Percutaneous Left Atrial appendage occlusion and anticoagulation therapy

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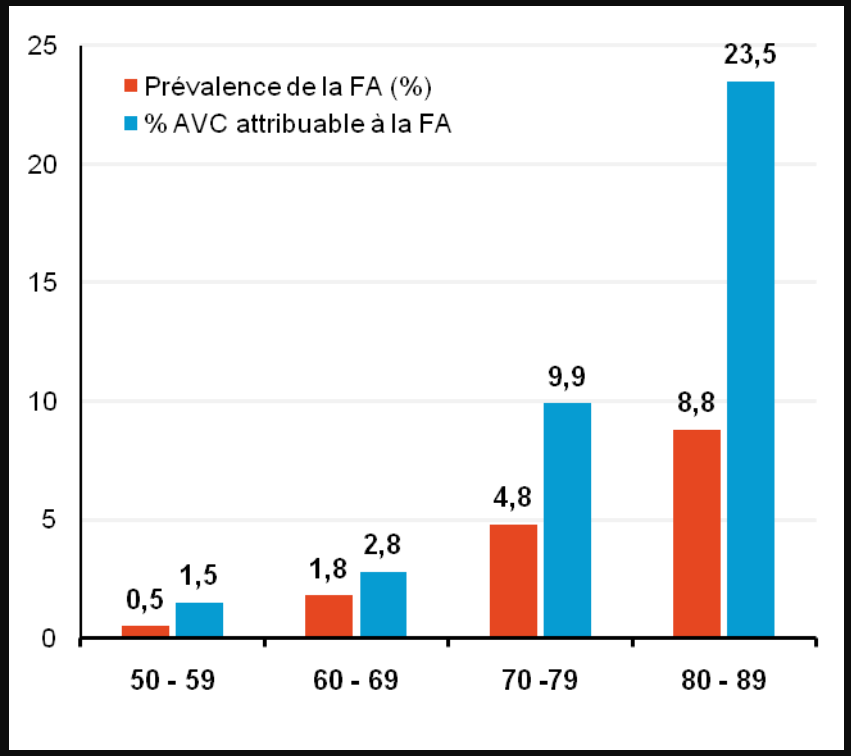
Atrial Fibrillation is a major cause of Stroke : (1,2)

- **AF is associated with a 5 fold increase risk of stroke (2)**
- **AF is responsable for 20 % of stroke (3)**
  - % of stroke due to AF increase with age

  (1,3,4)
- **In France, every 20 minutes 1 stroke due to AF***

Prévalence de la FA en fonction de l'âge et % d'AVC attribuable à la FA (7)



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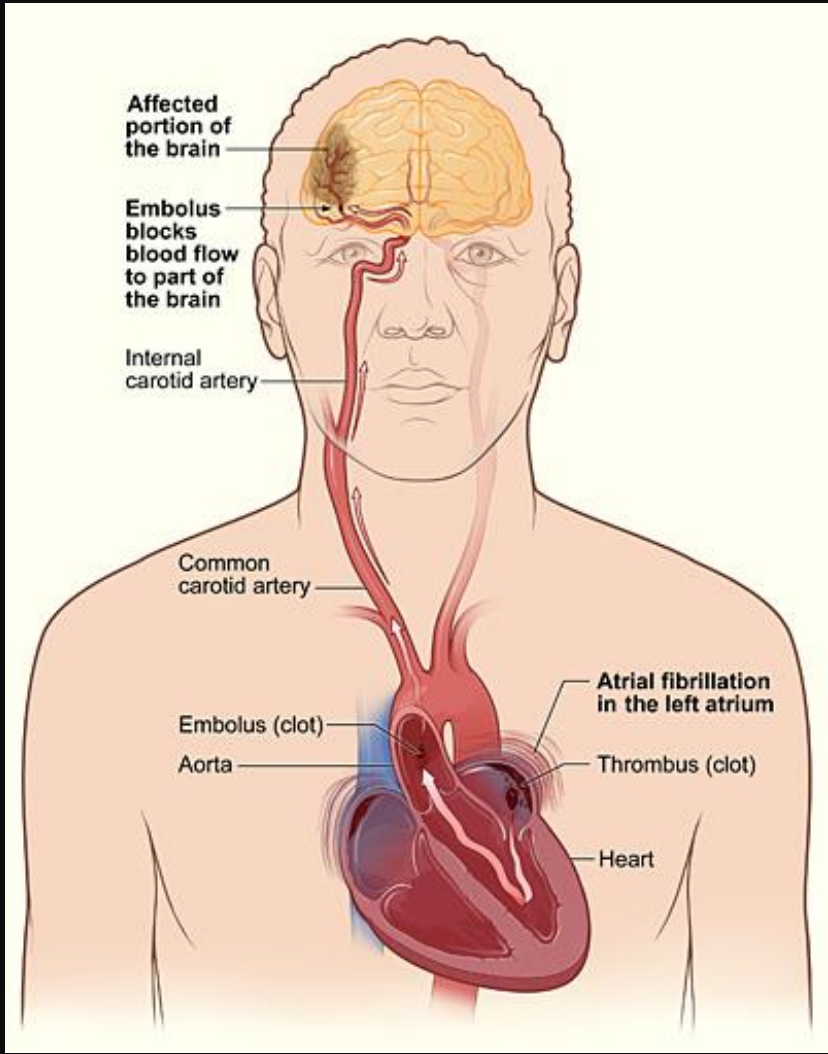
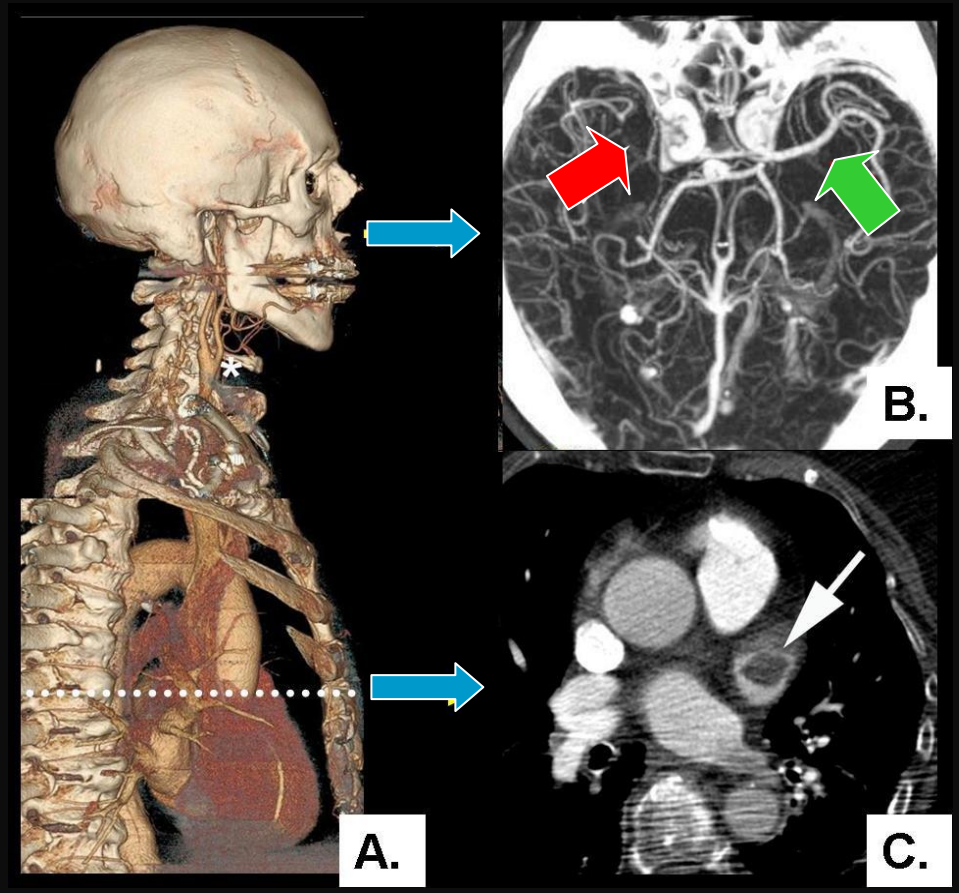
Association between AF and Stroke

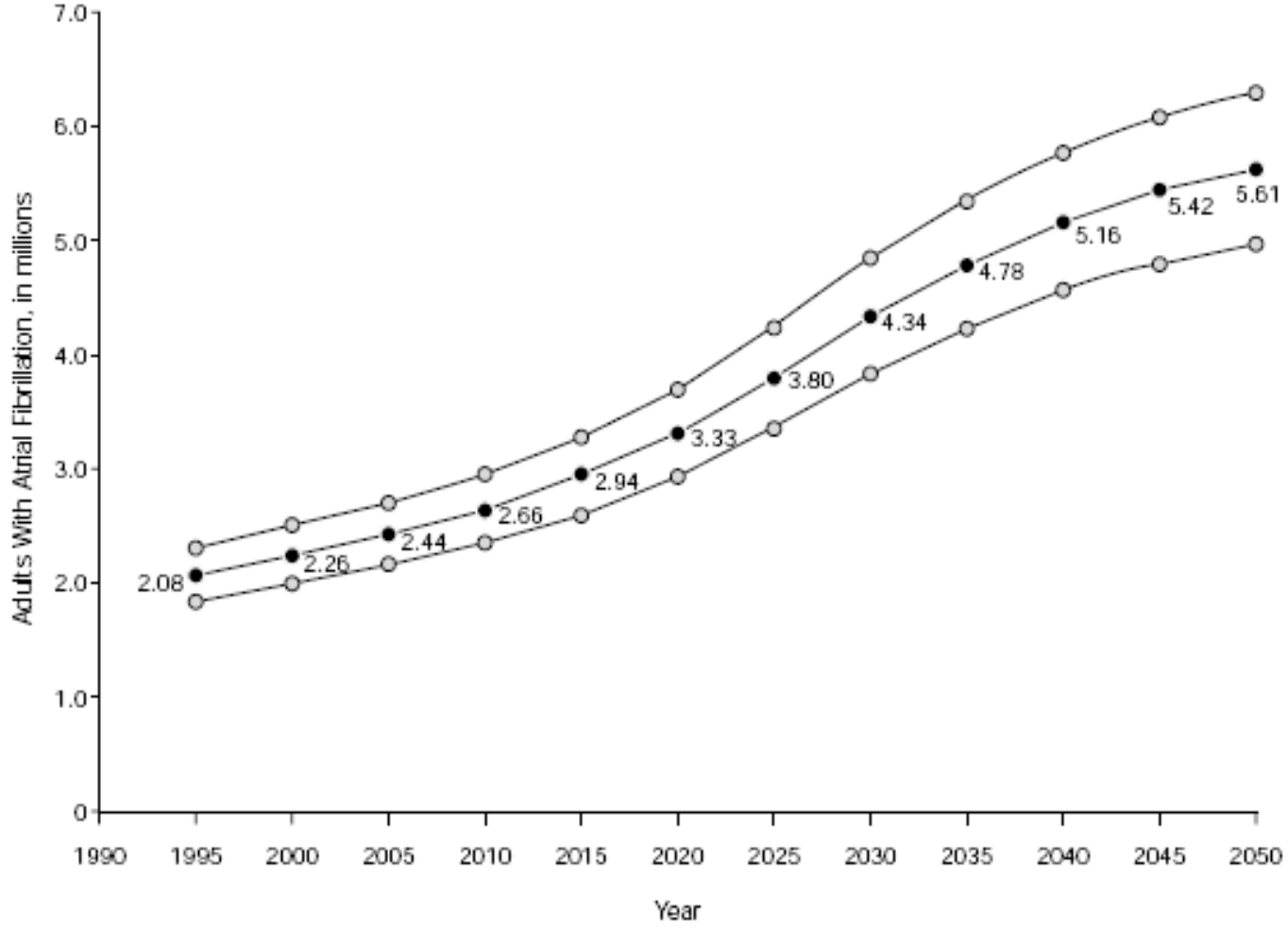




A: 3-D CT
B: Angio: ➡ - normal MCA
➡ - absence of MCA
C: CAT scan: Arrow showing LAA clot

Atrial Fibrillation prevalence is increasing

Figure 3. Projected Number of Adults With Atrial Fibrillation in the United States Between 1995 and 2050



AF prevalence is increasing due to old population

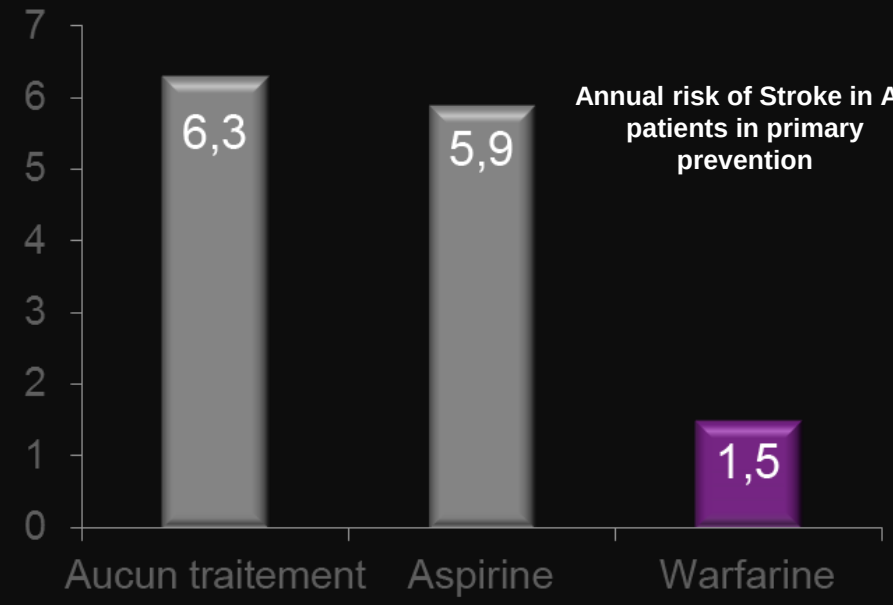
Table 2. Projected Age and Sex Distribution of Adults With Atrial Fibrillation in the United States Between 2000 and 2050*

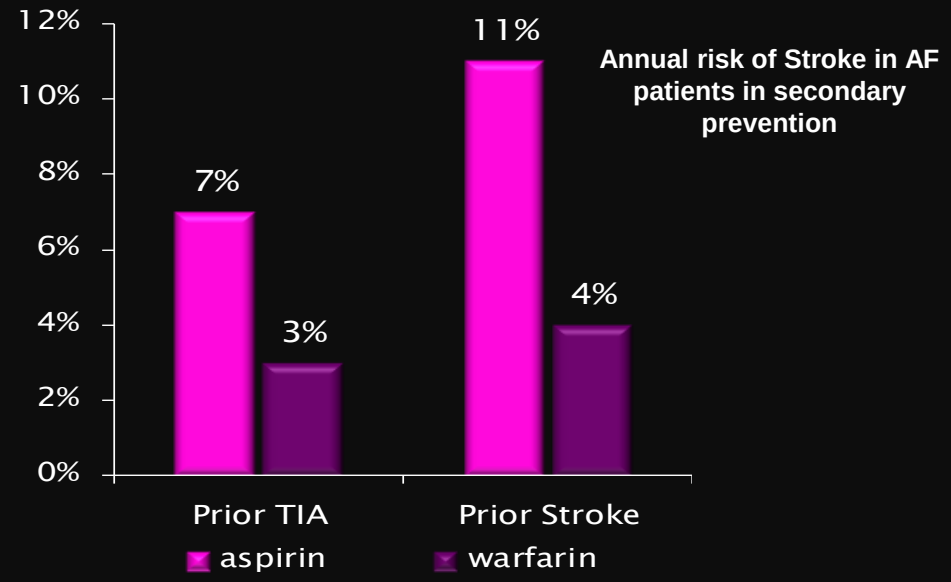
	Year		
	2000	2025	2050
Women	48.6	46.3	47.4
Age group, y			
<65	18.0	15.5	11.5
65-79	45.3	48.7	36.0
≥80	36.7	35.8	52.6

*Data are presented as percentage.

Stroke Prevention during AF

- Oral anticoagulation (VKA) reduces the risk of stroke during AF :
  - 60% reduction of stroke
  - 25% reduction of overall mortality





OTHER OPTIONS FOR STROKE PREVENTION IN AF PATIENTS

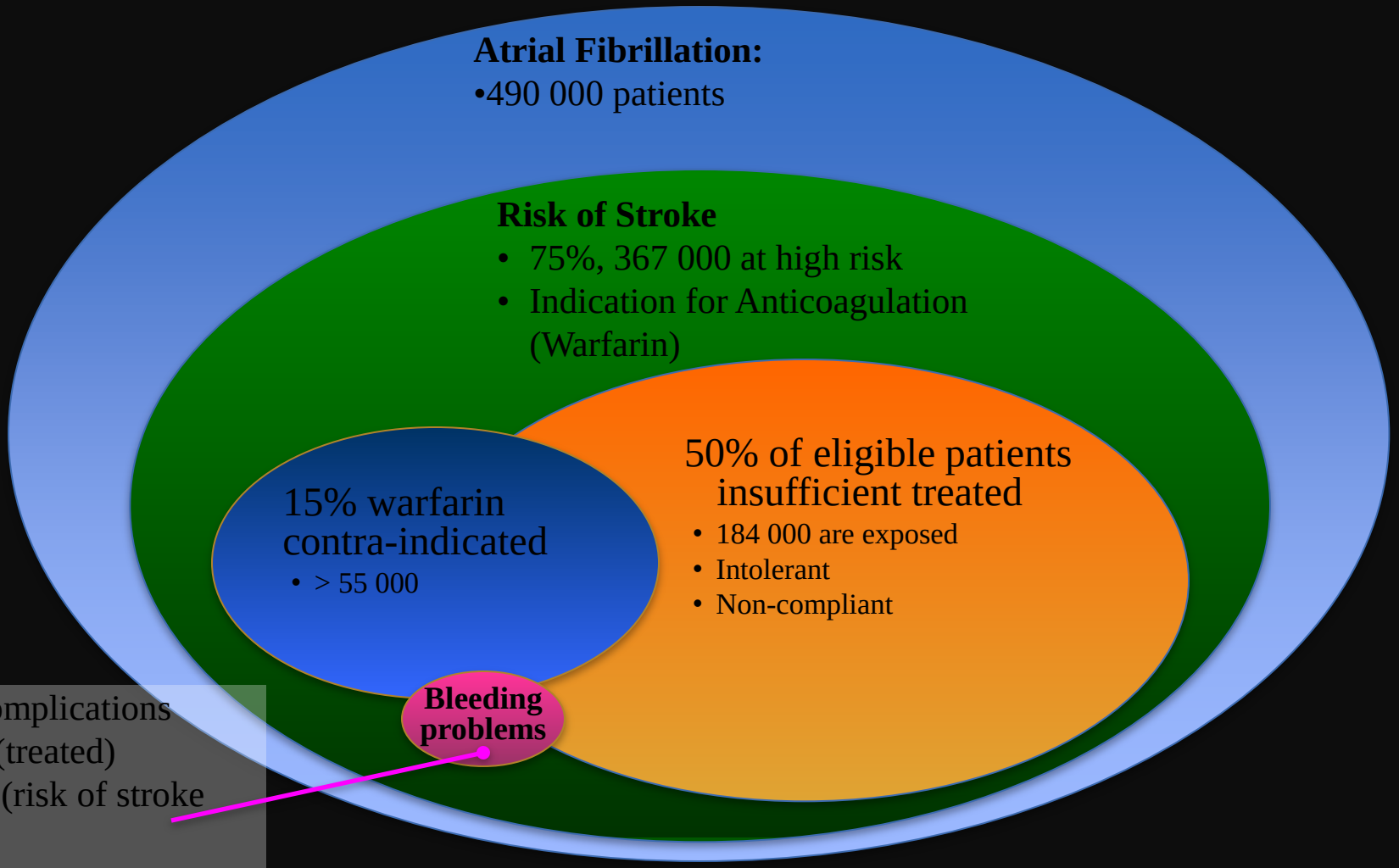
-New oral anticoagulant agents

-Percutaneous left atrial appendage occlusion (90% of thrombi are located in LAA during AF)

Even with NOACs hemorragic risk still persist

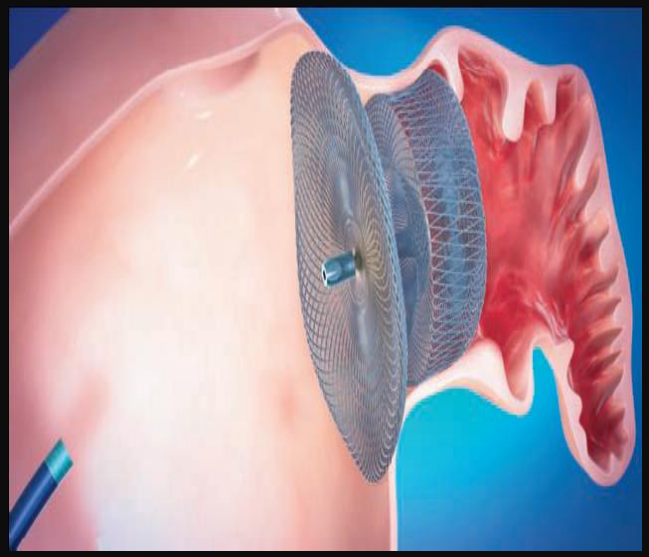
Event	Dabigatran, 110 mg		Dabigatran, 150 mg		Warfarin	
	no. of patients	%/yr	*no. of patients*	%/yr	*no. of patients*	%/yr
Major bleeding	322	2.71	375	3.11	397	3.36
Life threatening	145	1.22	175	1.45	212	1.80
Non–life threatening	198	1.66	226	1.88	208	1.76

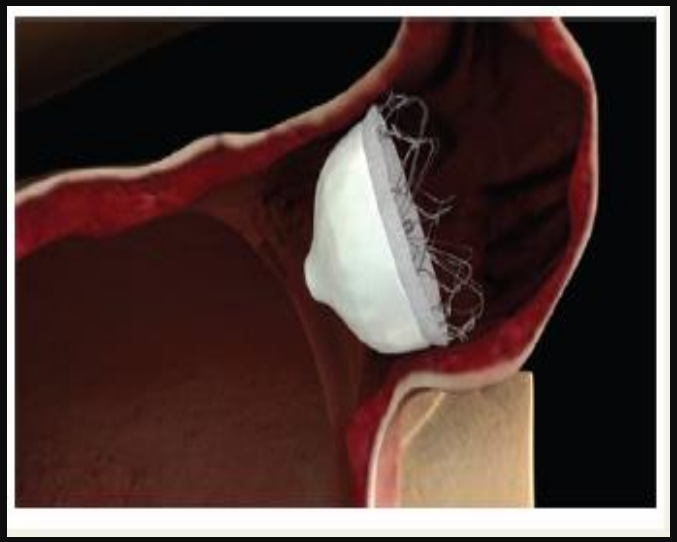
Patient Population *France*

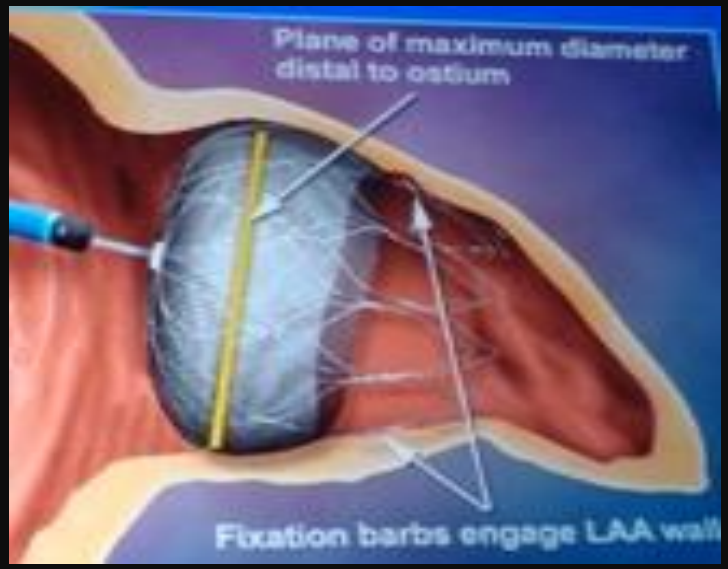


Bleeding Complications
- 5 500 /yr (treated)
- 11 000/yr (risk of stroke group)

Principle of transcatheter approach







EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion

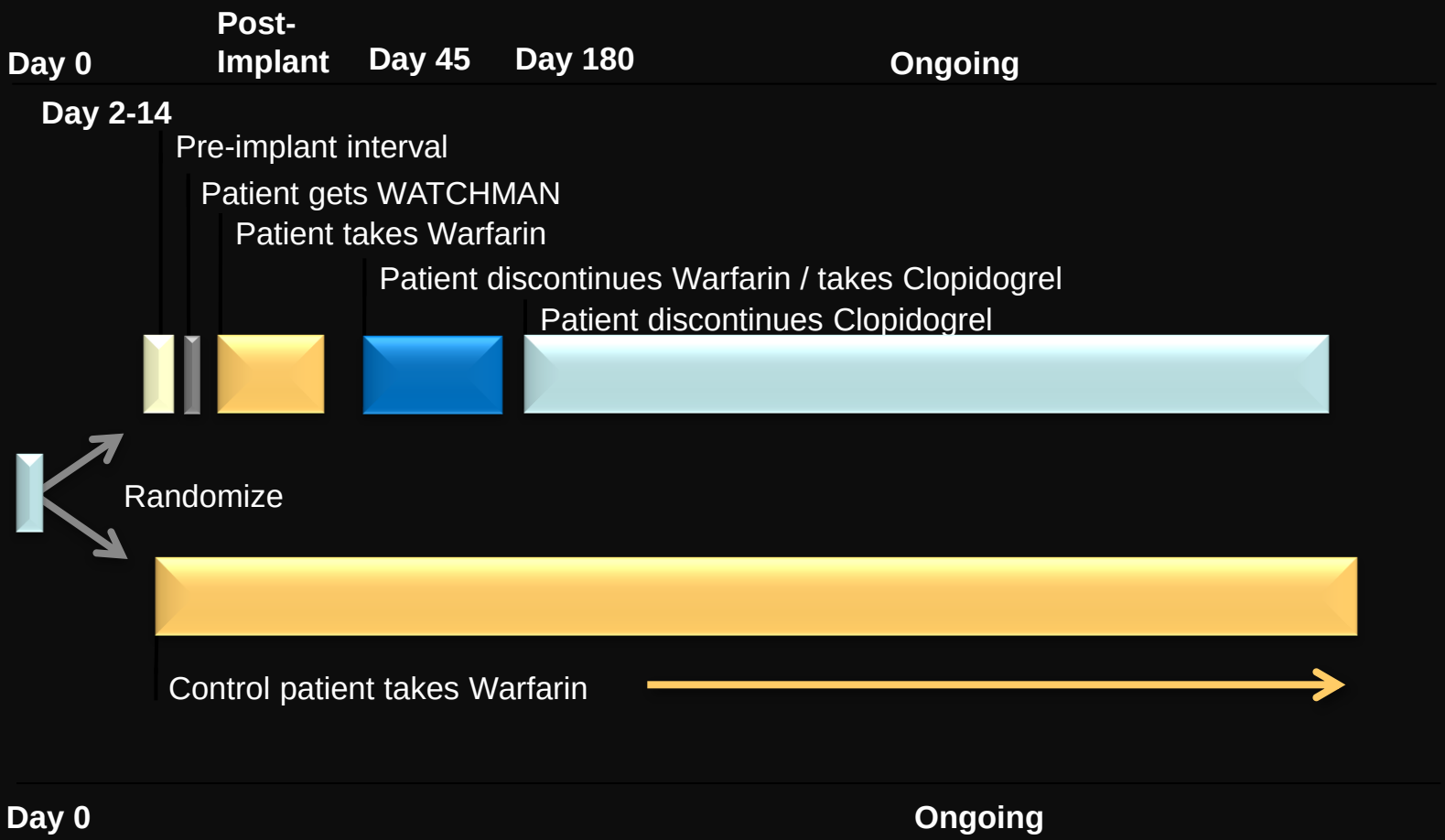
Bernhard Meier (EAPCI Chairperson) (Switzerland)[1], Yuri Blaauw (The Netherlands)[2], Ahmed A. Khattab (Switzerland)[1], Torsten Lewalter (Germany)[3], Horst Sievert (Germany)[4], Claudio Tondo (Italy)[5], Michael Glikson (EHRA Chairperson) (Israel)[6]*

Document Reviewers: Gregory Y. H. Lip (UK), Jose Lopez-Minguez (Spain), Marco Roffi (Switzerland), Carsten Israel (Germany), Dariusz Dudek (Poland), Irene Savelieva (on behalf of EP-Europace, UK)

PROTECT AF

Study Objective:	Evaluate the efficacy and safety of the WATCHMAN LAA Closure Device as compared to long-term warfarin therapy in patients with non-valvular atrial fibrillation and $CHADS_2$ score $\geq$ 1
Study Design:	Prospective, randomized (2 Device: 1 Control), non-inferiority study of the Watchman device compared to long-term warfarin therapy
Primary Endpoint:	Non-inferiority of the WATCHMAN device to warfarin therapy for the composite of ischemic stroke, hemorrhagic stroke, systemic embolism and cardiovascular/unexplained death
Additional Endpoints:	Life-threatening events including device embolization requiring retrieval, pericardial effusion requiring intervention, cranial and GI bleeding, and bleeding requiring transfusion $\geq$ 2 units PRBCs
Patient Population:	WATCHMAN n=463 Control n=244 Roll-in n=93
Number of Sites:	59 (55 U.S., 4 EU)

Design of the study



Long term Protect AF follow-up

Importance While effective in preventing stroke in patients with atrial fibrillation (AF), warfarin is limited by a narrow therapeutic profile, a need for lifelong coagulation monitoring, and multiple drug and diet interactions.
Objective To determine whether a local strategy of mechanical left atrial appendage (LAA) closure was noninferior to warfarin.
Design, Setting, and Participants PROTECT AF was a multicenter, randomized (2:1), unblinded, Bayesian-designed study conducted at 59 hospitals of 707 patients with nonvalvular AF and at least 1 additional stroke risk factor ($CHADS_2$ score ≥1). Enrollment occurred between February 2005 and June 2008 and included 4-year follow-up through October 2012. Noninferiority required a posterior probability greater than 97.5% and superiority a probability of 95% or greater; the noninferiority margin was a rate ratio of 2.0 comparing event rates between treatment groups.
Interventions Left atrial appendage closure with the device (n=00000059 farin (n=244; target international normalized ratio, 2-3).
Main Outcomes and Measures A composite efficacy end point including stroke, systemic embolism, and cardiovascular/unexplained death, analyzed by intention-to-treat.
Results At a mean (SD) follow-up of 3.8 (1.7) years (2621 patient-years), there were 39 events among 463 patients (8.4%) in the device group for a primary event rate of 2.3 events per 100 patient-years, compared with 34 events among 244 patients (13.9%) for a primary event rate of 3.8 events per 100 patient-years with warfarin (rate ratio, 0.60; 95% credible interval, 0.41-1.05), meeting prespecified criteria for both noninferiority (posterior probability, >99.9%) and superiority (posterior probability, 96.0%). Patients in the device group demonstrated lower rates of both cardiovascular mortality (1.0 events per 100 patient-years for the device group [17/463 patients, 3.7%] vs 2.4 events per 100 patient-years with warfarin [22/244 patients, 9.0%]; hazard ratio [HR], 0.40; 95% CI, 0.21-0.75; *P*= .005) and all-cause mortality (3.2 events per 100 patient-years for the device group [57/466 patients, 12.3%] vs 4.8 events per 100 patient-years with warfarin [44/244 patients, 18.0%]; HR, 0.66; 95% CI, 0.45-0.98; *P*= .04)
Conclusions and Relevance After 3.8 years of follow-up among patients with nonvalvular AF at elevated risk for stroke, percutaneous LAA closure met criteria for both noninferiority and superiority, compared with warfarin, for preventing the combined outcome of stroke, systemic embolism, and cardiovascular death, as well as superiority for cardiovascular and all-cause mortality.

JAMA, 2014

Left Atrial Appendage Closure with the Watchman Device in Patients with a Contraindication for Oral Anticoagulation: ASA Plavix Feasibility Study with Watchman
Left Atrial Appendage Closure Technology (ASAP Study)

Objectives: To assess the safety and efficacy of left atrial appendage closure (LAA) in nonvalvular atrial fibrillation (AF) patients ineligible for warfarin therapy.
Background: The PROTECT AF trial demonstrated that LAA closure with the Watchman device was non-inferior to warfarin therapy. However, PROTECT AF only included patients that were candidates for warfarin, and even patients randomized to the LAA closure arm received concomitant warfarin for 6 weeks after Watchman implantation.
Methods: Multi-center, prospective, non-randomized study of LAA closure with the Watchman device in 150 patients with non-valvular AF and CHADS2 ≥1, who were considered ineligible for warfarin. The primary efficacy endpoint was the combined events of ischemic stroke, hemorrhagic stroke, systemic embolism, and cardiovascular/unexplained death.
Results: The mean CHADS2 and CHA2DS2-VASc scores were 2.8 ± 1.2 and 4.4±1.7, respectively. History of hemorrhagic/bleeding tendencies (93%) was the most common reason for warfarin ineligibility. Mean duration of follow-up was 14.4 ± 8.6 months. Serious procedureor device-related safety events occurred in 8.7% of patients (13/150 patients). All-cause stroke or systemic embolism occurred in 4 patients (2.3% per year); ischemic stroke in 3 patients (1.7% per year) and hemorrhagic stroke in 1 patient (0.6% per year). This ischemic stroke rate was less than that expected (7.3% per year) based on the CHADS2 scores of the patient cohort.
Conclusions: LAA closure with the Watchman device can be safely performed without a warfarin transition, and is a reasonable alternative to consider for patients at high risk for stroke but with contraindications to systemic oral anticoagulation.

Device/Procedure Related Safety Events

	≤7 Days Post Procedure	>7 days Post Procedure	Total
Peri-procedural Stroke / TIA*	0 (0.0%)	0 (0.0%)	0 (0.0%)
Serious Pericardial Effusion	3 (1.5%)	0 (0.0%)	3 (1.5%)
Device Embolization	3 (1.5%)	0 (0.0%)	3 (1.5%)
Device Related Thrombus	0 (0.0%)	5 (2.4%)	5 (2.4%)
Total Safety Events	**6 (2.9%)**	**5 (2.4%)**	**11 (5.4%)**

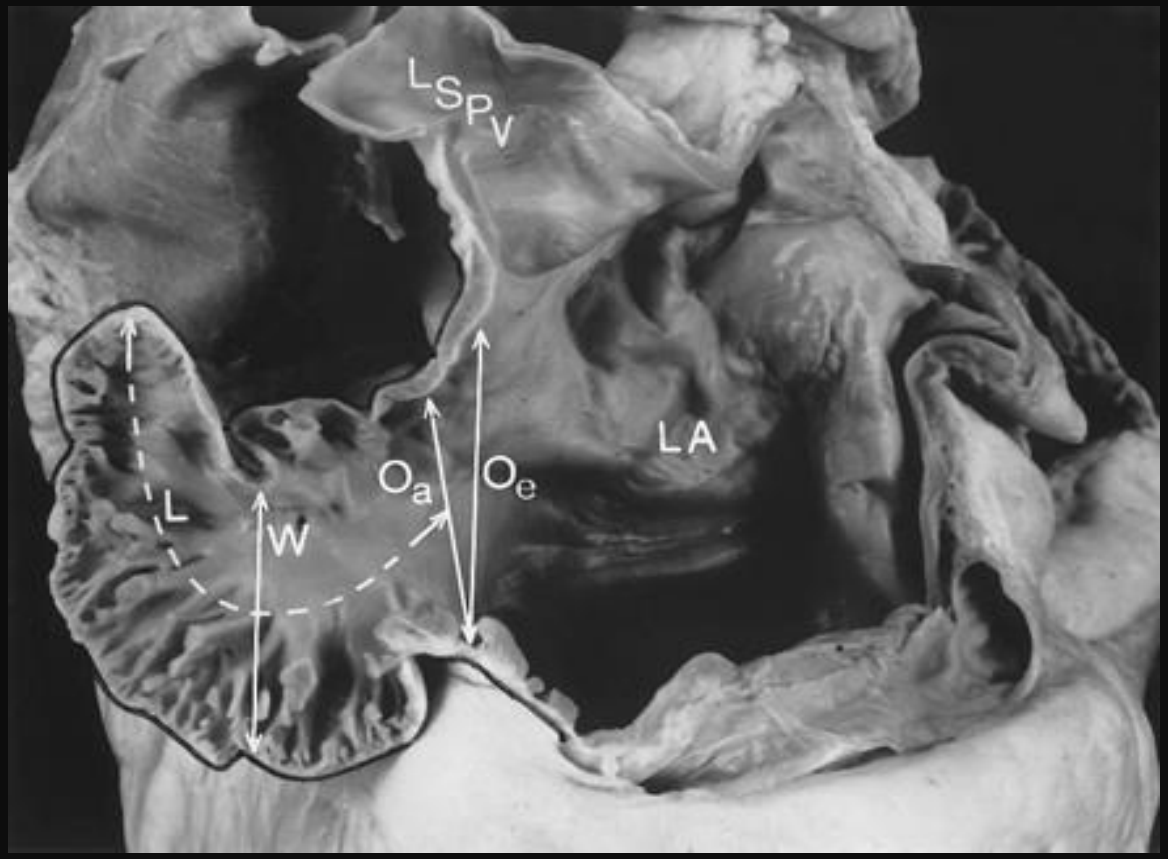
N=204

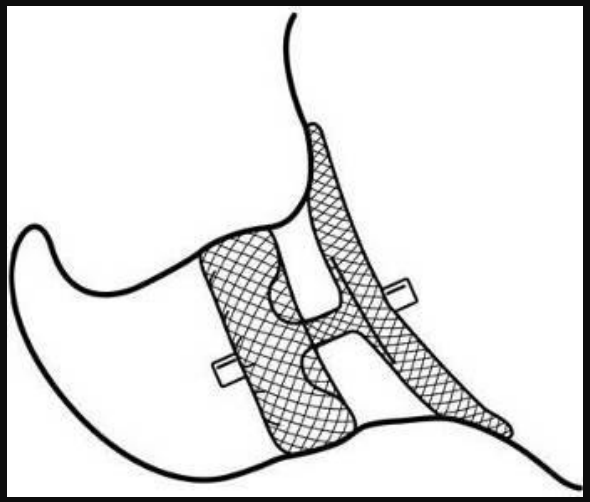
* The stroke/TIA is reference to device or procedure related strokes as adjudicated by the AE Review Committee.

Learning curve confirmed

	Initial European Registry[1]	**EU Prospective Observational Study**
Number of patients (Follow-up period)	N = 143 (Discharge or < 24 hrs)	N = 204 (< 7 days)
Enrollment Period	December 2008 – December 2009	August 2009 – September 2011
Stroke	N = 3 (2.1%)	N = 0 (0.0%)
Serious Pericardial Effusion	N = 5 (3.5%)	N = 3 (1.5%)
Device Embolization	N = 2 (1.4%)	N = 3 (1.5%)
Device Related Thrombus	N= 0 (0.0%)	N = 0 (0.0%)
Total reported Safety Events	**N = 10 (7%)**	**N = 6 (2.9%)**

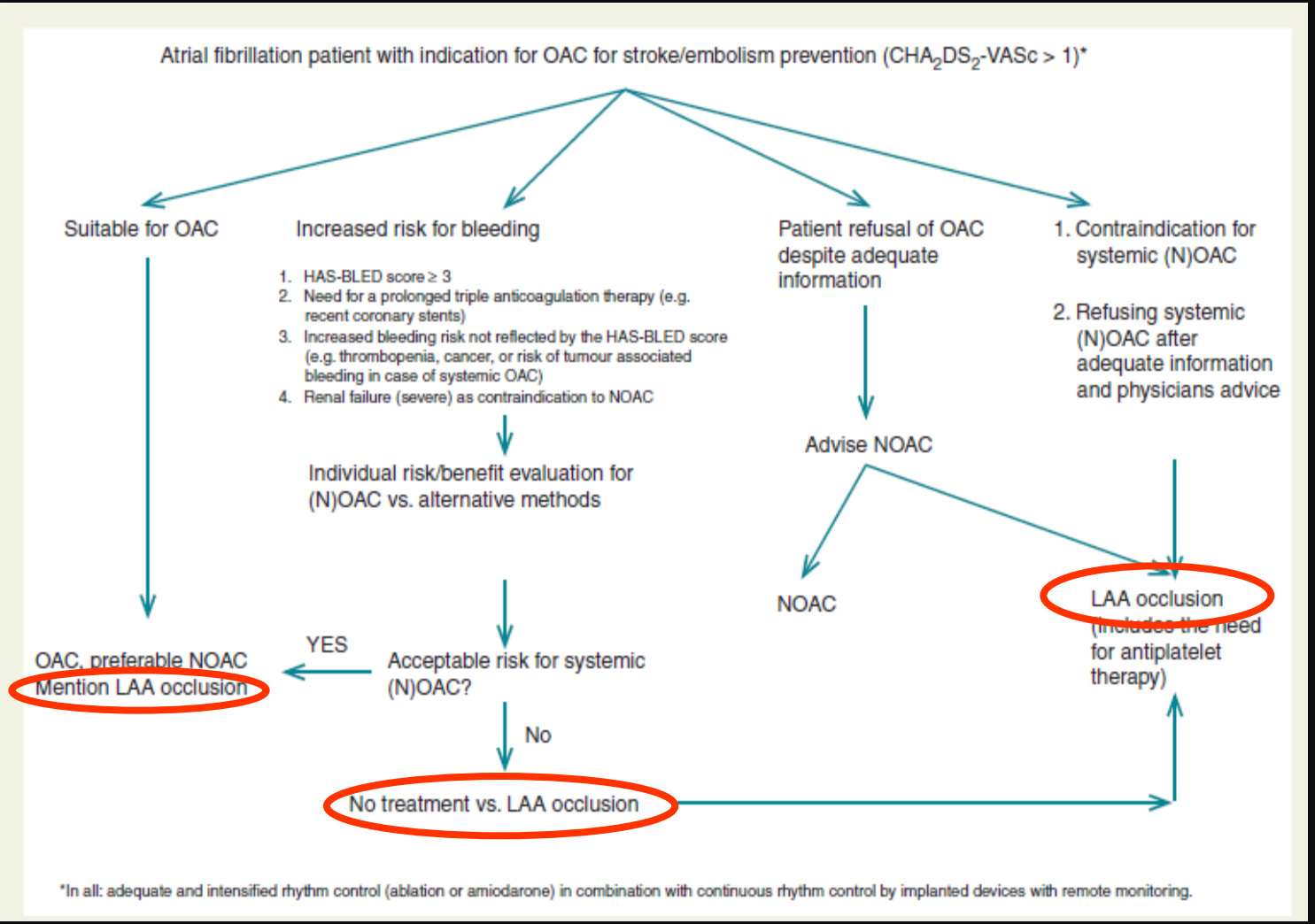
Anatomy of the Normal LAA





Veinot JP, et al: Anatomy of the Normal Left Atrial Appendage A Quantitative Study of Age-Related Changes in 500 Autopsy Hearts: Implications for Echocardiographic Examination. Circulation 1997;96:3112

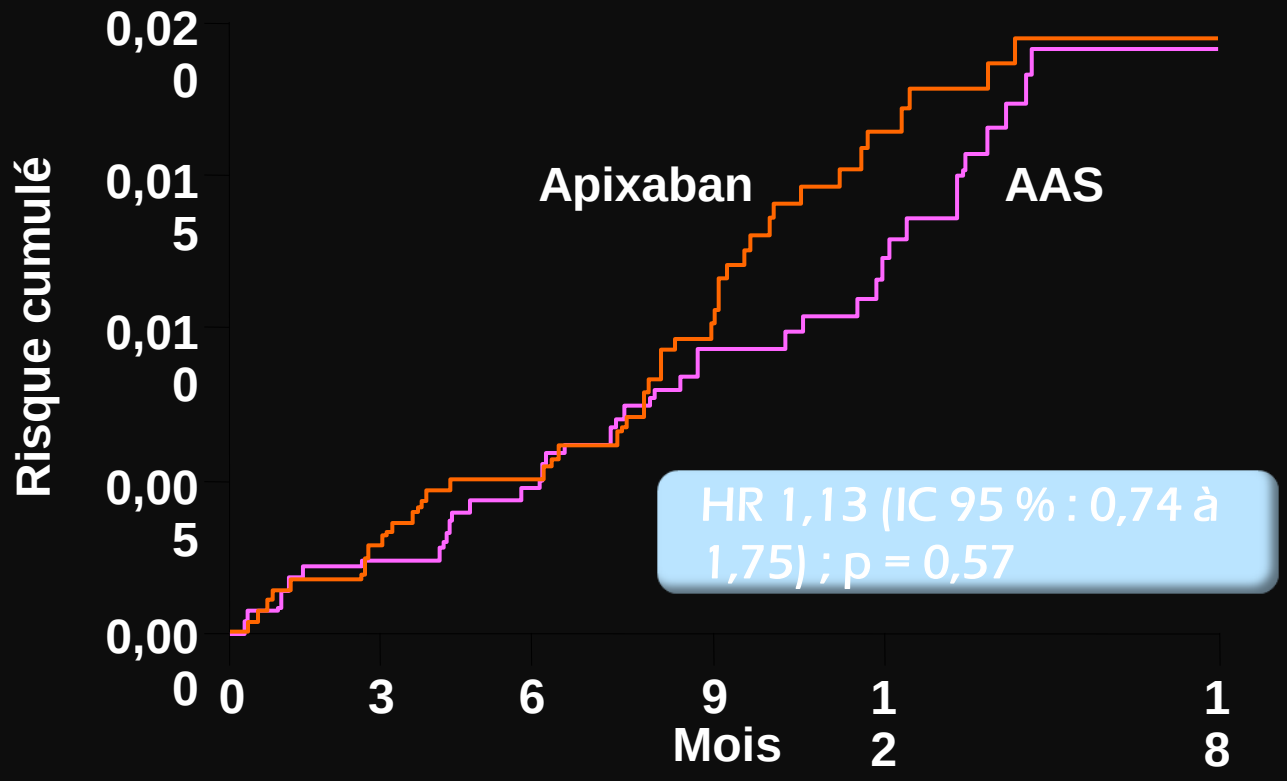
LAA Closure Indication



POST PROCEDURAL TREATMENT

- If possible OAC for 6 weeks
- Otherwise Aspirin+Plavix for 1-6 mois
- Otherwise Aspirin alone or nothing (depending on clinical situation)
- Follow-up with TTE before discharge and CT scan at 3, 6, 12 months
- Same bleeding risk with aspirin than apixaban?
- Place of NOAC following the procedure?

AVERROES STUDY: NO DIFFRENCE BETWEEN APIXABAN AND ASPIRIN IN HEMORRAGIC RISK IN AF PATIENTS

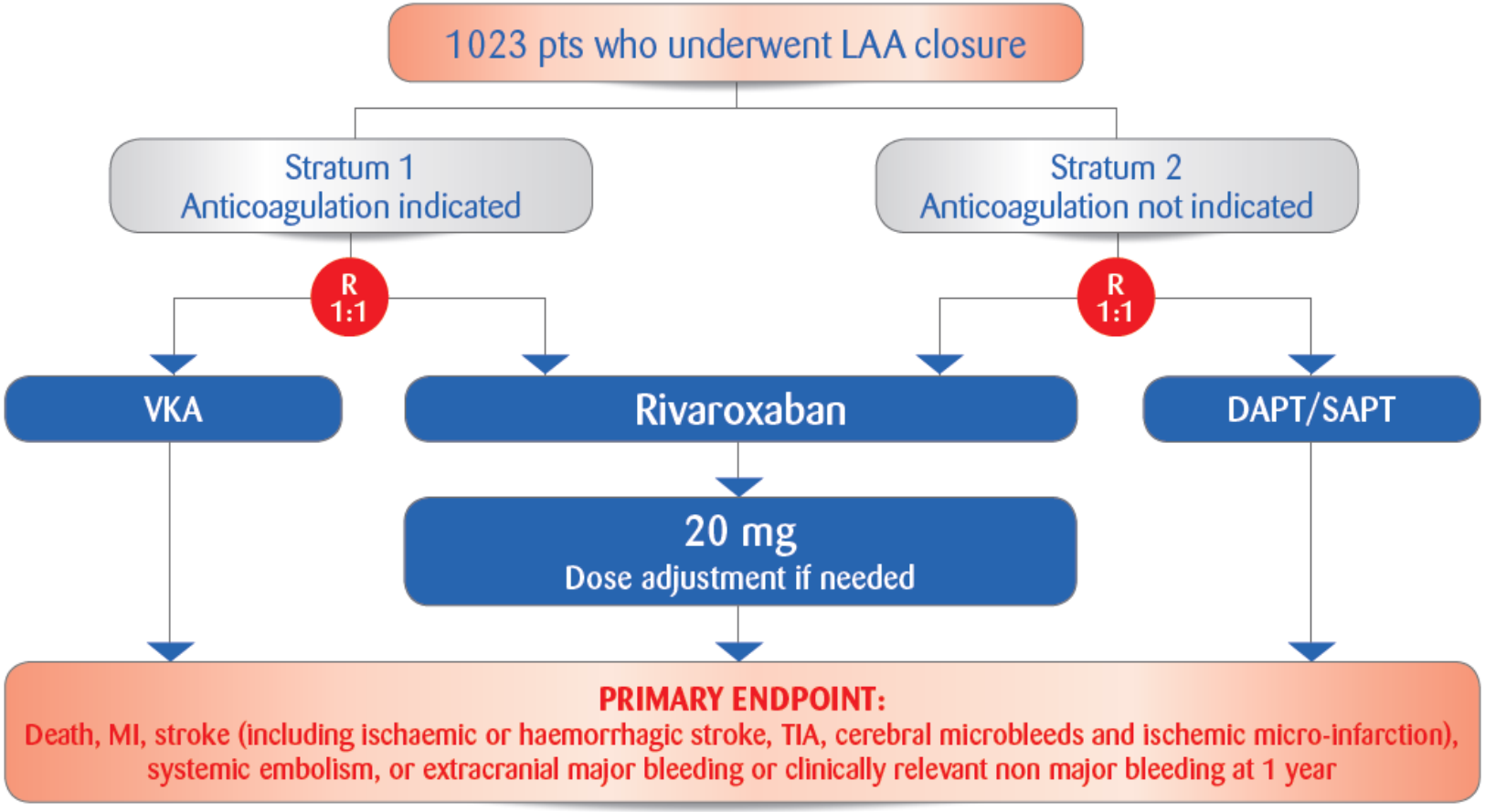


Nb. à risque						
Apixaban	2 808	2 759	2 566	2 120	1 521	622
AAS	2 791	2 738	2 557	2 140	1 571	642

*Critère de sécurité primaire

Anticoagulation with Rivaroxaban versus **D**ual or single antiplatelet therapy to **R**educe **I**schemic and bleeding events in **A**trial fibrillation patients **T**reated with **I**nvasive **C**losure of the left atrial appendage:

The randomized ADRIATIC Study



Design :

- PROBE study design (Prospective Randomised Open, Blinded End-point).
- 80 high volume centers, International

Activity in France

- More centers are practicing this procedure in France: 35
- Reimbursement of the prosthesis soon
- National registry with actually 850 patients included

In US

- Watchman just FDA approved

CONCLUSION

- New technology with promising future
- In France only for patients with CI for oral anticoagulation
- Multidisciplary approach for patients selection and implantation (Heart team)
- More data are needed to completely validate the efficacy and safety of the technique
- Post operative anticoagulation/ antiagregants best strategy still need to be assessed

Thank you for your attention!!!!