Left atrial appendage closure

P. Widimsky

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P. Widimsky – Potential conflicts of interest

Occasional speakers honoraria / advisory boards:

- **AstraZeneca**
- **Bayer**
- **Boehringer Ingelheim**
- **Daiichi Sankyo**
- **Novartis**
- **Pfizer**
- **Servier**

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Left atrial appendage

- Complex structure with effective contractions during sinus rhythm, contractions disappear during AF
- Variable shape and size (volume, length, width, orifice size)

- Neurohumoral activity: atrial natriuretic factor (ANF, ANP) secretion in response to ↑ atrial volume / pressure → vasodilator and diuretic activity → ↓ blood pressure.
- (X brain natriuretic peptide – similar, produced by ventricles).

- LAA visualization: TEE, CT, MR
- 92% of LA thrombi are localized in the LAA !

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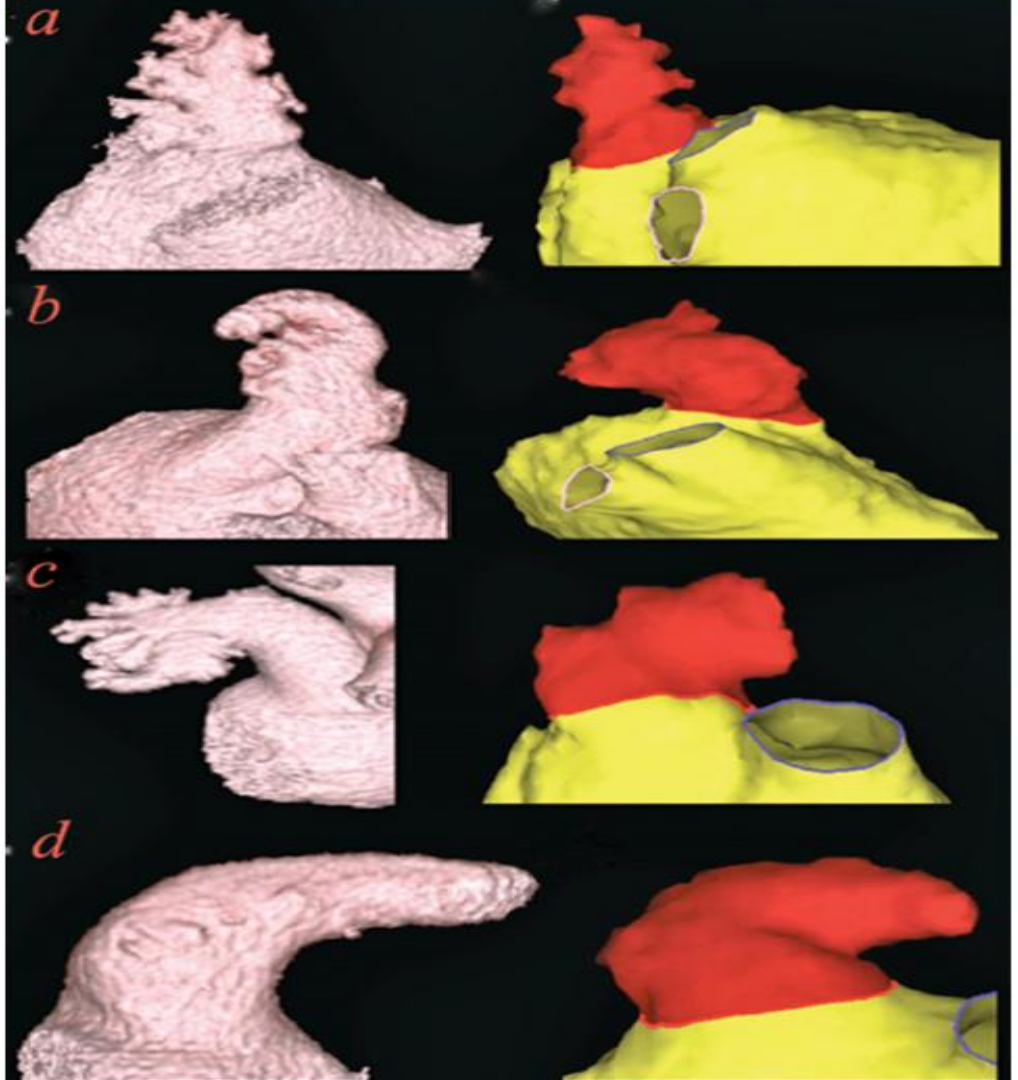
Morphologies (Di Biase et al.):

- cactus (30%)
- chicken wing (48%)
- cauliflower (3%)
- windsock (19%)



Why LAA occlusion ?

- LAA is frequent source of systemic emboli
- Occlusion or removal of LAA may decrease the risk of systemic embolization
- It may be an alternative to OAC in patients with high bleeding risk
- It may be an additional treatment on top of OAC to reduce the risk of stroke

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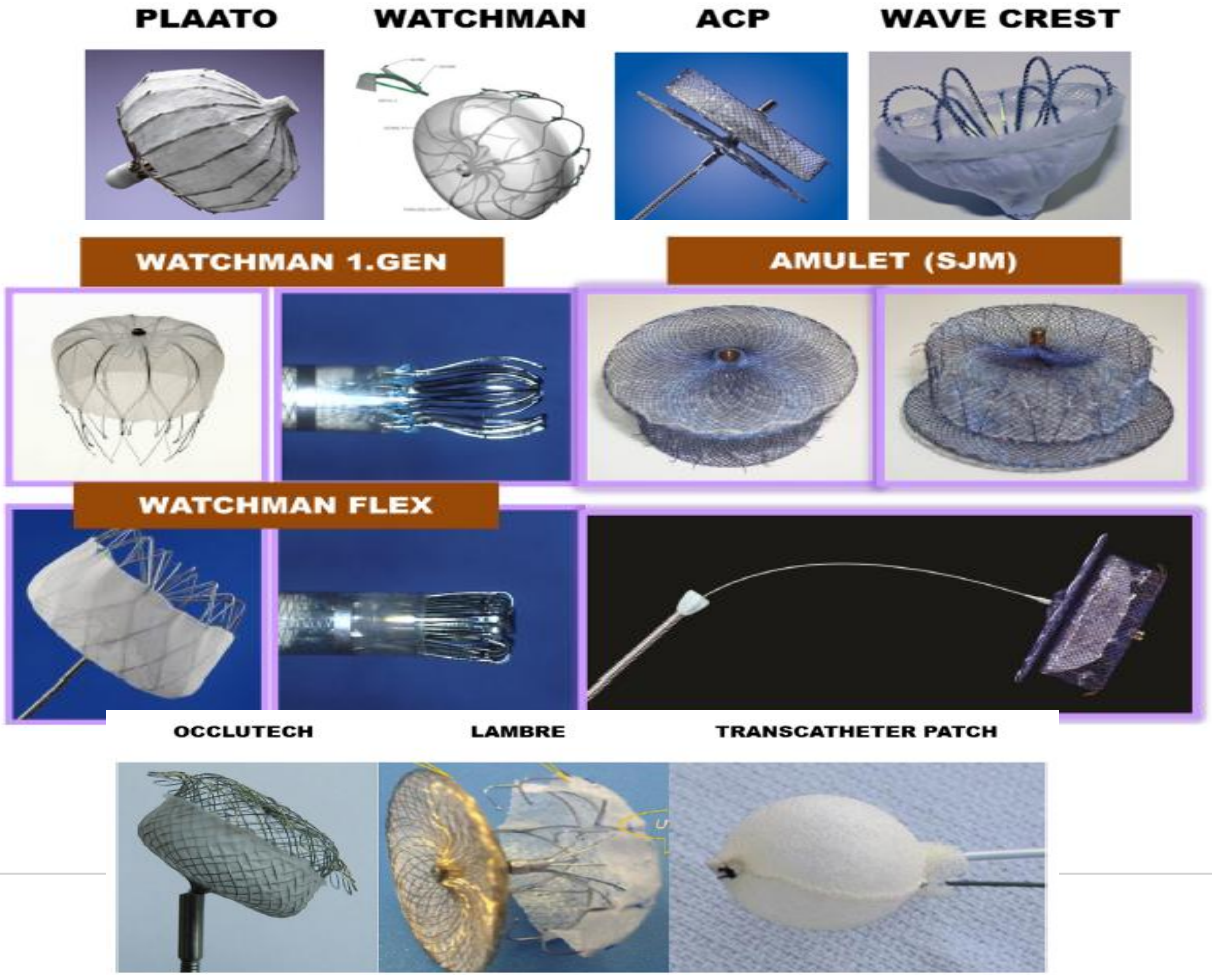
Types of occluders



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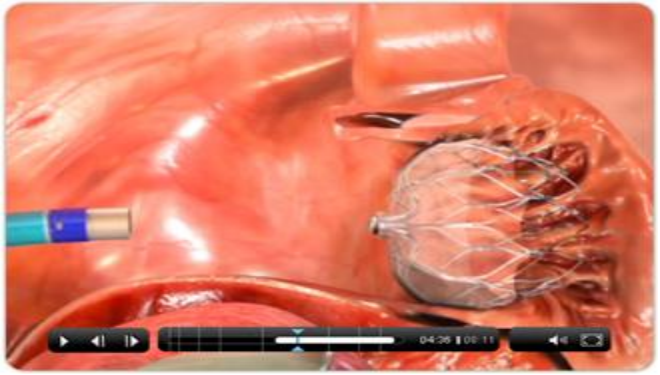

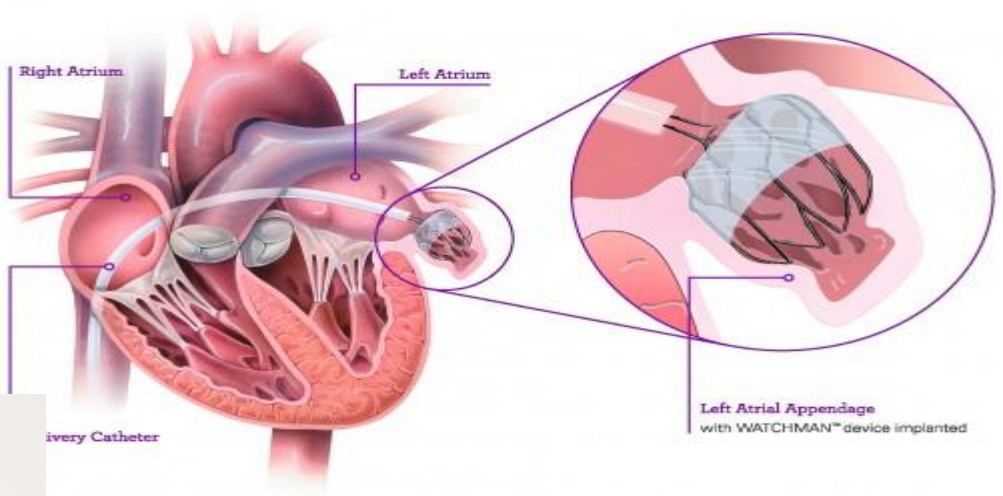

Watchman™, Boston Scientific

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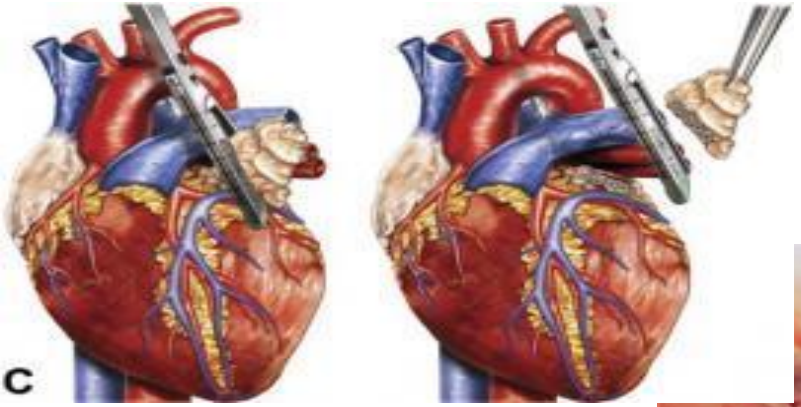
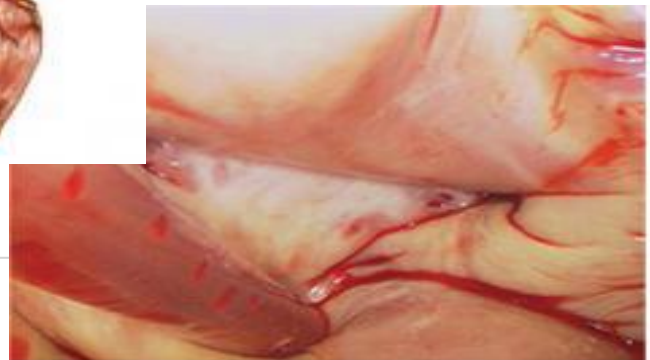
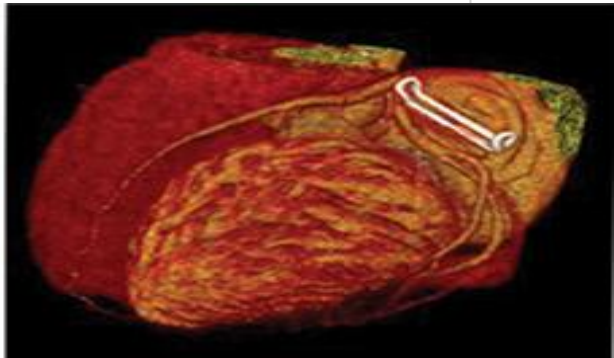
AtriClip® (AtriCure)



Surgical (epicardial) LAA ligation





Potential indications for LAA occlusion in patients with AF

Secondary stroke prevention:

- **Failed OAC: ischemic stroke in patients using OAC**
- **Severe bleeding occurred during OAC treatment**
- **Alternative to OAC in patients with high bleeding risk**
- **On top of OAC to further decrease risk of stroke recurrence**

Primary stroke prevention:

- **High bleeding risk AND high risk of stroke**

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Case from our center

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Male, 61 years with 3 small strokes while on 3 different antithrombotic drugs

- 3/2010 first AF paroxysm, CHA_2DS_2-VASc = 0, → ASA alone.
- 12/2010 **TIA on aspirin** → warfarin (INR 2.3 on 6.5 mg/d)
- 2/2012 **TIA on warfarin** → dabigatran 300 mg/d
- 1/2015 small ischemic **stroke on dabigatran**, TEE: spontaneous contrast in LAA
- 6/2015 LAA closure

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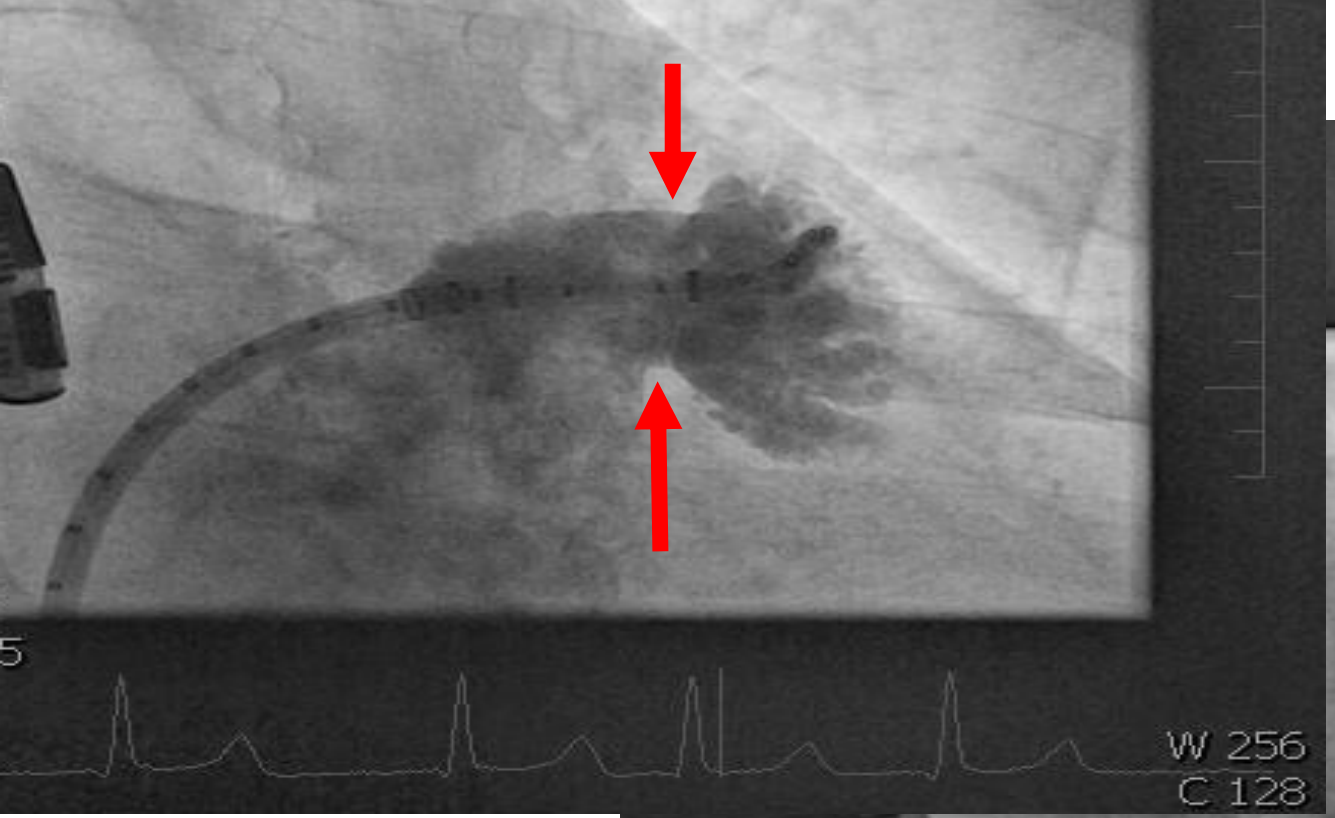
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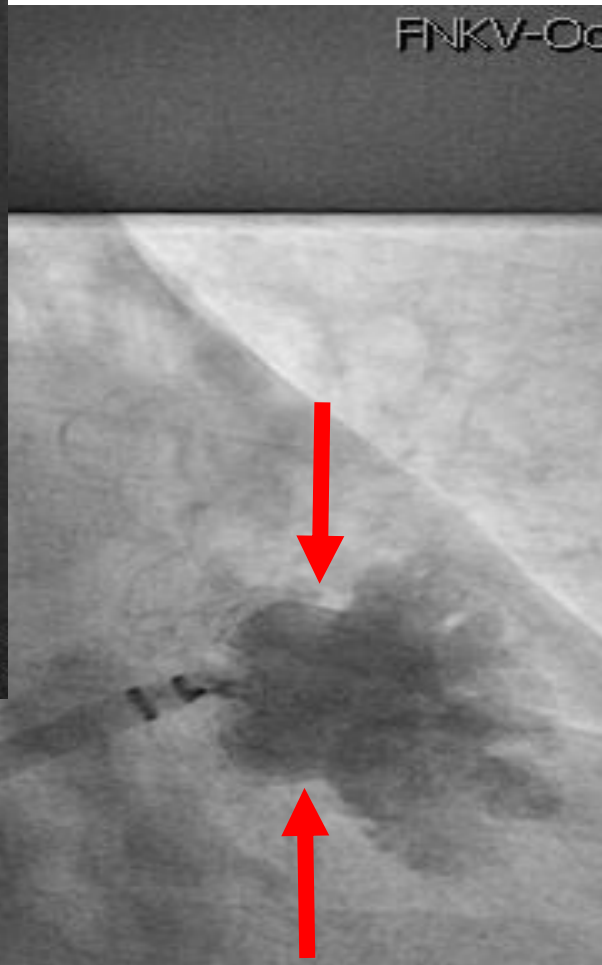
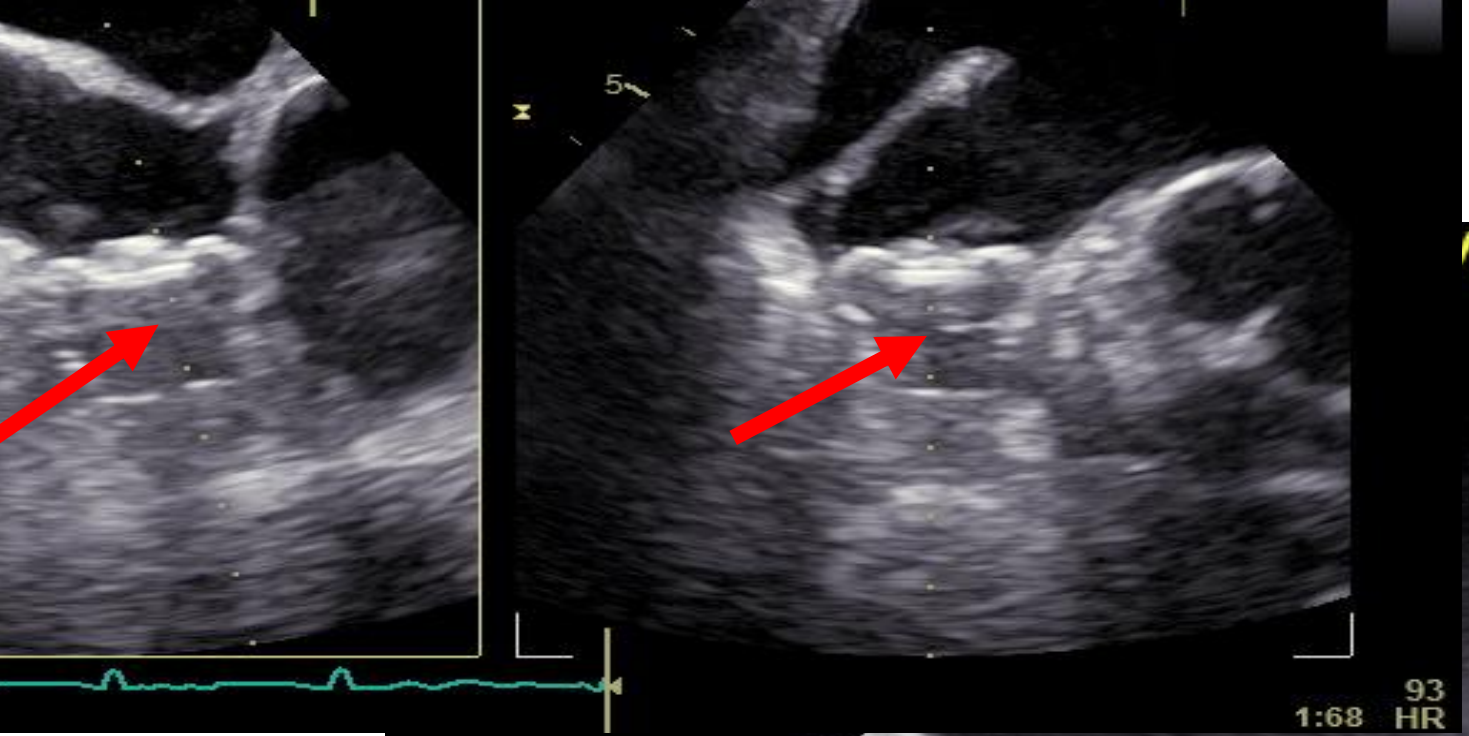

FNKV-Oc


5
93
1:68 HR

10

Published evidence

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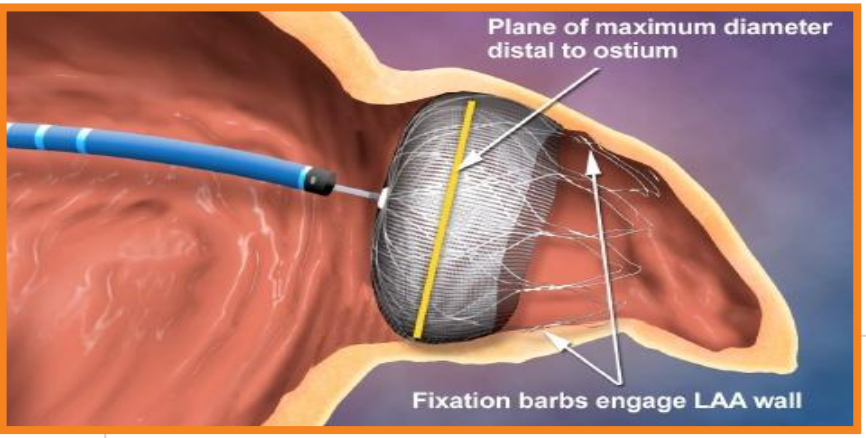
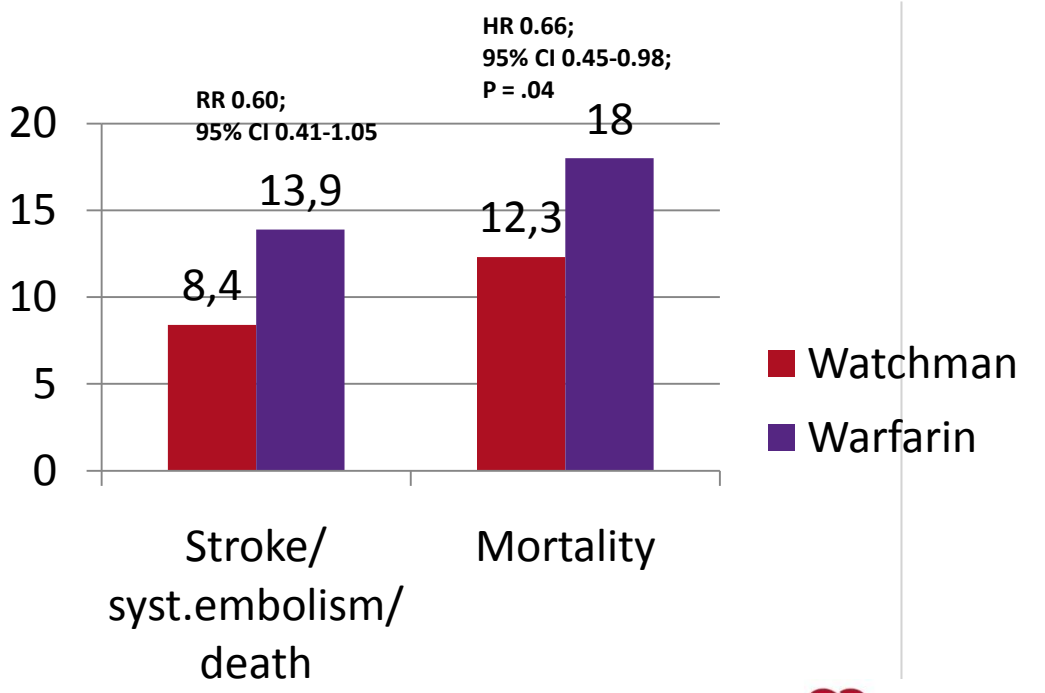
Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: PROTECT AF trial.

Reddy VY et al. JAMA 2014; 312: 1988-98.

- **Nonvalvular AF + $CHADS_2$ ≥1, f-u 4 yrs.**
- **LAA occluder (n = 463) or warfarin target INR 2-3 (n = 244).**





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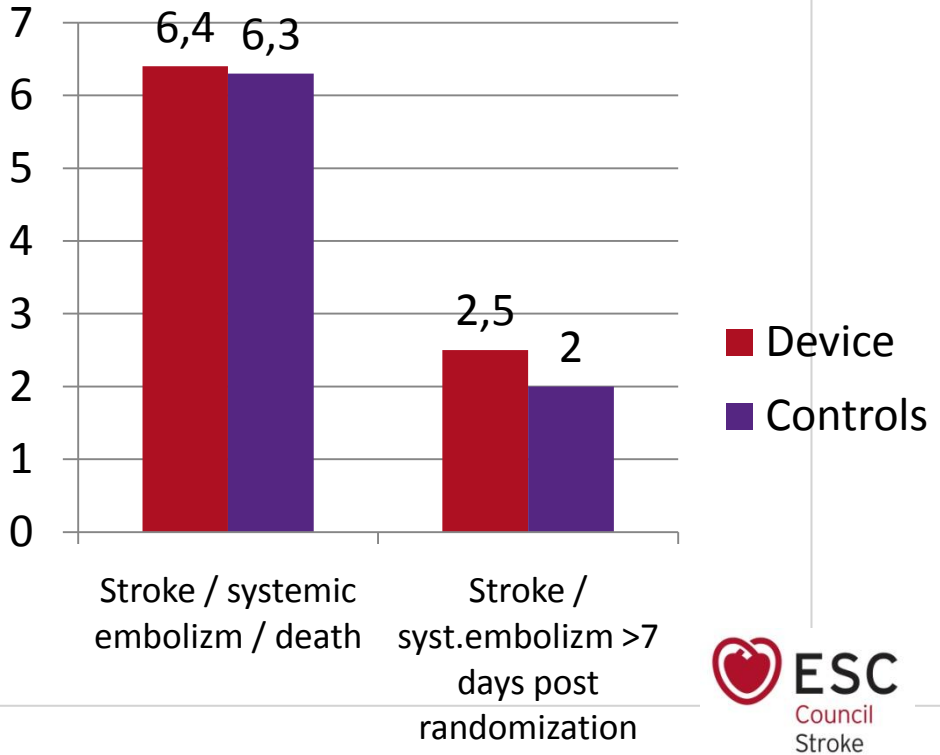
PREVAIL trial

CHADS2 ≥2 and CHADS2=1 patients not eligible for aspirin therapy alone
Composite of stroke, systemic embolism, and cardiovascular/ unexplained death

Holmes et al. JACC 2014 Jul 8;64(1):1-12

- **A = Watchman (n=269)**
- **B = Warfarin (n=138).**
- **Complications: 2.2% (Watchman arm)**
- **Pericardial effusions requiring surgical repair 0.4% (those requiring pericardiocentesis 1.5%)**



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LAA Closure as an Alternative to Warfarin for Stroke Prevention in Atrial Fibrillation: Meta-Analysis.

Holmes et al. JACC 2015; 65: 2614-23.

- **2406 pts from the PROTECT AF and PREVAIL trials, and their registries. Mean follow-up 2.7 years.**
- **Watchman: fewer hemorrhagic strokes, but more ischemic strokes in the device group.**
- **Watchman: fewer cardiovascular/unexplained death (1.1 vs. 2.3 events/100 PY; HR: 0.48; p = 0.006)**
- **Watchman: fewer nonprocedural bleeding (6.0% vs. 11.3%; HR: 0.51; p = 0.006) compared with warfarin.**

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LAAO for stroke prevention in AF: a systematic review and network meta-analysis of randomized controlled trials

Hanif H et al., J Cardiovasc Surg (Torino) 2018

Network meta-analysis (NMA) of randomized trials evaluating the efficacy of LAA occlusion compared with oral anticoagulant, antiplatelet, and placebo for stroke prevention.

Impact of LAA occlusion on mortality, major bleeding, and operative time.

Trend towards reduction in stroke (OR 0.84, 95% CrI 0.47-1.55) and mortality (OR 0.69, 95% CrI 0.44-1.10) for LAA occlusion versus warfarin, but no statistically significant effect.

LAA occlusion appears to preserve the benefits of OAC therapy for stroke prevention in patients with AF, but the current evidence is of low quality.

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Outcomes and costs of LAAO from randomized trial and real-world experience relative to oral anticoagulation.

Panniker S et al., Eur Heart J 2016

Registry of LAAO from two centres (n=110). Follow-up 2 years.

Pts suitable and unsuitable for long-term OAC, CHA_2DS_2VASc 4.5 ± 1.6, and HAS-BLED 3.8 ± 1.1

Procedural success rate 92%.

Annual rates: stroke 0.9%, major bleeding 0.9%, all-cause mortality 1.8%.

Anticoagulant therapy was successfully stopped in 91% of implanted patients by 12 months.

Registry study stroke and major bleeding rates were lower than PROTECT AF results

Left atrial appendage closure achieved cost parity between 4.9 years vs. dabigatran 110 mg and 8.4 years vs. warfarin. At 10 years, LAAC was cost-saving against all therapies.

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Bleeding After LAAO Compared With Long-Term Warfarin: Analysis of the WATCHMAN Randomized Trials.

Price MJ et al., JACC Cardiovasc Interv 2015

1,114 patients, median follow-up of 3.1 years.

No difference in major bleeding rate from randomization to the end of follow-up: 3.5 events vs. 3.6 events per 100 patient-years.

LAA closure significantly reduced bleeding >7 days post-randomization (1.8 events vs. 3.6 events per 100 patient-years), with the difference emerging 6 months after randomization (1.0 events vs. 3.5 events per 100 patient-years), when patients assigned to LAA closure were able to discontinue adjunctive oral anticoagulation and antiplatelet therapy.

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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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European Heart Journal - doi:10.1093/eurheartj/ehw210

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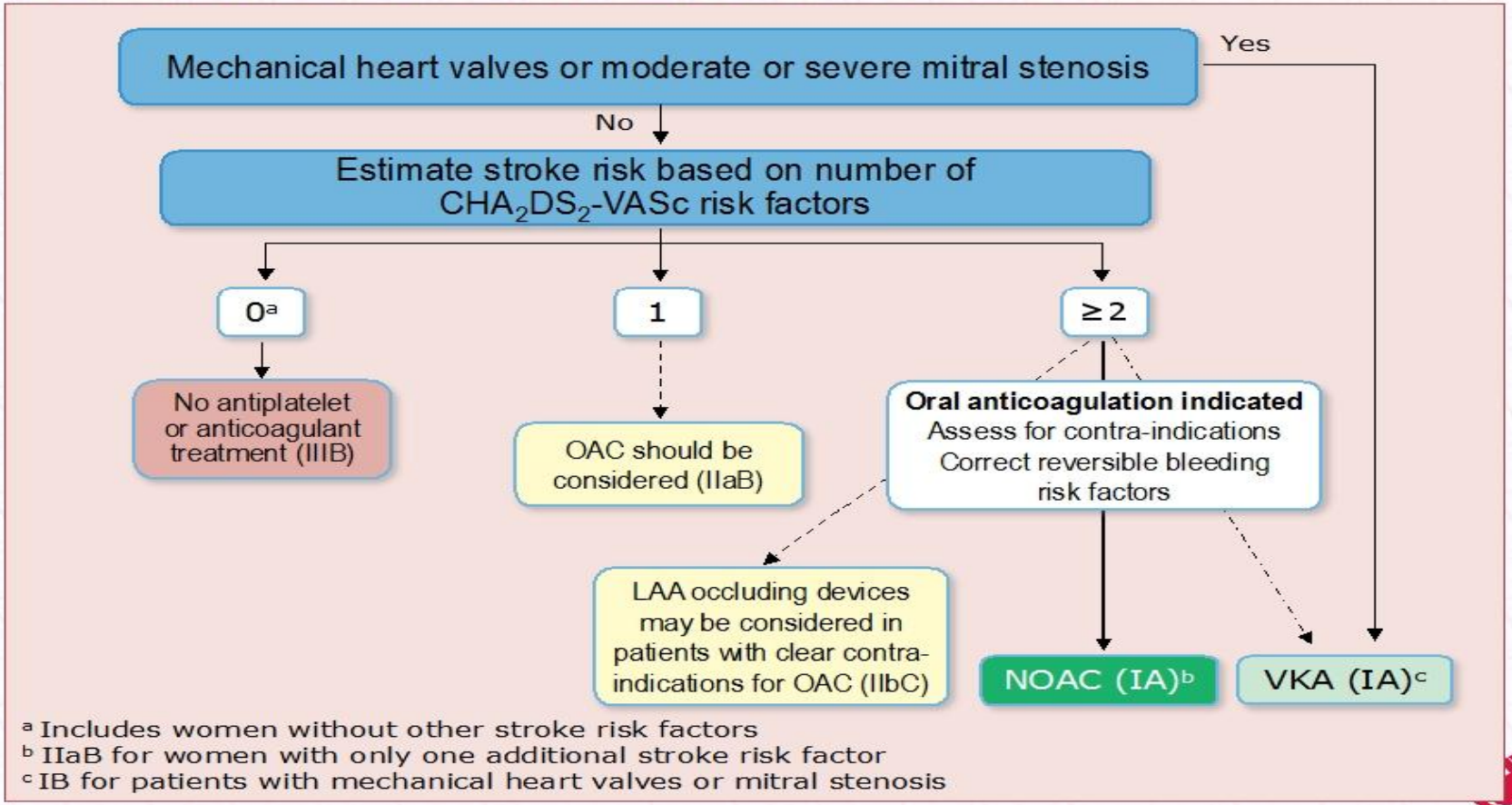
Stroke prevention in atrial fibrillation



[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

European Heart Journal - doi:10.1093/eurheartj/ehw210
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Main characteristics and outcomes in the PROTECT-AF trial comparing LAAO and warfarin

Study characteristics		
Study design	Randomized, unblinded (2:1)	
Number of patients	707	
Follow-up period, years	2.3	
Randomized treatments	Dose-adjusted warfarin or Watchman® left atrial appendage occlusion device (LAAO)	
Baseline patient characteristics		
Age, years (mean ± SD)	Warfarin: 73 ± 9; LAAO: 72 ± 8 years	
Male sex, %	Warfarin: 70 ; LAAO: 70	
$CHADS_2$ (mean)	Warfarin: 2.3; LAAO: 2.2	
Outcomes		
Events per 100 patient-years (rate ratio and 95% credible interval)	**Warfarin (n = 244)**	**LAAO device (n = 463)**
All stroke	2.7 (1.5–4.1)	2.0 (1.3–3.1)
Ischaemic stroke	1.4 (0.6–2.4)	1.9 (1.1–2.9)
Haemorrhagic stroke	1.2 (0.5–2.3)	0.3 (0.1–0.7)
Mortality	4.5 (2.8–6.2)	3.2 (2.3–4.5)

$CHADS_2$ = congestive heart failure, hypertension, age ≥75, diabetes, prior stroke/ transient ischaemic attack [2 points]; LAAO = left atrial appendage occlusion device; PROTECT-AF = System for Embolic PROTECTion in patients with Atrial Fibrillation; SD = standard deviation.

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Occlusion or exclusion of the left atrial appendage

Recommendations	Class	Level
After surgical occlusion or exclusion of the LAA, it is recommended to continue anticoagulation in at-risk patients with AF for stroke prevention.	I	B
LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term anticoagulant treatment (e.g. those with a previous life-threatening bleed without a reversible cause).	IIb	B
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery.	IIb	B
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients undergoing thoracoscopic AF surgery.	IIb	B

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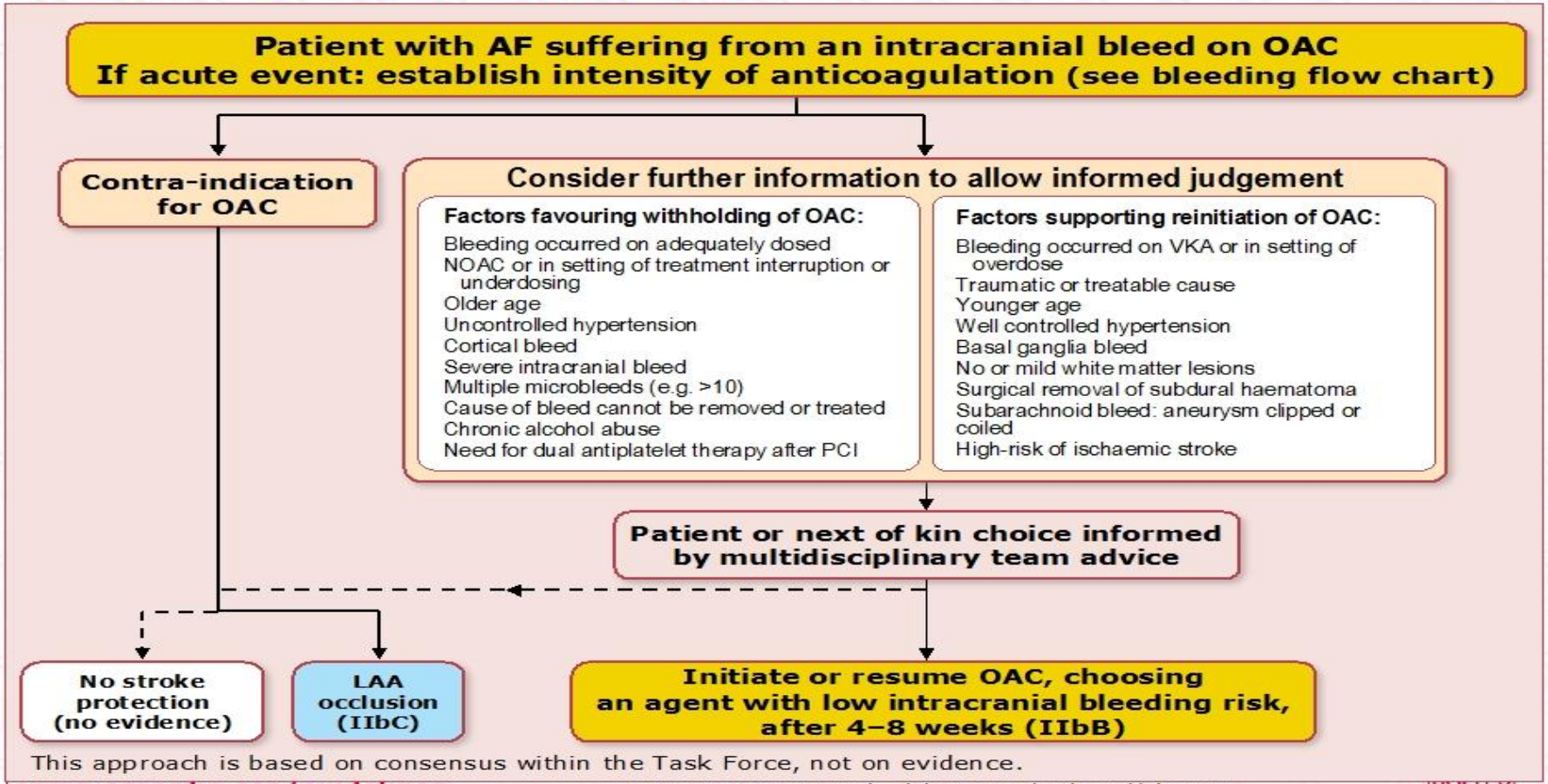
Initiation or resumption of anticoagulation in atrial fibrillation patients after an intracranial bleed



European Heart Journal - doi:10.1093/eurheartj/ehw210

Perspectives

- **Longer follow-up (>5 years) may favor LAA occlusion as its complications occur early after implantation, while bleeding complications after OAC occur constantly over time.**

- **Randomized comparisons device vs. NOAC needed**

- **Randomized comparisons device vs. endoscopic epicardial surgical LAA closure needed**

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Interventional left atrial appendage closure vs novel anticoagulation agents in patients with atrial fibrillation indicated for long-term anticoagulation (PRAGUE-17 study)

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Background Atrial fibrillation (AF), with a prevalence of 1% to 2%, is the most common cardiac arrhythmia. Without antithrombotic treatment, the annual risk of a cardioembolic event is 5% to 6%. The source of a cardioembolic event is a thrombus, which is usually formed in the left atrial appendage (LAA). Prevention of cardioembolic events involves treatment with anticoagulant drugs: either vitamin K antagonists or, recently, novel oral anticoagulants (NOAC). The other (nonpharmacologic) option for the prevention of a cardioembolic event involves interventional occlusion of the LAA.

Objective To determine whether percutaneous LAA occlusion is noninferior to treatment with NOAC in AF patients indicated for long-term systemic anticoagulation.

Study design The trial will be a prospective, multicenter, randomized noninferiority trial comparing 2 treatment strategies in moderate to high-risk AF patients (ie, patients with history of significant bleeding, or history of cardiovascular event(s), or a with $CHA_2DS_2VASc \geq 3$ and HAS-BLED score ≥ 2). Patients will be randomized into a percutaneous LAA occlusion (group A) or a NOAC treatment (group B) in a 1:1 ratio; the randomization was done using Web-based randomization software. A total of 396 study participants (198 patients in each group) will be enrolled in the study. The primary end point will be the occurrence of any of the following events within 24 months after randomization: stroke or transient ischemic attack (any type), systemic cardioembolic event, clinically significant bleeding, cardiovascular death, or a significant periprocedural or device-related complications.

Conclusion The PRAGUE-17 trial will determine if LAA occlusion is noninferior to treatment with NOAC in moderate- to high-risk AF patients. (Am Heart J 2017;183:108-14.)

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