Fibrillation atriale

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FA : étiologies et mécanismes

Stroke

Diabetes

Heart failure

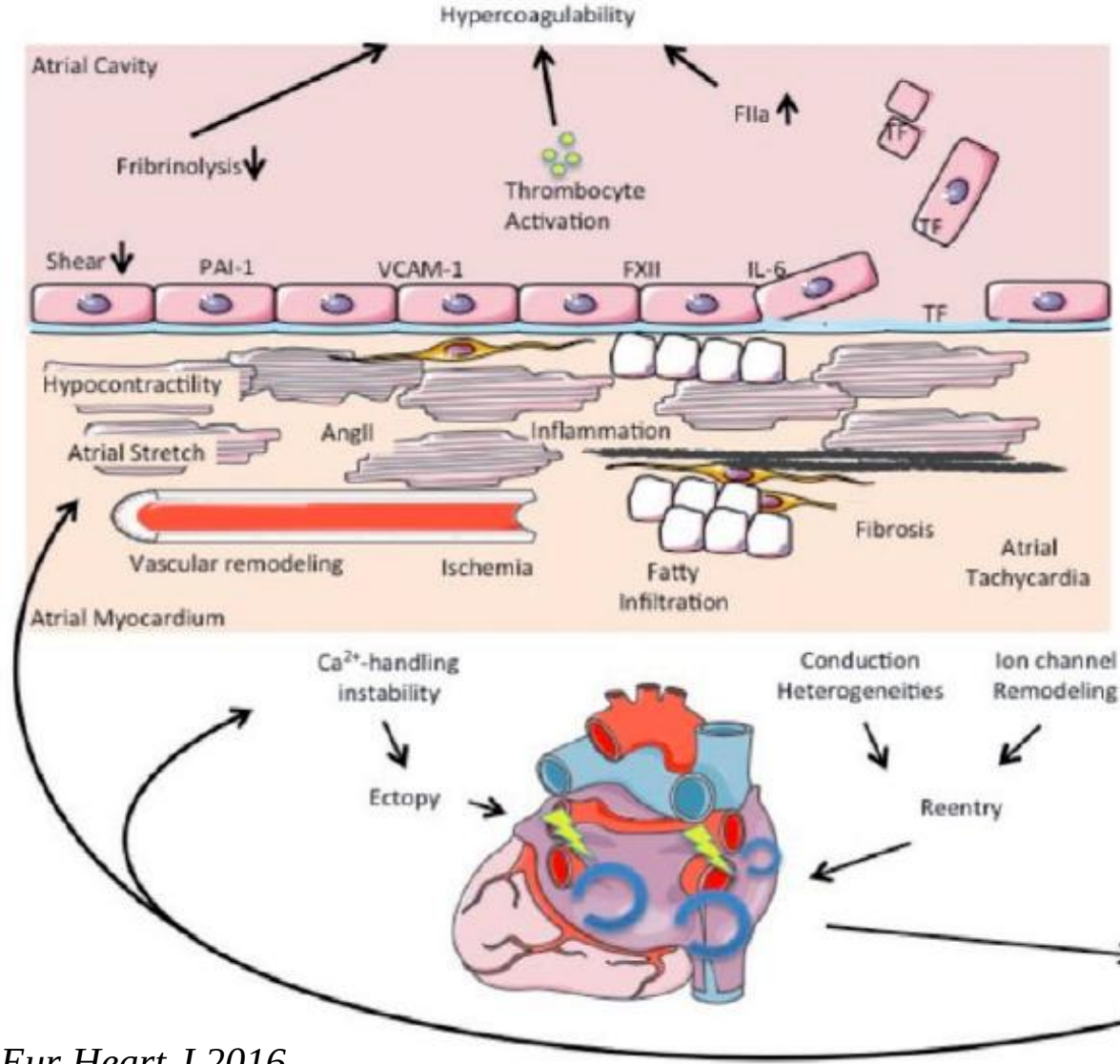
Obesity

Coronary artery disease

Hypertension

Ageing

Genetic predisposition



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Occurrence of death and stroke in pts in 47 countries 1 year after presenting with AF: a cohort study

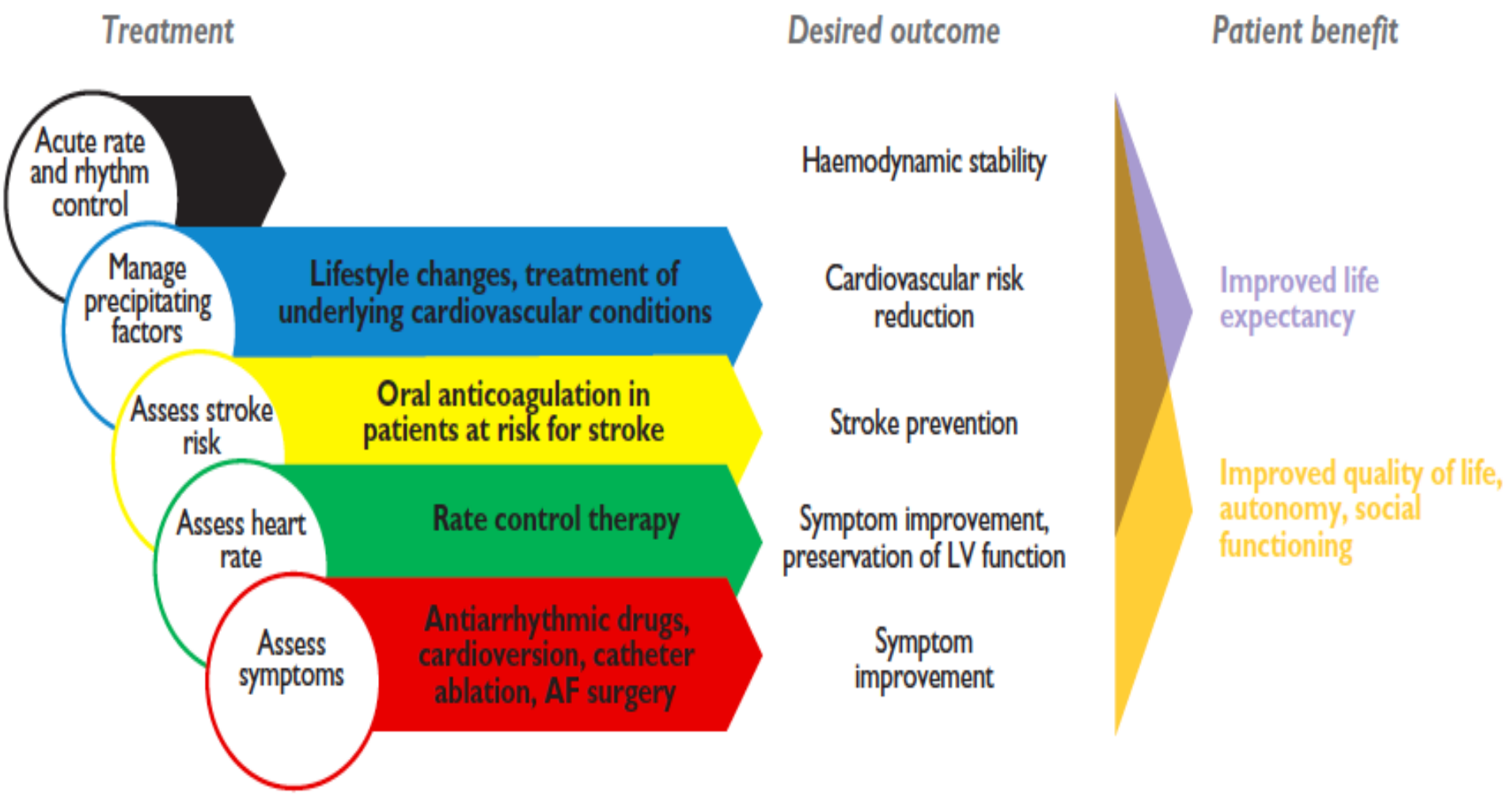
	North America, western Europe, or Australia (n=3800)	South America (n=1132)	Eastern Europe (n=2538)	Middle East (n=864)	Africa (n=1137)	India (n=2536)	China (n=2023)	South-east Asia (n=1331)	Overall (n=15361)	p value*
Death	366 (10%)	192 (17%)†	220 (9%)	113 (13%)†	225 (20%)†	231 (9%)	285 (14%)†	126 (9%)	1758 (11%)	<0·0001
Stroke	94 (2%)	31 (3%)	111 (4%)†	28 (3%)	89 (8%)†	20 (1%)†	143 (7%)†	88 (7%)†	604 (4%)	<0·0001
Systemic embolism	15 (<1%)	3 (<1%)	29 (1%)†	4 (<1%)	10 (1%)	2 (<1%)	14 (1%)	7 (1%)	84 (1%)	<0·0001‡
Major bleeding	111 (3%)	26 (2%)	48 (2%)	12 (1%)	22 (2%)	8 (<1%)†	26 (1%)†	68 (5%)†	321 (2%)	<0·0001
Admission to hospital for heart failure	411 (11%)	78 (7%)†	337 (13%)†	97 (11%)	391 (34%)†	92 (4%)†	336 (17%)†	180 (14%)	1922 (13%)	<0·0001
Admission to hospital for myocardial infarction	75 (2%)	16 (1%)	73 (3%)	16 (2%)	20 (2%)	9 (<1%)†	21 (1%)	38 (3%)	268 (2%)	<0·0001

Suivi de 15 361 patients/47 pays vus aux urgences avec une FA ou un flutter atrial comme diagnostic primaire ou associé. Moins de décès lorsque FA est le diagnostic primaire : (377: 6% de 6825 patients vs 1381: 16% de 853, p<0·0001). Principales causes de décès : ins card. : 519 (30% de 1758) et AVC : 148 (8%).

JS Healey et al . Lancet 2016; 388: 1161–69.

Acute and chronic management of AF

Desired cardiovascular outcomes, and patient benefits



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Anticoagulants : ce que nous savons (1)

- Le traitement anticoagulant prévient la plupart des accidents ischémiques chez les patients présentant une FA et améliore le pronostic vital.

- Le traitement anticoagulant est supérieur au placebo et à l'aspirine chez les patients à risque de complications thrombo-emboliques.

- Le bénéfice clinique est démontré chez tous les patients, exceptés les patients à très faible risque et ce traitement doit donc être très largement proposé aux patients en cas de FA.

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Recommendations for prediction of stroke and bleeding risk

Recommendations	Class[a]	Level[b]
The CHA_2DS_2-VASc score is recommended for stroke risk prediction in patients with AF.	I	A
Bleeding risk scores should be considered in AF patients on oral anticoagulation to identify modifiable risk factors for major bleeding.	IIa	B
Biomarkers such as high-sensitivity troponin and natriuretic peptide may be considered to further refine stroke and bleeding risk in AF patients.	IIb	B

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FA et risque thrombo-embolique

Score $CHADS_2$

Critère $CHADS_2$	Score
C : Insuffisance cardiaque congestive	1
H : Hypertension artérielle	1
A : Âge >75 ans	1
D : Diabète	1
S : AVC/AIT/ Thrombo-embolie	2

Score CHA_2DS_2-VASC

Critères CHA_2DS_2-VASc	Score
C : IC congestive : dysfonction VG	1
H : Hypertension artérielle	1
A : Âge ≥75 ans	2
D : Diabète	1
S : AVC/AIT/ Thrombo-embolie	2
V : Maladie vasculaire (ATCD d'IDM, maladie artérielle périphérique ou plaque aortique)	1
A : Âge 65–74 ans	1
S : Sexe (féminin)	1

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Eur Heart J 2010 ; 31 : 2369-2449

Pourquoi le score CHA_2DS_2-VASc ?

- **Afin de mieux identifier les patients à faible risque de complications thromboemboliques.**
- **Un score $CHADS_2$ = 0 peut correspondre à un score CHA_2DS_2-VASc compris entre 0 et 3 avec des taux d'évènements annuels variant de 0.78 % à 5.9 %.**
  - CHA_2DS_2-VASc = 0 : 0.78%
  - CHA_2DS_2-VASc = 1 : 2.01%
  - CHA_2DS_2-VASc = 2 : 3.71%
  - CHA_2DS_2-VASc = 3 : 5.92%

Risque hémorragique : score HAS-BLED

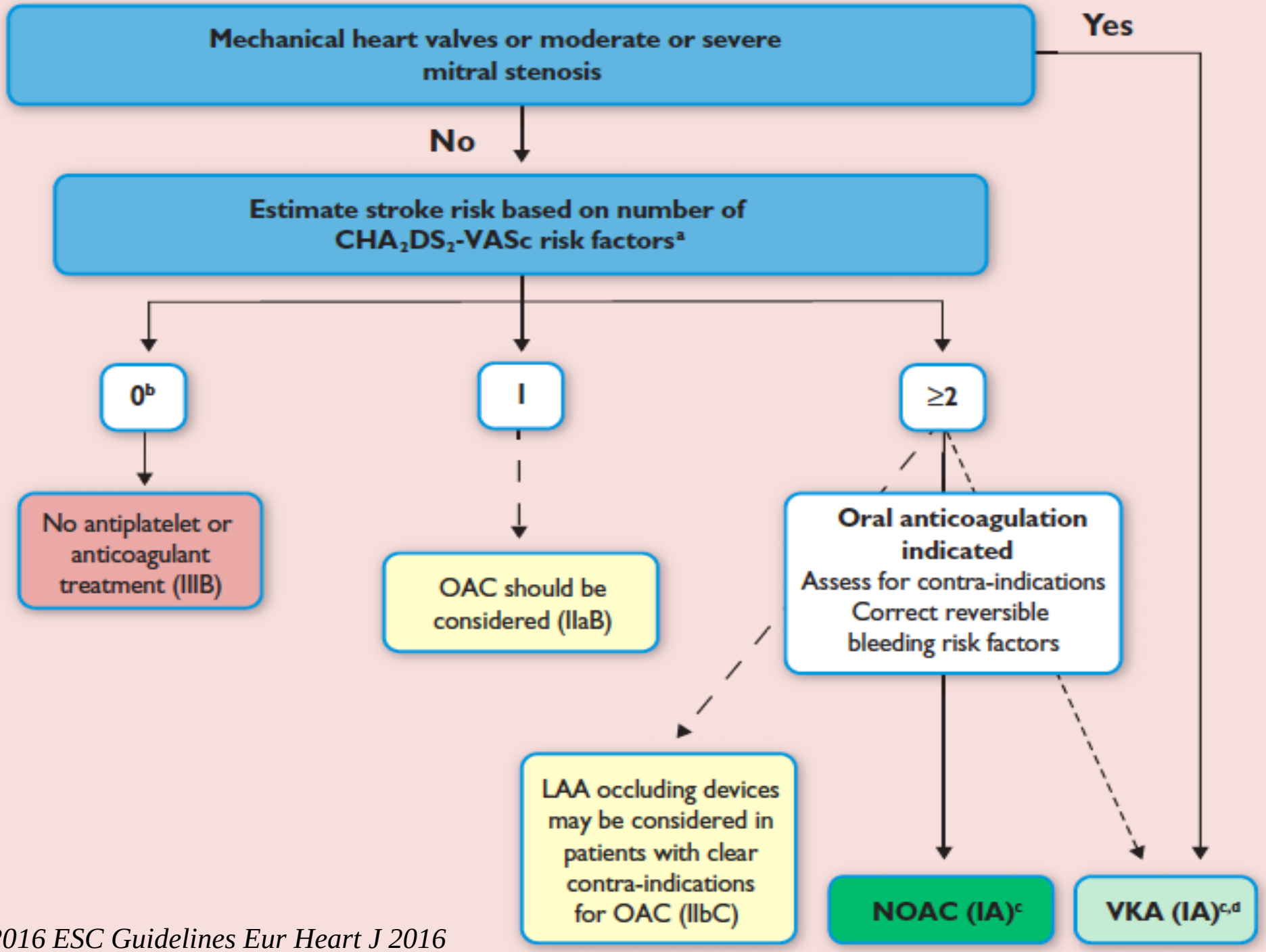
Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

HAS-BLED Score	Hémorragies 100 pts/ an
0	1,13
1	1,02
2	1,88
3	3,74
4	8,70
5	12,5

HTA = PAS > 160 mmHg **IR = Créat > 200 µmol/**

IH = ASAT/ALATx3N, biliX2N, cirrhose

Eur Heart J 2010 ; 31 : 2369-449



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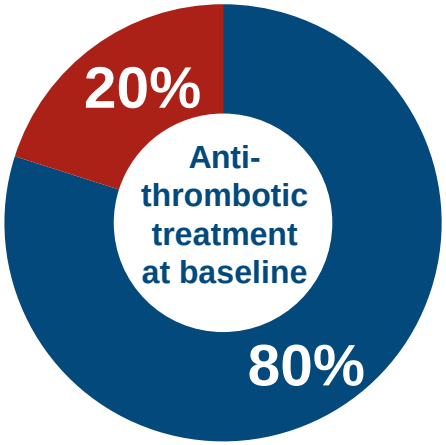
Despite the demonstrated safety and efficacy of NOACs, many patients at risk of stroke do not receive OACs

Analysis of data from observational registries has shown an increasing uptake of NOACs, but many patients with AF who are at risk of stroke do not receive OACs[1–4]

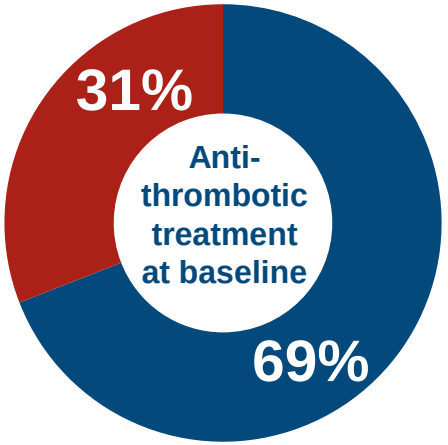
GLORIA™-AF (10 675 patients)[1]



Receiving OAC

Not receiving OAC

GARFIELD-AF (17 475 European patients)[2]



Similar proportions of patients did not receive OACs in the PREFER in AF (17.7%) and EORP--AF (20.0%) registries[3,4]

1. Huisman MV et al. Am J Med 2015; 2. Camm AJ et al. Poster P85323, ESC 2015; 3. Kirchhof P et al. Europace 2014; 4. Lip GHY et al. Europace 2014

Anticoagulants : ce que nous savons ? (2)

- La sous-utilisation ou l'arrêt prématuré du traitement anticoagulant sont encore fréquents.
- Néanmoins le risque majeur d'accident embolique sans anticoagulant est souvent supérieur au risque hémorragique, même chez des sujets âgés, ou les patients ayant des problèmes cognitifs ou faisant des chutes.
- Le risque hémorragique d'une thérapeutique par aspirine n'est pas différent de celui sous AVK ou AOD.
- Les AVK et les AOD, mais pas l'aspirine, préviennent efficacement les accidents thrombo-emboliques.

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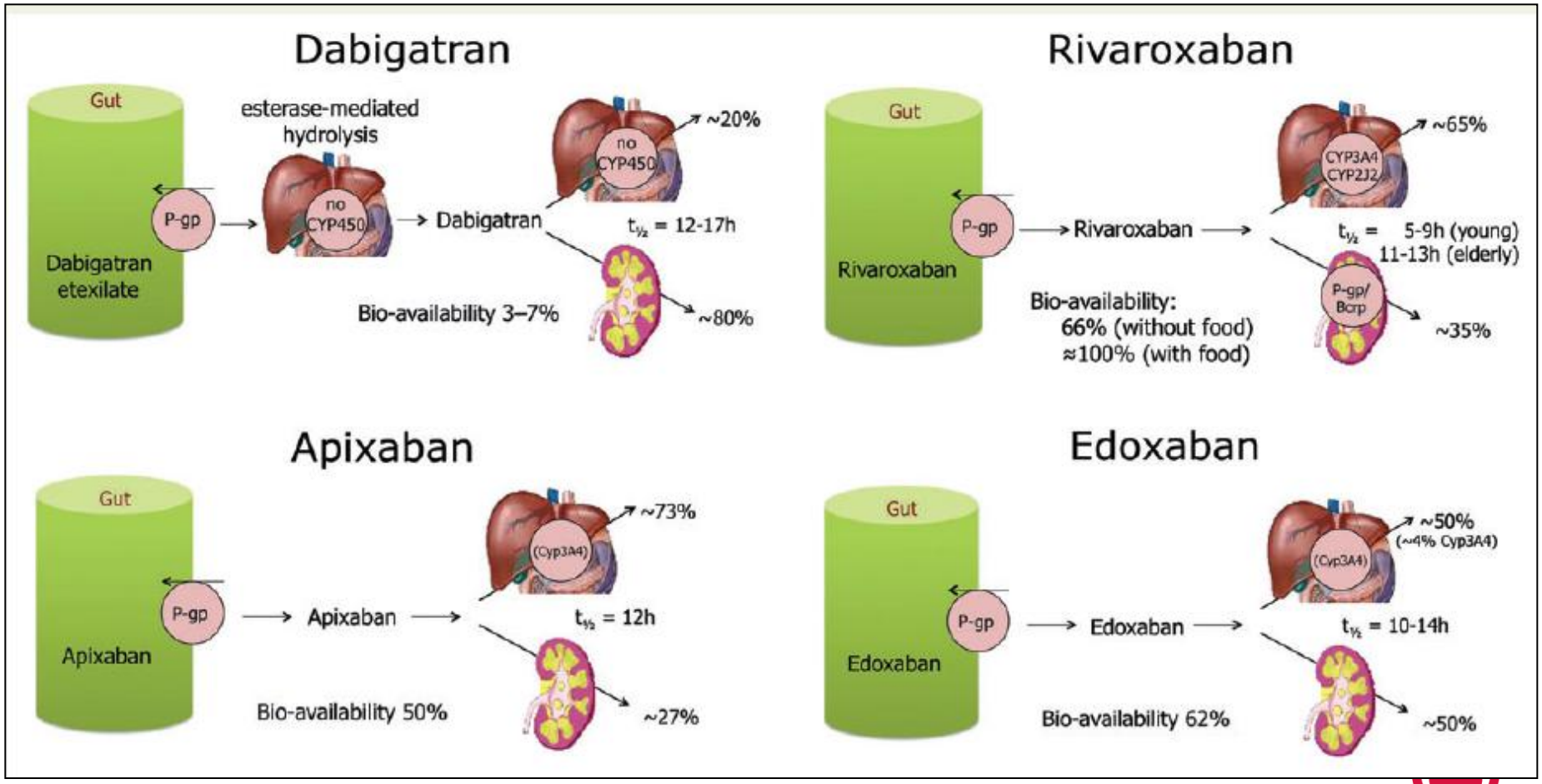
Non-VKA oral anticoagulant drugs, approved for prevention of systemic embolism or stroke in patients with non-valvular AF

	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
Action	Direct thrombin inhibitor	Activated factor Xa inhibitor	Activated factor Xa inhibitor	Activated factor Xa inhibitor
Dose	150 mg BID 110 mg BID[a,b] (75 mg BID)[b]	5 mg BID 2.5 mg BID[a]	60 mg OD[c] 30 mg OD[a]	20 mg OD 15 mg OD[a]
Phase III clinical trial	RE-LY[25]	ARISTOTLE[26] AVERROES[27]	ENGAGE-AF[28]	ROCKET-AF[29]

From H Heidbuchel et al. Europace 2015

Absorption et métabolisme des AOD



P-gp inhibitors : verapamil, dronedarone, amiodarone, and quinidine.
Inducers of P-gp and CYP3A4 : rifampicin, carbamazepine…

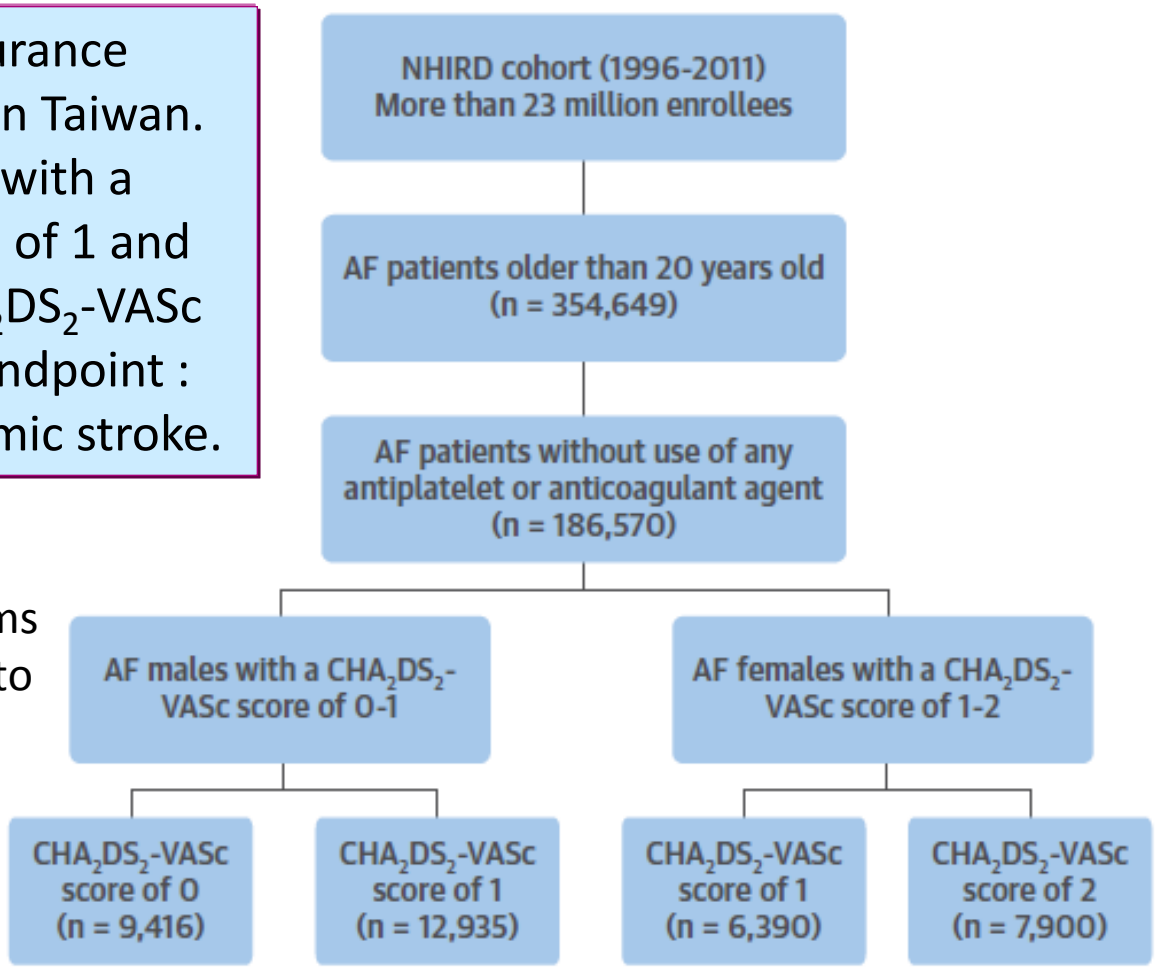
EHRA Practical Guide. Europace 2015

Recommendations for stroke prevention in patients with atrial fibrillation **ESC 2016**	Class[a]	Level[b]
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
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

Should AF patients with 1 additional risk factor of the CHA_2DS_2-VASc score (beyond sex) receive OAC ?

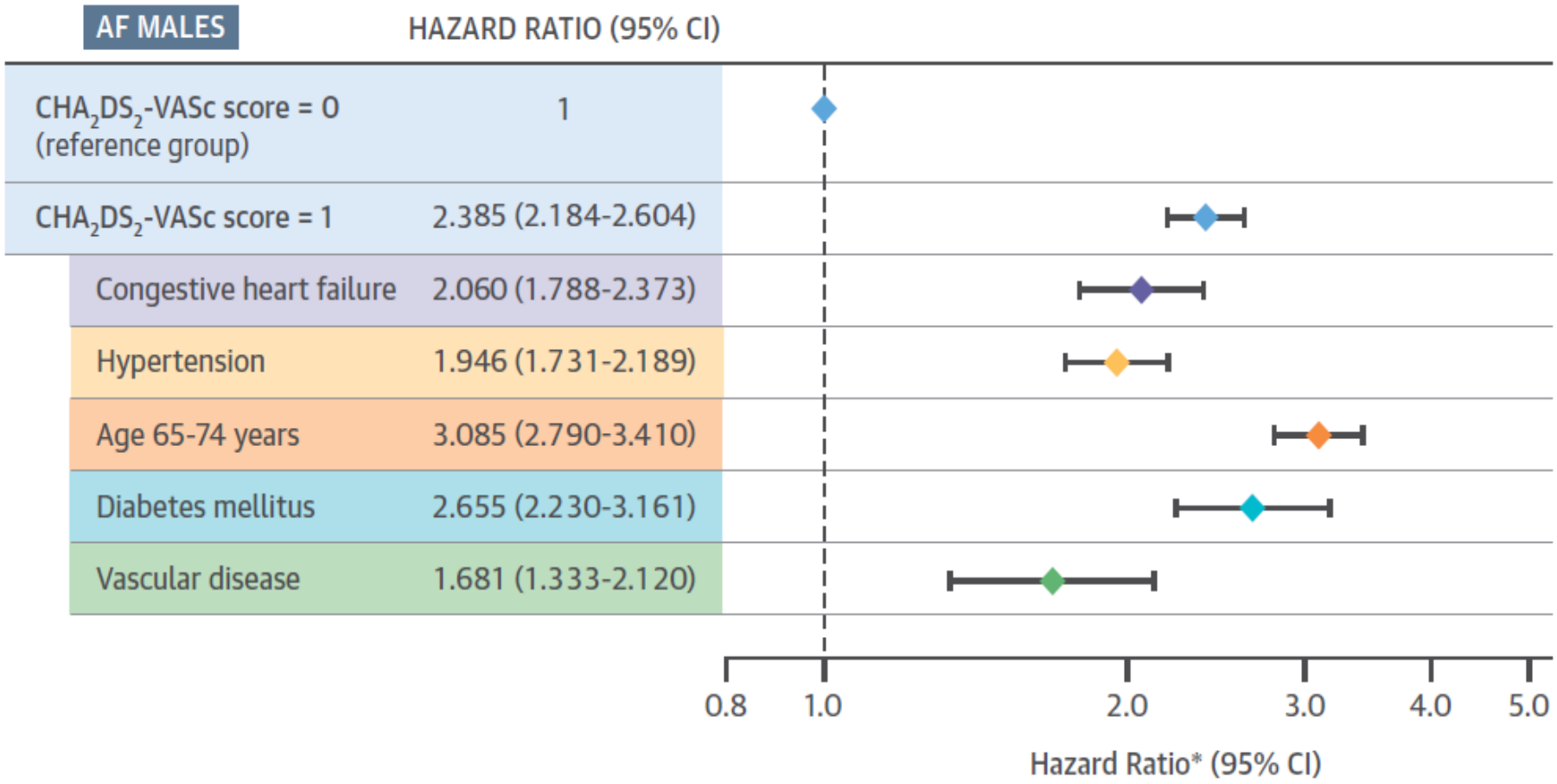
National Health Insurance Research Database in Taiwan. Evaluation of males with a CHA_2DS_2-VASc score of 1 and females with a CHA_2DS_2-VASc score of 2. Clinical endpoint : occurrence of ischemic stroke.

Drug treatment status from prescription claims from 180 days before to 90 days after the AF diagnosis.
F-up: 5.2 ± 4.3 years.



Chao T-F. et al. J Am Coll Cardiol. 2015; 65: 635–42.

Risk of ischemic stroke in AF patients stratified by CHA_2DS_2-VASc components



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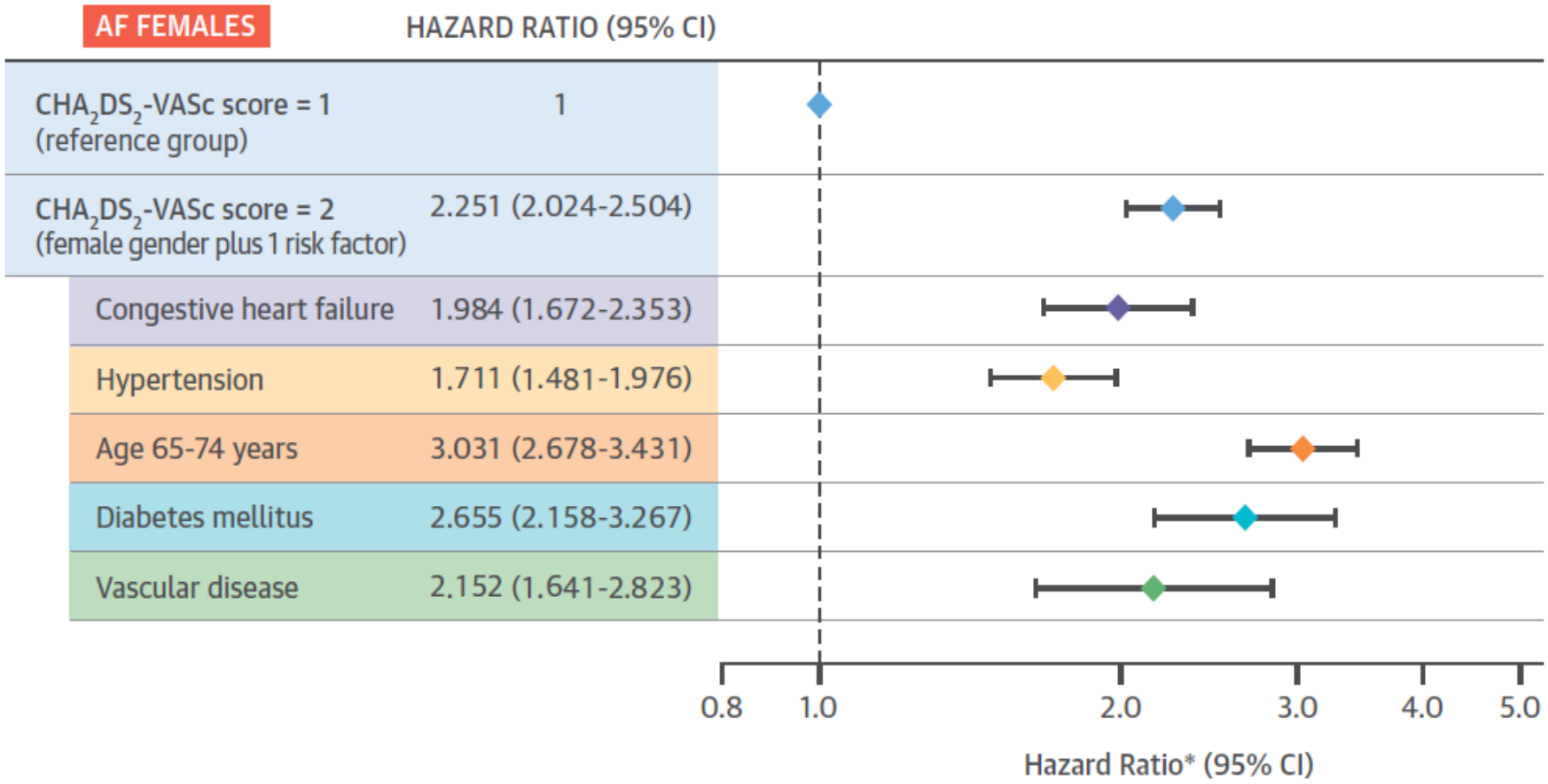
Risk of ischemic stroke in AF patients stratified by CHA_2DS_2-VASc components



Chao T-F. et al. J Am Coll Cardiol. 2015; 65: 635–42.

Independent FDA study of Medicare mirrors the favourable benefit–risk profile of dabigatran established in RE-LY®

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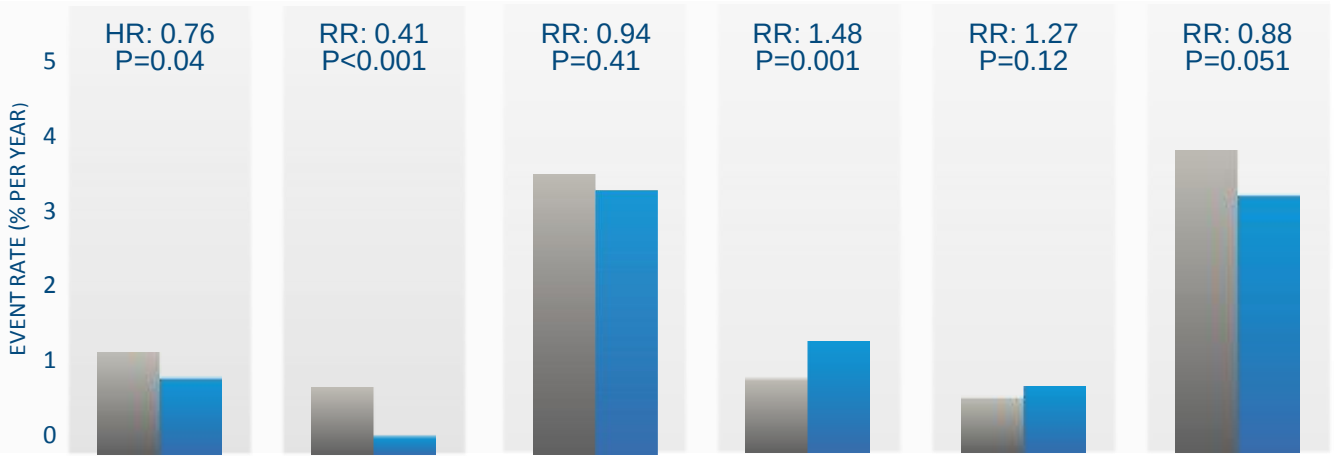
RE-LY®1–4

N>18 000
Warfarin
D150 BID

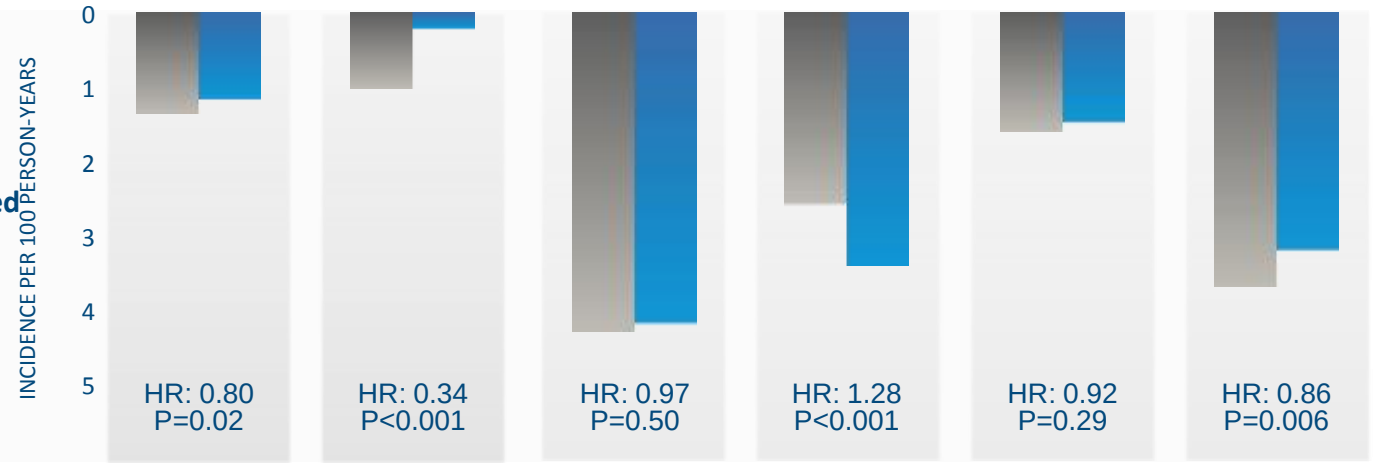
RCT



MEDICARE*5

N>134 000
Warfarin
D150 & D75 BID combined

Real-world data



*Primary findings for dabigatran are based on analysis of both 75 mg &150 mg together without stratification by dose

1. Connolly SJ et al. N Engl J Med 2009; 2. Connolly SJ et al. N Engl J Med 2010; 3. Pradaxa®: EU SPC, January 2015 4. Connolly SJ et al. N Engl J Med 2014; 5. Graham DJ et al. Circulation 2015

Comparative effectiveness and safety of non-VKA OAC and warfarin in patients with AF

Safety outcomes

- Major bleeding, any bleeding (intracranial, major, GI bleeding, traumatic intracranial), and all-cause mortality

Methods

- Prospective analysis of three Danish health registries (Aug 2011–Nov 2015)
- Follow up until outcome of interest, emigration, death, or end of study
- Cox regression and inverse probability-of-treatment weighted analysis

Patients

- New users of dabigatran, apixaban, rivaroxaban, or warfarin
- **N=61 678** (12 701 dabigatran, 6349 apixaban, 7192 rivaroxaban, 35 436 warfarin); **only patients on standard NOAC doses were included**

Limitations

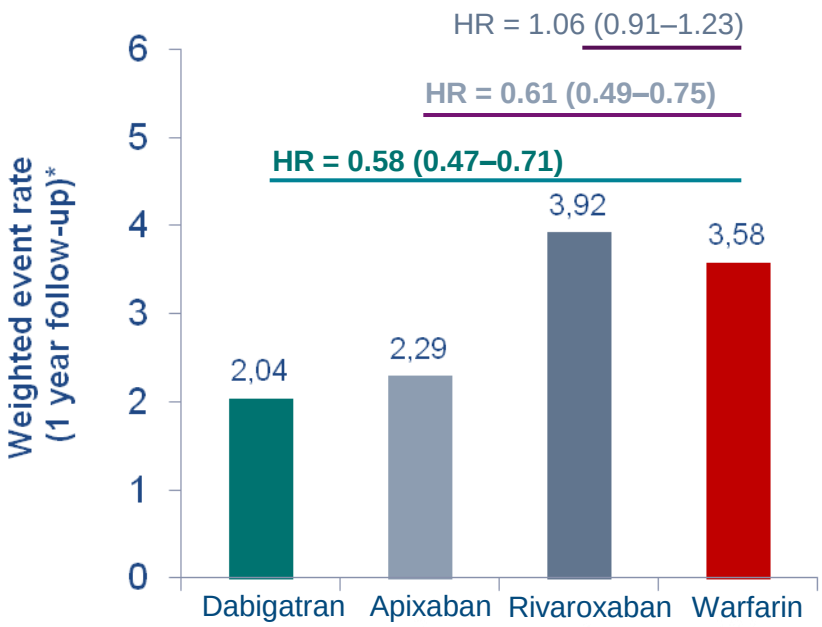
- Only ITT analysis presented
- Limited variables for adjustment
- Follow-up duration limited for some patients
- Patients included prior to availability of apixaban

TB Larsen et al. BMJ 2016;355:i3189

Safety profile of dabigatran and apixaban, more favourable than rivaroxaban in Danish registries

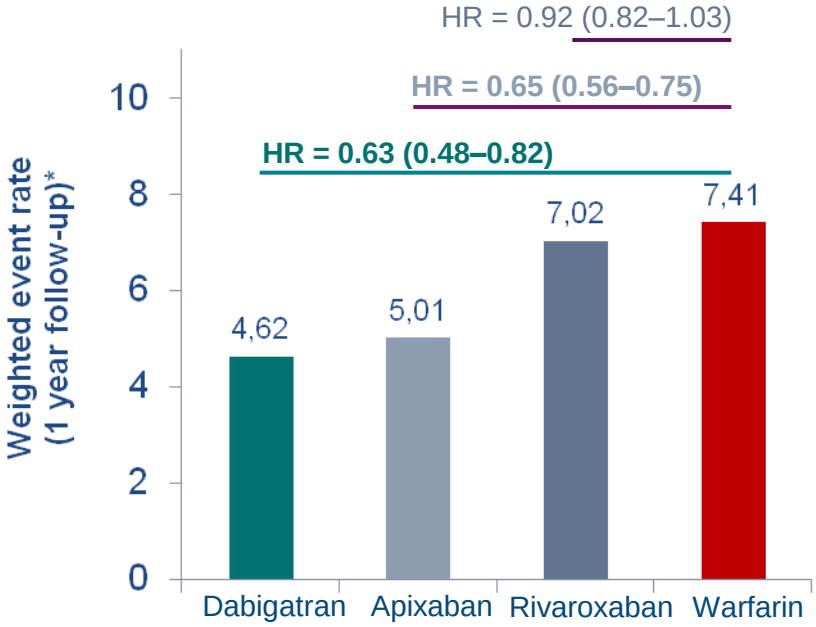
Major bleeding

Adjusted HR (95% CI) vs warfarin



All-cause mortality

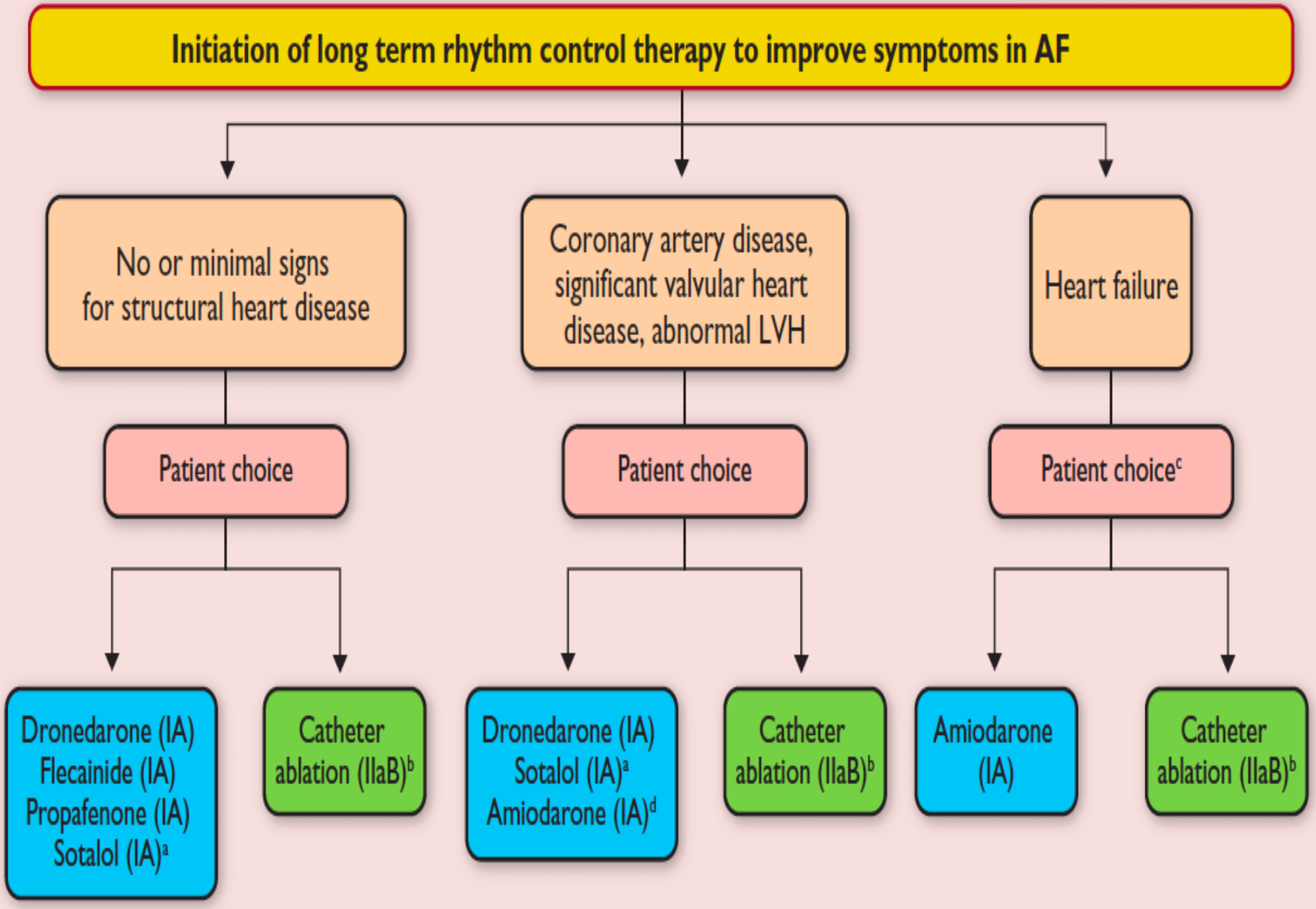
Adjusted HR (95% CI) vs warfarin



Dabigatran and apixaban were associated with a statistically significantly lower risk of any bleeding, major bleeding, and death compared with rivaroxaban or warfarin

Only standard doses of NOACs were compared in this study. *Inverse probability of treatment weighted and expressed as population average treatment rates per 100 years. Adjusted HR (95% CI), bold values indicate statistical significance. Limitations: ITT analysis; limited variables for adjustment; limited follow-up; patients included prior to availability of apixaban.

TB Larsen et al. BMJ 2016;353:i3189



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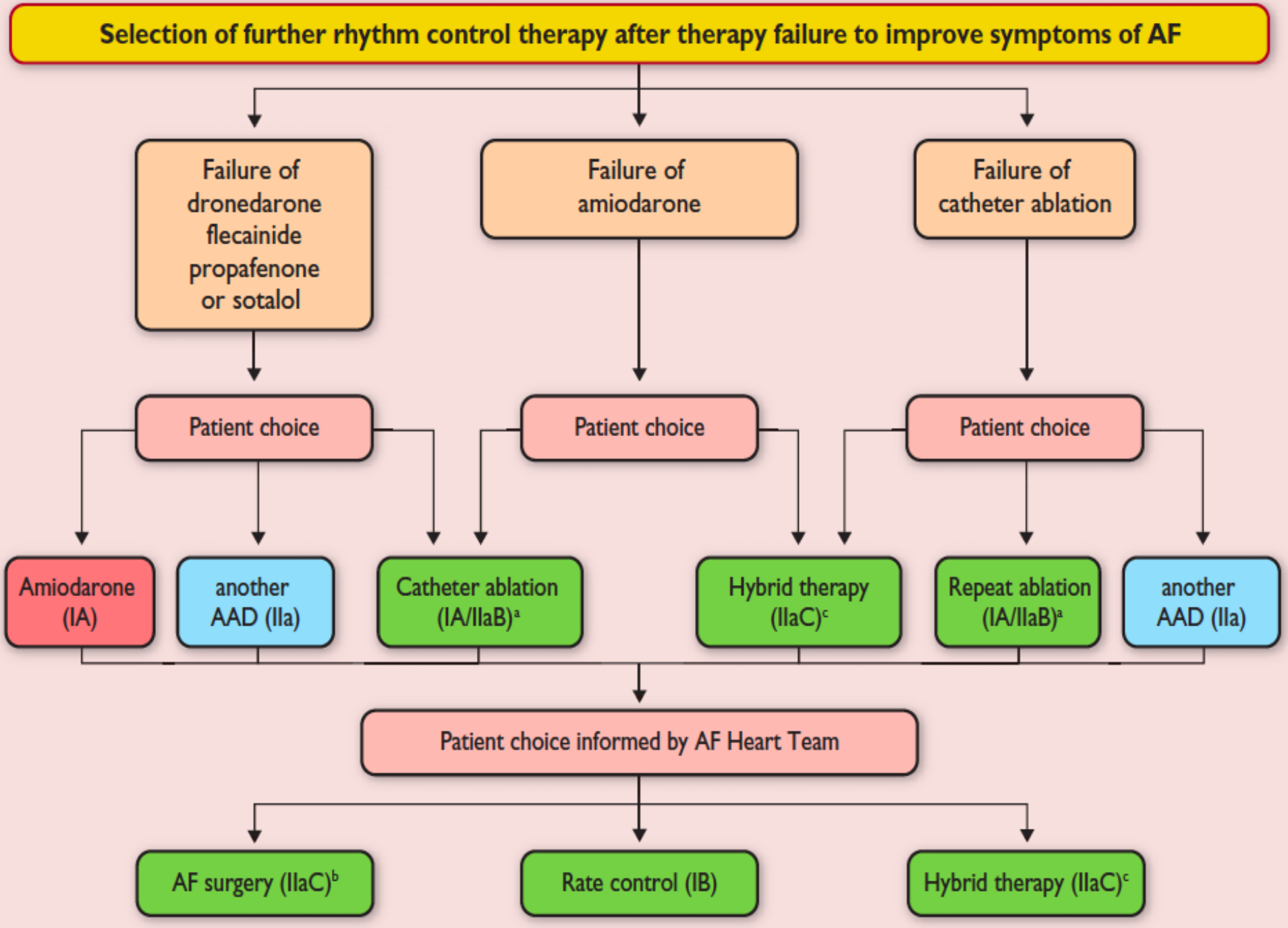
Recommendations for AF ablation

	Class[a]	Level[b]
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 documented or occurring 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
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



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Taille oreillette gauche et risque d'AVC

Table 3 OR (95% CI) for stroke according to CHA_2DS_2-VASc score, indexed left atrial size and atrial fibrillation combined: the Tromsø Study 1994–2012

	Model 1	Model 2
CHA_2DS_2-VASc and LA size		
CHA_2DS_2-VASc=0, Group 1 (n=957)	1 (Ref.)	1 (Ref.)
CHA_2DS_2-VASc ≥1		
LA size <2.8, Group 2 (n=1713)	3.9 (2.7 to 5.5)	3.7 (2.6 to 5.3)
LA size ≥2.8, Group 3 (n=96)	9.7 (5.6 to 16.7)	9.4 (5.3 to 16.4)
Atrial fibrillation (AF)*		
No AF, Group 1 (n=2391)	1 (Ref.)	1 (Ref.)
Late AF, Group 2 (n=266)	1.0 (0.7 to 1.6)	1.0 (0.6 to 1.5)
Early AF, Group 3 (n=142)	2.8 (1.9 to 4.2)	2.6 (1.7 to 3.9)
Previous AF, Group 4 (n=45)	2.4 (1.2 to 5.0)	2.2 (1.1 to 4.5)

Model 1: Unadjusted.
Model 2: Adjusted for smoking, Total/HDL cholesterol ratio, BMI, GFR.

Participants with CHA_2DS_2-VASc ≥1 and LA size <2.8 had ~4 times increased odds of stroke, whereas participants with CHA_2DS_2-VASc ≥1 and LA size ≥2.8 had ~9 times increased odds of stroke, compared with participants with CHA_2DS_2-VASc score 0 (2844 participants from the Tromsø Study).

Tiwari S, et al. Open Heart 2016;3:e000439

Taille OG et risque AVC embolique et cryptogénique

	Left Atrial Size	Model 1, Unadjusted, Hazard Ratio (95% Confidence Interval)	Model 2,* Hazard Ratio (95% Confidence Interval)	Model 3,† Hazard Ratio (95% Confidence Interval)
Recurrent ischemic stroke of any subtype	Normal left atrial size	Reference	Reference	Reference
	Mild left atrial enlargement	1.15 (0.67–1.97)	1.10 (0.63–1.90)	1.06 (0.60–1.87)
	Moderate to severe left atrial enlargement	1.24 (0.61–2.52)	1.06 (0.51–2.19)	1.06 (0.48–2.30)
	Left atrial size (per SD increase)	1.09 (0.84–1.41)	1.03 (0.79–1.34)	1.03 (0.76–1.38)
Recurrent cardioembolic or cryptogenic stroke	Normal left atrial size	Reference	Reference	Reference
	Mild left atrial enlargement	1.56 (0.64–3.84)	1.53 (0.61–3.80)	1.32 (0.51–3.39)
	Moderate to severe left atrial enlargement	4.35 (1.81–10.48)	3.83 (1.54–9.54)	2.83 (1.03–7.81)
	Left atrial size (per SD increase)	1.76 (1.25–2.48)	1.73 (1.21–2.49)	1.55 (1.01–2.37)

*Adjusted for age, sex, and race-ethnicity.

†Adjusted for age, sex, race-ethnicity, hypertension, diabetes mellitus, hypercholesterolemia, smoking, atrial fibrillation, and congestive heart failure.

655 first ischemic stroke patients.

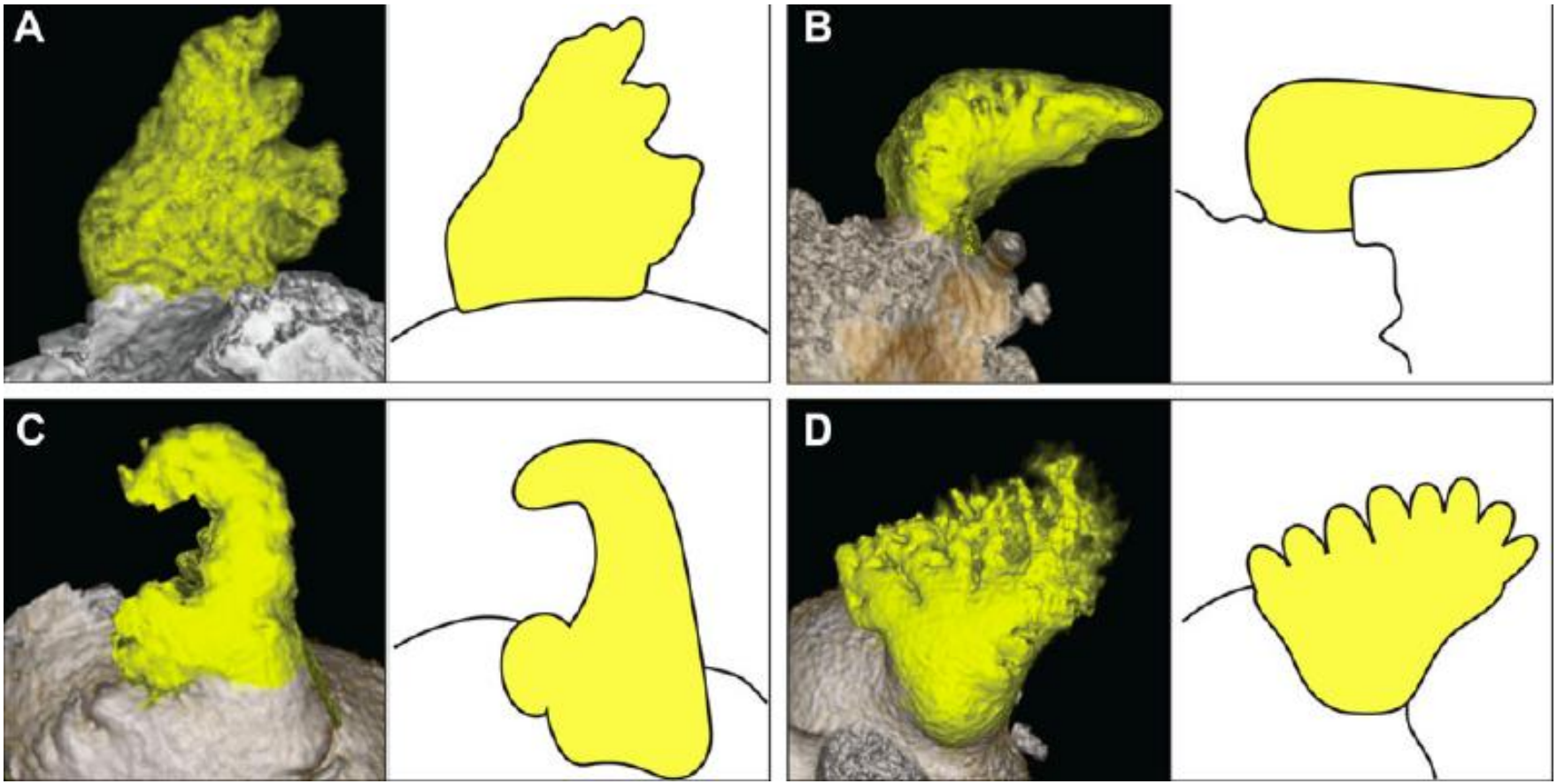
S. Yaghi et al. Stroke. 2015;46:1488-93.

Taille OG et risque AVC embolique et cryptogénique

- **Mécanismes expliquant la relation taille OG et risque AVC :**
  - Association dilatation OG et fibrillation atriale. Néanmoins relation persiste indépendamment de la FA mais FA recherchée de manière sommaire.
  - Réduction de la vélocité sanguine dans un auricule dilaté : relation dilatation OG-contraste OG-accidents emboliques.
  - Relation dilatation OG et HTA. Néanmoins relation persiste indépendamment de l'HTA.
  - Taille de l'OG marqueur de la cardiopathie atriale.

S. Yaghi et al. Stroke. 2015;46:1488-93.

Classification des morphologies de l'auricule gauche



(A) cactus; (B) chicken wing; (C) wind sock; (D) cauliflower.

JM Lee et al. J Cardiovasc Electrophysiol, 2015; 26: 922-7,

Facteurs de risque d'AVC

Variable	Univariate OR (95% CI)	P Value
Women	1.46 (0.94–2.29)	0.095
Hypertension	2.18 (1.40–3.41)	0.001
Diabetes mellitus	2.22 (1.33–3.71)	0.002
Prestroke CHA_2DS_2-VASc score	1.41 (1.18–1.70)	<0.001
Persistent AF	2.11 (1.37–3.27)	0.001
LA anterior–posterior diameter (cm)	2.50 (1.68–3.74)	<0.001
LA volume (cm^3)	1.01 (1.0–1.02)	0.014
LAA orifice area (cm^2)	1.38 (1.22–1.57)	<0.001
LAA volume (cm^3)	1.10 (1.04–1.16)	<0.001
LAA velocity (cm/s)	0.96 (0.95–0.98)	<0.001
Chicken wing vs. others	0.52 (0.34–0.80)	0.003
Cauliflower vs. others	1.89 (1.03–3.46)	0.040

AF patients with ischemic strokes (n = 160) and age-matched AF patients without ischemic strokes (n = 200).

JM Lee et al. J Cardiovasc Electrophysiol, 2015; 26: 922-7,

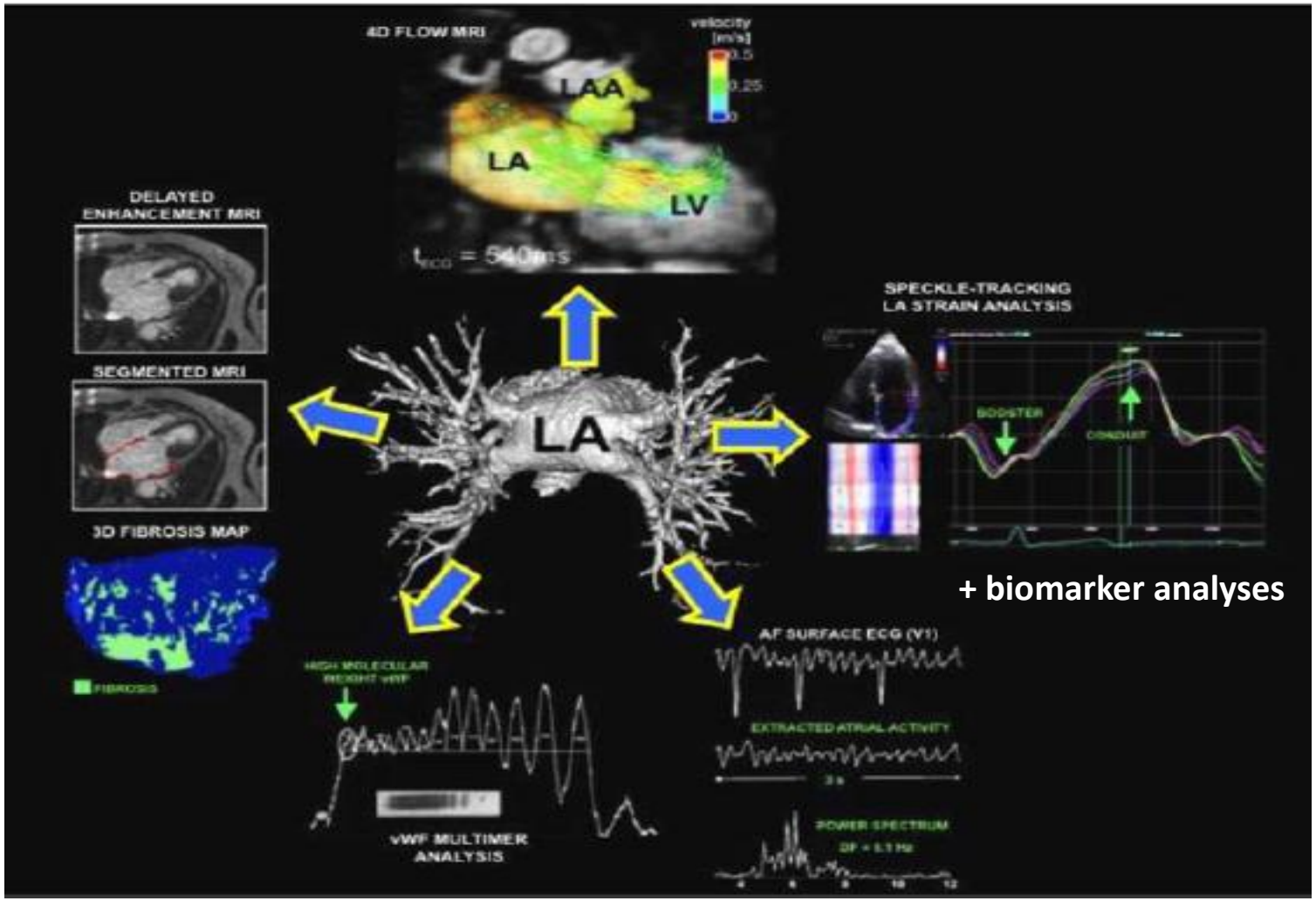
Univariate and multivariate analysis for prediction of post stroke AF

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Age, year	1.05	0.99–1.12	0.09	1.04	0.98–1.10	0.190
Gender	1.56	0.37–6.48	0.55			
Global LALS, %	0.92	0.85–0.98	0.04	0.90	0.83–0.97	< 0.01
LA volume index, mL/m^2	1.15	1.01–1.31	0.04	1.03	0.98–1.08	0.16
Log NIHSS	1.36	1.05–1.78	0.02	1.23	0.26–5.71	0.79
CHA_2DS_2-VASc ≥ 4	3.94	0.95–16.23	0.05	2.01	0.59–6.78	0.26
E/e'	1.14	0.98–1.32	0.10			

227 patients (132 males, age 67 ± 12) with acute ischemic stroke without a history of AF. Global LALS as a marker of LA mechanical function has incremental predictive value for post-stroke AF in these patients.

D.Kim et al. J Cardiovasc Ultrasound 2016;24:20-7.

Techniques d'analyse d'une atriomyopathie



Adapted from JL Goldberger et al. Circulation. 2015;132:278-91.

Recommendations for patients with kidney disease and atrial fibrillation

Recommendations	Class[a]	Level[b]	Ref[c]
The assessment of kidney function by serum creatinine or creatinine clearance is recommended in all AF patients to detect kidney disease and to support correct dosing of AF therapy.	I	A	316, 318–321
All AF patients treated with oral anticoagulation should be considered for at least yearly renal function evaluation to detect chronic kidney disease.	IIa	B	

2016 ESC Guidelines Eur Heart J 2016

Algorithme décisionnel pour FA et insuffisance rénale

Patient with atrial fibrillation and chronic kidney disease

Determine stroke risk (CHA_2DS_2-VASc Score)
Consider oral anticoagulation if score is ≥ 1 in males / ≥ 2 in females

Determine bleeding risk (HAS-BLED Score)

Estimate creatinine clearance (CrCl) to determine appropriate oral anticoagulant (OAC)

OAC options:	CrCl < 15 ml/min or ESRD on RRT	CrCl 15–29 ml/min	CrCl 30–49 ml/min	CrCl ≥ 50 ml/min
Vitamin K antagonist	When time in therapeutic range >70%	When time in therapeutic range >70%	When time in therapeutic range >70%	When time in therapeutic range >70%
Apixaban	5 mg, b.i.d.*	2.5 mg, b.i.d.	5 mg, b.i.d.†	5 mg, b.i.d.†
Dabigatran	✖	75 mg, b.i.d.‡	150 or 110 mg, b.i.d.§	150 mg, b.i.d.‖
Edoxaban	✖	30 mg, o.d.	30 mg, o.d.	60 mg, o.d.¶
Rivaroxaban	✖	15 mg, o.d.	15 mg, o.d.	20 mg, o.d.

Address bleeding risk factors, frequent follow up, and closely monitor renal function in NOAC users

YC Lau et al. J Am Coll Cardiol 2016;68:1452–64,

Gaps in evidence

15. Gaps in evidence

There are some areas of AF management that are supported by excellent evidence from multiple, adequately powered randomized trials (e.g. oral anticoagulation). Other areas, such as rhythm control therapy, integrated AF management, and lifestyle modifications are clearly developing the required evidence, while areas such as rate control are in dire need of better studies to underpin future guidelines. Here, we identify areas in need of further research.

15.1 Major health modifiers causing atrial fibrillation

Atrial fibrillation has different causes in different patients. More research is needed into the major causes (and electrophysiological mechanisms) of AF in different patient groups.[176,1024] Such research should consider the major comorbidities associated with AF, and characterize the response to AF therapy in patients with different, pathophysiologically distinct types of AF.

15.2 How much atrial fibrillation constitutes a mandate for therapy?

Technological advances allow screening for an irregular pulse using patient-operated ECG devices, smartphones, and a variety of other technologies. These may be very useful to detect silent, undiagnosed AF.[157] Adequately powered studies evaluating the diagnostic accuracy of such technologies, the diagnostic yield in different populations, the shortest duration and pattern of atrial arrhythmias conveying a stroke risk, and the effect of ECG screening on outcomes are needed.

15.3 Atrial high-rate episodes (AHRE) and need for anticoagulation

All of the information on the benefit of OAC has been generated in patients with AF diagnosed by ECG. Technological advances allow ready detection of AHRE in patients with implanted devices and an atrial lead. Such patients are at increased stroke risk, but it is unclear whether they benefit from OAC. Controlled trials evaluating OAC in AHRE patients are ongoing and will provide evidence on the best antithrombotic therapy in these patients.

15.4 Stroke risk in specific populations

Several specific AF groups should be studied to better characterize their risk for AF, stroke, and other AF-related complications (e.g. patients with one stroke risk factor, and non-Caucasian patients). Confounding factors (e.g. different therapy of concomitant cardiovascular diseases) may help to explain the variability in the reported rates of incident AF, prevalent AF, and AF complications. This also applies to the effect of gender in AF patients.[47]

15.5 Anticoagulation in patients with severe chronic kidney disease

The use of NOACs has not been tested in patients with creatinine clearance <30 mL/min, and there is very little evidence on the effects of OAC in patients on haemodialysis or on other forms of renal replacement therapy. Studies evaluating OAC in patients with severe CKD are needed to inform the best management in this patient group at high risk for stroke and bleeding.

15.6 Left atrial appendage occlusion for stroke prevention

The most common justification for LAA occlusion devices in clinical practice is a perceived high bleeding risk and, less often, contraindications for OAC.[459] Unfortunately, LAA occluders have not been tested in such populations. Furthermore, LAA occluders have not been compared with NOAC therapy in patients at risk for bleeding, or with thoracoscopic LAA clipping. There is a clear need to conduct adequately designed and powered trials to define the clinical role of LAA occluders compared with NOAC therapy in patients with relative or absolute contraindications for anticoagulation, and/or in those suffering from an ischaemic stroke on anticoagulant therapy.

15.7 Anticoagulation in atrial fibrillation patients after a bleeding or stroke event

At least 2% of anticoagulated patients with AF will experience a serious bleeding event per year. Observational data suggest that OAC can be reinitiated even after an intracerebral bleeding event.[460,484] Controlled studies evaluating different anticoagulation and stroke prevention interventions are urgently needed to provide evidence on the best management of patients who have suffered a bleeding event that would usually lead to withholding OAC. Some studies (e.g. APACHE-AF [Apixaban versus Antiplatelet drugs or no antithrombotic drugs after anticoagulation-associated intraCerebral HaEmorrhage in patients with Atrial Fibrillation][1025]) are ongoing, but adequately powered trials are needed. Similarly, prospectively collected data are needed on the stroke prevention and bleeding risk following (re-)initiation of OAC after stroke or intracranial bleeding.

15.8 Anticoagulation and optimal timing of non-acute cardioversion

Based on retrospective data, previous recommendations on the safe time-window in which a cardioversion can be performed in new-onset AF used $\leq$48 h as the 'gold standard' for non-protected cardioversion. However, new evidence has emerged that initiating pre-cardioversion anticoagulation in patients with AF episodes of $<$24 h or even $<$12 h would provide even better safety.[642,647,1026–1028] Further research is needed to establish a clear safety margin in this clinical situation.

15.9 Competing causes of stroke or transient ischaemic attack in atrial fibrillation patients

Prospective RCTs have demonstrated the superiority of carotid endarterectomy compared to stenting in patients with symptomatic high-degree stenosis of the internal carotid artery.[1029] As endarterectomy minimizes the need for combination therapy with OAC and antiplatelets,[1030] this approach has appeal in patients with AF to reduce bleeding risk. However, few of these studies included patients with AF. In a large observational study, the composite of in-hospital mortality, post-procedural stroke, and cardiac complications was higher in AF patients undergoing carotid stenting (457/7668; 6.0%) compared with endarterectomy (4438/51 320; 8.6%; $P<0.0001$).[1031] Despite adjustment for baseline risk, this may just reflect the type of patients referred for each procedure, and further randomized studies are needed to confirm the optimal treatment strategy in AF patients with carotid disease.

15.10 Anticoagulation in patients with biological heart valves (including transcatheter aortic valve implantation) and specific forms of valvular heart disease

The optimal antithrombotic therapy in the first months after biological valve replacement (including after catheter-based valve replacement) is not known. VKAs remain the mainstay during the initial post-operative period; NOACs probably deliver the same protection. In patients without AF, many centres use platelet inhibitors only. NOACs appear to be equally effective as VKAs in patients with moderate aortic stenosis, based on a subanalysis from the ROCKET-AF trial,[1032] as well as the Loire Valley AF project.[1033] Further data would be helpful to confirm these observations.[1034] The safety and efficacy of NOACs in patients with rheumatic mitral valve disease has not been evaluated and should be studied.

15.11 Anticoagulation after 'successful' catheter ablation

In view of the long-term recurrence rates of AF, this Task Force recommends that OAC is continued in AF patients after 'successful' catheter ablation. Nonetheless, observational data suggest that the stroke risk may be lower after catheter ablation of AF compared with other AF patients. The ongoing EAST – AFNET 4 trial will inform, in a more general way, whether rhythm control therapy can reduce stroke rates in anticoagulated AF patients. In addition, there seems to be a place for a controlled trial evaluating the termination of OAC therapy at an interval after 'successful' catheter ablation.

15.12 Comparison of rate control agents

Although the use of rate control therapy is very common in AF patients, robust data comparing rate control therapies are scant, with the majority of studies being small uncontrolled trials over short periods of follow-up. Some studies are ongoing [e.g. RATE-AF (Rate Control Therapy Evaluation in Permanent Atrial Fibrillation)[559]] and will investigate the potential benefits of different rate-controlling agents, characteristics, or biomarkers that can help to personalize the use of rate control, and the adverse event profile of specific drugs in defined groups of patients.

15.13 Catheter ablation in persistent and long-standing persistent AF

While a few recent randomized studies support the use of catheter or surgical ablation in patients with persistent AF and long-standing persistent AF,[1042] there is a clear need for more data evaluating this intervention in adequately powered randomized trials.

15.14 Optimal technique for repeat catheter ablation

PVI emerges as the most important target for catheter ablation of AF. Although a plethora of different additional ablation techniques have been published, their added value is questionable in patients undergoing a first catheter ablation, including those with persistent AF.[735,1042] Many patients are in need of multiple catheter ablation procedures, and such interventions often follow local or operator-specific protocols without clear evidence to support the choice of ablation target or intervention. There is a clear clinical need to define the best approach in patients who are in need of a second ablation procedure.

15.15 Combination therapy for maintenance of sinus rhythm

In the follow-up after initially successful catheter ablation, even when done in experienced centres, many patients will experience symptomatic recurrences of AF. These patients are often managed with antiarrhythmic drugs. There is a surprising paucity of data evaluating different rhythm control interventions in patients with recurrent AF after catheter ablation. Such studies seem reasonable and feasible.

15.16 Can rhythm control therapy convey a prognostic benefit in atrial fibrillation patients?

The progress in rhythm control therapy (catheter ablation, new antiarrhythmic drugs) and observational long-term analyses suggest that rhythm control therapy may have a prognostic benefit in anticoagulated AF patients. Ongoing trials such as CABANA and EAST – AFNET 4 will provide initial answers to this important question, but more data are needed, including trials of surgical ablation techniques.

15.17 Thoracoscopic 'stand-alone' atrial fibrillation surgery

Minimally invasive epicardial ablation surgery for the treatment of stand-alone AF was reported a decade ago.[1035] The procedure has since evolved towards a totally thoracoscopic procedure,[1036] and lesion sets were extended to a complete left atrial maze.[822] Randomized trials using a standardized procedure are urgently needed to clearly define the benefits and risks of thoracoscopic AF ablation, and to further support decisions of the AF Heart Team.

15.18 Surgical exclusion of the left atrial appendage

Exclusion of the LAA has been performed by cardiothoracic surgeons for decades, but prospective randomized studies comparing the rate of ischaemic stroke with or without left appendage exclusion are presently lacking. The LAAOS (Left Atrial Appendage Occlusion Study) III is currently randomizing cardiac surgery patients with AF to undergo concomitant occlusion or no occlusion of the appendage.[467] More data are also needed to confirm the safety and efficacy of thoracoscopic exclusion, following early positive observational data.[1037]

15.19 Concomitant atrial fibrillation surgery

Adequately powered randomized trials are needed, employing systematic follow-up with uniform lesion sets and energy sources, to evaluate the benefits and risks of concomitant AF surgery in symptomatic AF patients. An RCT on non-uniform lesion sets with long-term follow-up is due to publish shortly.[1038] Such trials will assist the AF Heart Team to decide on optimal therapy for individual patients, including the full repertoire of medical and surgical options for the treatment of AF.

Fibrillation atriale - Conclusions

- Recommandations anticoagulants ESC 2016 de classe IA dès que score CHADSVasc ≥ 2.
- Pas de limites d'âge mais prendre en compte le risque hémorragique : score HASBLED, les 4C : Cockcroft, Cognition, Comédications, Chutes. Arrivée des antidotes : sujet évolutif ++.
- Efficacité et sécurité démontrées pour les 4 AOD dans des études prospectives randomisées et dans la « vraie vie ».
- Recommandations ablation FA pour les patients symptomatiques et après échec d'un traitement antiarythmique loyal. Indication posée chez un patient informé, avec une équipe expérimentée.
- Encore de nombreux sujets à débattre !