

ICT 2023

28th International Congress on Thrombosis

Lisbon

1-3 June 2023



Left appendage closure for stroke prevention

E. Infante de Oliveira

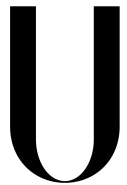
Head of Cardiology, Lusíadas Lisbon Hosp

Interv. Cardiologist, H Santa Cruz, CHLO

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Secretary-General 23-25 – Portuguese Society Cardiology

EAPCI 22-24 International Affairs Committee Member



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Left atrial appendage closure: why?

- pathophysiology relevance
- unmet therapeutical need
- technical feasibility & evidence
- future directions

Left atrial appendage closure: why?

Etiology – Nonrheumatic AFib

Table 1. Review of Published Reports Detailing the Frequency and Site of Thrombus Location in Patients With Nonrheumatic Atrial Fibrillation

| Setting | No. of Patients | Thrombus Location | | Reference No. |
|--------------------|-----------------|-------------------|-----------|---------------|
| | | LA Appendage | LA Cavity | |
| TEE ^a | 317 | 66 | 1 | 40 |
| TEE | 233 | 34 | 1 | 25 |
| Autopsy | 506 | 35 | 12 | 39 |
| TEE | 52 | 2 | 2 | 28 |
| TEE | 48 | 12 | 1 | 41 |
| TEE and Operation | 171 | 8 | 3 | 24 |
| SPAF III TEE Study | 359 | 19 | 1 | 42 |
| TEE | 272 | 19 | 0 | 26 |
| TEE | 60 | 6 | 0 | 43 |
| Total | 1,288 | 201 | 21 | |

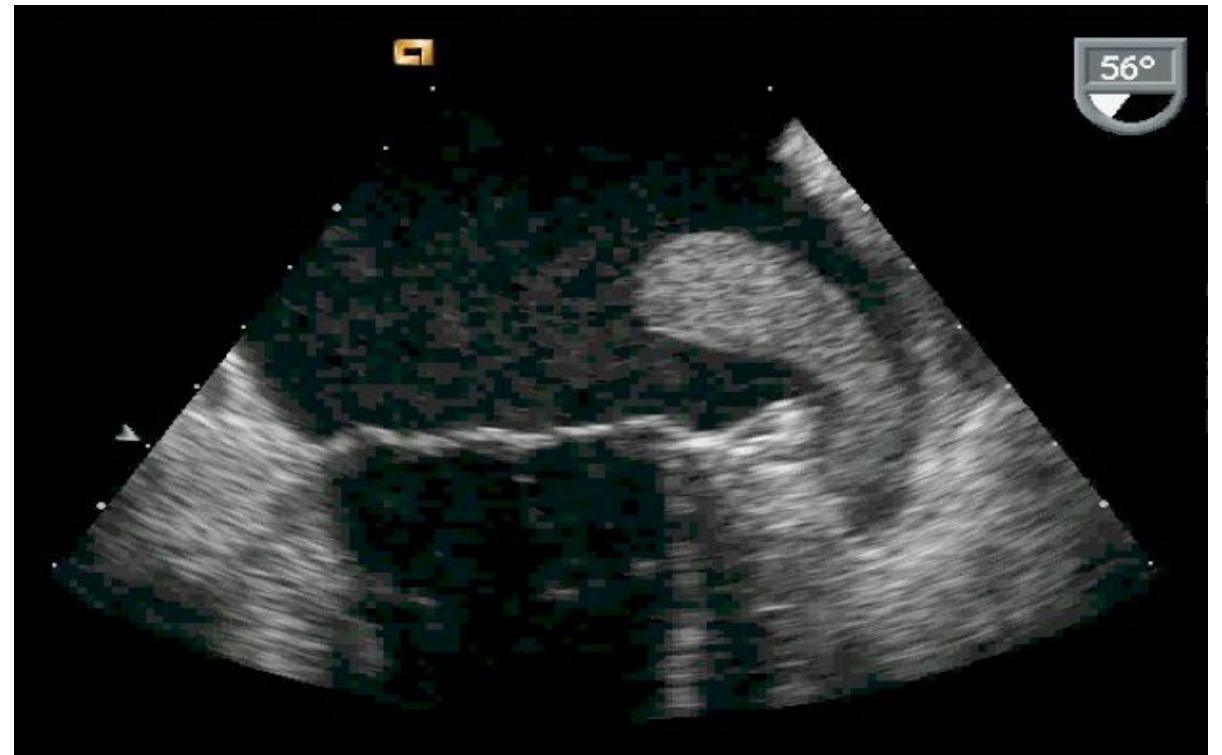
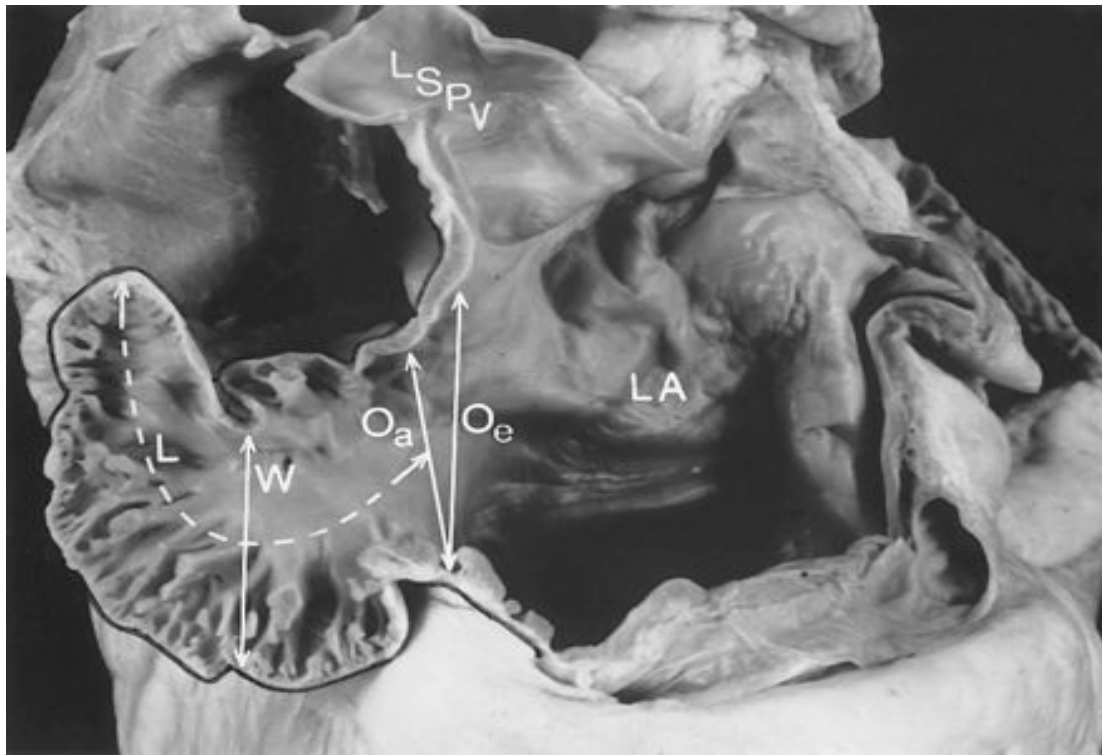
 **LAA 91%**

^a 5% of this cohort had mitral stenosis or a prosthetic mitral valve.

LA = left atrium; SPAF III = Stroke Prevention in Atrial Fibrillation Trial; TEE = transesophageal echocardiography.

Left atrial appendage closure: why?

Atrial fibrillation thrombus formation occurs $> 90\%$ in the LAA



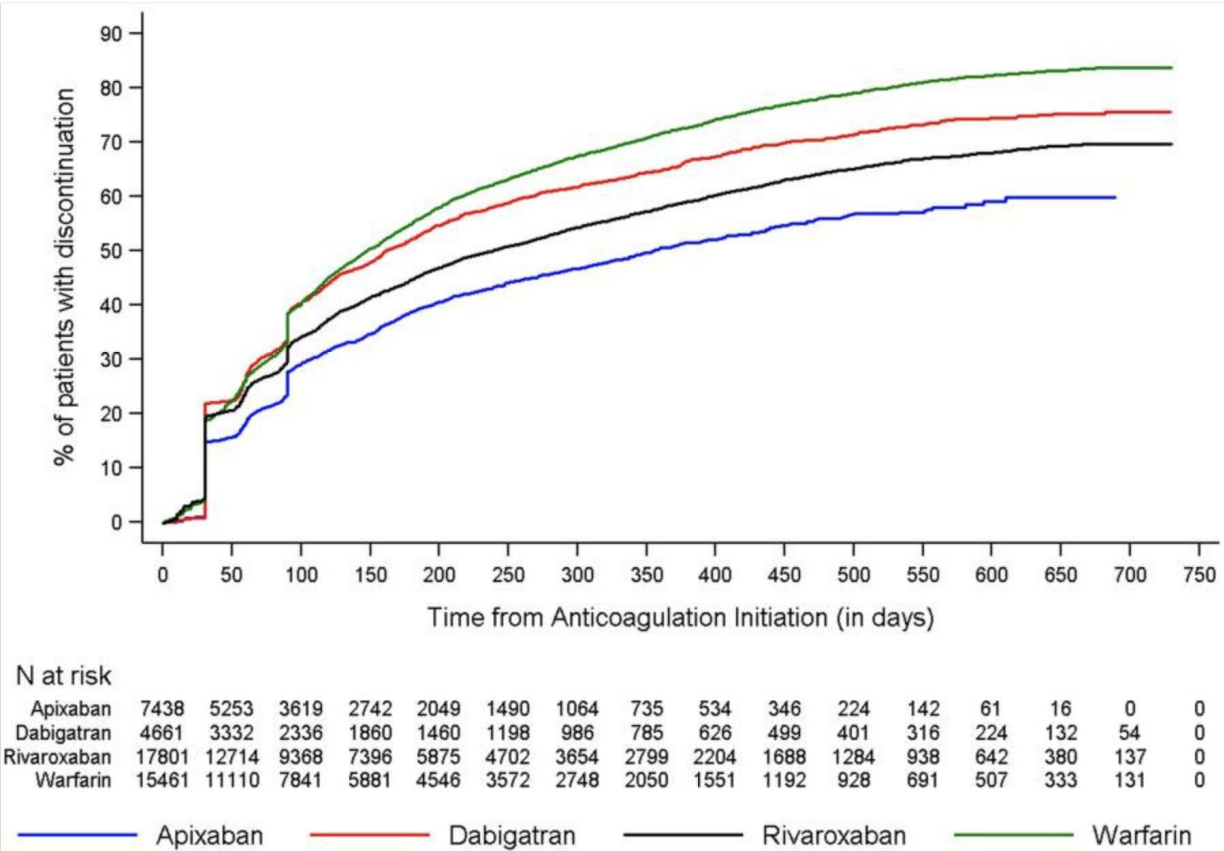
Left atrial appendage closure: why?

Stroke prevention in atrial fibrillation, unmet needs:

- high bleeding risk
- intolerance to anticoagulants
- anticoagulant residual risk

Left atrial appendage closure: why?

Anticoagulant therapy discontinuation



Lip GYH, Pan X, Kamble S, et al. *PLoS One*. 2018;13(4):e0195950.

Left atrial appendage closure: why?

Table 1: Residual Thromboembolic Risk in Landmark Clinical Trials of AF

| Study | Year | No. Patients | Mean CHADS ₂ score | Residual thromboembolic Risk* | |
|---------------------------------|------|--------------|-------------------------------|-------------------------------|----------|
| | | | | DOAC | Warfarin |
| RE-LY ²⁰ | 2008 | 18,113 | 2.1 | 1.11–1.53 [†] | 1.69 |
| ROCKET AF ²¹ | 2011 | 14,264 | 3.5 | 2.10 | 2.40 |
| ARISTOTLE ¹⁹ | 2011 | 18,201 | 2.1 | 1.27 | 1.60 |
| ENGAGE AF-TIMI 48 ¹⁸ | 2013 | 21,105 | 2.8 | 1.18–1.61 [†] | 1.50 |

*Expressed as percentage per year or event rate per 100 patient-years. [†]Dose dependent. DOAC = direct oral anticoagulant.

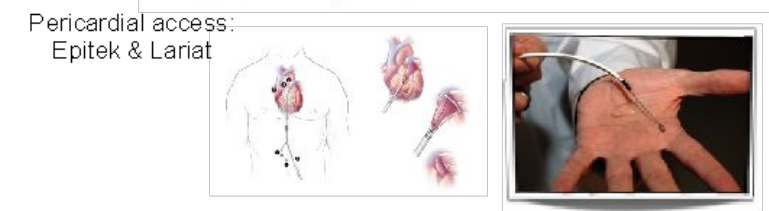
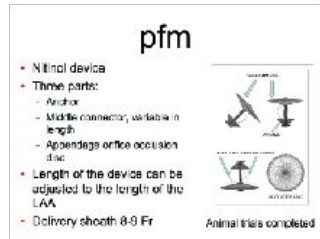
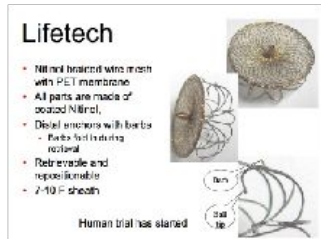
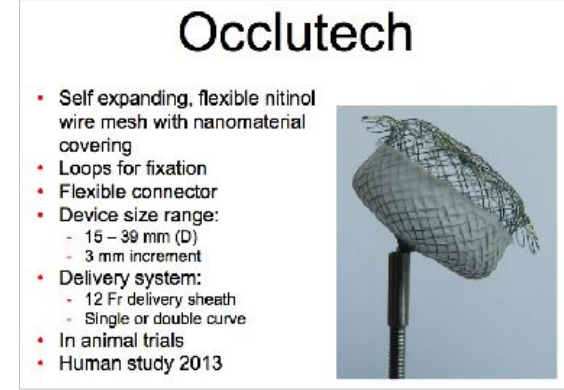
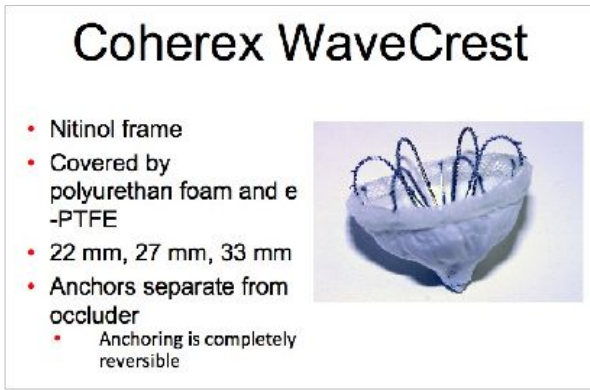
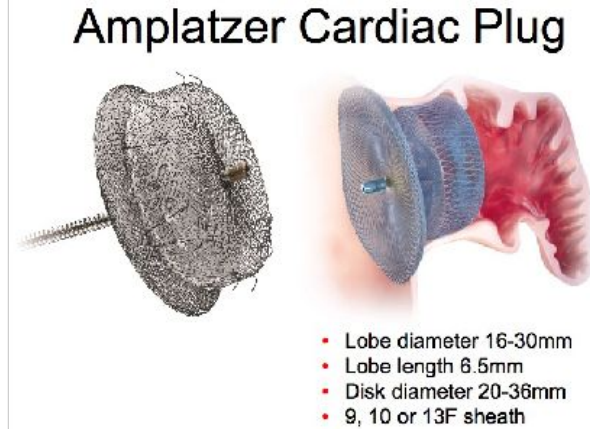
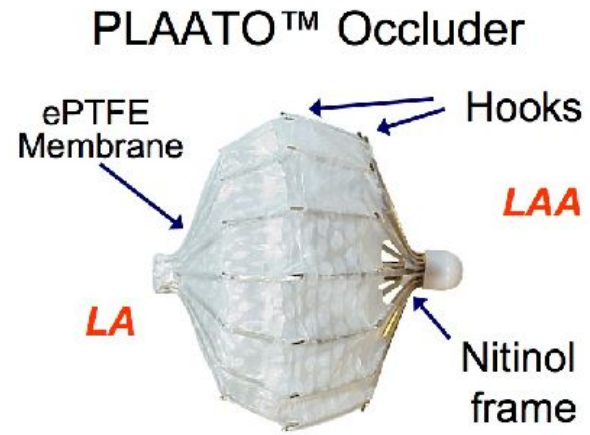
Arrhythmia & Electrophysiology Review 2021;10(3):147–53.

Table 1: CHA2DS2-VASc Score and Annual Stroke Rates

| CHA2DS2-VASc Score | Adjusted Annual Stroke Rate |
|--------------------|-----------------------------|
| 0 | 0 % |
| 1 | 1.3 % |
| 2 | 2.2 % |
| 3 | 3.2 % |
| 4 | 4.0 % |
| 5 | 6.7 % |
| 6 | 9.8 % |
| 7 | 9.6 % |
| 8 | 6.7 % |
| 9 | 15.2 % |

Modified from the European Society of Cardiology guidelines for the management of atrial fibrillation.²⁴

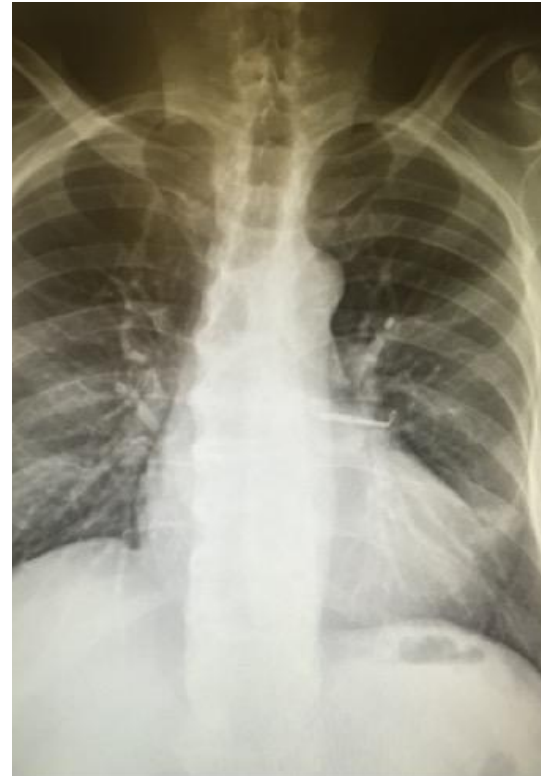
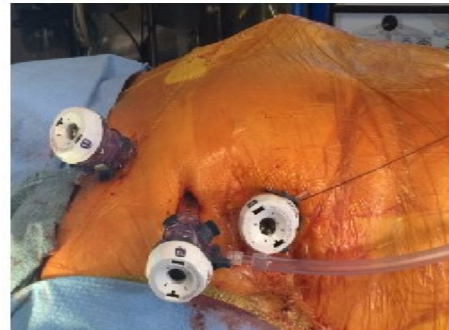
Left atrial appendage closure: why?



Left atrial appendage closure: why?

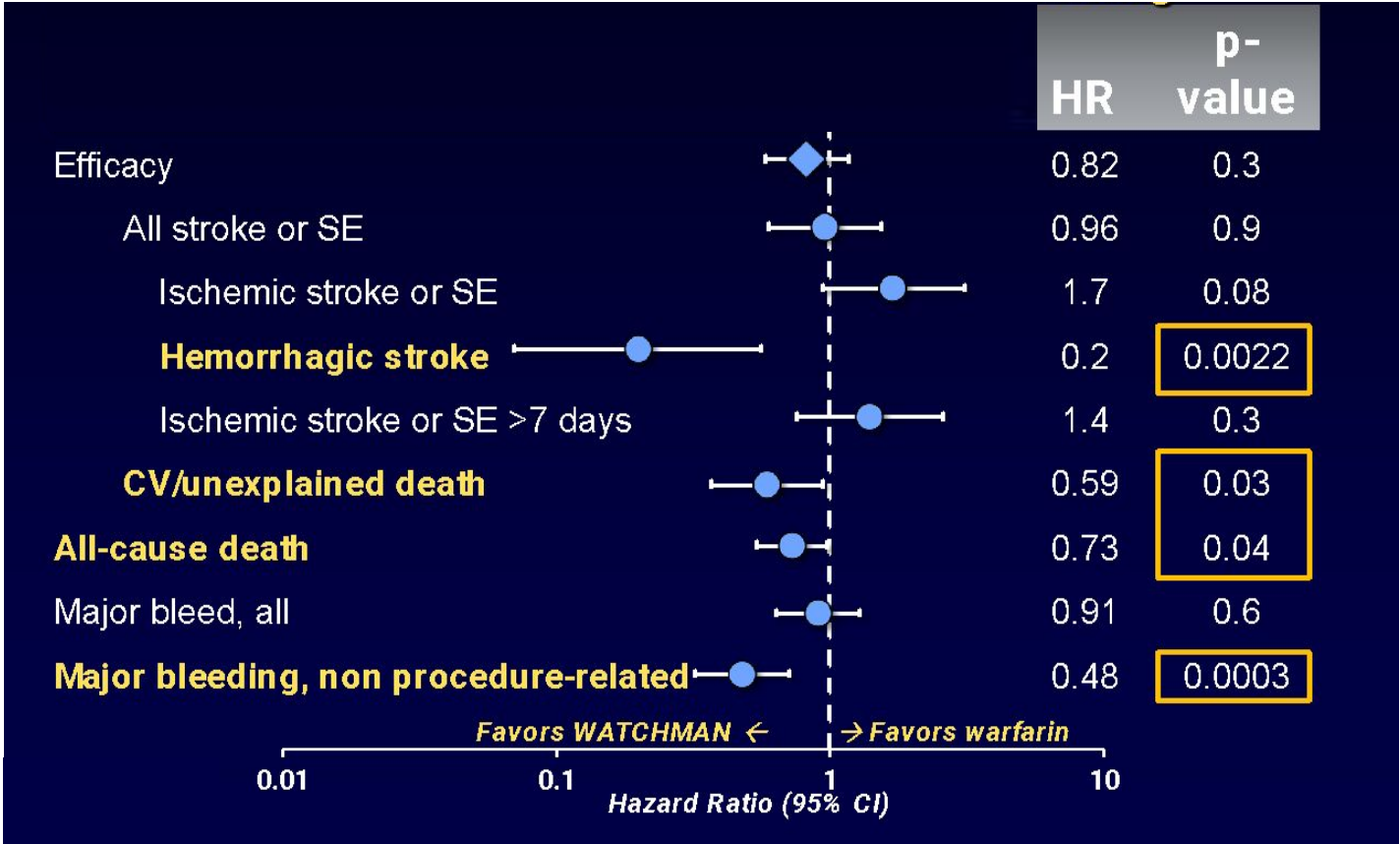
Atriclip

- Mini-thoracotomy
- Thoracoscopic



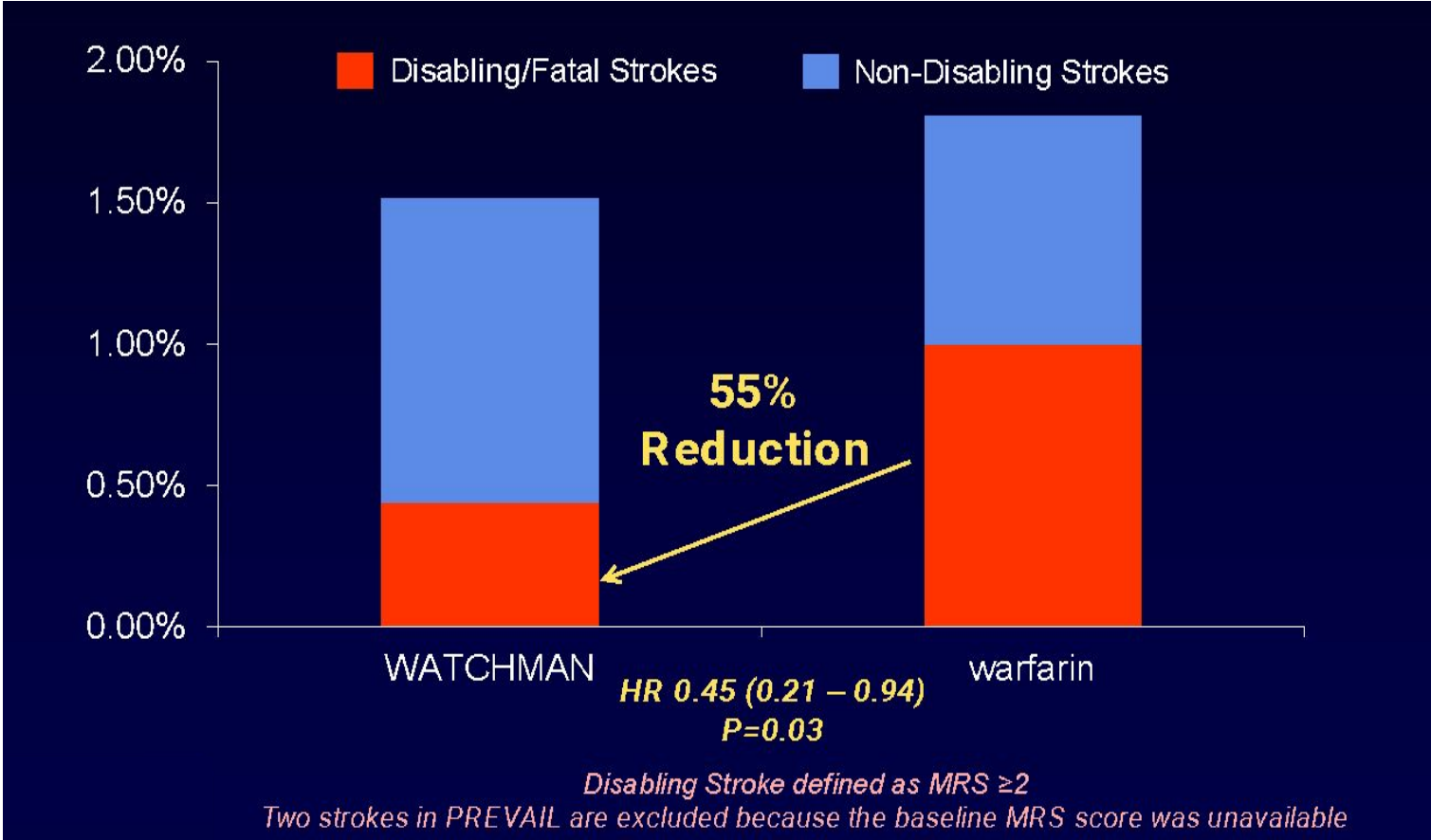
Current evidence and indications for LAA closure

PROTECT AF & PREVAIL - patient-level meta-analysis Patients eligible to oral anticoagulation



Current evidence and indications for LAA closure

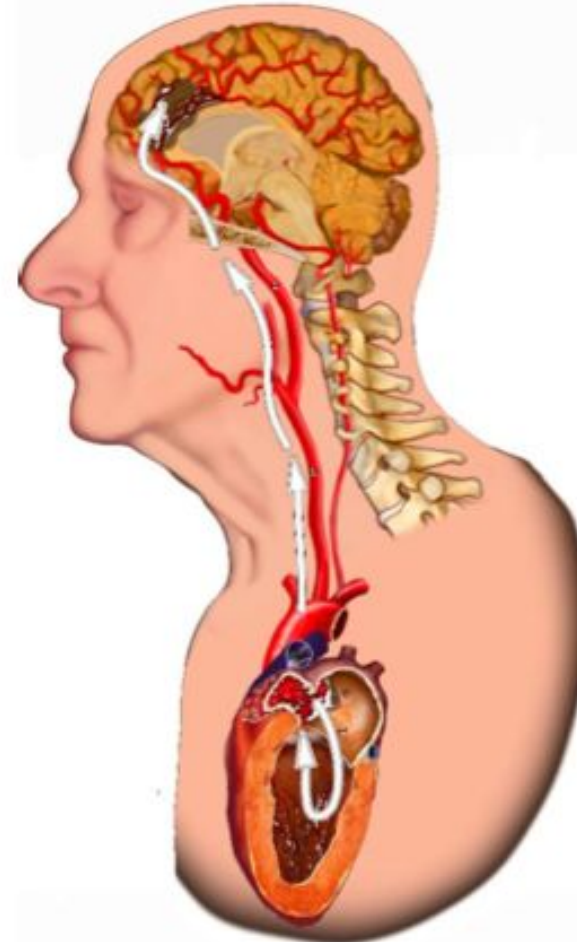
Superior reduction in disabling strokes



J Am Coll Cardiol. 2017 Nov 4

Current evidence and indications for LAA closure

Fatal / Disabling stroke – thrombus size matters!



Current evidence and indications for LAA closure

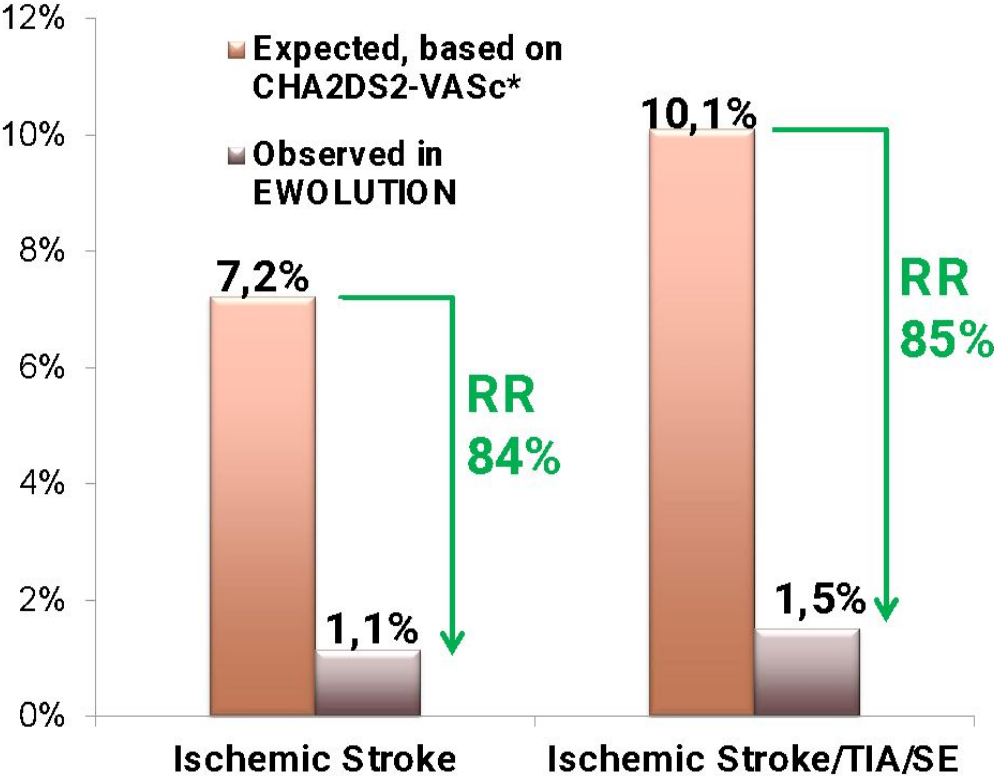
LAA closure – ESC guidelines

| Recommendations for LAA closure/occlusion/excision | | |
|--|-------|-------|
| Recommendations | Class | Level |
| Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation. | IIb | B |
| Surgical excision of the LAA may be considered in patients undergoing open heart surgery. | IIb | C |

Current evidence and indications for LAA closure

Pts ineligible to OAC (73%)

EWOLUTION – Annual Stroke Rate



Boersma Heart Rhythm. 2017 Sep;14(9):1302-1308.

Current evidence and indications for LAA closure

The Assessment of the Watchman Device in Patients Unsuitable for Oral Anticoagulation (ASAP-TOO) trial



David R. Holmes, MD,^a Vivek Y. Reddy, MD,^b Maurice Buchbinder, MD,^c Kenneth Stein, MD,^d Myriah Elletson^d Martin W. Bergmann, MD,^c Boris Schmidt, MD,^f and Jacqueline Saw, MD, FRCPC^g *Rochester, Minneapolis, MN; New York, NY; Stanford, CA; Hamburg, Frankfurt, Germany; and British Columbia, Canada*

Background Oral anticoagulants (OACs) reduce stroke risks with nonvalvular atrial fibrillation (AF); however, they are underused because of absolute or relative contraindications due to real or perceived risk of bleeding. Although left atrial appendage closure is increasingly performed in OAC-ineligible patients, this has not been studied in a randomized controlled trial.

Study objectives The ASAP-TOO study is designed to establish the safety and effectiveness of the Watchman left atrial appendage closure device in patients with nonvalvular AF who are deemed ineligible for OAC. The primary effectiveness end point is the time to first occurrence of ischemic stroke or systemic embolism. The primary safety end point includes all-cause death, ischemic stroke, systemic embolism, or device- or procedural-related event requiring open cardiac surgery or major endovascular intervention.

Study design This is a multinational, multicenter prospective randomized trial. Patients meeting the inclusion criteria with CHA₂DS₂-VASc score ≥ 2 and who are deemed by 2 study physicians to be unsuitable for OAC will be randomized in a 2:1 allocation ratio to Watchman versus control. Control patients will be prescribed single antiplatelet therapy or no therapy at the discretion of the study physician. Up to 888 randomized subjects will be enrolled from up to 100 global investigational sites. Both device group and control patients will have follow-up visits at 3, 6, and 12 months and then every 6 months through 60 months.

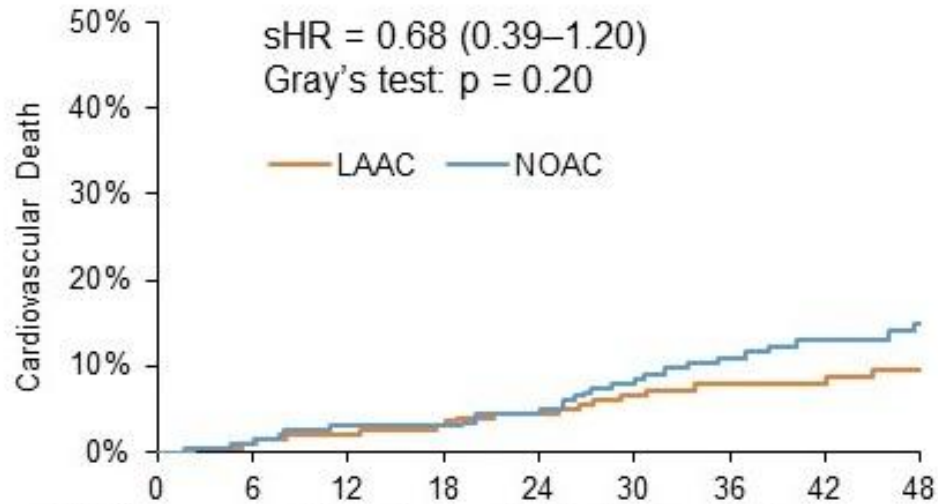
Summary This trial will assess the safety and efficacy of Watchman in this challenging population of high-stroke risk AF patients. (Am Heart J 2017;189:68-74.)

PRAGUE-17: Three-Year Outcomes From A Randomized Trial of Left Atrial Appendage Closure Versus Direct Acting Oral Anticoagulation in Patients With Atrial Fibrillation

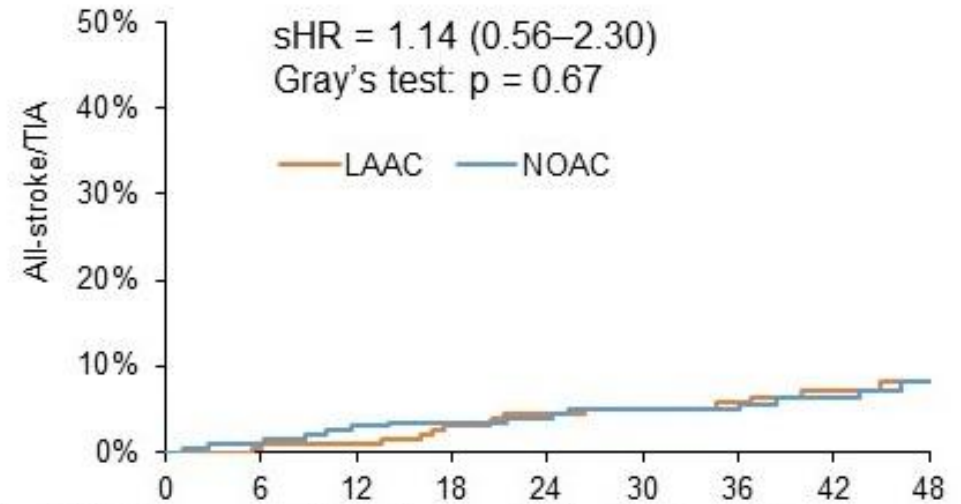
Pavel Osmancik, Dalibor Herman, Petr Neuzil, Pavel Hala, Milos Taborsky, Petr Kala, Martin Poloczek, Josef Stasek, Ludek Haman, Marian Branny, Jan Chovancik, Pavel Cervinka, Jiri Holy, Tomas Kovarnik, David Zemanek, Stepan Havranek, Vlastimil Vancura, Petr Peichl, Petr Tousek, Veronika Lekesova, Jiri Jarkovsky, Martina Novackova, Klara Benesova, Petr Widimsky & Vivek Y. Reddy

*Clinic of Cardiology, Charles University and University Hospital
Kralovske Vinohrady, Prague, Czech Republic*

Cumulative incidence function for cardiovascular death and all-stroke/TIA in ITT populations



| No. at Risk* | | Time since randomisation (months) | | | | |
|--------------|---------|-----------------------------------|----------|----------|---------|----|
| | | 0 | 6 | 12 | 18 | 24 |
| LAAC | 201 (0) | 191 (4) | 180 (9) | 130 (15) | 73 (17) | |
| NOAC | 201 (0) | 191 (4) | 181 (10) | 125 (15) | 65 (21) | |



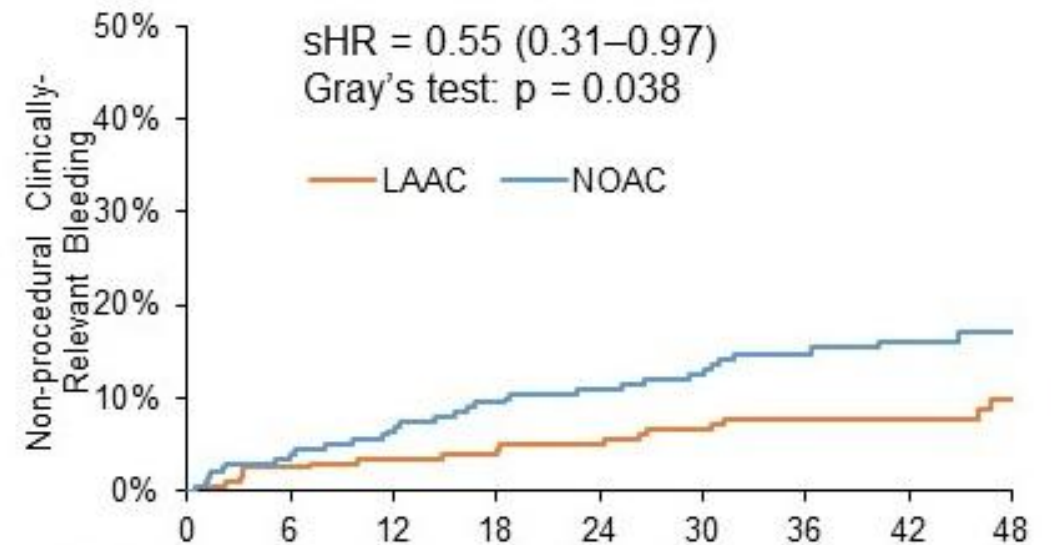
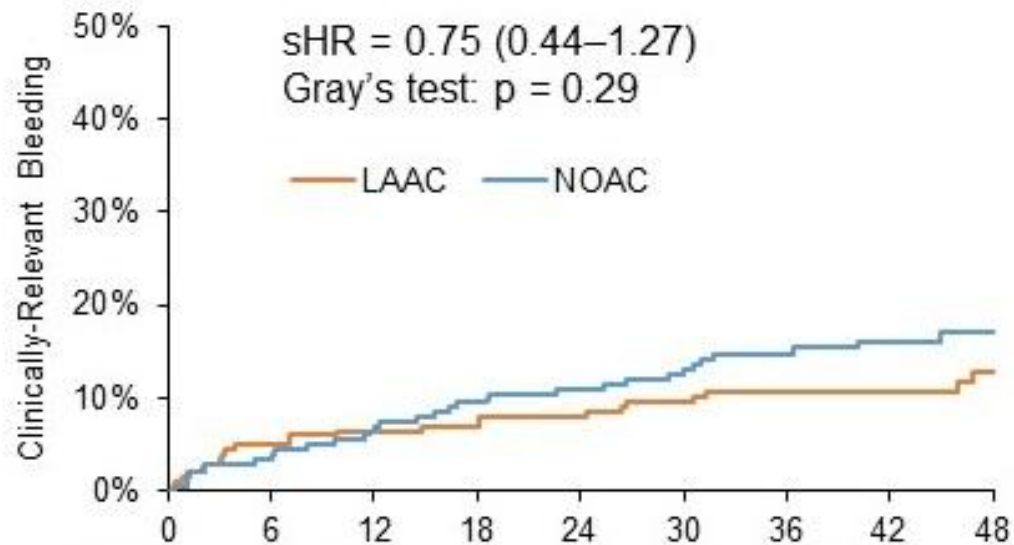
| No. at Risk* | | Time since randomisation (months) | | | | |
|--------------|---------|-----------------------------------|----------|----------|---------|----|
| | | 0 | 6 | 12 | 18 | 24 |
| LAAC | 201 (0) | 190 (7) | 174 (15) | 125 (25) | 68 (28) | |
| NOAC | 201 (0) | 185 (10) | 174 (18) | 119 (32) | 61 (42) | |

*Number of patients who are free of any event is supplemented (in brackets) by number of patients with competing risk up to given time.

LAAC: 3.0 events per 100 pt-years
NOAC: 4.4 events per 100 pt-years

LAAC: 2.4 events per 100 pt-years
NOAC: 2.7 events per 100 pt-years

Cumulative incidence function for clinically-relevant, and non-procedural clinically-relevant bleeding in ITT populations



| No. at Risk* | | Time since randomisation (months) | | | | |
|--------------|---------|-----------------------------------|----------|----------|---------|----|
| | 0 | 6 | 12 | 18 | 24 | 30 |
| LAAC | 201 (0) | 180 (6) | 168 (14) | 121 (22) | 64 (26) | |
| NOAC | 201 (0) | 181 (7) | 165 (13) | 110 (26) | 56 (33) | |

| No. at Risk* | | Time since randomisation (months) | | | | |
|--------------|---------|-----------------------------------|----------|----------|---------|----|
| | 0 | 6 | 12 | 18 | 24 | 30 |
| LAAC | 201 (0) | 184 (8) | 172 (16) | 124 (24) | 66 (28) | |
| NOAC | 201 (0) | 181 (7) | 165 (13) | 110 (26) | 56 (33) | |

*Number of patients who are free of any event is supplemented (in brackets) by number of patients with competing risk up to given time.

LAAC: 4.3 events per 100 pt-years
NOAC: 5.9 events per 100 pt-years

LAAC: 3.4 events per 100 pt-years
NOAC: 5.9 events per 100 pt-years



ACC.21

Left Atrial Appendage Occlusion Study (LAAOS) III

Richard Whitlock MD PhD

On Behalf of the LAAOS III Investigators

Professor of Surgery

Twitter: @RichardWhitloc2

N Engl J Med 2021; 384:2081-2091



AMERICAN
COLLEGE of
CARDIOLOGY

LAAOS III Intervention

N Engl J Med 2021; 384:2081-2091

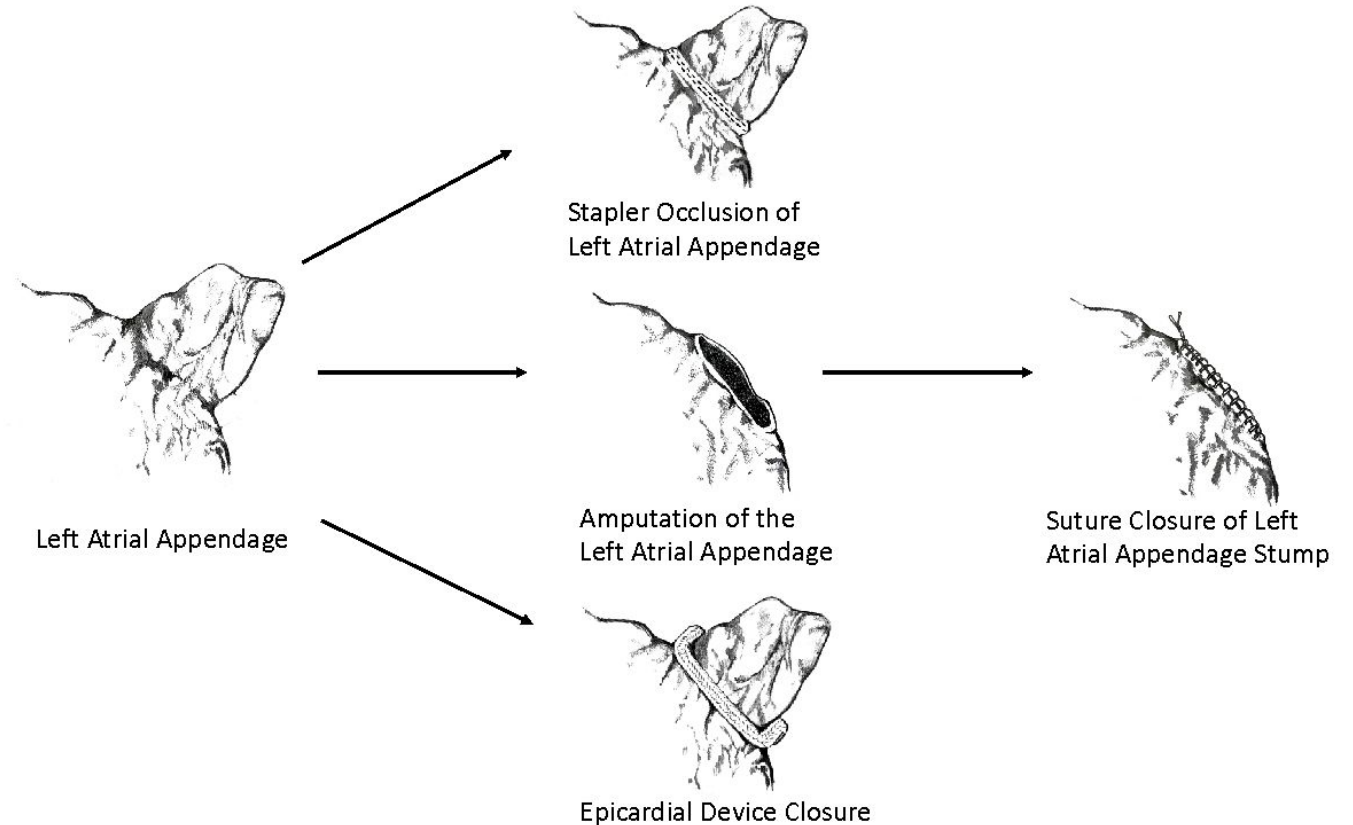
Epicardial Occlusion Techniques

$CHA_2DS_2-VASc \geq 2$

- LAA occlusion
 Ⓡ
- No occlusion

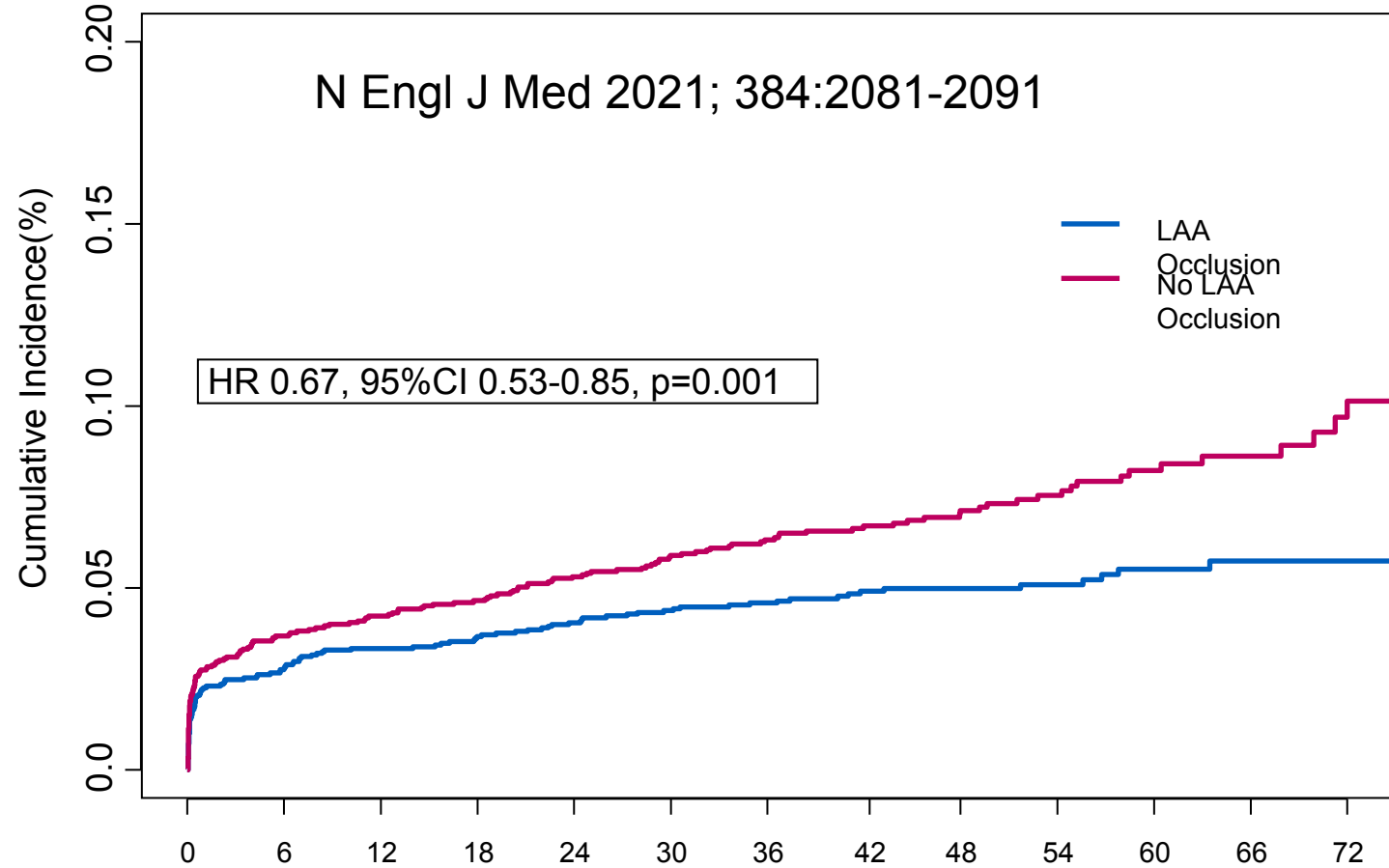
Blinding of:

- Patient
- Research team
- Treating team



ACC.21

Stroke or Systemic Embolism



at
 Risk
 Occlusion
 Occlusion

| | Time since surgery(months) | | | | | | | | | | | | | |
|-----------|----------------------------|------|------|------|------|------|------|------|------|-----|-----|-----|-----|--|
| | 0 | 6 | 12 | 18 | 24 | 30 | 36 | 42 | 48 | 54 | 60 | 66 | 72 | |
| Occlusion | 2379 | 2163 | 2105 | 2059 | 2020 | 1948 | 1642 | 1322 | 1046 | 781 | 550 | 349 | 199 | |
| Occlusion | 2391 | 2134 | 2081 | 2030 | 1981 | 1897 | 1607 | 1291 | 1016 | 751 | 540 | 348 | 205 | |

ACC.21

Left atrial appendage closure: when and to whom?

LAAO – who can benefit? **MAIN STREAM**

Alternative to anticoagulation in non-valvular AF with high bleeding risk

or OAC intolerance

Recurrent GI bleeding

- a) unknown origin
- b) angiodysplasia
- c) lesions not accessible to endoscopic therapy

Intracranial bleeding

- a) non-traumatic subdural hemorrhage
- b) cerebral amyloid angiopathy
- c) (N)OAC hemorrhagic stroke

Recurrent hematuria

- a) unknown origin
- b) lesions not amenable to intervention

Left atrial appendage closure: when and to whom?

LAAO – who can benefit? **MAIN STREAM**

Alternative to anticoagulation in non-valvular AF with high bleeding risk

or OAC intolerance

Coagulopathies

- a) low platelet count
- b) myelodysplastic syndrome
- c) genetic disorders

Chronic renal failure (ClCreat < 30 ml/min)

Chronic corticosteroid or NSAID therapy

Long-term DAPT

(N)OAC intolerance

Left atrial appendage closure: when and to whom?

LAAO – who can benefit?

- Add-on strategy (LAA closure plus (N)OAC)

Stroke or systemic embolism under adequate (N)OAC

AF pts submitted to cardiac surgery (LAAOS III strategy)

Very high embolic risk

Left atrial appendage closure: when and to whom?

LAAO – who can benefit?

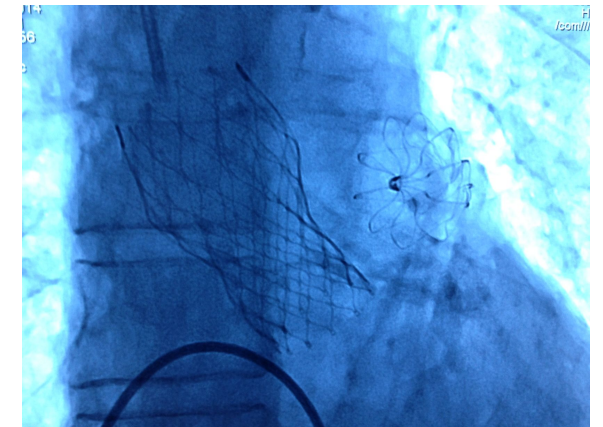
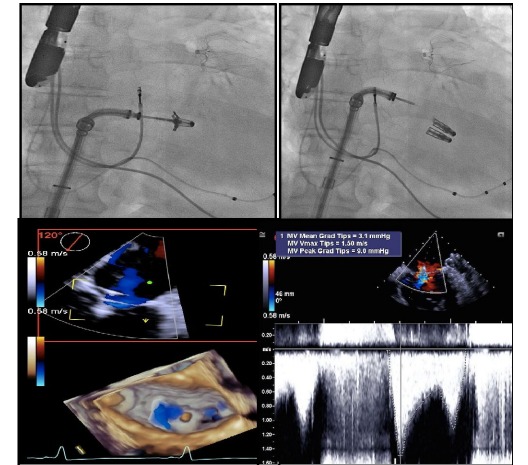
Percutaneous hybrid-procedures

AF ablation (LAAOS III concept)

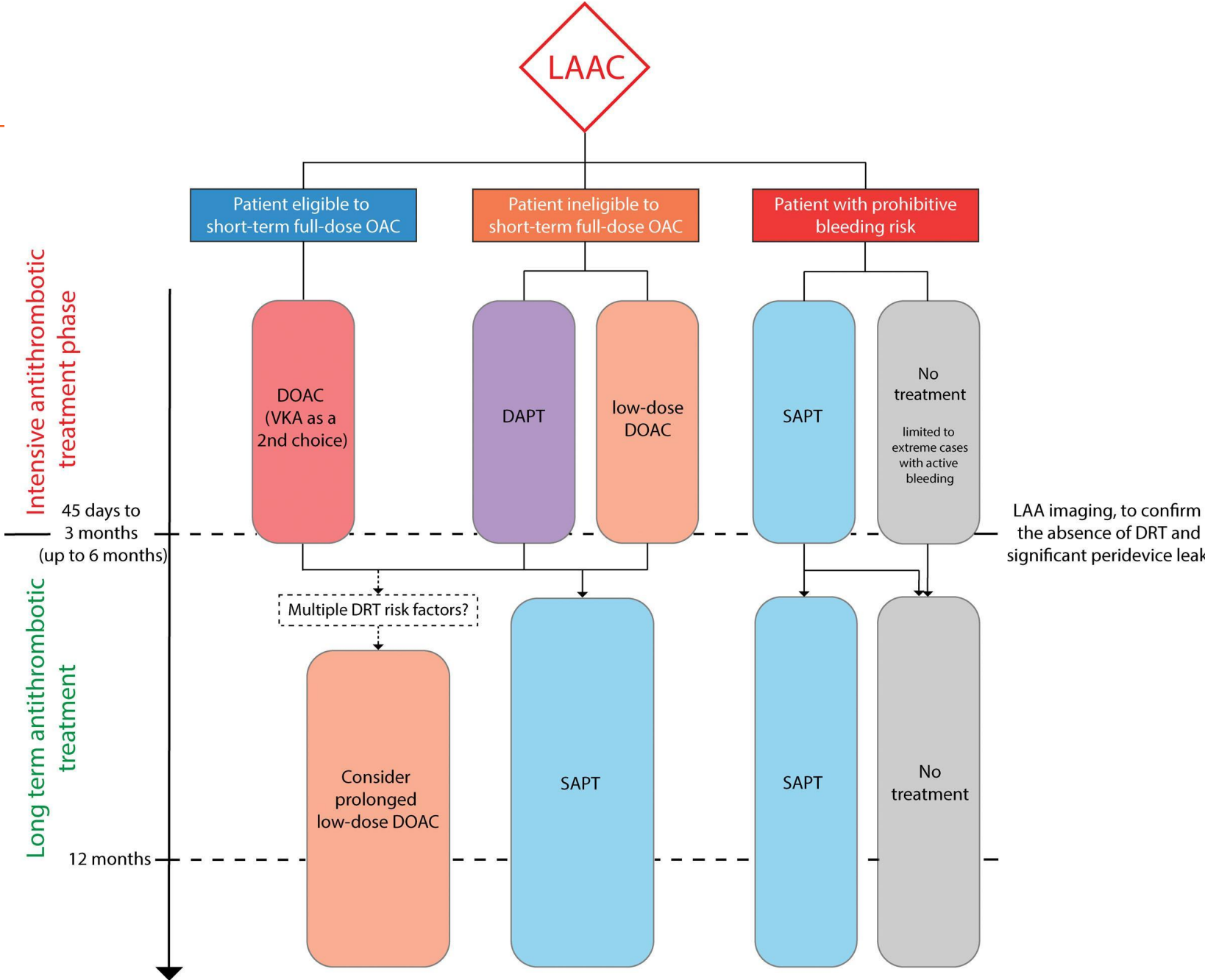
Mitral intervention (ex: edge-to-edge repair) (LAAOS III concept)

Septal closure (opportunity and compromise of future access)

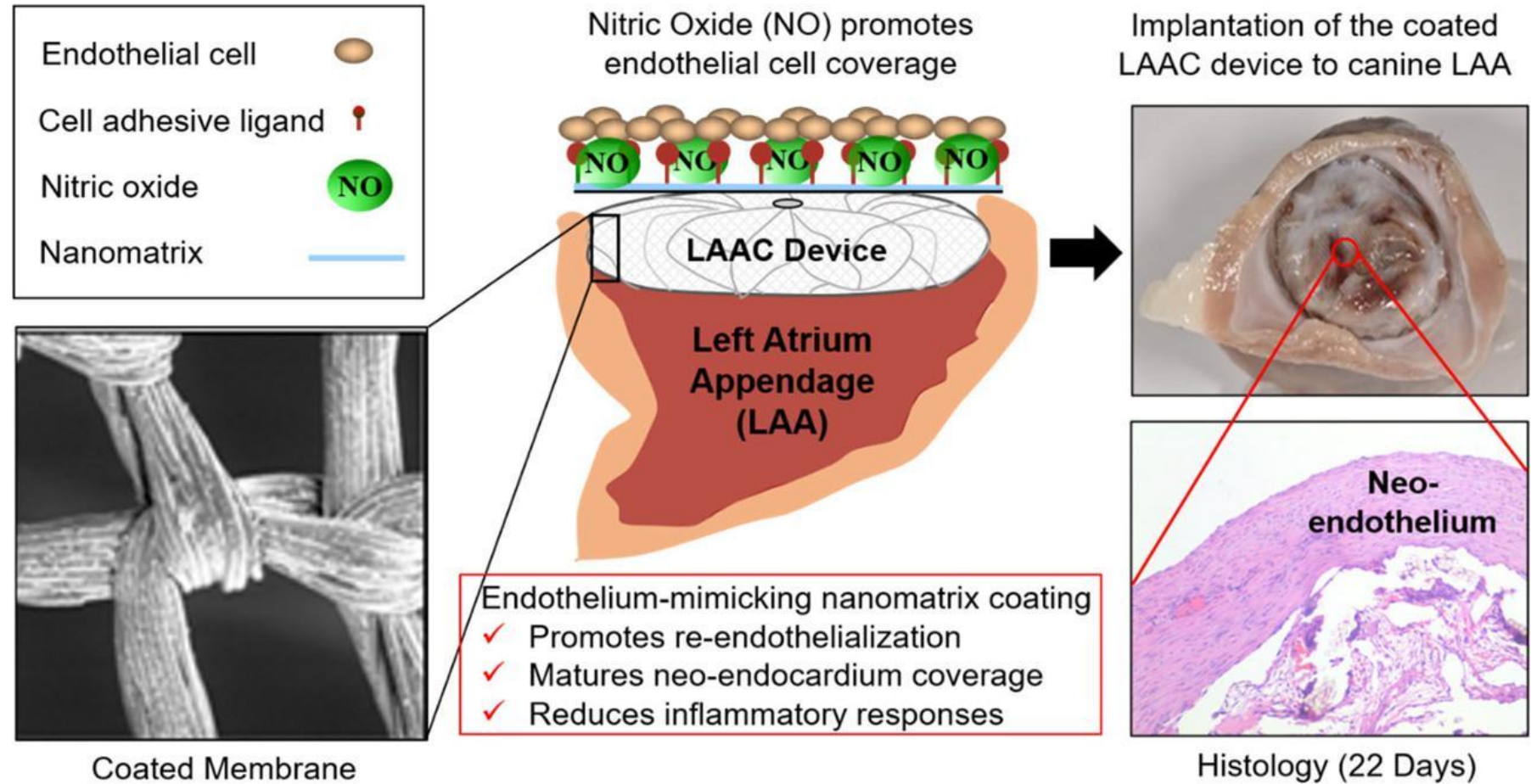
TAVI (frailty and bleeding risk)



Future directions



Left atrial appendage closure: future directions



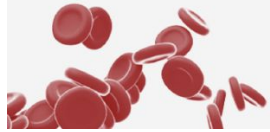
Nanomatrix Composition: PA-YIGSR (endothelial cell adhesive ligand)
PA-KKKKK (NO-producing donor sequence)

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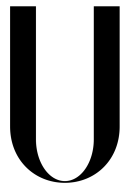
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