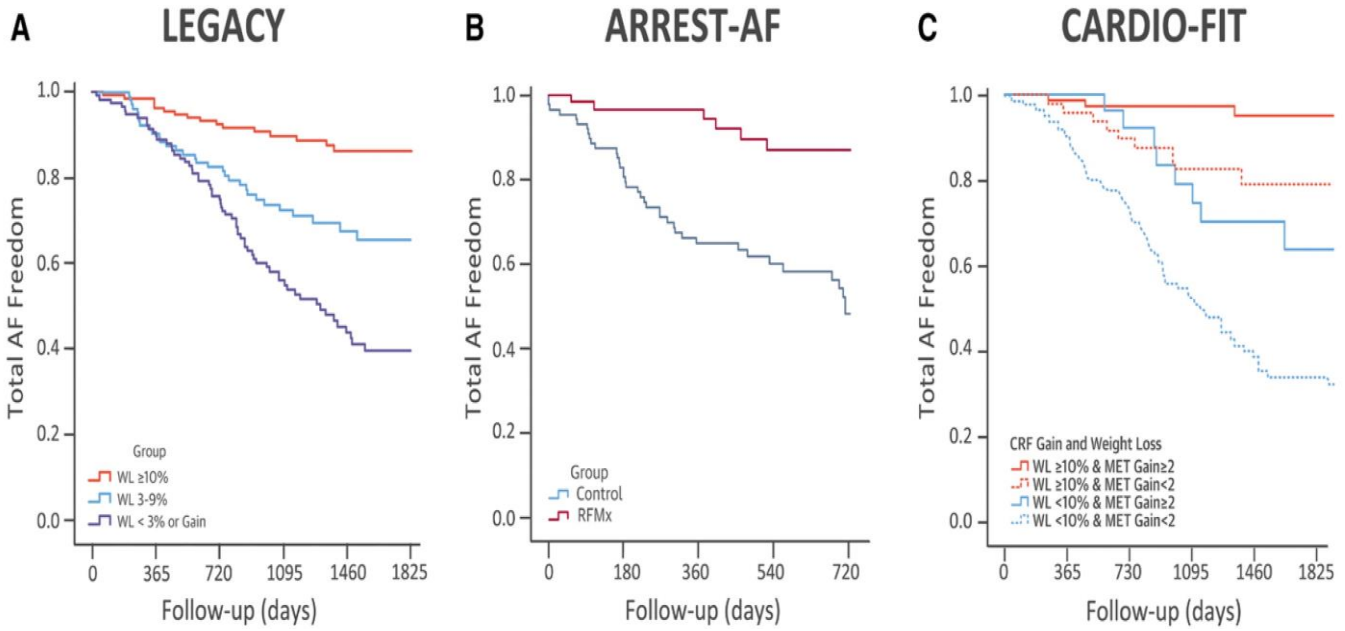
STATE OF THE ART
Dennis H. Lau, MBBS, PhD
Stanley Nattel, MD, PhD
Jonathan M Kalman, MBBS, PhD
Prashanthan Sanders, MBBS, PhD

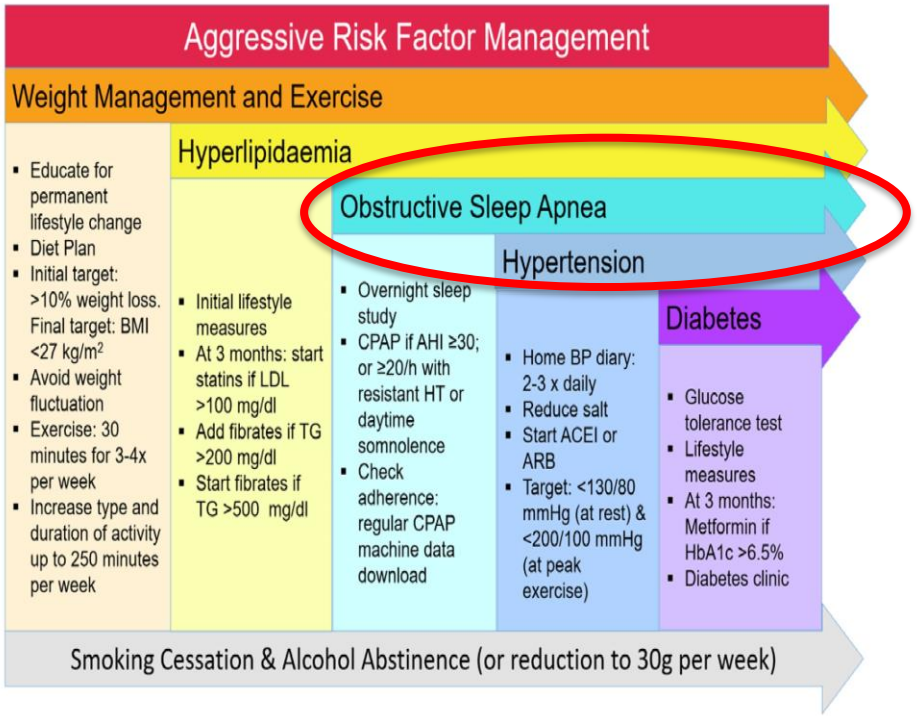


Major AF mechanisms related to risk factors.

Circulation 2017;136:583–596

Kaplan-Meier curves of various lifestyle modifications





Components of risk factor modification in ARREST-AF and LEGACY studies

Lau DH. Circulation. 2017;136:583–596.

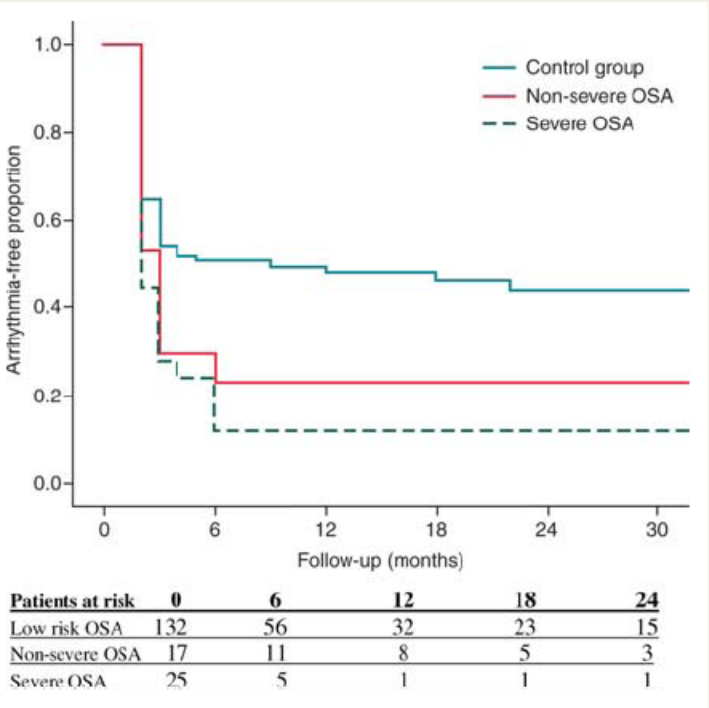
The rate of non-response to pharmacologic treatment increases with the increase in OSA severity

Characteristic	Entire Cohort (n = 61)	Nonsevere OSA (n = 38)	Severe OSA (n = 23)
Age (years)	64 ± 9	64 ± 11	65 ± 7
Women*	34%	42%	22%
Caucasian	89%	90%	87%
Body mass index (kg/m^2)	34 ± 7	33 ± 8	36 ± 6
Hypertension*	66%	58%	78%
Coronary artery disease†	31%	18%	52%
Heart failure	20%	15%	26%
AF			
Paroxysmal	61%	63%	57%
Persistent	25%	21%	30%
Permanent	15%	16%	13%
Baseline AF burden score	19 ± 8	18 ± 9	20 ± 8
Response to AADs‡	49%	61%	30%
Echocardiographic parameters			
Left atrial dimension (mm)	46 ± 8	46 ± 8	47 ± 8
Left ventricular ejection fraction (%)	50 ± 11	52 ± 10	47 ± 14
Left ventricular hypertrophy	47%	43%	52%

Monahan K Am J Cardiol 2012, 110:369-72

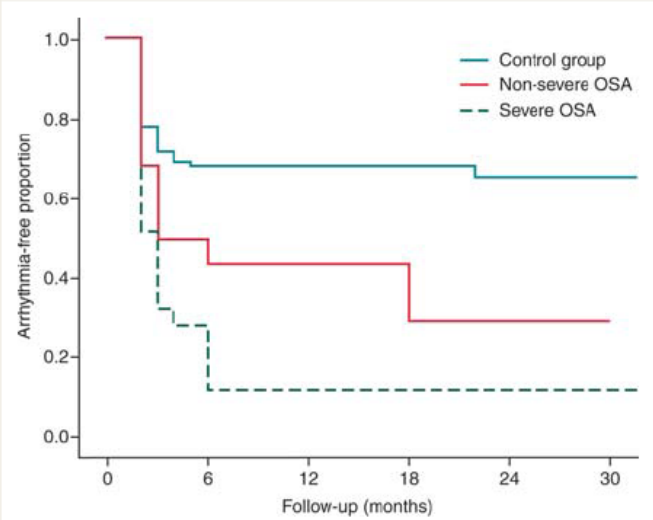
Low efficacy of atrial fibrillation ablation in severe obstructive sleep apnoea patients

Maria Matiello[1†], Mercé Nadal[1†], David Tamborero[1], Antonio Berruezo[1], Josep Montserrat[1,2], Cristina Embid[1,2], Jose Rios[3], Julián Villacastín[4], Josep Brugada[1], and Lluís Mont[1*]



Patients at risk	0	6	12	18	24
Low risk OSA	132	56	32	23	15
Non-severe OSA	17	11	8	5	3
Severe OSA	25	5	1	1	1

Figure 1 Freedom from arrhythmia recurrences after a single ablation procedure.



Patients at risk	0	6	12	18	24
Low risk OSA	132	76	42	27	19
Non-severe OSA	17	15	10	5	3
Severe OSA	25	6	1	1	1

Figure 2 Freedom from arrhythmia recurrences including the performance of a second ablation procedure.

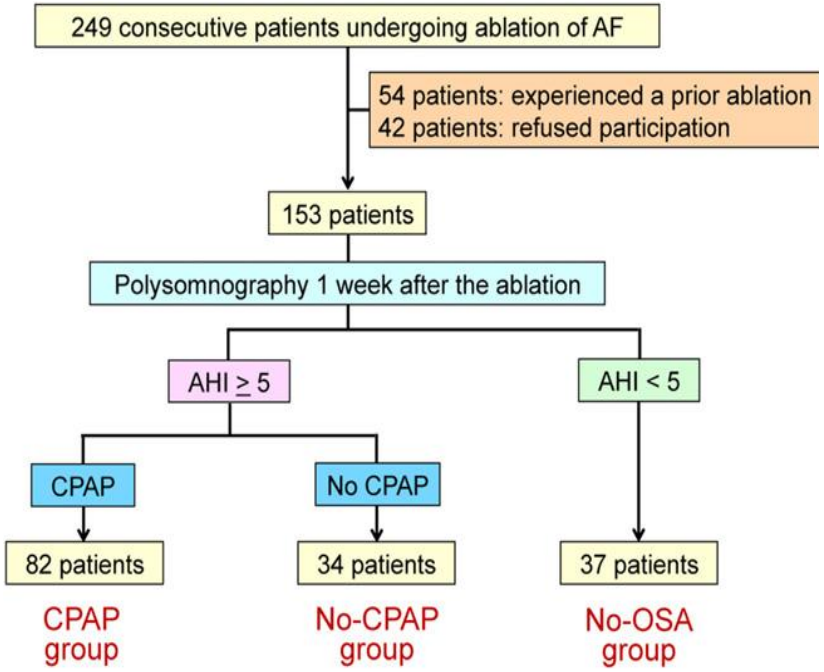
Table 3 Final model of Cox's regression model for arrhythmia recurrence

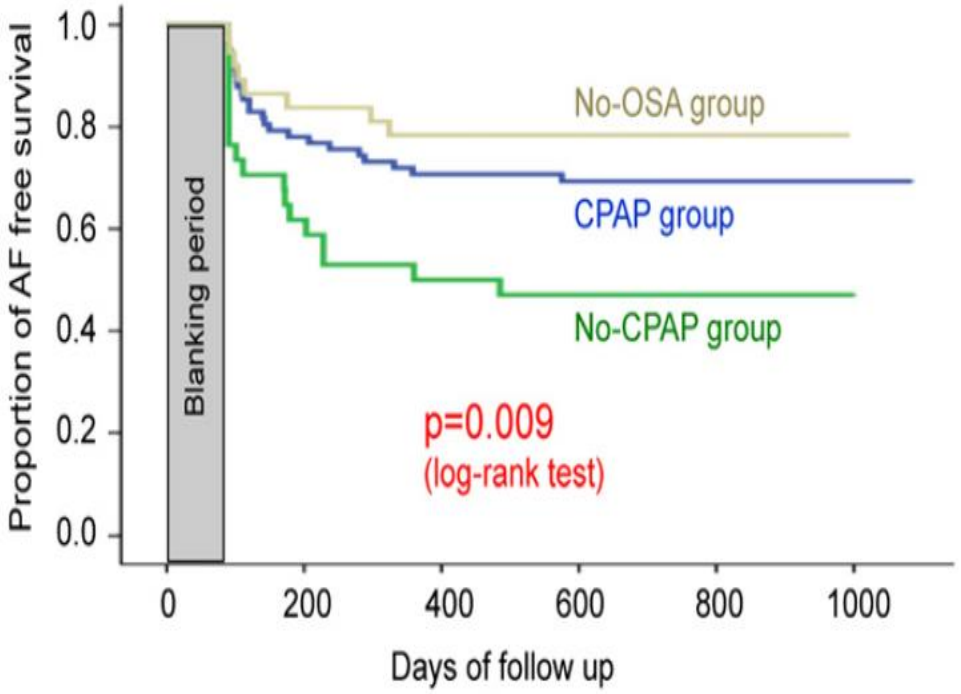
	HR (95% CI)	*P*-value
Left atrial diameter	1.046 (1.005–1.089)	0.029
OSA group		
Low risk for OSA	1 (—)	—
Non-severe OSA	1.574 (0.826–3.000)	0.168
Severe OSA	1.870 (1.106–3.161)	0.019

OSA, obstructive sleep apnoea.

Europace 2010; 12: 1084-89

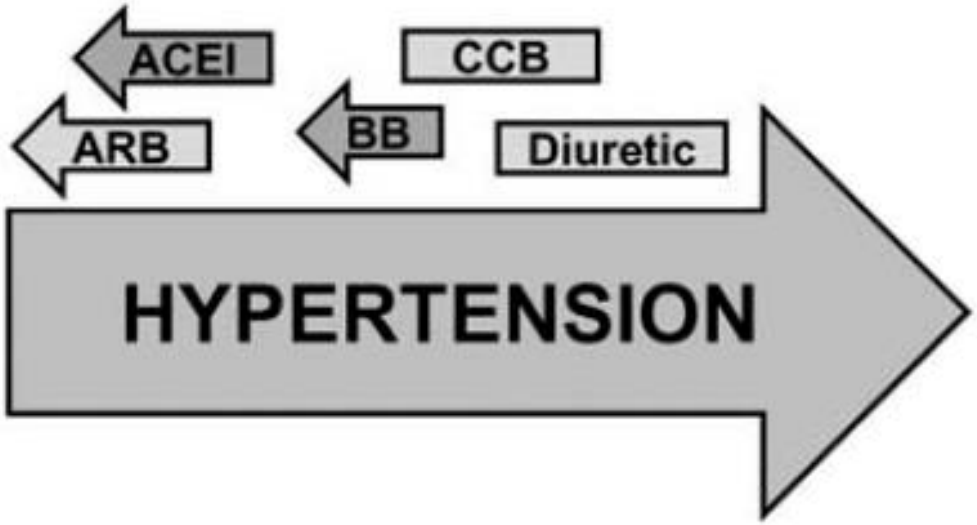
Concomitant obstructive sleep apnea increases the recurrence of atrial fibrillation following RF catheter ablation





Patients with untreated OSA have a higher recurrence of AF after ablation
N=153, prospective study

Naruse Y et al *Heart Rhythm 2013;10:331–337*

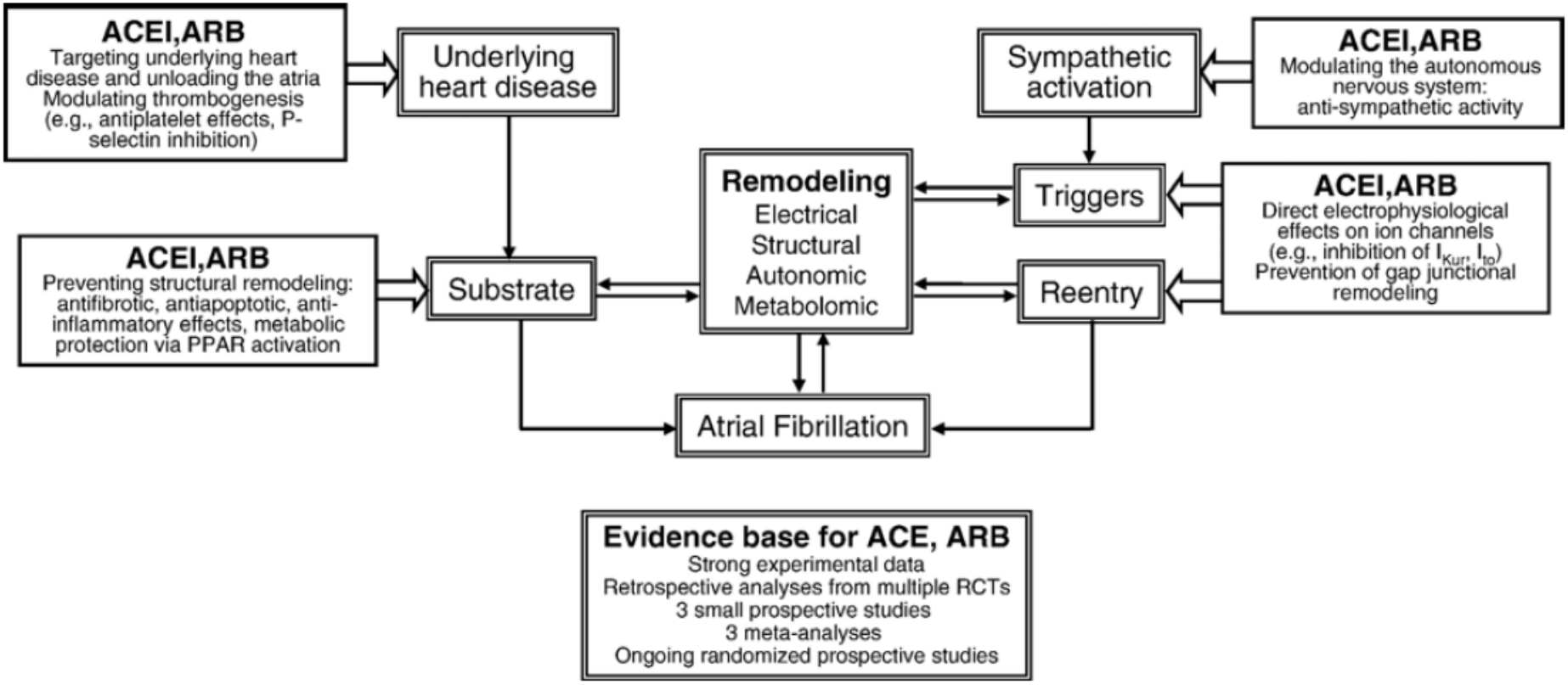


ATRIAL FIBRILLATION

« Upstream therapy » for the treatment of AF

Drug Class	Mechanism of Action	Clinical Evidence
ACE inhibitors	Reduced production of angiotensin II	Reduction in the incidence AF for patients with LV dysfunction[66]
		Reduction in the incidence AF for post-MI patients with LV dysfunction[67]
Angiotensin receptor blockers	Angiotensin I receptor antagonist	Reduction in the incidence of AF for patients with LV dysfunction[66]
		No reduction in recurrent AF[68]
Statins	HMG-CoA reductase inhibitor, antioxidant, anti-inflammatory	Reduction in the incidence of AF[69]
		Reduction in postoperative or post-MI AF[70]
w-3 Polyunsaturated fatty acids	Lipid lowering, antiarrhythmic, antioxidant, anti-inflammatory	Reduction in postoperative AF[71]
Glucocorticoids	Anti-inflammatory	Reduction in recurrent and permanent AF[72]
		Reduction in postoperative AF[73]
Spironolactone	Aldosterone antagonist	None
Pirfenidone	Unknown (anti-inflammatory?)	None

Rôle potentiel IEC et ARA2



Effets arythmogènes de l'ATII

Angiotensine II

Facteurs de croissance

Myocytes

Cellules musculaires lisses

Fibroblastes

Remodelage structurel

Effets arythmogènes de l'ATII

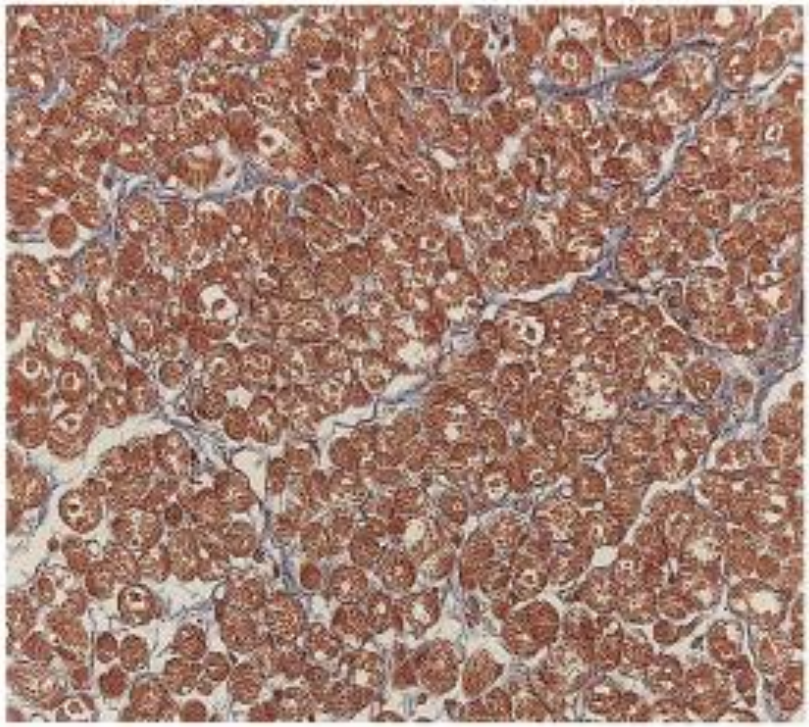
Augmentation de la post-charge

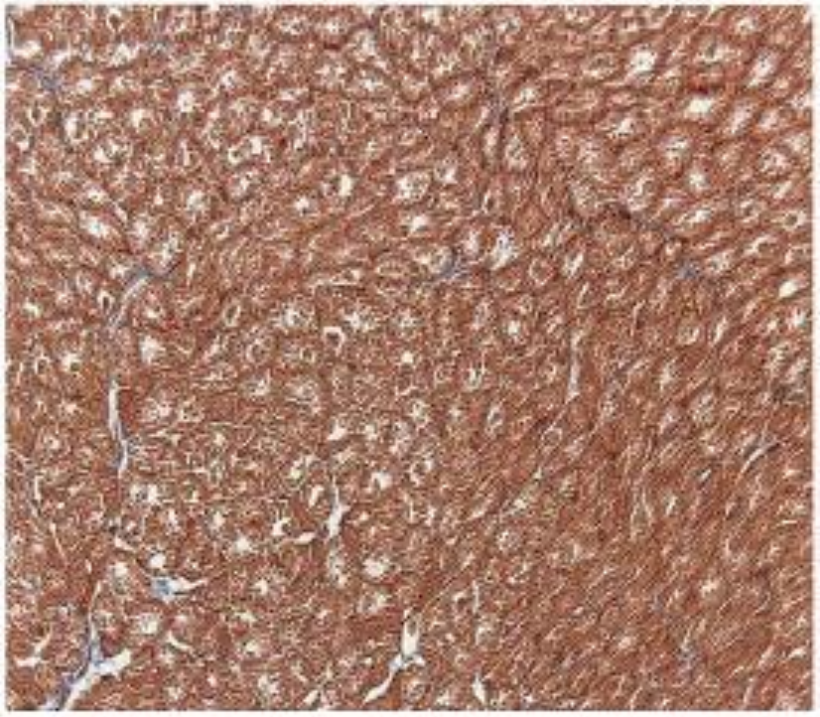
Dilatation et hyperpression VG

Dispersion des périodes réfractaires
Raccourcissement du potentiel d'action
Post dépolarisations

Remodelage électrophysiologique

FA expérimentale et ARA II





Placebo

Candesartan 5 sem.

Kumagai, JACC, 2003

AF and RAS inhibition

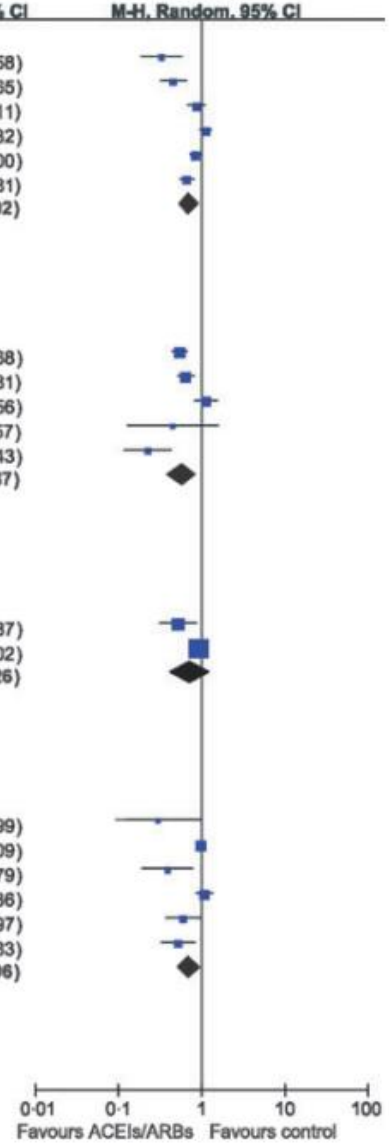
Hypertension

Ins. cardiaque

Post-IDM

FA

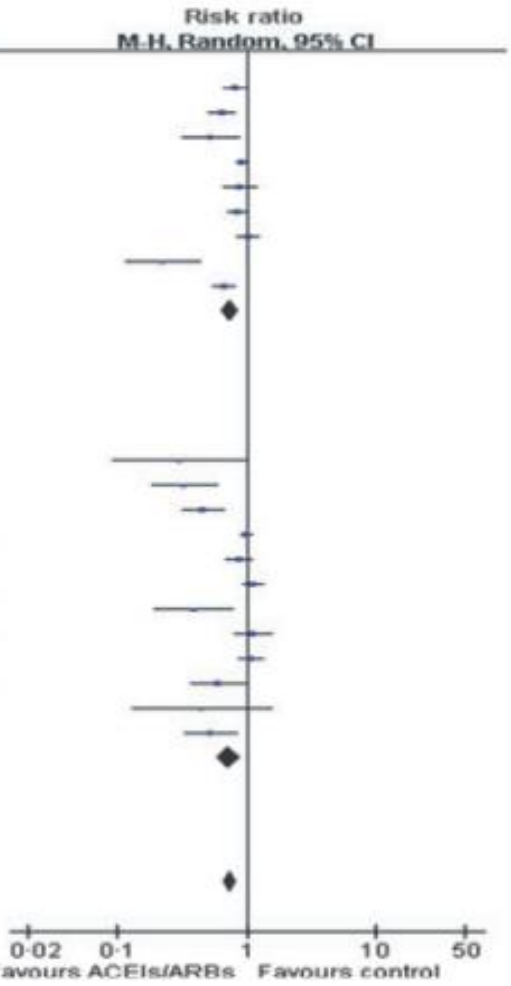
Study or subgroup	ACEIs/ARBs Events	Total	Control Events	Total	Weight	Risk ratio M-H, Random, 95% CI
1.2.1 Hypertension						
Fogari 2006	13	107	39	106	9·9%	0·33 (0·19, 0·58)
Fogari 2008	42	246	46	123	14·7%	0·46 (0·32, 0·65)
Hansson(CAPPP) 1999	117	5492	135	5493	17·6%	0·87 (0·68, 1·11)
Hansson(STOP-H2) 1999	200	2205	357	4409	19·5%	1·12 (0·95, 1·32)
Schmieder(VALUE) 2008	252	6872	299	6888	19·6%	0·84 (0·72, 1·00)
wachtell(LIFE) 2005	150	4298	221	4182	18·7%	0·66 (0·54, 0·81)
Subtotal (95% CI)		**19220**		**21201**	**100·0%**	**0·71 (0·54, 0·92)**
Total events	774		1097			
Heterogeneity: $\tau^2 = 0·09$; $\chi^2 = 38·51$, df = 5 ($P < 0·00001$); $I^2 = 87\%$ (74%, 94%) ($P < 0·001$)						
Test for overall effect: $Z = 2·55$ ($P = 0·01$)						
1.2.2 Chronic heart failure						
Ducharme(CHARM) 2006	117	3191	215	3188	28·8%	0·54 (0·44, 0·68)
Maggioni (Val-HeFT) 2005	113	2205	174	2190	28·4%	0·65 (0·51, 0·81)
Massie(I-PRESERVE) 2008	77	2067	68	2061	24·6%	1·13 (0·82, 1·56)
Van den berg 1995	2	7	7	11	5·0%	0·45 (0·13, 1·57)
Vermes(SOLVD) 2003	10	186	45	188	13·2%	0·22 (0·12, 0·43)
Subtotal (95% CI)		**7656**		**7638**	**100·0%**	**0·58 (0·39, 0·87)**
Total events	319		509			
Heterogeneity: $\tau^2 = 0·15$; $\chi^2 = 24·34$, df = 4 ($P < 0·0001$); $I^2 = 84\%$ (63%, 93%) ($P < 0·001$)						
Test for overall effect: $Z = 2·66$ ($P = 0·008$)						
1.2.3 Post myocardial infarction						
Pedersen(TRACE) 1999	22	790	42	787	34·9%	0·52 (0·31, 0·87)
Pizzetti(GISSI-3) 2001	665	8865	721	8846	65·1%	0·92 (0·83, 1·02)
Subtotal (95% CI)		**9655**		**9633**	**100·0%**	**0·73 (0·43, 1·26)**
Total events	687		763			
Heterogeneity: $\tau^2 = 0·13$; $\chi^2 = 4·64$, df = 1 ($P = 0·03$); $I^2 = 78\%$ ($P = 0·03$)						
Test for overall effect: $Z = 1·12$ ($P = 0·26$)						
1.2.4 Atrial fibrillation						
Belluzzi 2009	3	31	10	31	4·7%	0·30 (0·09, 0·99)
GISSI-AF 2009	371	722	375	720	28·2%	0·99 (0·89, 1·09)
Madrid 2002	9	79	22	75	10·3%	0·39 (0·19, 0·79)
Tveit (CAPRAF) 2007	48	68	45	69	24·4%	1·08 (0·86, 1·36)
Ueng 2003	18	70	32	75	16·0%	0·60 (0·37, 0·97)
Yin 2006	25	118	24	59	16·3%	0·52 (0·33, 0·83)
Subtotal (95% CI)		**1088**		**1029**	**100·0%**	**0·71 (0·52, 0·96)**
Total events	474		508			
Heterogeneity: $\tau^2 = 0·09$; $\chi^2 = 22·27$, df = 5 ($P = 0·0005$); $I^2 = 78\%$ (50%, 90%) ($P < 0·001$)						
Test for overall effect: $Z = 2·22$ ($P = 0·03$)						



Huang et al, Eur J Clin Invest 2011

AF and RAS inhibition

Study or subgroup	Favours ACEIs/ARBs Events	Total	Control Events	Total	Weight	Risk ratio M-H, Random, 95% CI
1.1.1 Primary prevention						
Ducharme(CHARM) 2006	177	3191	215	3188	6·4%	0·82 (0·68, 1·00)
Maggioni (Val-HeFT) 2005	113	2205	174	2190	6·0%	0·65 (0·51, 0·81)
Pedersen(TRACE) 1999	22	790	42	787	3·3%	0·52 (0·31, 0·87)
Pizzetti(GISSI-3) 2001	665	8865	721	8846	7·3%	0·92 (0·83, 1·02)
Salehian(HOPE) 2007	86	4291	91	4044	5·4%	0·89 (0·67, 1·19)
Schmieder(VALUE) 2008	252	6872	299	6888	6·7%	0·84 (0·72, 1·00)
TRANSCEND 2008	182	2954	180	2972	6·4%	1·02 (0·83, 1·24)
Vermes(SOLVD) 2003	10	186	45	188	2·4%	0·22 (0·12, 0·43)
wachtell(LIFE) 2005	150	4298	221	4182	6·3%	0·66 (0·54, 0·81)
Subtotal (95% CI)		**33652**		**33285**	**50·3%**	**0·76 (0·65, 0·88)**
Total events	1657		1988			
Heterogeneity: $\tau^2 = 0·04$; $\chi^2 = 36·36$, df = 8 ($P < 0·0001$); $I^2 = 78\%$ (58%, 88%) ($P < 0·001$)						
Test for overall effect: $Z = 3·52$ ($P = 0·0004$)						
1.1.2 Secondary prevention						
Belluzzi 2009	3	31	10	31	0·9%	0·30 (0·09, 0·99)
Fogari 2006	13	107	39	106	2·9%	0·33 (0·19, 0·58)
Fogari 2008	42	246	46	123	4·7%	0·46 (0·32, 0·65)
GISSI-AF 2009	371	722	375	720	7·3%	0·99 (0·89, 1·09)
Hansson(CAPPP) 1999	117	5492	135	5493	5·9%	0·87 (0·68, 1·11)
Hansson(STOP-H2) 1999	200	2205	357	4409	6·7%	1·12 (0·95, 1·32)
Madrid 2002	9	79	22	75	2·2%	0·39 (0·19, 0·79)
Massie(I-PRESERVE) 2008	77	2067	68	2061	5·0%	1·13 (0·82, 1·56)
Tveit (CAPRAF) 2007	48	68	45	69	6·0%	1·08 (0·86, 1·36)
Ueng 2003	18	70	32	75	3·6%	0·60 (0·37, 0·97)
Van den berg 1995	2	7	7	11	0·9%	0·45 (0·13, 1·57)
Yin 2006	25	118	24	59	3·7%	0·52 (0·33, 0·83)
Subtotal (95% CI)		**11212**		**13232**	**49·7%**	**0·73 (0·59, 0·89)**
Total events	925		1160			
Heterogeneity: $\tau^2 = 0·08$; $\chi^2 = 57·61$, df = 11 ($P < 0·00001$); $I^2 = 81\%$ (68%, 89%) ($P < 0·001$)						
Test for overall effect: $Z = 3·03$ ($P = 0·002$)						
Total (95% CI)		**44864**		**46517**	**100·0%**	**0·75 (0·66, 0·85)**
Total events	2582		3148			
Heterogeneity: $\tau^2 = 0·05$; $\chi^2 = 99·53$, df = 20 ($P < 0·00001$); $I^2 = 80\%$ [70%, 87%] ($P < 0·001$)						
Test for overall effect: $Z = 4·54$ ($P < 0·00001$)						

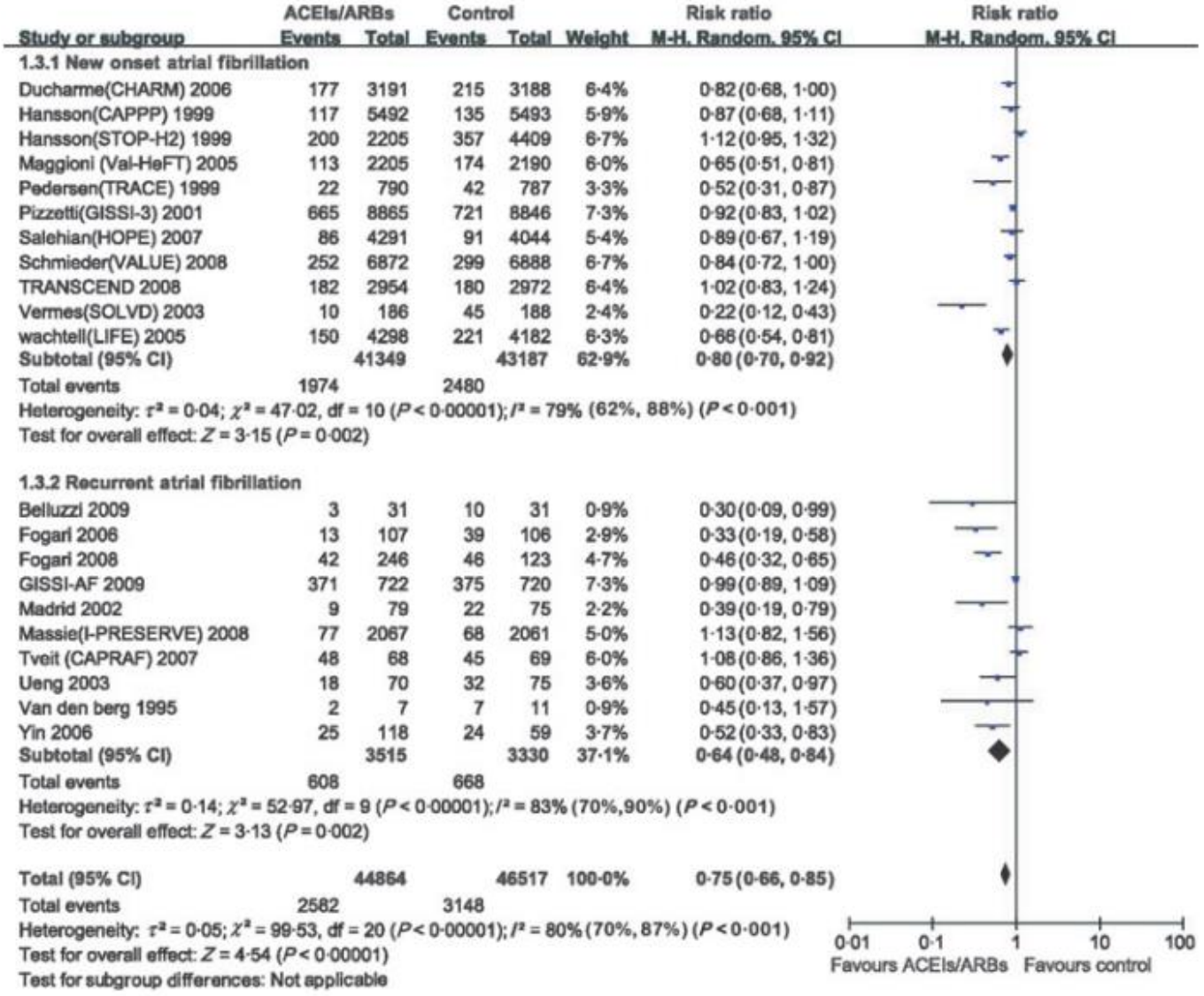


Huang et al, Eur J Clin Invest 2011

AF and RAS inhibition

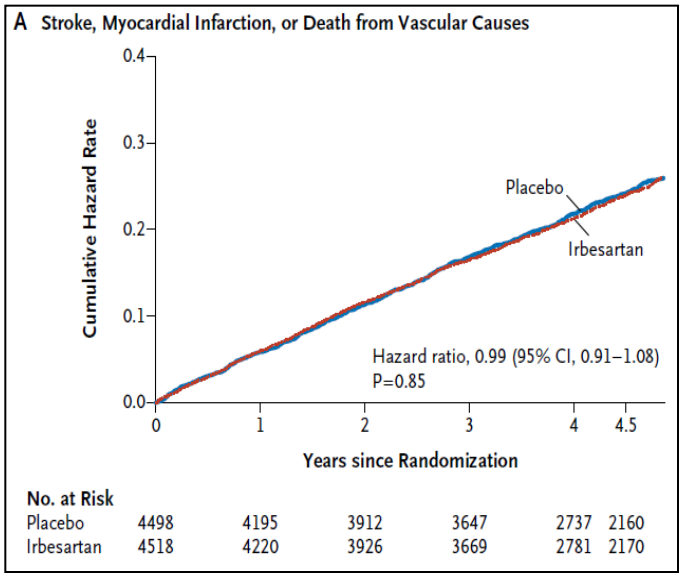
Nouvelle FA

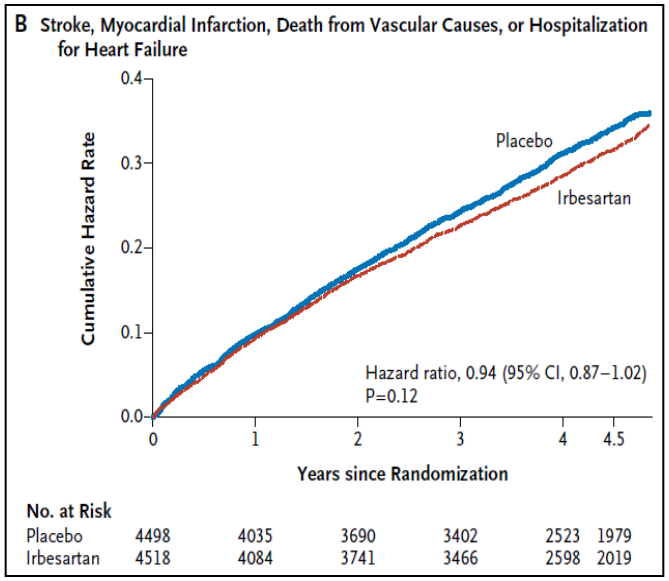
Récidive de FA



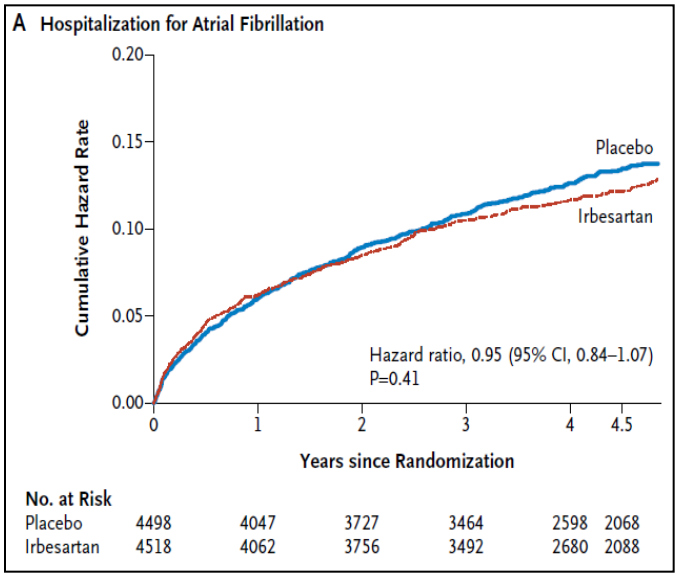
Study or subgroup	ACEIs/ARBs Events	Total	Control Events	Total	Weight	Risk ratio M-H, Random, 95% CI
1.3.1 New onset atrial fibrillation						
Ducharme(CHARM) 2006	177	3191	215	3188	6·4%	0·82 (0·68, 1·00)
Hansson(CAPPP) 1999	117	5492	135	5493	5·9%	0·87 (0·68, 1·11)
Hansson(STOP-H2) 1999	200	2205	357	4409	6·7%	1·12 (0·95, 1·32)
Maggioni (Val-HeFT) 2005	113	2205	174	2190	6·0%	0·65 (0·51, 0·81)
Pedersen(TRACE) 1999	22	790	42	787	3·3%	0·52 (0·31, 0·87)
Pizzetti(GISSI-3) 2001	665	8865	721	8846	7·3%	0·92 (0·83, 1·02)
Salehian(HOPE) 2007	86	4291	91	4044	5·4%	0·89 (0·67, 1·19)
Schmieder(VALUE) 2008	252	6872	299	6888	6·7%	0·84 (0·72, 1·00)
TRANSCEND 2008	182	2954	180	2972	6·4%	1·02 (0·83, 1·24)
Vermes(SOLVD) 2003	10	186	45	188	2·4%	0·22 (0·12, 0·43)
wachtell(LIFE) 2005	150	4298	221	4182	6·3%	0·66 (0·54, 0·81)
Subtotal (95% CI)		**41349**		**43187**	**62·9%**	**0·80 (0·70, 0·92)**
Total events	1974		2480			
Heterogeneity: $\tau^2 = 0·04$; $\chi^2 = 47·02$, df = 10 ($P < 0·00001$); $I^2 = 79\%$ (62%, 88%) ($P < 0·001$)						
Test for overall effect: $Z = 3·15$ ($P = 0·002$)						
1.3.2 Recurrent atrial fibrillation						
Belluzzi 2009	3	31	10	31	0·9%	0·30 (0·09, 0·99)
Fogari 2006	13	107	39	106	2·9%	0·33 (0·19, 0·58)
Fogari 2008	42	246	46	123	4·7%	0·46 (0·32, 0·65)
GISSI-AF 2009	371	722	375	720	7·3%	0·99 (0·89, 1·09)
Madrid 2002	9	79	22	75	2·2%	0·39 (0·19, 0·79)
Massie(I-PRESERVE) 2008	77	2067	68	2061	5·0%	1·13 (0·82, 1·56)
Tveit (CAPRAF) 2007	48	68	45	69	6·0%	1·08 (0·86, 1·36)
Ueng 2003	18	70	32	75	3·6%	0·60 (0·37, 0·97)
Van den berg 1995	2	7	7	11	0·9%	0·45 (0·13, 1·57)
Yin 2006	25	118	24	59	3·7%	0·52 (0·33, 0·83)
Subtotal (95% CI)		**3515**		**3330**	**37·1%**	**0·64 (0·48, 0·84)**
Total events	608		668			
Heterogeneity: $\tau^2 = 0·14$; $\chi^2 = 52·97$, df = 9 ($P < 0·00001$); $I^2 = 83\%$ (70%,90%) ($P < 0·001$)						
Test for overall effect: $Z = 3·13$ ($P = 0·002$)						
Total (95% CI)		**44864**		**46517**	**100·0%**	**0·75 (0·66, 0·85)**
Total events	2582		3148			
Heterogeneity: $\tau^2 = 0·05$; $\chi^2 = 99·53$, df = 20 ($P < 0·00001$); $I^2 = 80\%$ (70%, 87%) ($P < 0·001$)						
Test for overall effect: $Z = 4·54$ ($P < 0·00001$)						
Test for subgroup differences: Not applicable						

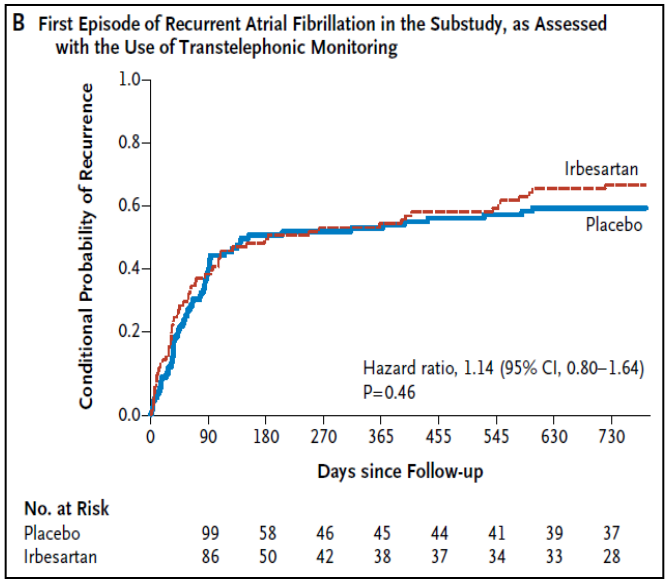
Huang et al, Eur J Clin Invest 2011





9016 pts (HTA 88%) suivis 4,1 ans en moyenne





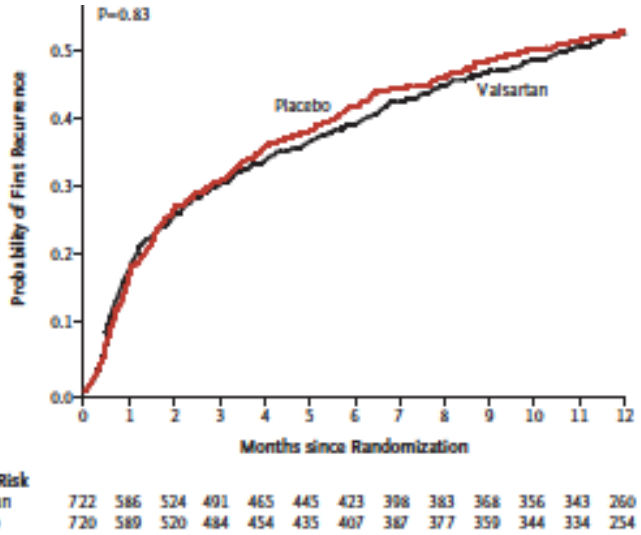
ACTIVE I investigators, NEJM 2011

Upstream therapy dans la FA : la fin??

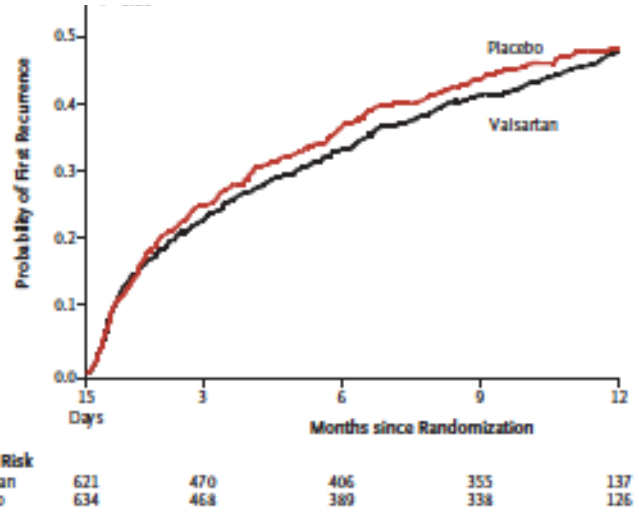
Valsartan for Prevention of Recurrent Atrial Fibrillation

The GISSI-AF Investigators*

A



No. at Risk													
Valsartan	722	586	524	491	465	445	423	398	383	368	356	343	260
Placebo	720	589	520	484	454	435	407	387	377	359	344	334	254



No. at Risk					
Valsartan	621	470	406	355	137
Placebo	634	468	389	338	126

Kaplan–Meier Curves for the Time to the First Recurrence of Atrial Fibrillation.

Panel A includes data from the whole cohort, and Panel B data from the 1255 patients who were in sinus rhythm at 15 days.

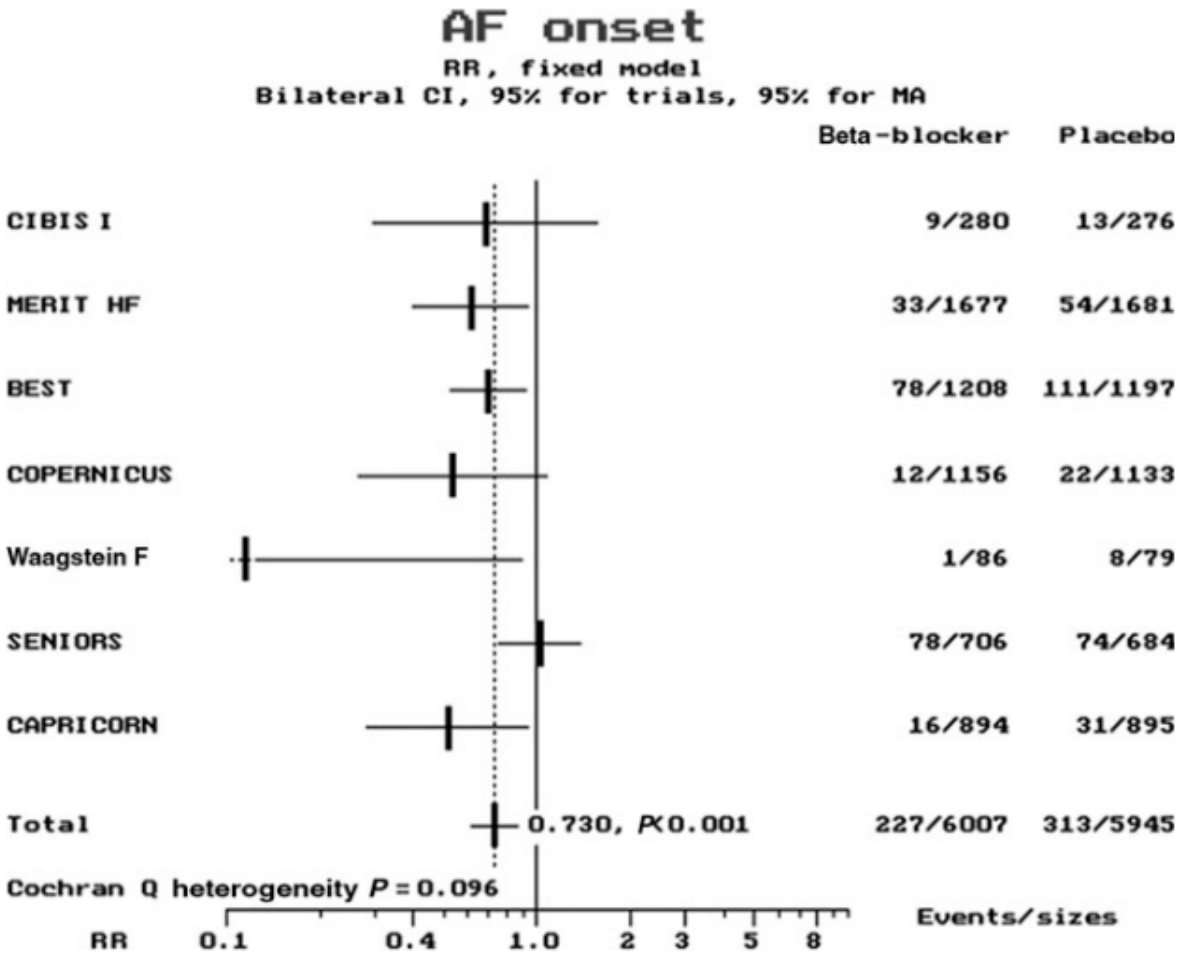
N Engl J Med 2009: 360;16

Rhythm control therapy : non antiarrhythmic drugs

Recommendations	Class	Level
Antiarrhythmic effects of non-antiarrhythmic drugs		
ACE-Is, ARBs and beta-blockers should be considered for prevention of new-onset AF in patients with heart failure and reduced ejection fraction.	**IIa**	**A**
ACE-Is and ARBs should be considered for prevention of new-onset AF in patients with hypertension, particularly with LV hypertrophy.	**IIa**	**B**
Pre-treatment with ACE-Is or ARBs may be considered in patients with recurrent AF undergoing electrical cardioversion and receiving antiarrhythmic drug therapy.	**IIb**	**B**
ACE-Is or ARBs are not recommended for the secondary prevention of paroxysmal AF in patients with little or no underlying heart disease.	**III (no benefit)**	**B**

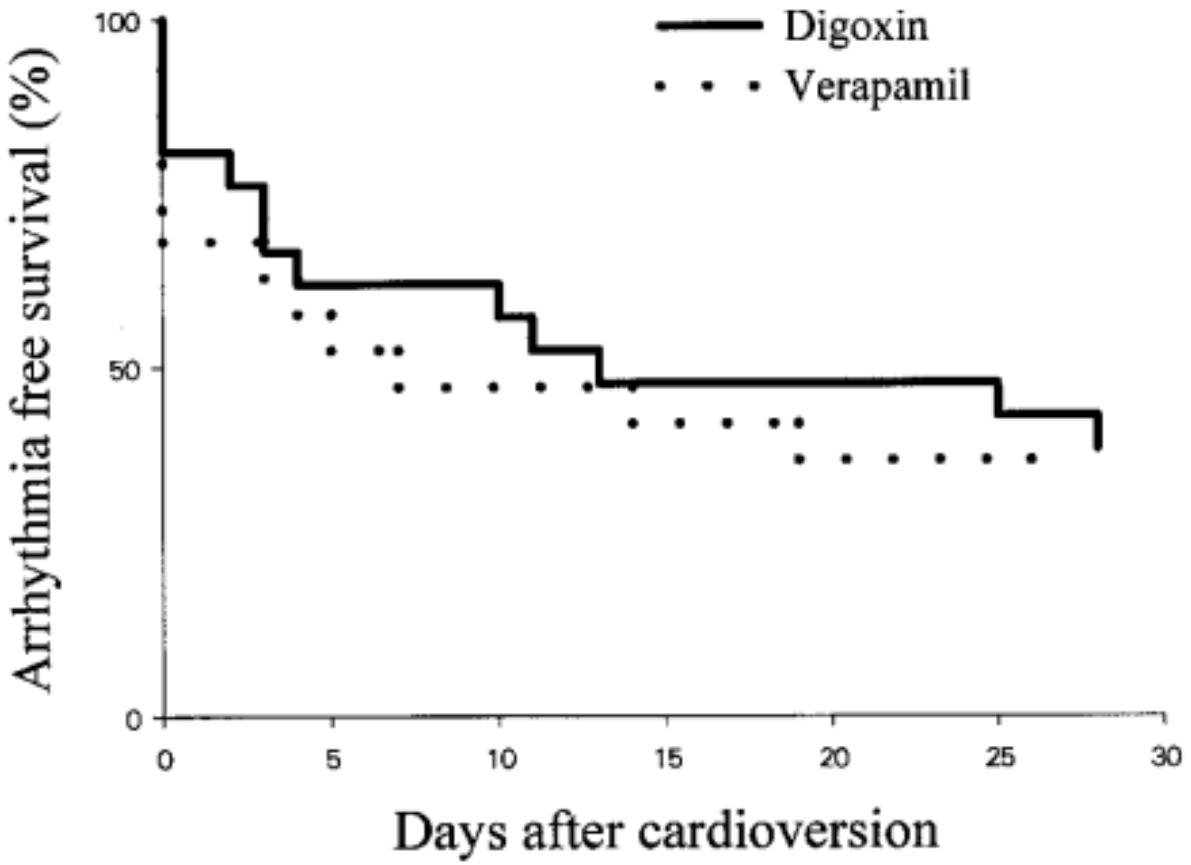
ESC 2016

AF and Beta-blockers in HF



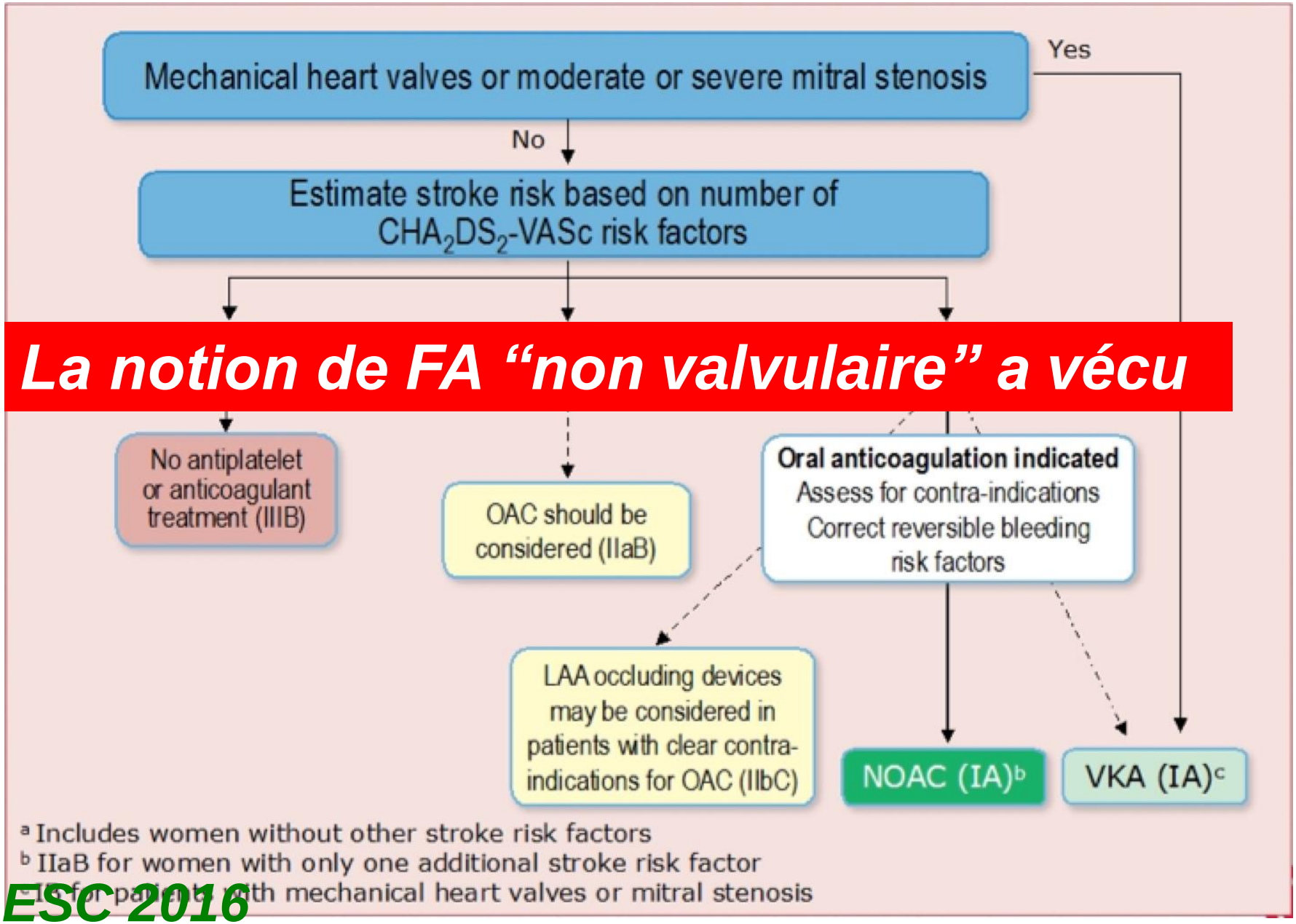
Nasr et al, Eur Heart J 2007

Verapamil vs Digoxin around cardioversion



Van Noor, J Cardiovasc Electrophysiol 2010

Qui anticoaguler?



ESC 2016

Qui anticoaguler?

Recommendations	Class	Level
Oral anticoagulation therapy to prevent thromboembolism is recommended for all male AF patients with a CHA_2DS_2-VASc score of 2 or more.	I	A
Oral anticoagulation therapy to prevent thromboembolism is recommended in all female AF patients with a CHA_2DS_2-VASc score of 3 or more.	I	A
Oral anticoagulation therapy to prevent thromboembolism should be considered in male AF patients with a CHA_2DS_2-VASc score of 1, considering individual characteristics and patient preferences.	IIa	B
Oral anticoagulation therapy to prevent thromboembolism should be considered in female AF patients with a CHA_2DS_2-VASc score of 2, considering individual characteristics and patient preferences.	IIa	B
Vitamin K antagonist therapy (INR 2.0–3.0 or higher) is recommended for stroke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valves.	I	B
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a Vitamin K antagonist.	I	A

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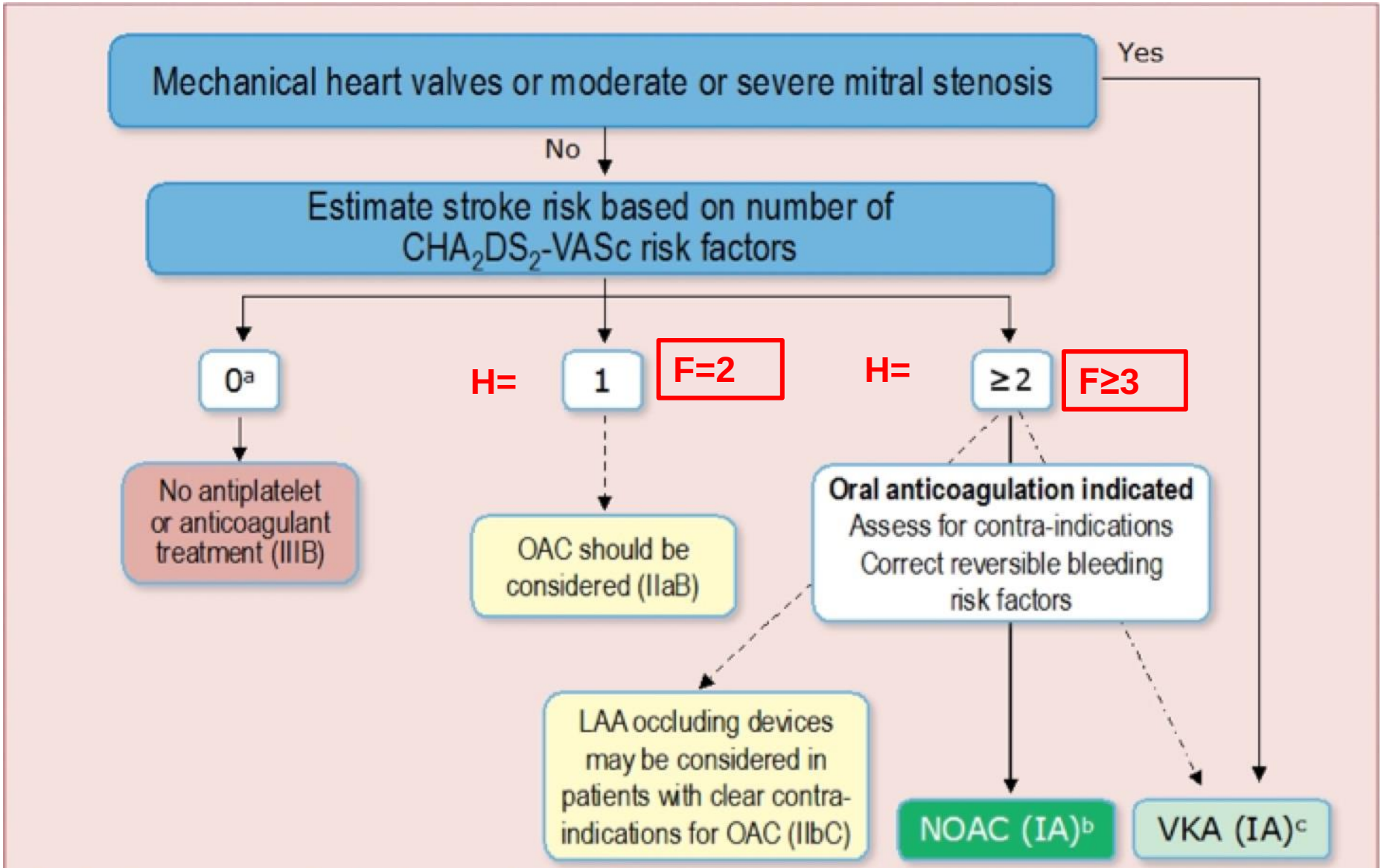
Qui anticoaguler?

Recommendations	Class	Level
When patients are treated with a vitamin K antagonist, time in therapeutic range (TTR) should be kept as high as possible and closely monitored.	I	A
AF patients already on treatment with a vitamin K antagonist may be considered for NOAC treatment if TTR is not well controlled despite good adherence, or if patient preference without contra-indications to NOAC (e.g. prosthetic valve).	IIb	A
Combinations of oral anticoagulants and platelet inhibitors increase bleeding risk and should be avoided in AF patients without another indication for platelet inhibition.	III (harm)	B
In male or female AF patients without additional stroke risk factors, anticoagulant or antiplatelet therapy is not recommended for stroke prevention.	III (harm)	B
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III (harm)	A
NOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are not recommended in patients with mechanical heart valves (Level of evidence B) or moderate-to-severe mitral stenosis (Level of evidence C).	III (harm)	B C

ESC 2016

Qui anticoaguler?

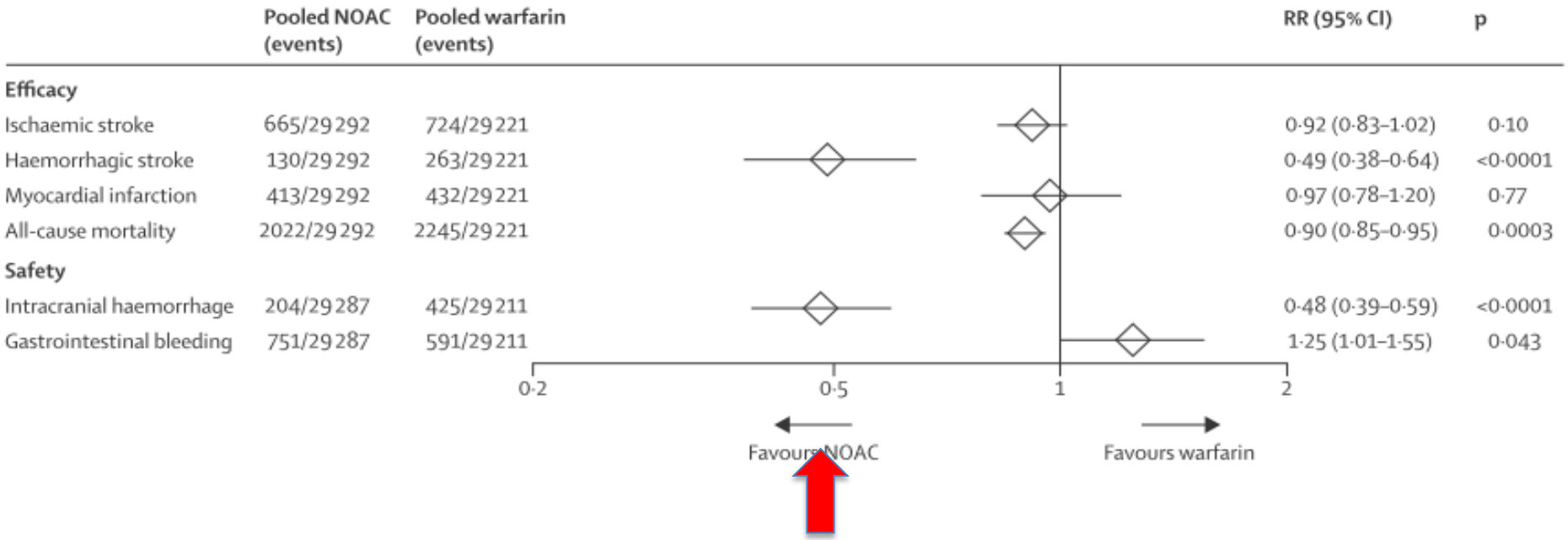
ESC 2016



[a] Includes women without other stroke risk factors
[b] IIaB for women with only one additional stroke risk factor
[c] IB for patients with mechanical heart valves or mitral stenosis

	Apixaban ARISTOTLE[1]	**Apixaban** AVERROES[2]	**Dabigatran** RE-LY[3]	**Edoxaban** ENGAGE AF-TIMI 48[4]	**Rivaroxaban** ROCKET AF[5]
N	18 201	5 599	18 113	21 105	14 264
Design	Double-blind, double-dummy	Double-blind, double-dummy	Blinded (dabigatran) Open-label (warfarin)	Double-blind, double-dummy	Double-blind, double-dummy
Treatments	• Apixaban 5 mg twice-daily (2.5 mg twice-daily in selected patients*) • Warfarin (INR target: 2–3)	• Apixaban 5 mg twice-daily (2.5 mg twice-daily in selected patients*) • ASA (81–324 mg per day)	• Dabigatran 110 mg twice-daily • Dabigatran 150 mg twice-daily • Warfarin (INR target: 2–3)	• Edoxaban high-dose (60 mg)† • Edoxaban low-dose (30 mg)† • Warfarin (INR target: 2–3)	• Rivaroxaban 20 mg once-daily (15 mg once-daily in selected patients‡) • Warfarin (INR target: 2–3)
Objective	Non-inferiority	Superiority	Non-inferiority	Non-inferiority	Non-inferiority

NOACs vs Warfarine N=71218



Ruff et al., Lancet 2013

ESC European Society of Cardiology
European Heart Journal (2018) 39, 3021–3104
doi:10.1093/eurheartj/ehy339

2018 ESC/ESH Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)

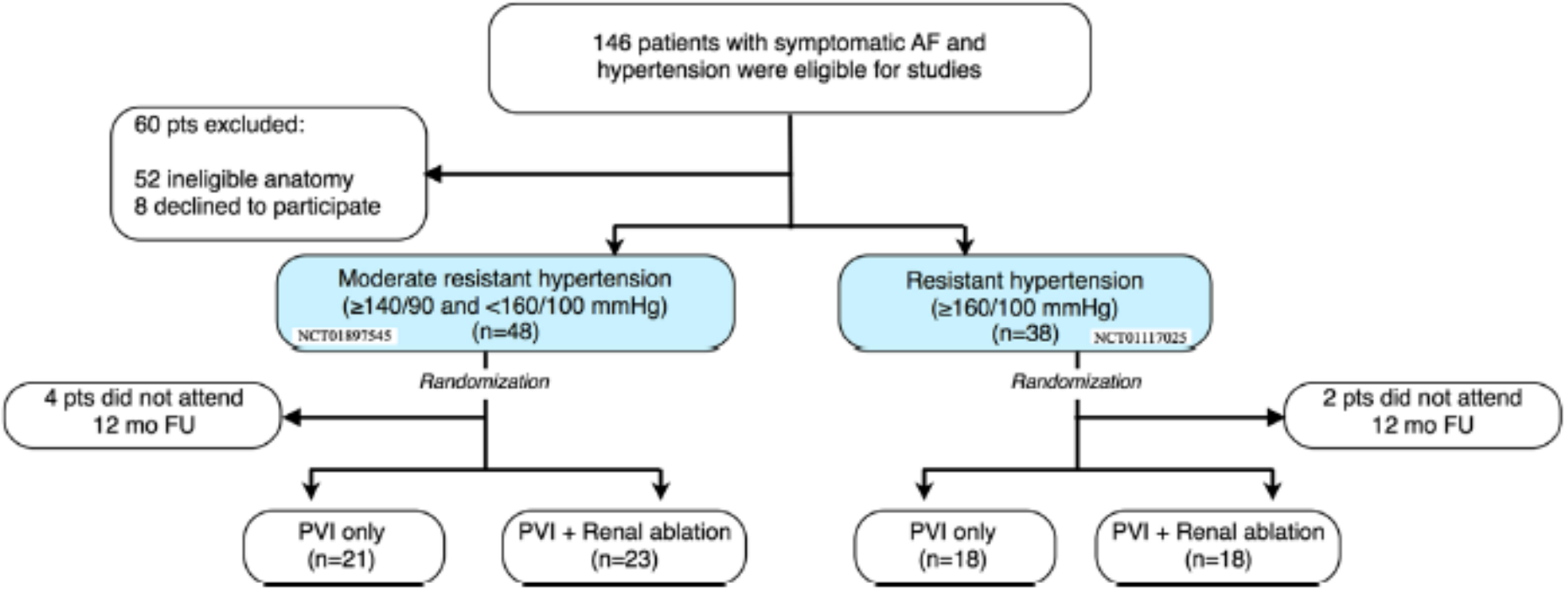
Authors/Task Force Members: Bryan Williams* (ESC Chairperson) (UK), Giuseppe Mancia* (ESH Chairperson) (Italy), Wilko Spiering (The Netherlands), Enrico Agabiti Rosei (Italy), Michel Azizi (France), Michel Burnier (Switzerland), Denis L. Clement (Belgium), Antonio Coca (Spain), Giovanni de Simone (Italy), Anna Dominiczak (UK), Thomas Kahan (Sweden), Felix Mahfoud (Germany), Josep Redon (Spain), Luis Ruilope (Spain), Alberto Zanchetti† (Italy), Mary Kerins (Ireland), Sverre E. Kjeldsen (Norway), Reinhold Kreutz (Germany), Stephane Laurent (France), Gregory Y. H. Lip (UK), Richard McManus (UK), Krzysztof Narkiewicz (Poland), Frank Ruschitzka (Switzerland), Roland E. Schmieder (Germany), Evgeny Shlyakhto (Russia), Costas Tsioufis (Greece), Victor Aboyans (France), and Ileana Desormais (France)

Therapeutic strategies in hypertensive patients with AF

Recommendation	Class[a]	Level[b]
In patients with AF, screening for hypertension is recommended.[536]	I	C
A beta-blocker or non-dihydropyridine CCB should be considered as part of the treatment of hypertension if rate control is needed.[536]	IIa	B
Stroke prevention with oral anticoagulation is recommended in patients with AF and hypertension, and a CHA_2DS_2-VASc score of ≥2 in men and ≥3 in women.[536,556]	I	A
Stroke prevention with oral anticoagulants should be considered in AF patients with hypertension, even when hypertension is the single additional risk factor (CHA_2DS_2-VASc score of 1).[536,556]	IIa	B
Oral anticoagulants should be used with caution in patients with marked BP elevation (SBP ≥180 mmHg and/or DBP ≥100 mmHg); the aim should be to lower SBP to at least <140 mmHg, and SBP lowering to <130 should be considered. If this is not possible, then patients should make an informed decision that they accept that the stroke protection provided by the anticoagulant will be associated with higher bleeding risk.[536]	IIa	B

Renal denervation for improving outcomes of catheter ablation in patients with atrial fibrillation and hypertension: Early experience

Evgeny Pokushalov, MD, PhD,* Alexander Romanov, MD,* Demosthenes G. Katritsis, MD, PhD,† Sergey Artyomenko, MD,* Sevda Bayramova, MD,* Denis Losik, MD,* Vera Baranova, MD,* Alexander Karaskov, MD, PhD,* Jonathan S. Steinberg, MD, FHRS‡



Study design and patient flow

Heart Rhythm2014;0:1–8

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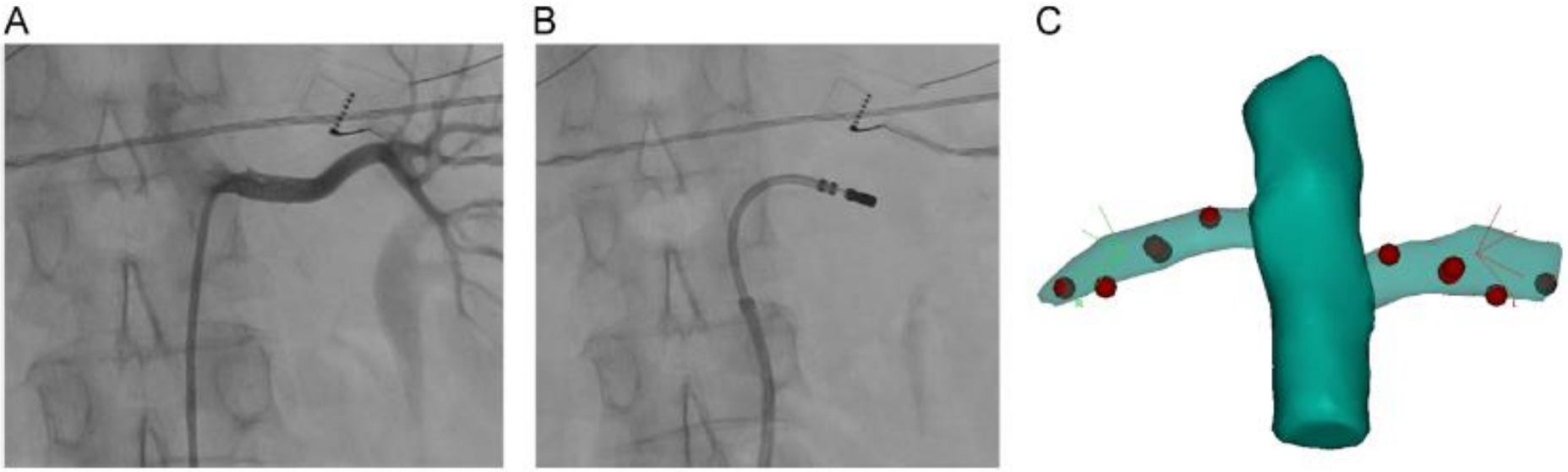

Figure 2 **A:** Angiography of the left renal artery. **B:** Renal ablation using the NaviStar ablation catheter. **C:** Three-dimensional reconstructions with sites of radiofrequency ablation represented in *red*.

Heart Rhythm2014;0:1–8

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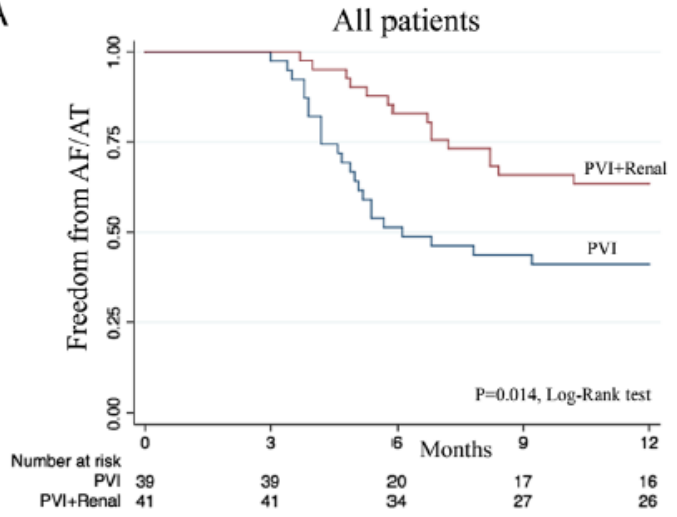
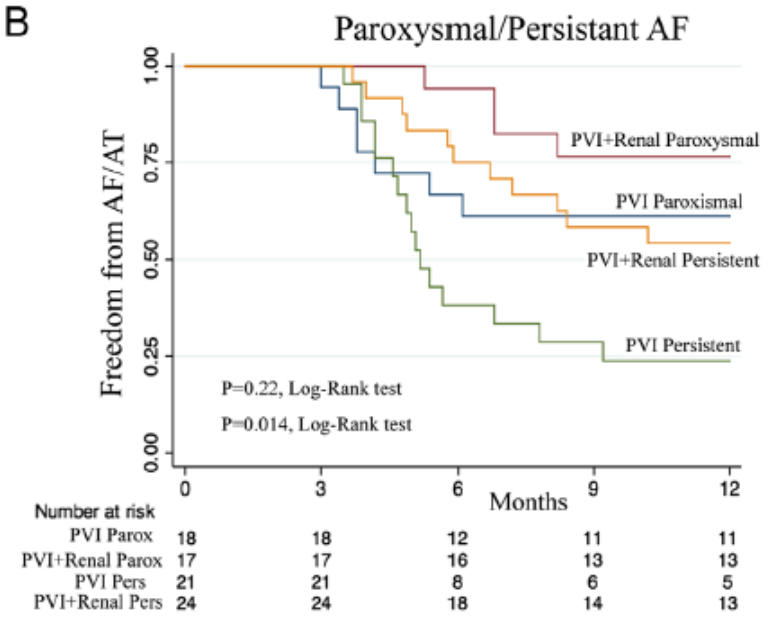
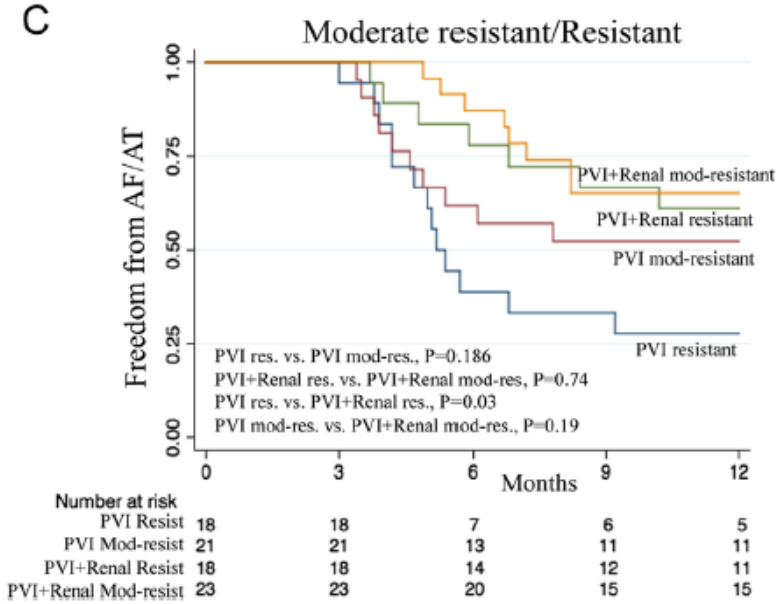
A



B



C



Heart Rhythm2014;0:1–8

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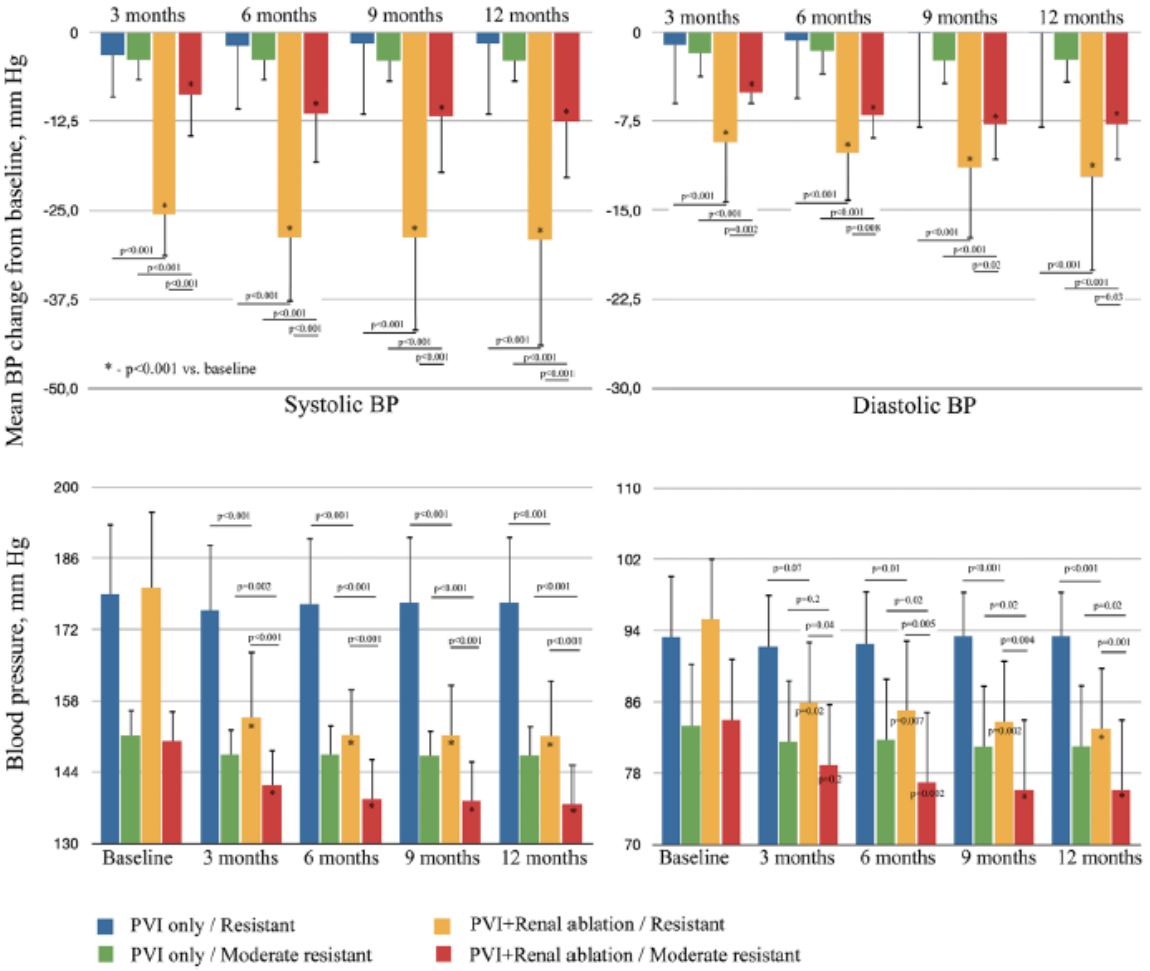

Figure 4 **A:** Change from baseline in systolic and diastolic blood pressures (BP) throughout follow-up. **B:** Office systolic and diastolic BP throughout up. PVI = pulmonary vein isolation.

Heart Rhythm2014;0:1–8

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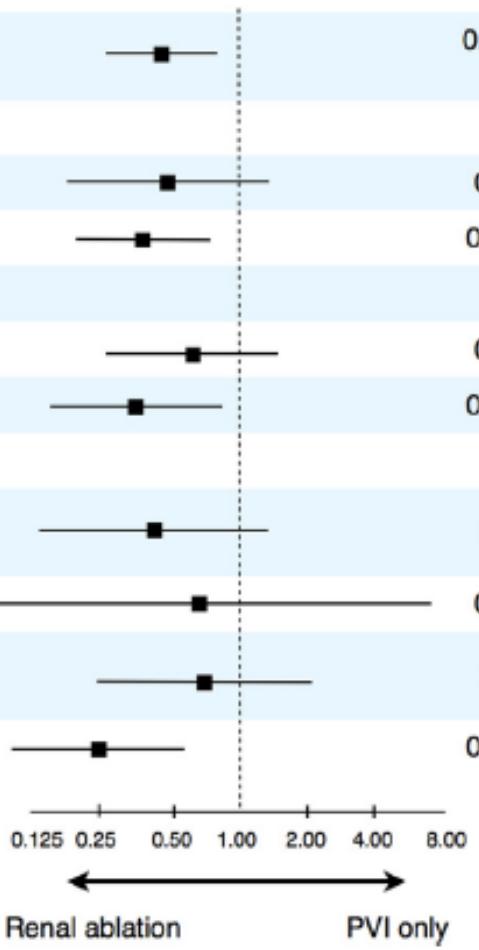
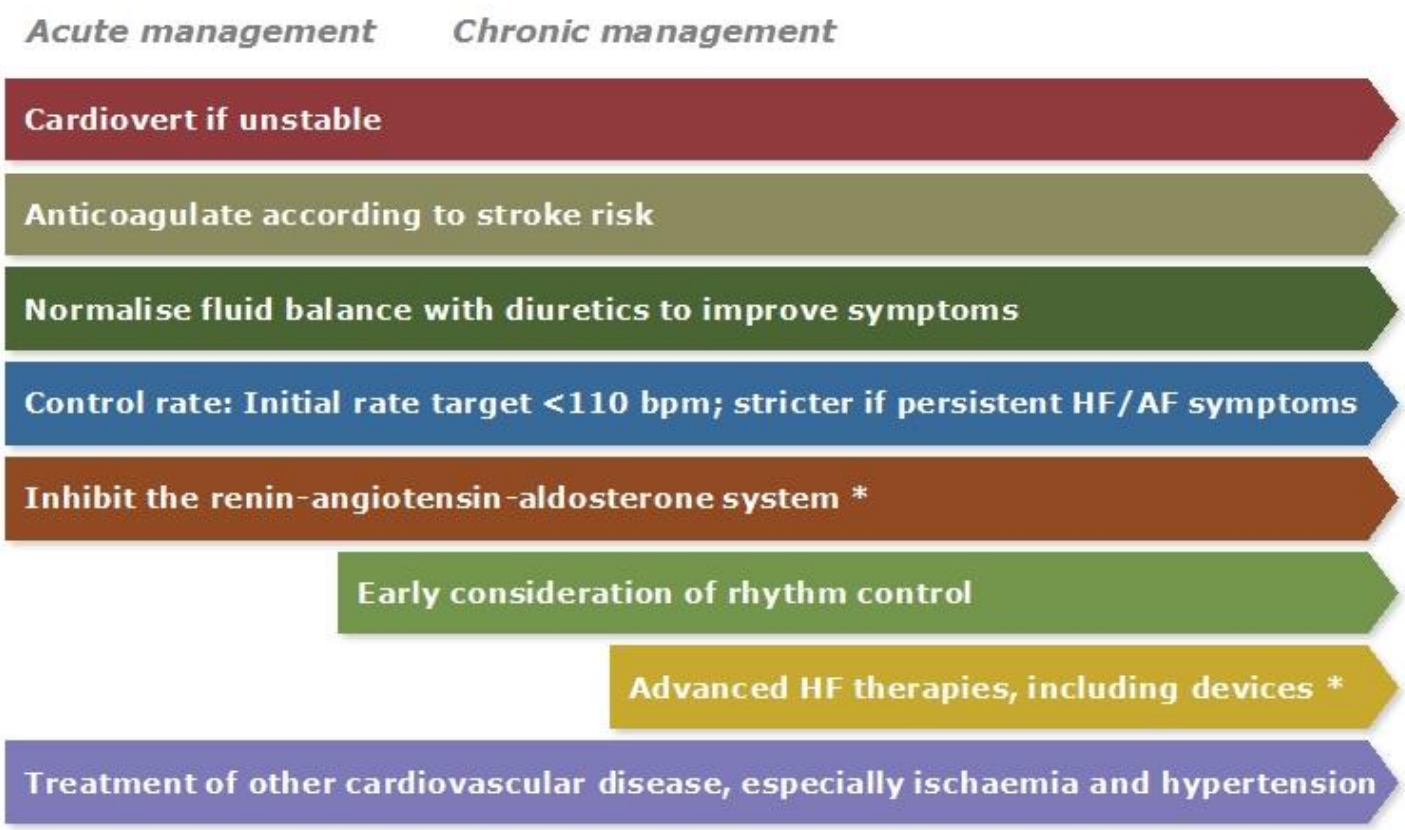
Subgroup	PVI only,n	PVI +RDN,n	Hazard Ratio (95%CI),p	*p for interaction
All subjects	39/23	41/15	0.45 (0.23-0.86), 0.009	
PAF/Pers AF				0.827
Paroxysmal	18/7	17/4	0.47 (0.14-1.6)	
Persistent	21/16	24/11	0.39 (0.18-0.85)	
Moderate resistant/Resistant				0.409
Moderate resistant	21/10	23/8	0.56 (0.22-1.4)	
Resistant	18/13	18/7	0.37 (0.14-0.93)	
Second level interaction				
Paroxysmal moderate resistant	12/5	13/3	0.43 (0.1-1.8)	
Paroxysmal resistant	6/2	4/1	0.61 (0.06-6.8)	
Persistent moderate resistant	9/5	10/5	0.69 (0.2-2.4)	
Persistent resistant	12/11	14/6	0.25 (0.09-0.72)	



Heart Rhythm2014;0:1–8

Initial management of patients presenyting acutely with AF and heart failur



* In patients with heart failure and reduced ejection fraction.

Guidelines ESC 2016

Fourth pillar of AF care.