



# **AVC chez le sujet âgé Fermeture de l'auricule gauche au cours de la fibrillation auriculaire non-valvulaire : une alternative au traitement anticoagulant ?**

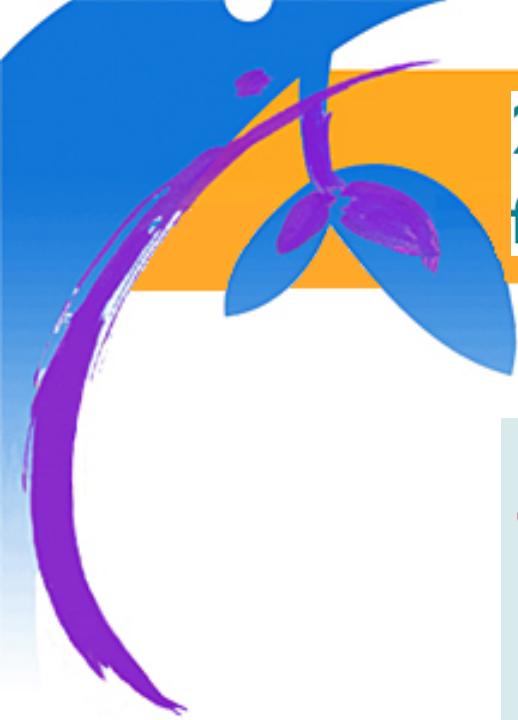
**Jean-Michel Juliard, Eric Brochet, Dominique Himbert, P Aubry,  
Alec vahanian**

**Département de Cardiologie  
Hôpital Bichat, Paris, France**

**3<sup>e</sup> JOURNÉE  
du  
CLUB NEUROVASCULAIRE**



**PROGRAMME  
27 mai 2014**  
**ASSISTANCE  
PUBLIQUE**  **HÔPITAUX  
DE PARIS**



# 2012 focused update of the ESC Guidelines for the management of atrial fibrillation

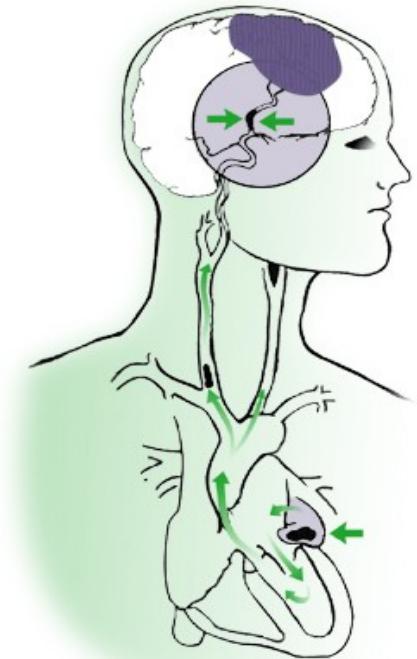
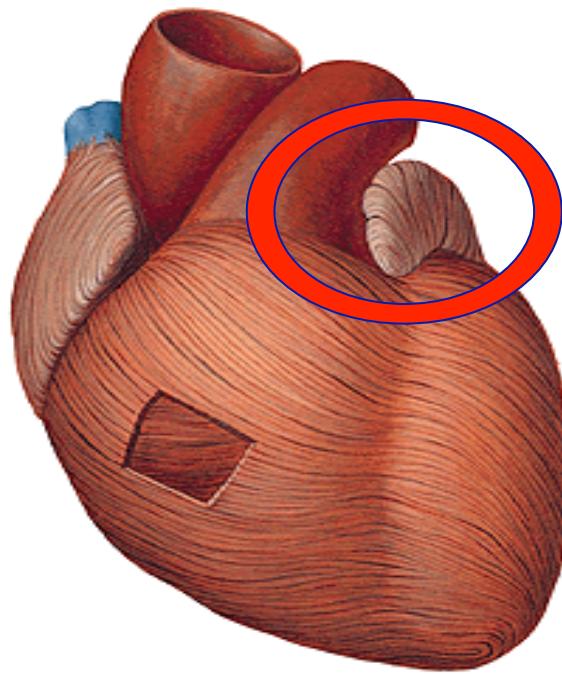
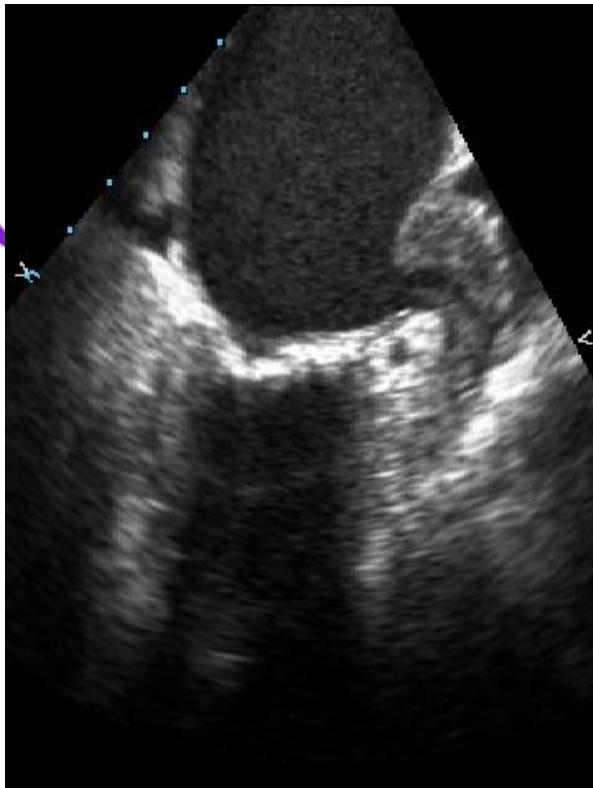
## Recommendations for LAA closure/occlusion/excision

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref <sup>c</sup>
Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.	IIb	B	115, 118
Surgical excision of the LAA may be considered in patients undergoing open heart surgery.	IIb	C	



European Heart Journal (2012) **33**, 2719–2747  
doi:10.1093/eurheartj/ehs253

# L'auricule gauche est la principale source de thrombi



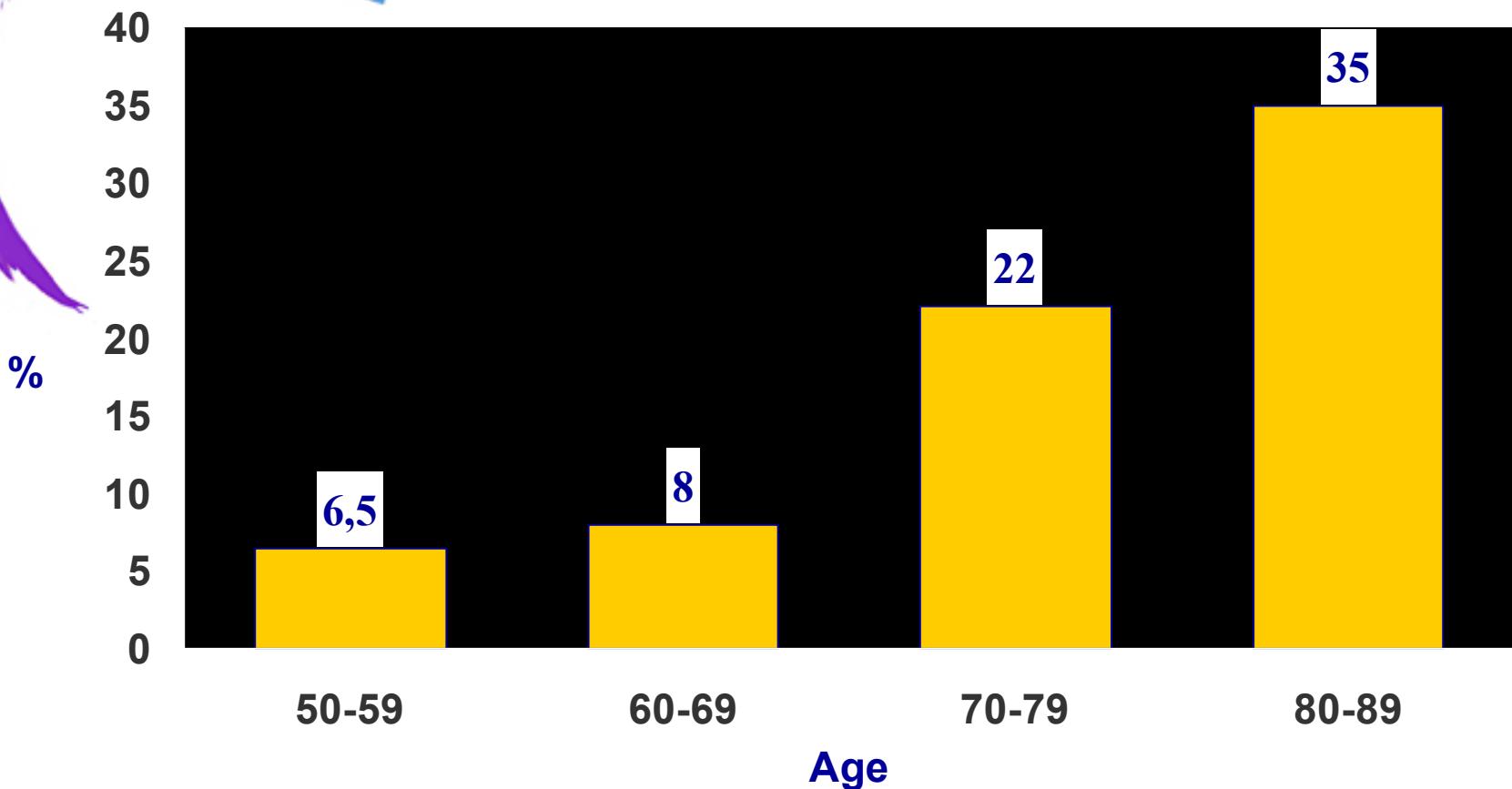


# AVC et FA

---

- AF : Prevalence of 0.4% of general population (> 80 years: 10%)
- 2/3 of the AF population is considered at high-risk of stroke
- AF accounts for approximately 15% of all strokes
- Anticoagulation (warfarin) therapy is proven effective but sometimes contraindicated and most often underutilized in clinical practice

# AVC et FA en fonction de l'âge



# Stroke Risk Assessment: CHA<sub>2</sub>DS<sub>2</sub>-VASc score



Letter	Risk factor	Points awarded
C	- Congestive heart failure/LV dysfunction	1
H	- Hypertension	1
A	- Age >75	2
D	- Diabetes mellitus	1
S	- Stroke/TIA/thrombo-embolism	2
V	- Vascular disease	1
A	- Age 65–74	1
Sc	- Sex-category (i.e. female sex)	1
	<b>Maximum score</b>	<b>9</b>

Camm AJ et al, Guidelines for the management of Atrial Fibrillation  
Eur Heart J 2010;31:2369-2429

# Adjusted Stroke Rate

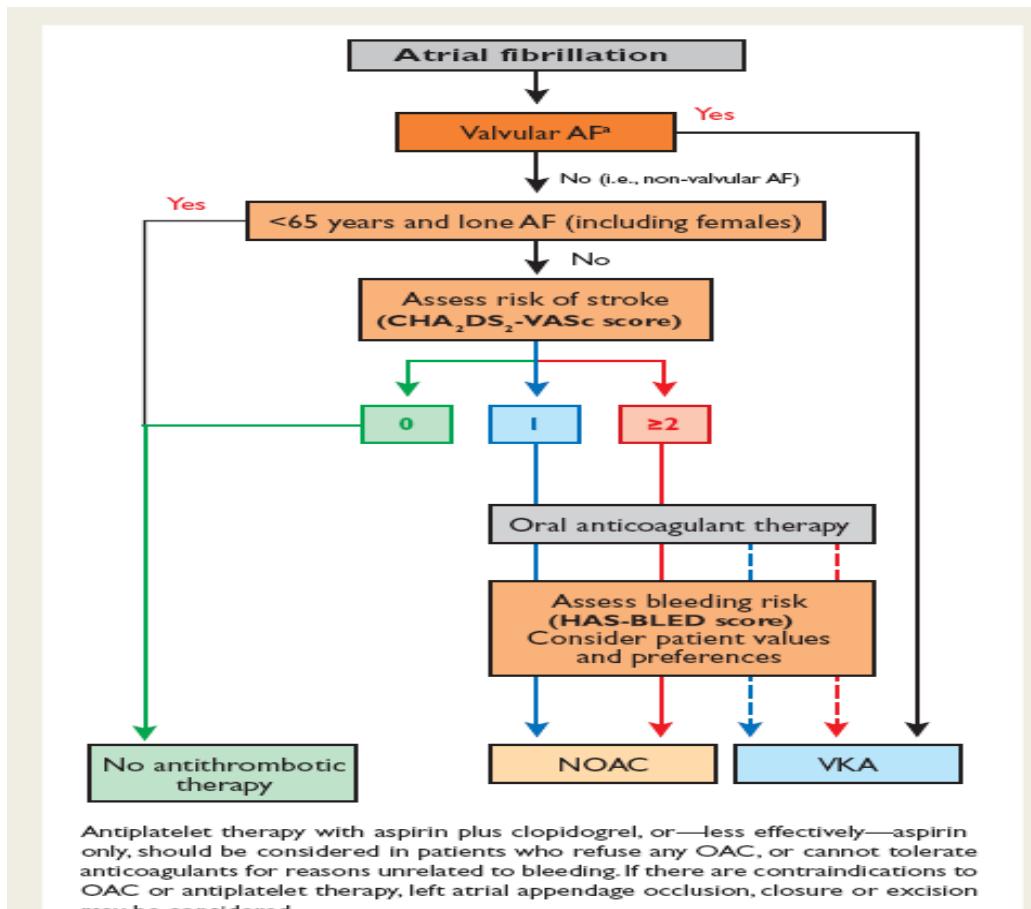
(c) Adjusted stroke rate according to CHA<sub>2</sub>DS<sub>2</sub>-VASc score

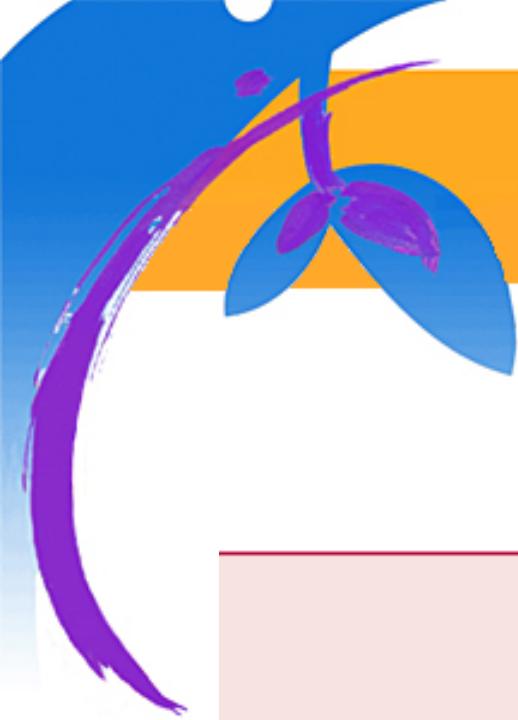
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	Patients (n = 7329)	Adjusted stroke rate (%/year) <sup>b</sup>
0	1	0%
1	422	1.3%
2	1230	2.2%
3	1730	3.2%
4	1718	4.0%
5	1159	6.7%
6	679	9.8%
7	294	9.6%
8	82	6.7%
9	14	15.2%

Camm AJ et al, Guidelines for the management of Atrial Fibrillation  
Eur Heart J 2010;31:2369-2429

# 2012 focused update of the ESC Guidelines for the management of atrial fibrillation

An update of the 2010 ESC Guidelines for the management  
of atrial fibrillation  
Developed with the special contribution of the European Heart  
Rhythm Association





# Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial

Jonathan Mant, FD Richard Hobbs, Kate Fletcher, Andrea Roalfe, David Fitzmaurice, Gregory YH Lip, Ellen Murray, on behalf of the BAFTA investigators\* and the Midland Research Practices Network (MidReC)\*

	Warfarin (n=488)		Aspirin (n=485)		Warfarin vs aspirin	
	n	Risk per year	n	Risk per year	RR (95% CI)	p
Stroke	21	1.6%	44	3.4%	0.46 (0.26-0.79)	0.003

## Haemorrhage (fatal and non-fatal)

Major extracranial haemorrhage	18	1.4%	20	1.6%	0.87 (0.43-1.73)	0.67
Other hospital admission for haemorrhage	24	1.8%	19	1.5%	1.22 (0.64-2.36)	0.52
All major haemorrhages (including intracranial and haemorrhagic stroke)	25	1.9%	25	2.0%	0.96 (0.53-1.75)	0.90

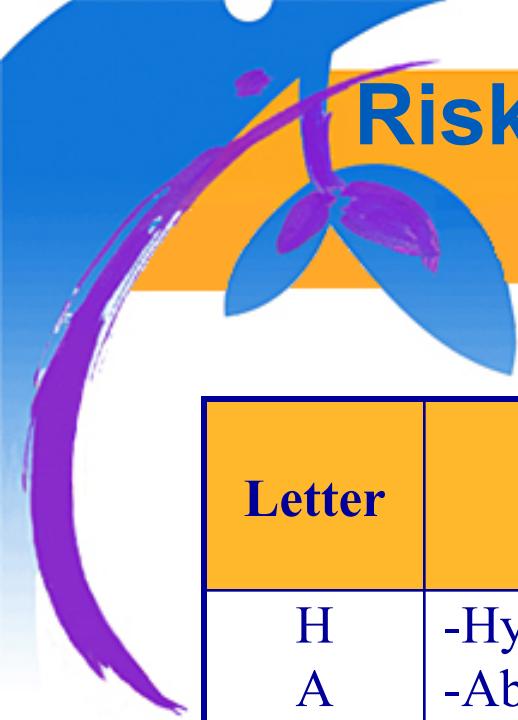


## Bleeding Risk During Oral Anticoagulation in Atrial Fibrillation Patients Older Than 80 Years

Daniela Poli, MD,\*† Emilia Antonucci, MS,\*† Elisa Grifoni, MD,\*† Rosanna Abbate, MD,\*†  
Gian Franco Gensini, MD,\*‡ Domenico Prisco, MD\*†  
*Florence, Italy*

### Odds Ratios associated with bleeding risk

	Odds Ratio	95% Confidence Interval	p Value
Age $\geq 80$ yrs	3.1	1.5-6.2	0.002
Stroke/TIA	2.5	1.3-4.8	0.007
Hypertension	1.3	0.6-2.7	0.5
Previous bleeding	1.0	0.1-6.9	0.9
CHADS <sub>2</sub> score	1.3	1.0-1.7	0.03



# Risk assessment 1 yr bleeding HAS-BLED score

Letter	Clinical characteristic	Points awarded
H	-Hypertension (systolic blood pressure > 160 mmHg)	1
A	-Abnormal renal & liver function (1 point each)	1 or 2
S	-Stroke	1
B	-Bleeding	1
L	-Labile INRs	1
E	-Elderly (age > 65 yrs)	1
D	-Drugs or alcohol (1 point each)	1 or 2
	Maximum	9 points

■ Score of  $\geq 3$  indicates ‘high risk’



# Randomized Clinical Trials

## ■ PROTECT AF (Holmes DR et al, Lancet 2009;374:534-42)

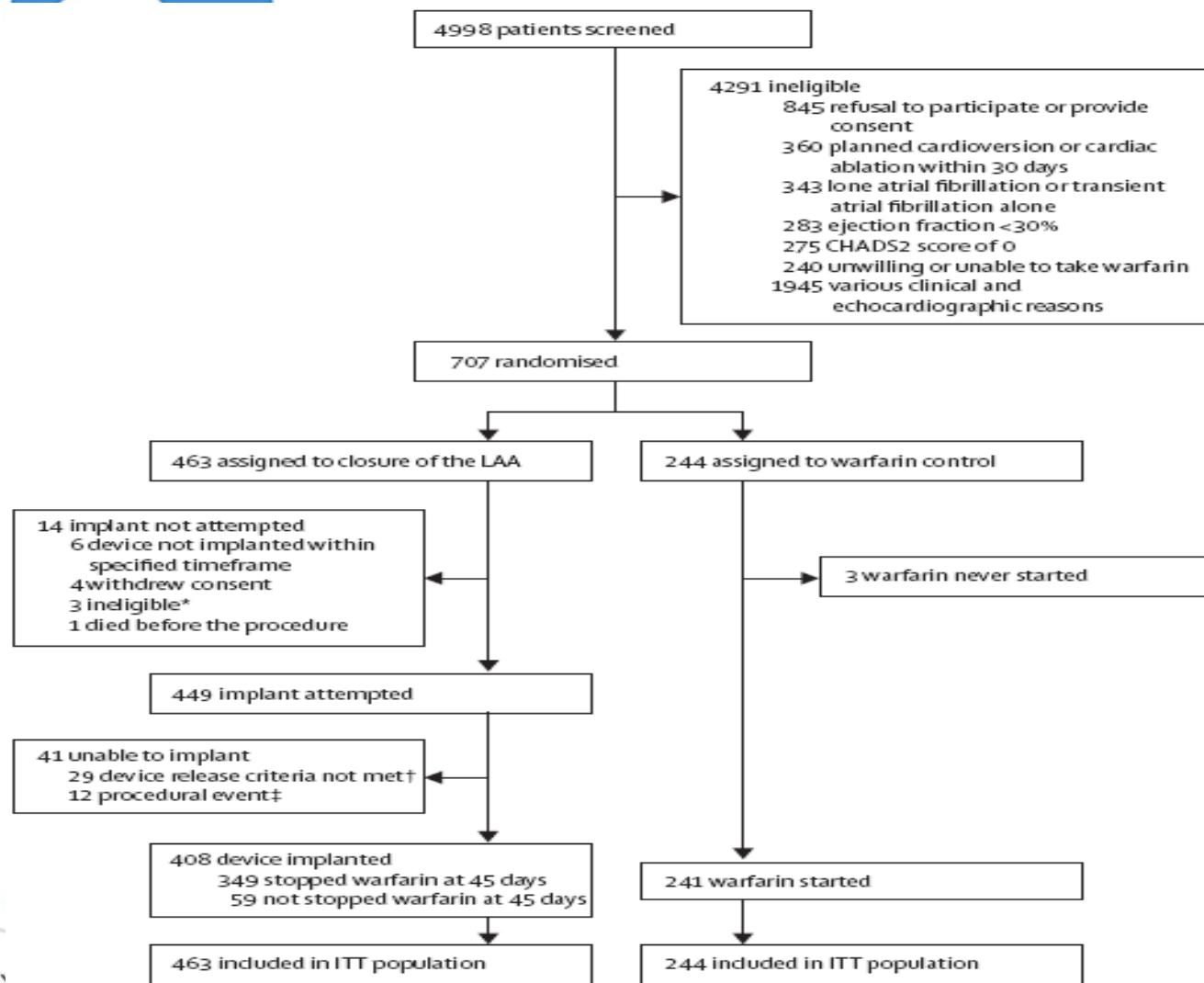
	Intervention group (n=463)	Control group (n=244)
Characteristics		
Age (years)	71.7(8.8;46.0-95.0)	72.7(9.2;41.0-95.0)
Male	326 (70.4%)	171 (70.1%)

- Nonvalvular atrial fibrillation
- Paroxysmal, permanent or persistent
- CHADS<sub>2</sub> ≥ 1
- No contraindication to warfarin

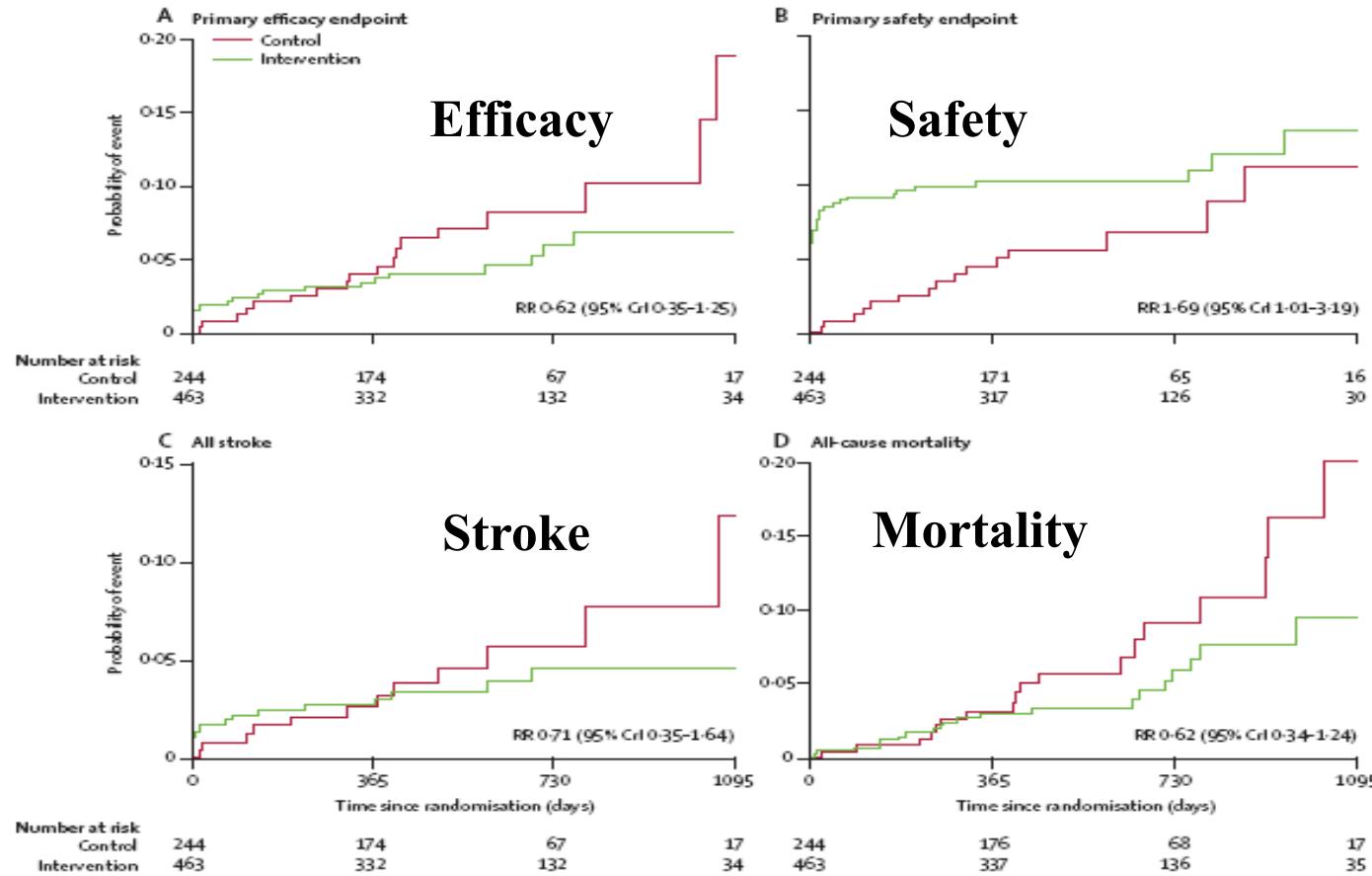
## ■ PREVAIL

- eCHADS<sub>2</sub> ≥ 2

# Selection of Patients in PROTECT-AF Trial



# Results



Primary endpoint: stroke, cardiovascular death and systemic embolism

# Safety

	Intervention (n=463)	Control (n=244)
Serious pericardial effusion*	22 (4.8%)	0
Major bleeding†	16 (3.5%)	10 (4.1%)
Procedure-related ischaemic stroke	5 (1.1%)	0
Device embolisation	3 (0.6%)	0
Haemorrhagic stroke‡	1 (0.2%)	6 (2.5%)
Other§	2 (0.4%)	0

\*Defined as the need for percutaneous or surgical drainage. †Major bleeding is defined as a bleeding event that required at least 2 units of packed red blood cells or surgery to correct. ‡Of the seven haemorrhagic strokes, six resulted in death (intervention group, n=1; control group, n=5). §An oesophageal tear and a procedure-related arrhythmia.

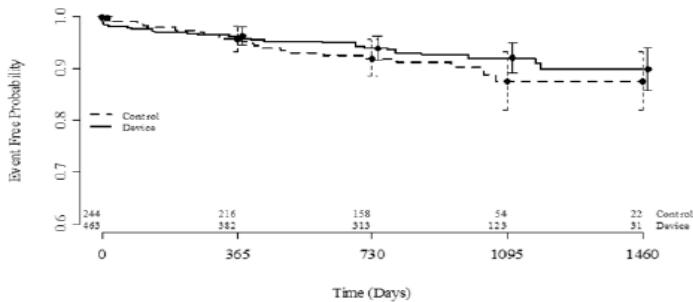
Table 3: Adverse events

# Percutaneous Left Atrial Appendage Closure for Stroke Prophylaxis in Patients With Atrial Fibrillation

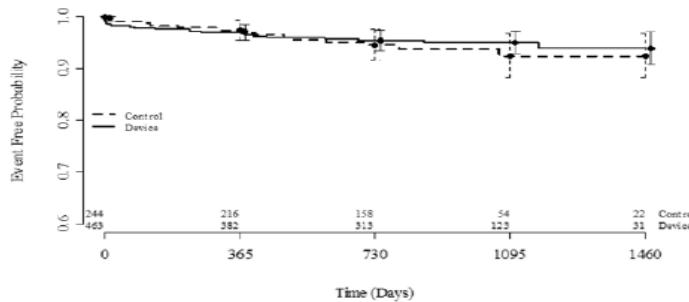
## 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) Trial

Vivek Y. Reddy, MD; Shephal K. Doshi, MD; Horst Sievert, MD; Maurice Buchbinder, MD; Petr Neuzil, MD, PhD; Kenneth Huber, MD; Jonathan L. Halperin, MD; David Holmes, MD; on behalf of the PROTECT AF Investigators

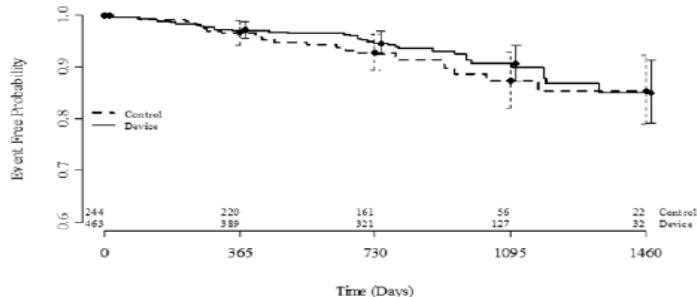
### Primary Efficacy



### Stroke



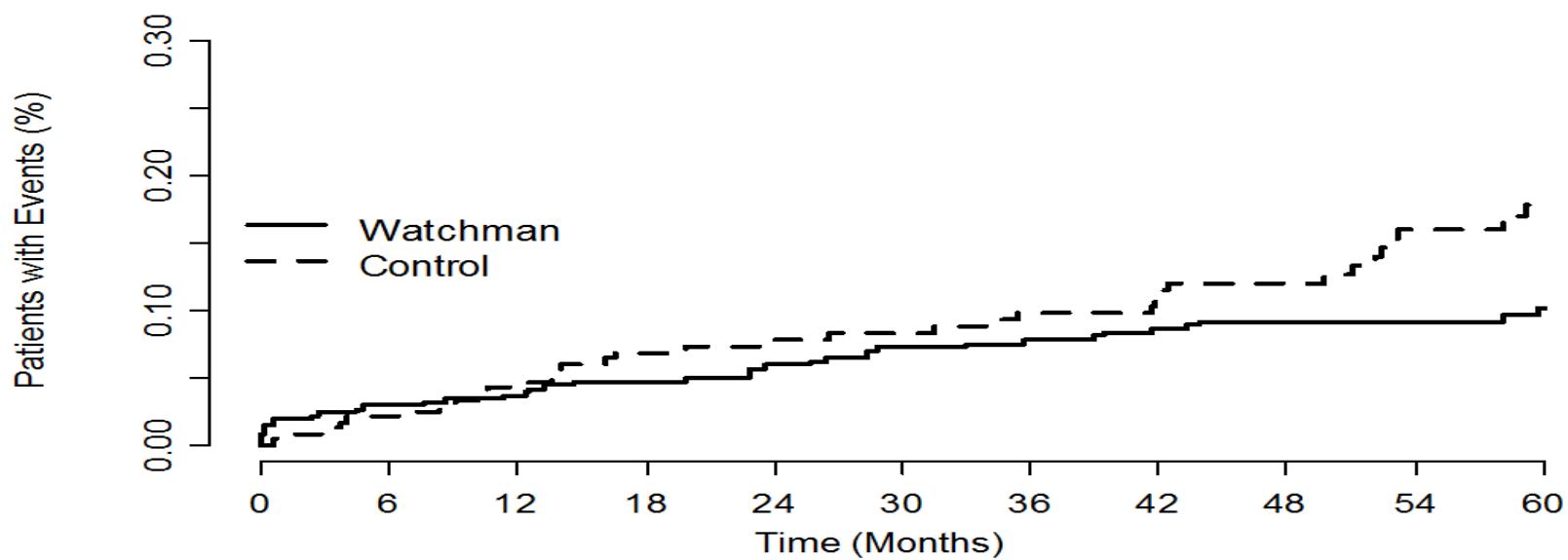
### All-Cause Mortality



Circulation 2013;127:720-29

# PROTECT-AF: Primary Efficacy Endpoint

Event	Watchman Group (n = 463)		Warfarin Group (n = 244)		Posterior Probabilities		
	Events/ Patient-Years	Observed Rate (Events per 100 Patient-Years) (95% CrI)	Events/ Patient-Years	Observed Rate (Events per 100 Patient-Years) (95% CrI)	Rate Ratio (Watchman/Warfarin) (95% CrI)	Non- inferiority	Superiority
Primary Efficacy Endpoint	39/1720.2	2.3 (1.7, 3.2)	34/900.8	3.8 (2.5, 4.9)	0.60 (0.41, 1.05)	>0.999	0.960



## No. at Risk

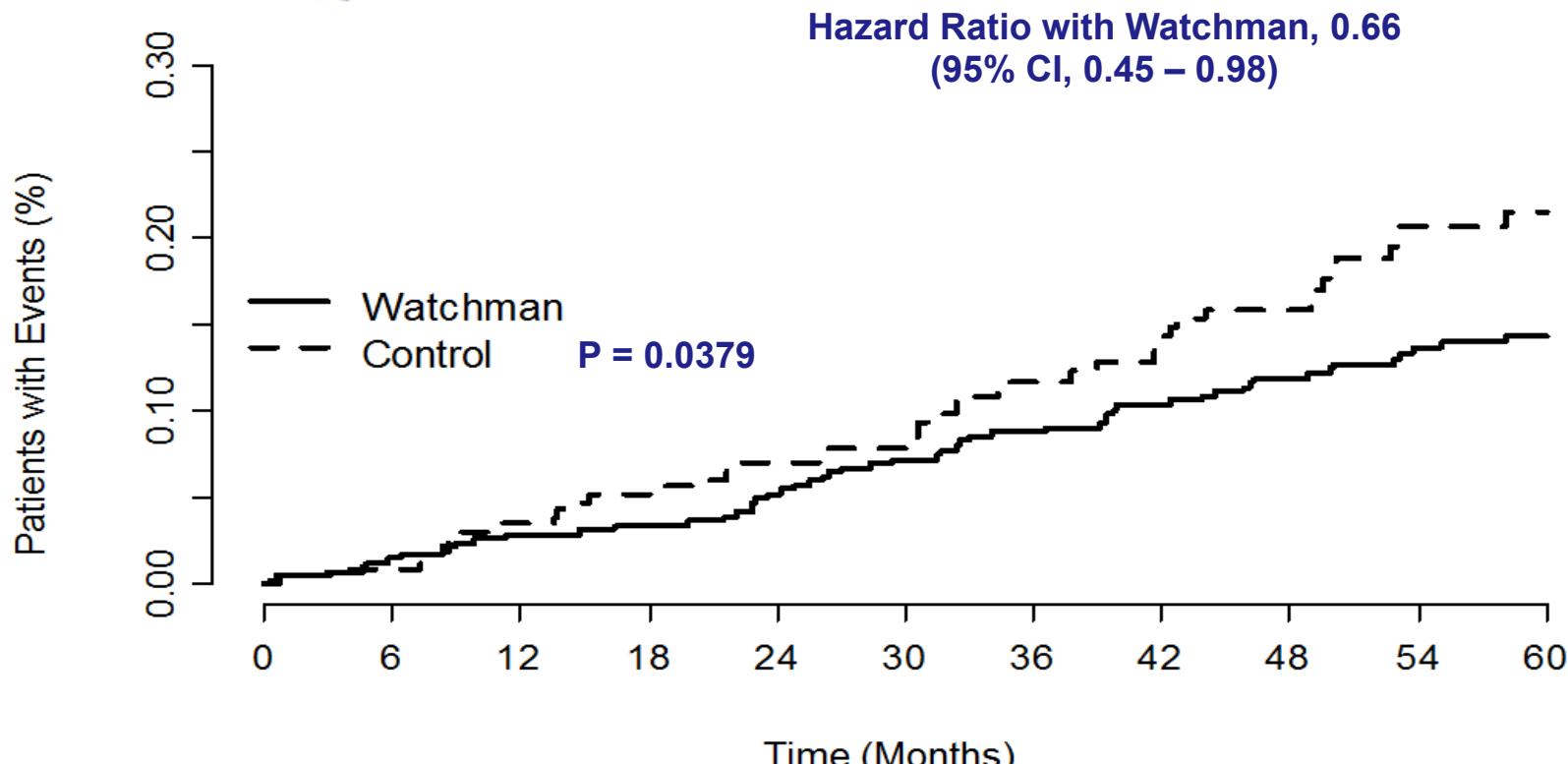
Watchman	463	398	382	370	360	345	337	327	317	285	196
Control	244	230	218	210	200	188	173	159	147	121	87

# PROTECT-AF:

## Primary Efficacy Endpoint

Event	Watchman Group (n = 463)		Warfarin Group (n = 244)		Rate Ratio (Watchman/Warfarin) (95% CrI)	Posterior Probabilities	
	Events/ Patient-Years	Observed Rate (Events per 100 Patient-Years) (95% CrI)	Events/ Patient-Years	Observed Rate (Events per 100 Patient-Years) (95% CrI)		Non- inferiority	Superiority
Primary Efficacy Endpoint	39/1720.2	2.3 (1.7, 3.2)	34/900.8	3.8 (2.5, 4.9)	0.60 (0.41, 1.05)	>0.999	0.960
Stroke	26/1720.7	1.5 (1.0, 2.2)	20/900.9	2.2 (1.3, 3.1)	0.68 (0.42, 1.37)	0.999	0.825
Ischemic Stroke	24/1720.8	1.4 (0.9, 2.1)	10/904.2	1.1 (0.5, 1.7)	1.26 (0.72, 3.28)	0.780	0.147
Hemorrhagic Stroke	3/1774.2	0.2 (0.0, 0.4)	10/916.2	1.1 (0.5, 1.8)	0.15 (0.03, 0.49)	>0.999	0.999
Systemic Embolization	3/1773.6	0.2 (0.0, 0.4)	0/919.5	0.0	NA	-	-
Cardiovascular Death	17/1774.3	1.0 (0.6, 1.5)	22/919.4	2.4 (1.4, 3.4)	0.40 (0.23, 0.82)	>0.999	0.995

# Intention-to-Treat: 5-year follow-up All-Cause Mortality



## No. at Risk

Watchman	463	404	389	381	373	360	352	341	330	294	202
Control	244	233	222	216	204	193	177	163	150	125	92



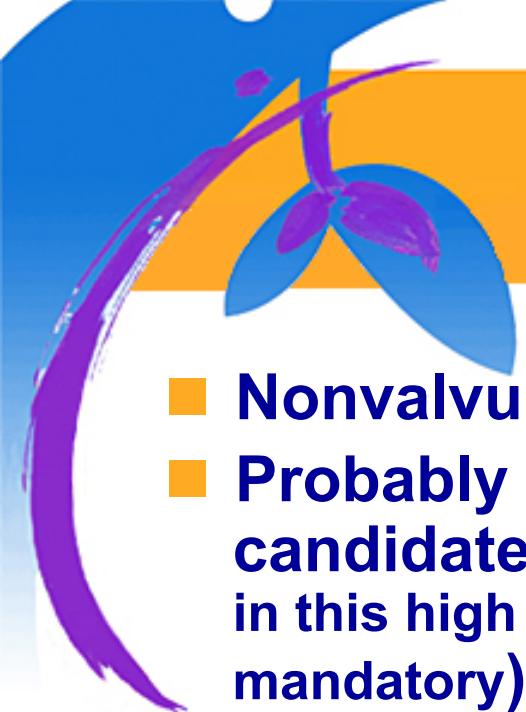
# Issues

- Are we ready to perform LAA occlusion in all nonvalvular AF patients chronically treated with warfarin ?
- We have no comparison with other new oral anticoagulants therapies
- Preference of the patient
- Cost-effectiveness ratio ?
- Safety of the technique on a large scale ?



# Conditions in which percutaneous LAA occlusion may be considered

- Previous ICH : acknowledging individual patient factors, and bleeding etiology
- Recurrent GI bleeding : bleeding from unknown origin or intestinal angiodyplasia despite endoscopic therapy. Lesions that are not accessible for endoscopic therapy
- Co-morbidities : uncontrolled hypertension, cerebral microbleeds, cerebral amyloid angiopathy
- Recurrent ischemic stroke despite well-controlled therapeutic OAC : after exclusion of other sources of embolism
- Coagulopathies : low platelet counts, myelodysplastic syndrome
- Intolerance to new OAC drugs : GI intolerance, severe liver or kidney dysfunction
- Elderly patient : which threshold of age ??



# **Left atrial appendage occlusion : alternative therapy to oral anticoagulation ? For which patients ?**

- **Nonvalvular atrial fibrillation**
- **Probably for those defined previously : poor candidate or ineligible to oral anticoagulation (even in this high risk subset of patients, a randomized study is mandatory)**
- **Patient selection should be carried out by a multidisciplinary team**
- **Registries must be implemented**
- **Comparison between LAA occlusion and NOAC is desirable**
- **Should we extend in the future LAA occlusion to all patients with no contraindication to OAC ?**

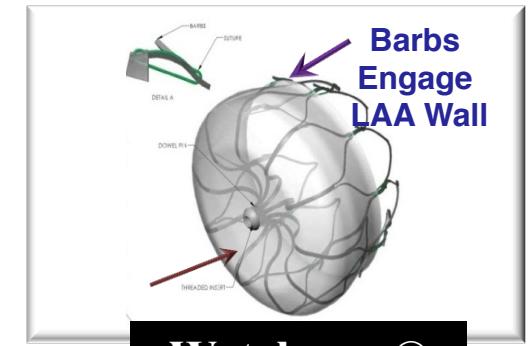


# Patients with a contraindication for oral anticoagulation

## Is LAA occlusion feasible, safe and efficient ?

### The ASAP Study

- 150 patients with nonvalvular AF, CHADS<sub>2</sub> ≥ 1
- Feasibility: successful implantation in 94.7%
- Safety: 2 cases of pericardial effusion (percutaneous drainage), 6 cases of device-related thrombus (5 discovered during TEE surveillance without clinical sequela)
- Efficacy: follow-up (men 14.4 months), ischemic stroke 1.7% versus expected rate of 7.3%.



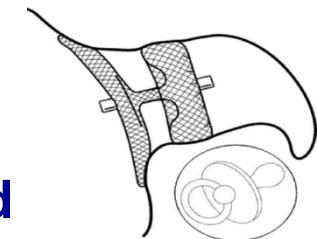
Watchman®

# Patients with a contraindication for oral anticoagulation

Is LAA occlusion feasible, safe and efficient ?

## Amplatzer Study

- 52 patients with nonvalvular AF, CHADS<sub>2</sub> ≥ 1 or CHADS<sub>2</sub>VAS<sub>c</sub> score ≥ 2
- Feasibility: successful implantation in 98.1%
- Safety: 1 patient with cardiac tamponade required pericardiocentesis at 1 month, no cases of device thrombosis
- Efficacy: follow-up (men 20 months), ischemic stroke 1.1% versus expected rate of 8.6%.



Urena M, et al J Am Coll Cardiol 2013;62:96-102

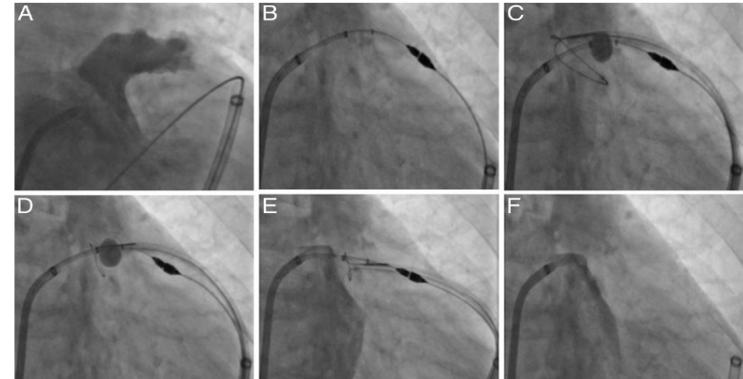


# Patients with a contraindication for oral anticoagulation

## Is LAA occlusion feasible, safe and efficient ?

### LARIAT Device

- 89 patients (62 yrs)
- Nonvalvular AF, CHADS<sub>2</sub> ≥ 1
- Poor candidate or ineligible for warfarin therapy
- Feasibility: successful implantation in 96%
- Safety: 2 patient with severe pericarditis post-operatively, 1-year TEE (n = 65) :98% LAA occlusion
- Efficacy: at 6 months, one sudden death, one hemorrhagic stroke



Bartus K et al J Am Coll Cardiol 2013;62:108-18