

Do We Need LAAO in the Era of NOAC?

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Korean Heart Rhythm Society COI Disclosure

Hee Tae Yu

The authors have no financial conflicts of interest
to disclose concerning the presentation

Safety Concerns with LAAO and OAC

Safety concerns with left atrial appendage occlusion

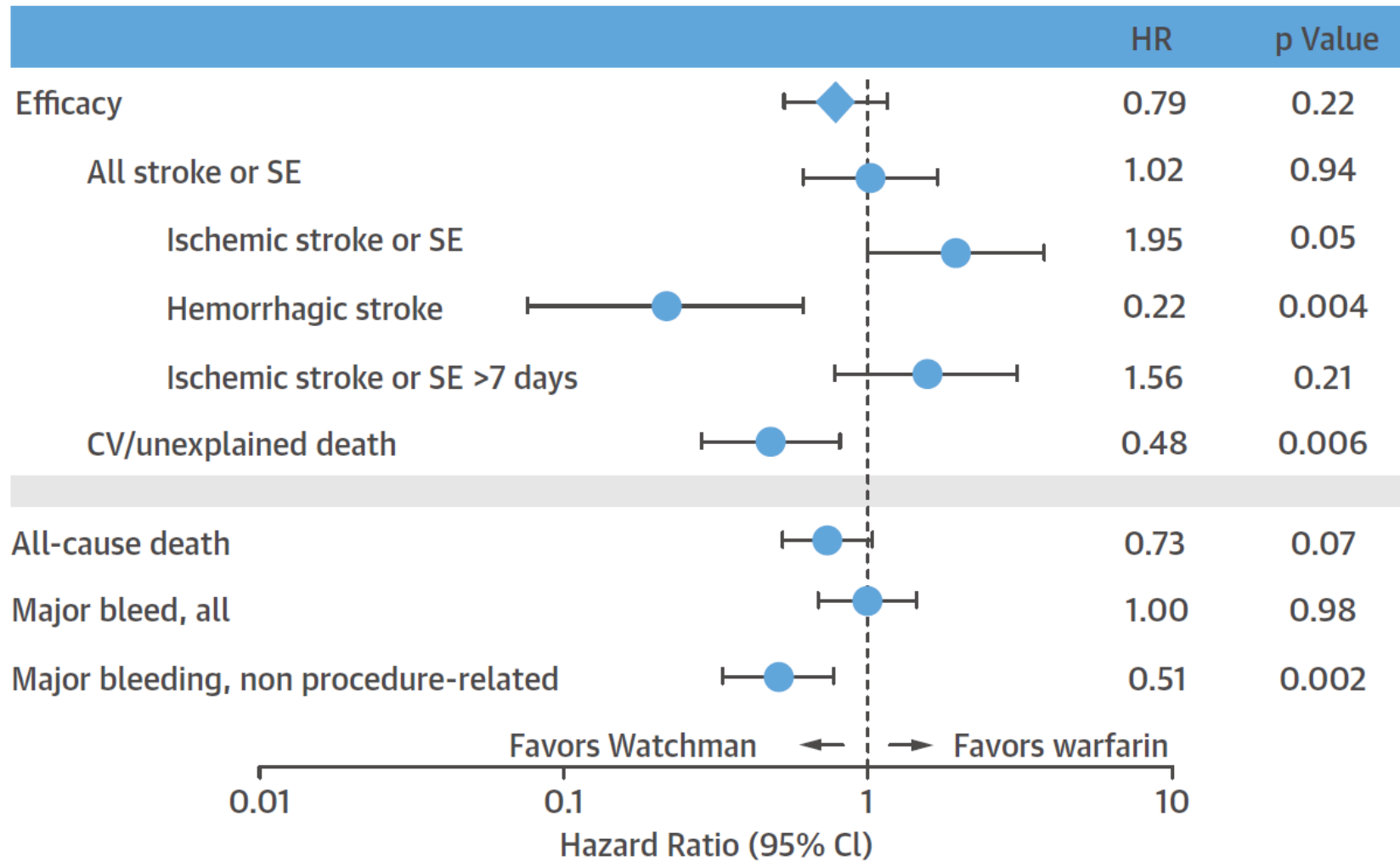
- Risk of infection at the access site
- Risk of device induced thrombus
- Risk of left atrial appendage rupture after device employment.
- Need of continuous oral anticoagulation even after device occlusion

Safety concerns with Oral anticoagulation

- Warfarin requires frequent monitoring of the INR and has a narrow therapeutic window.
- NOAC requires frequent dosing and skipping a dose can put the patient at risk for thrombus formation.
- Both vitamin K and non vitamin K anticoagulants can lead to episodes of major bleeding during long term treatment.

Sandhu O et al. Cureus 2020;12:e10437

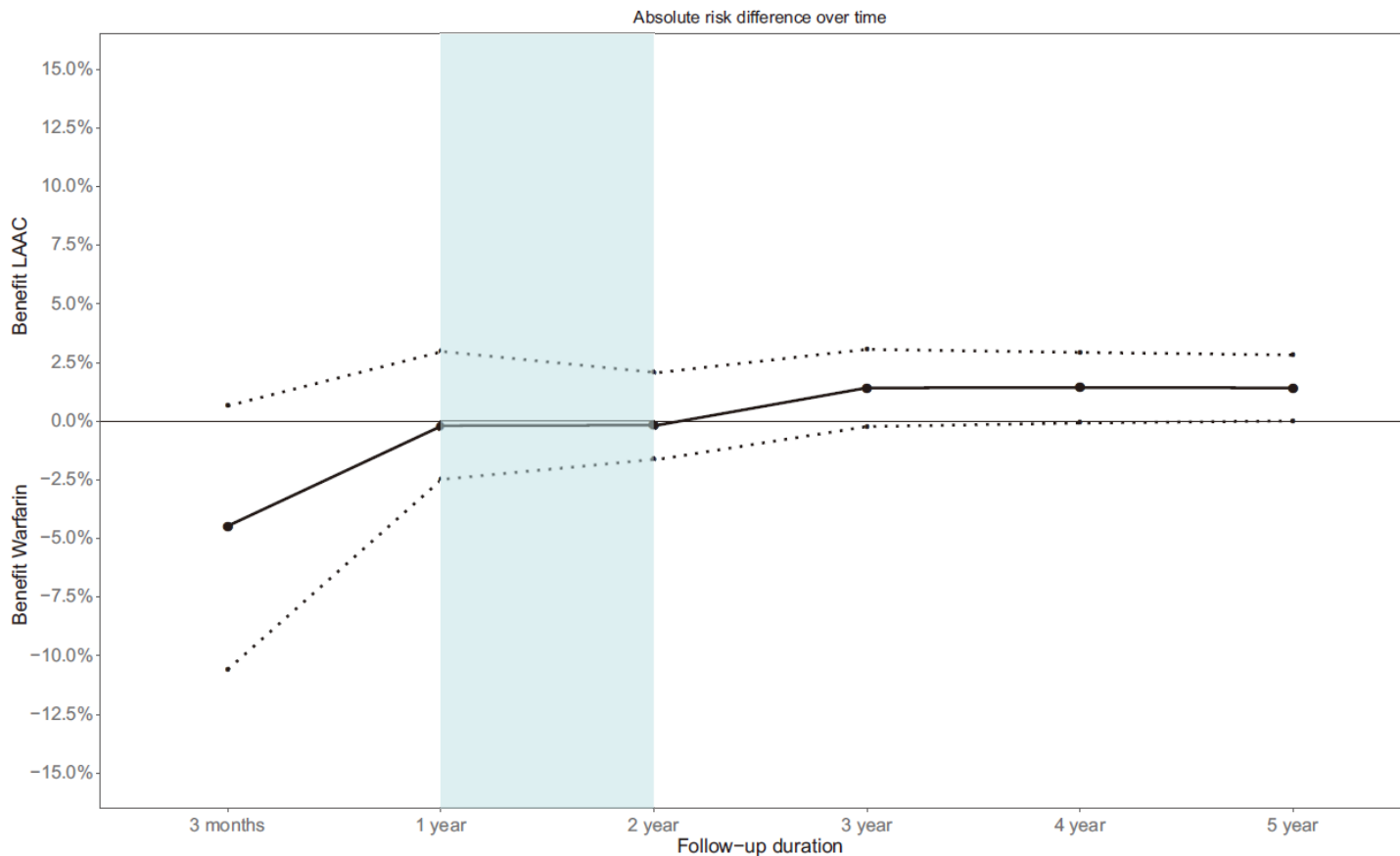
Meta-analysis of PREVAIL and PROTECT-AF



Holmes DR et al. J Am Coll Cardiol 2015;65:2614-2623

Meta-analysis of PREVAIL and PROTECT-AF

Net Clinical Benefit of Left Atrial Appendage Closure Versus Warfarin in Patients With Atrial Fibrillation: A Pooled Analysis of the Randomized PROTECT-AF and PREVAIL Studies



Brouwer TF et al. J Am Heart Assoc 2019;8:e013525

Recent Guideline Recommendations

COR	LOE	Recommendation
Ib	B-NR	<p>1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation.</p> <p>NEW: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.</p>

2019 AHA/ACC/HRS AF Guidelines

Recommendations for occlusion or exclusion of the LAA

LAA occlusion may be considered for stroke prevention in patients with AF and contraindications for long-term anticoagulant treatment (e.g. intracranial bleeding without a reversible cause).^{448,449,481,482}

Ib

B

Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery.^{459,483}

Ib

C

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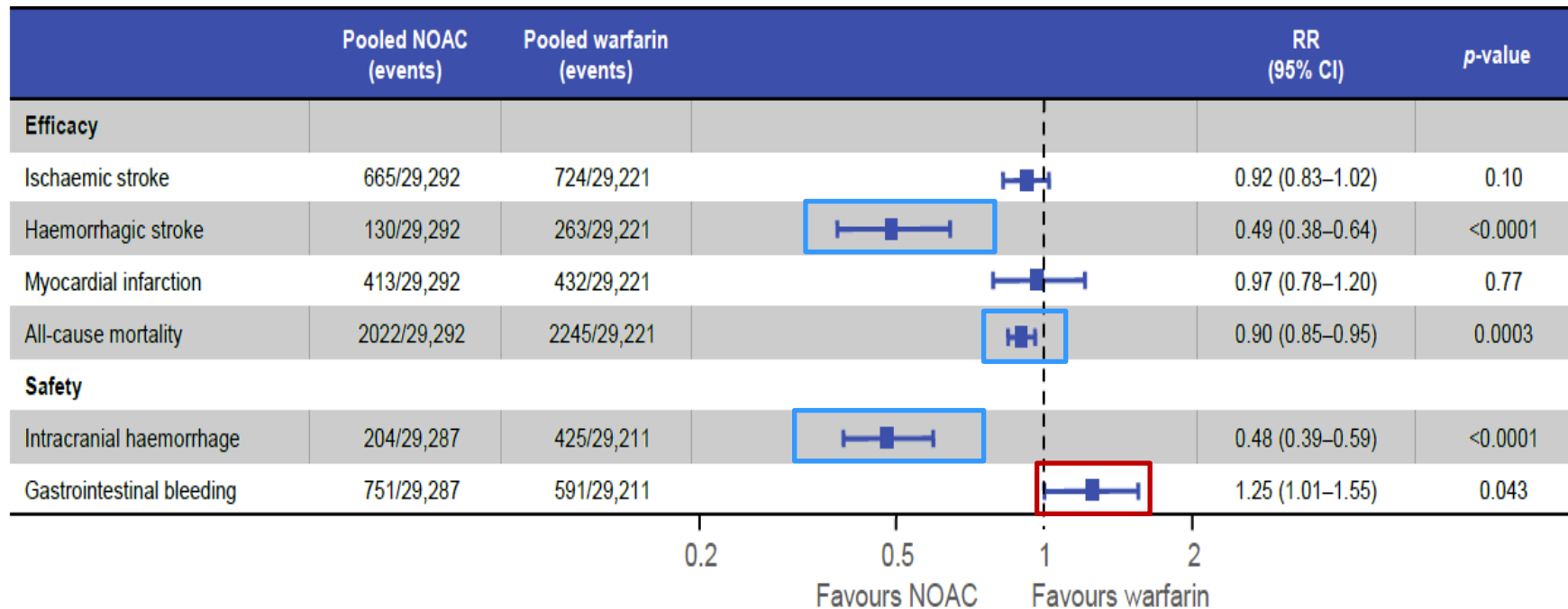
2020 ESC AF Guidelines

NOAC, A Game Changer for SPAF

NOACs are associated with significant reductions in:

- ◆ Haemorrhagic stroke (with a strong trend towards lower rates of ischaemic stroke)
- ◆ Intracranial haemorrhage
- ◆ All-cause mortality (with a trend towards lower rates of myocardial infarction)

Whereas the **risk of gastrointestinal bleeding is increased (not in Asian, only in Western)**



Ruff CT et al. Lancet 2014;383:955-962

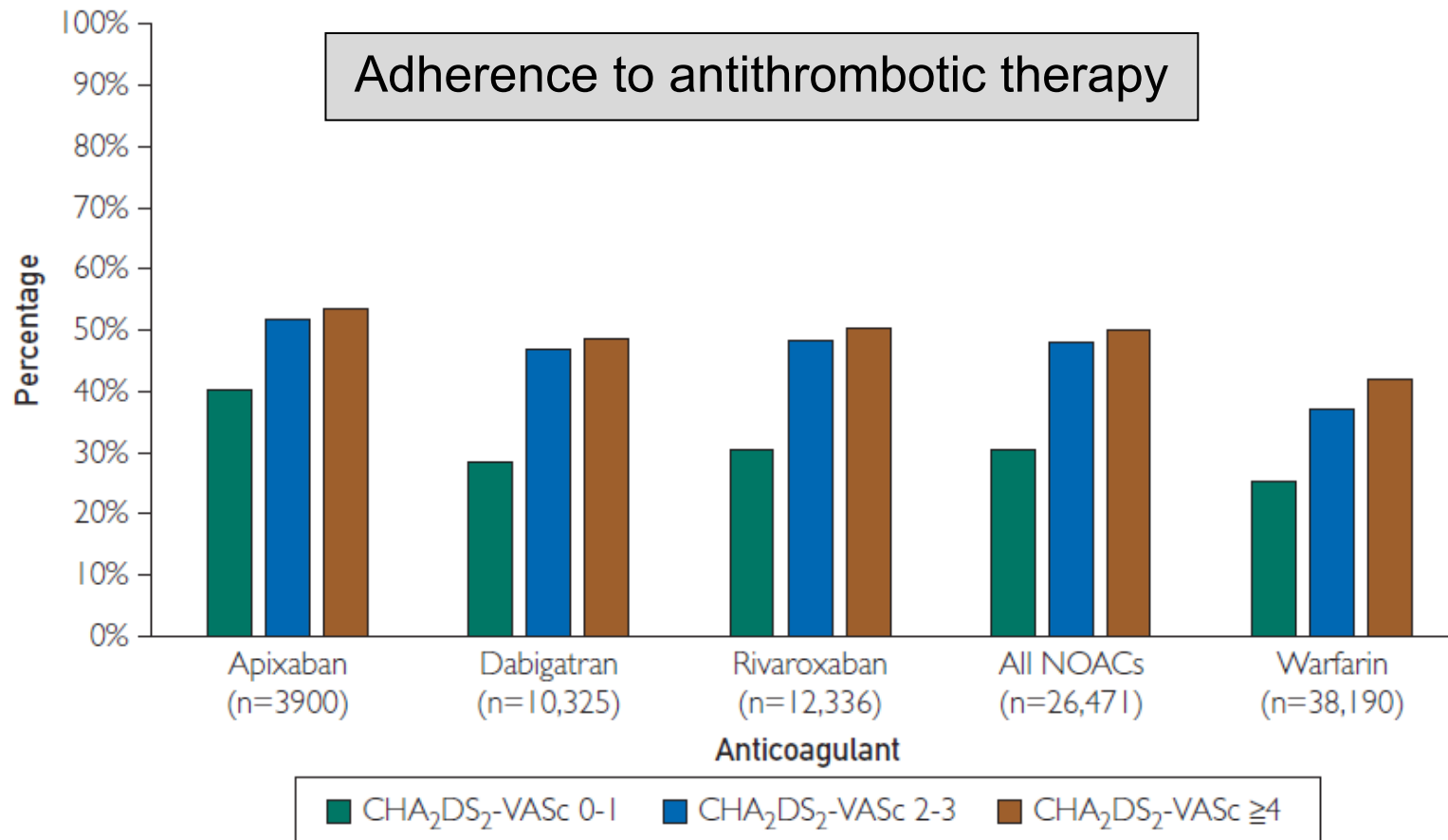
Problems with oral anticoagulation

- Incomplete efficacy
 - Intracranial bleeding
 - Life threatening bleeding
 - Drug-drug and food-drug interactions
 - Poor adherence and persistence with therapy
 - Failure to be prescribed
 - Use of low dose
 - Expensive reversal agents – relatively unavailable
- Worse with VKA
- Worse with NOACs

Inadequate use, too many strokes, too many bleeds and too many deaths

Nonadherence to OAC therapy

A retrospective cohort analysis by using a large US commercial insurance database (N=64,661) from Nov 2010 to Dec 2014

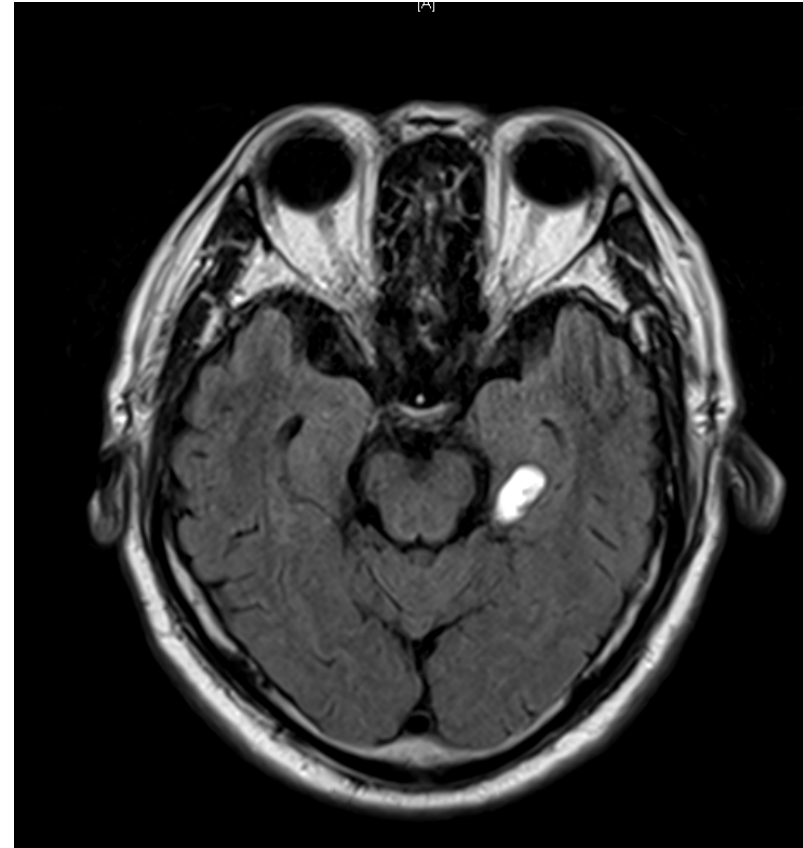


Yao X et al. *J Am Heart Assoc.* 2016;5:e003074

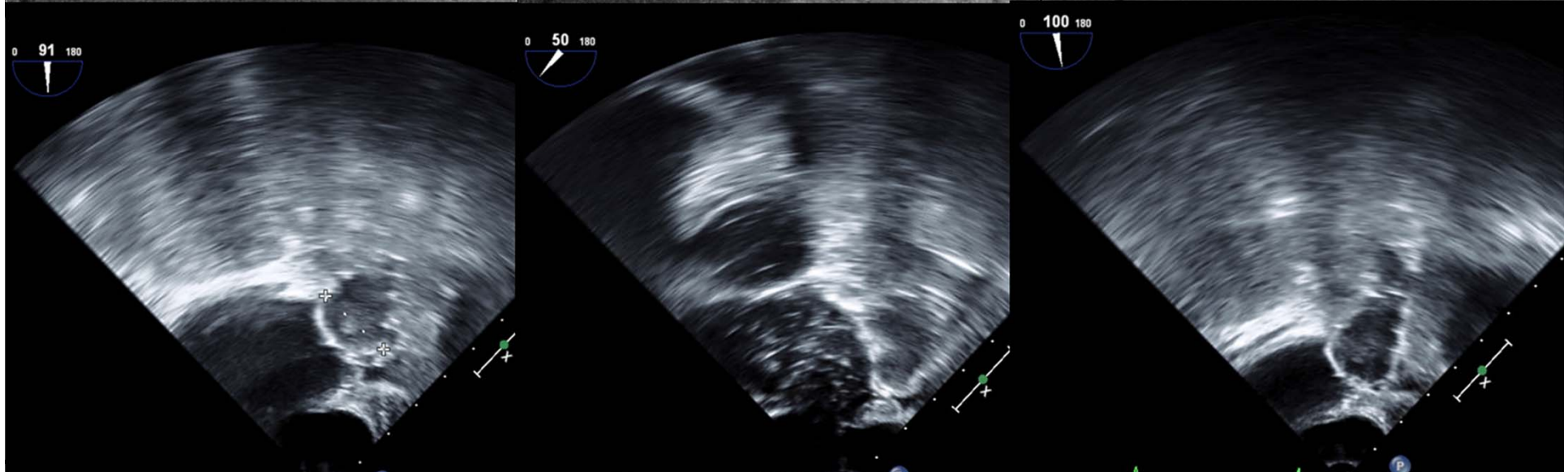
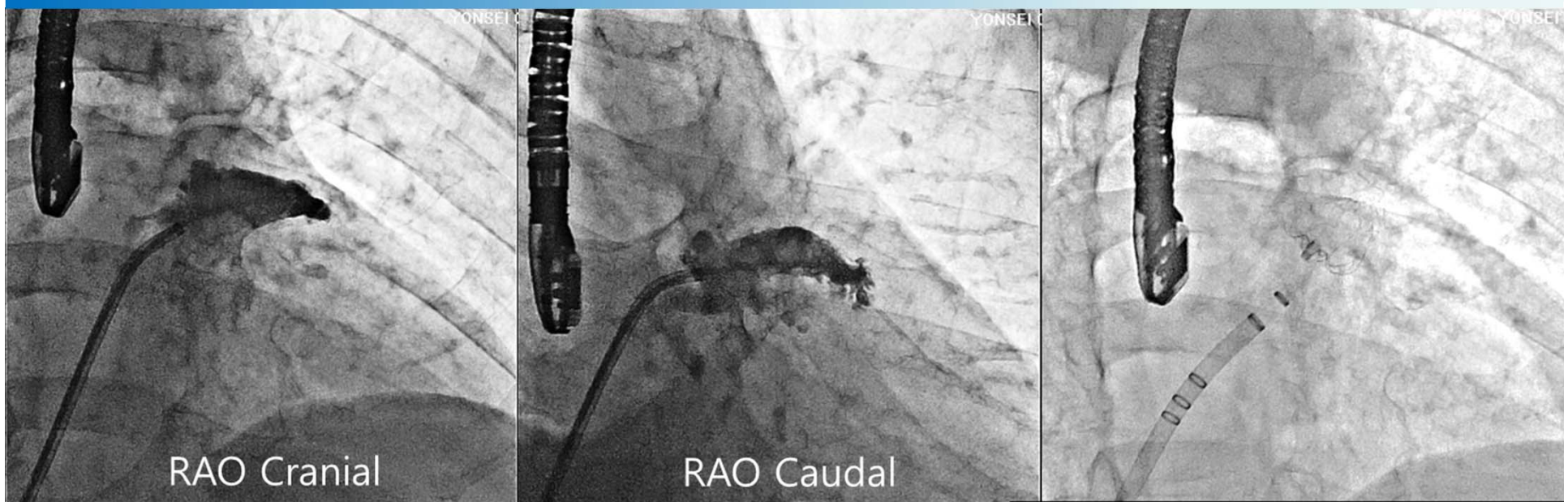
Case: M/72, ICH under NOAC

- Persistent AF, S/P DC cardioversion
- CAD (left main 50% stenosis)
- Hypertension, DM, CKD (eGFR 62)
- CHA₂DS₂-VASc 3

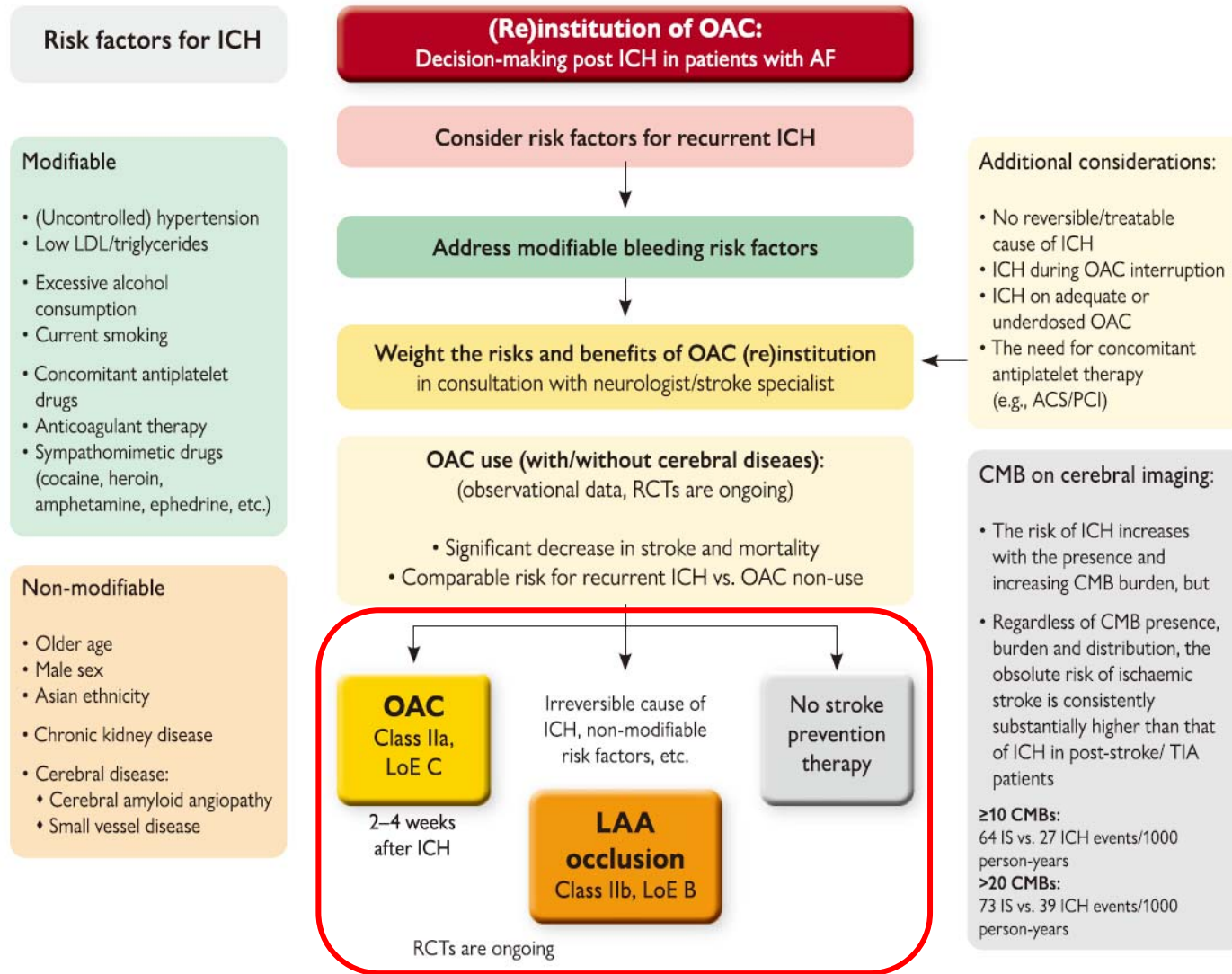
- Subacute ICH d/t Hemangioma
- Under Rivaroxaban 15mg QD



Case: WATCHMAN 24mm Device

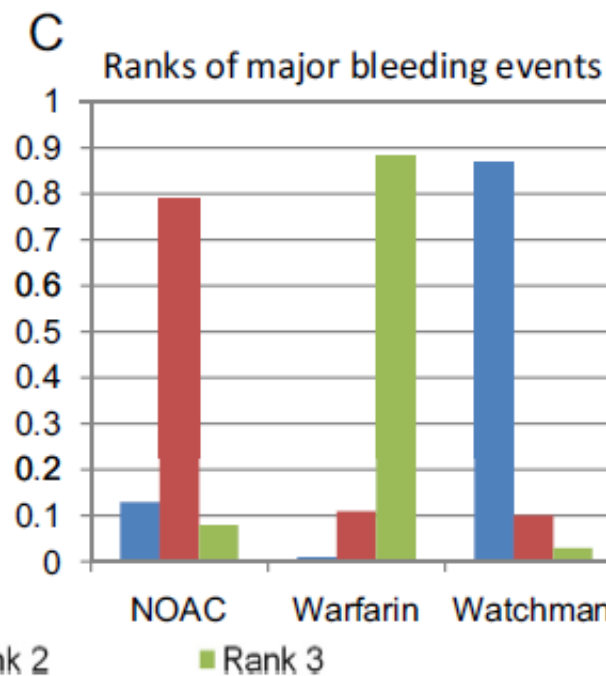
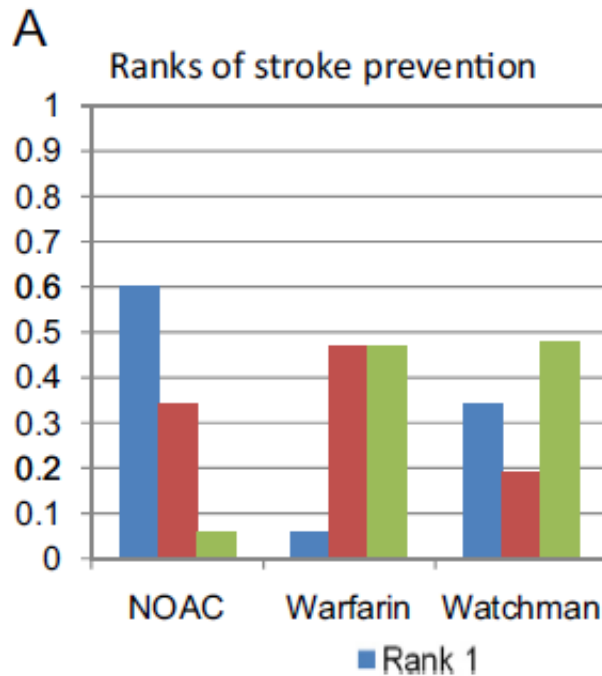


Post-ICH Stroke Prevention



2020 ESC AF Guidelines

Network meta-analyses of the NOAC vs. warfarin and LAAO vs. warfarin RCTs



B
ORs of stroke prevention

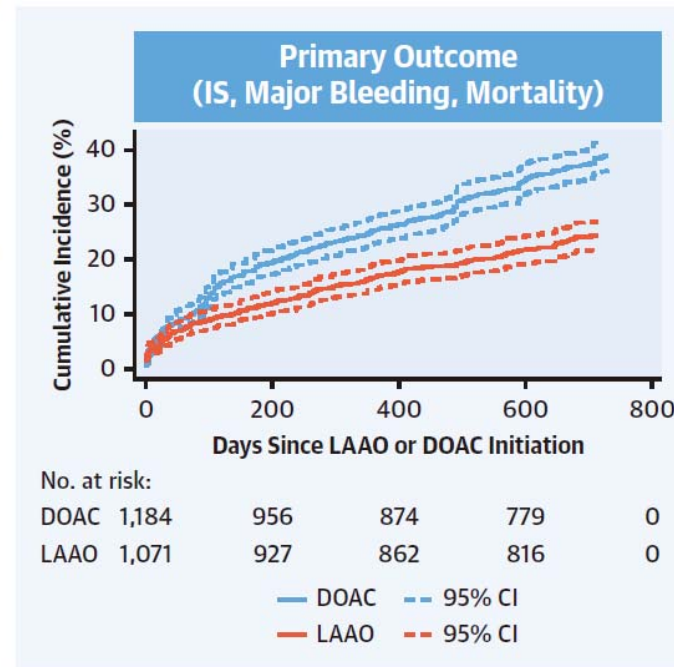
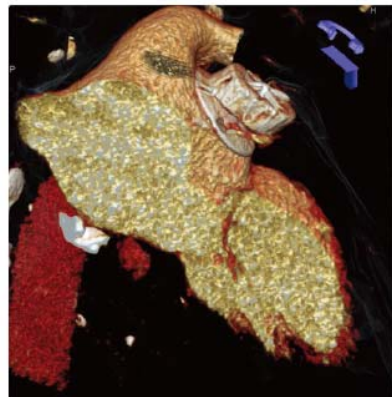
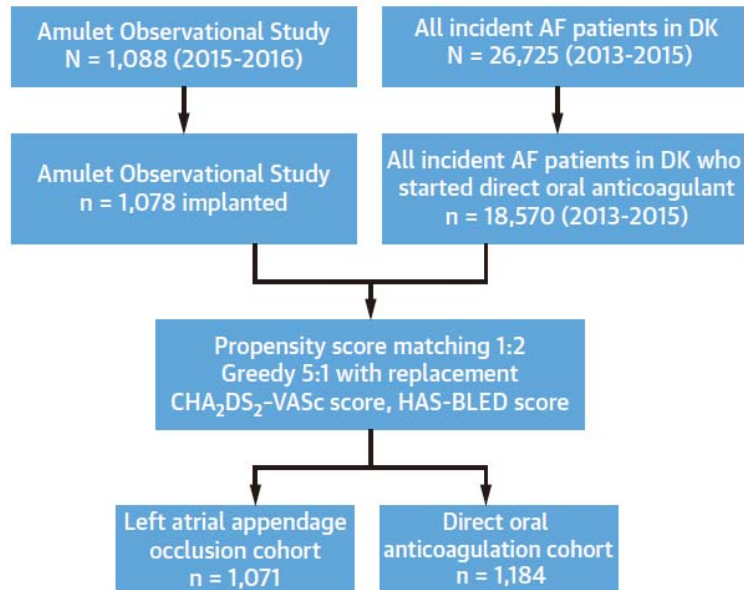
NOAC	1.17 (0.85,1.67)	1.16 (0.57,2.97)
0.86 (0.60,1.18)	Warfarin	0.99 (0.52,2.28)
0.86 (0.34,1.75)	1.01 (0.44,1.94)	Watchman

D
ORs of major bleeding events

NOAC	1.27 (0.84,1.88)	0.66 (0.29,1.45)
0.79 (0.53,1.19)	Warfarin	0.52 (0.26, 1.06)
1.52 (0.69,3.42)	1.93 (0.94,3.89)	Watchman

Li X et al. Heart Rhythm 2016;13:1203-1214

LAAO vs. NOAC: A Propensity Score-Matched Study



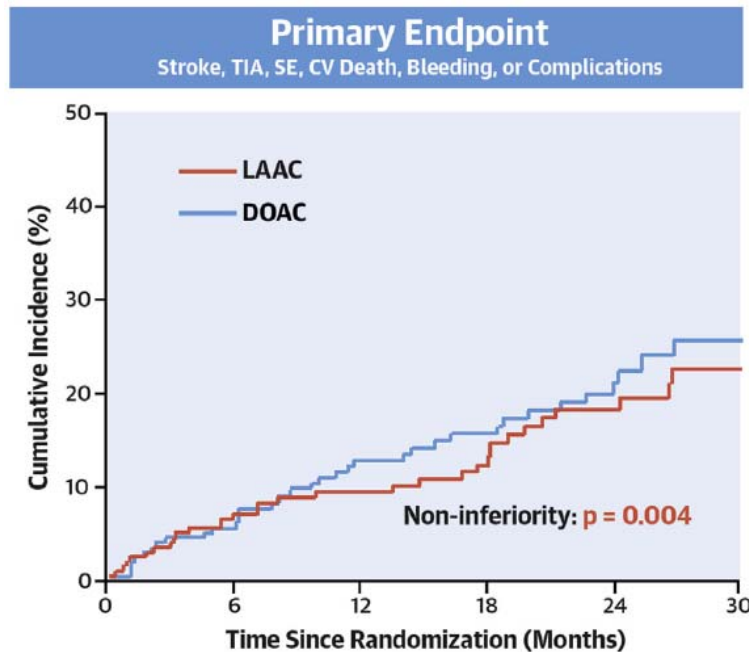
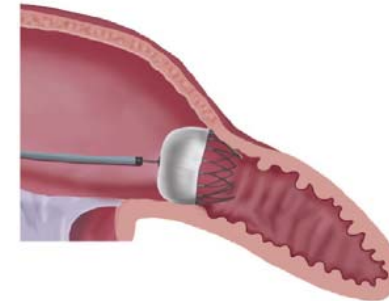
Clinical Outcomes	Hazard Ratio (95% CI)
IS, major bleeding, mortality	0.57 (0.49-0.67)
Ischemic stroke	1.11 (0.71-1.75)
Major bleeding	0.62 (0.49-0.79)
All-cause mortality	0.53 (0.43-0.64)
Cardiovascular mortality	0.51 (0.37-0.70)

Nielsen-Kudsk JE et al. *J Am Coll Cardiol Interv* 2021;14:69-78

LAAO vs. NOAC RCT in high-risk AF patients : PRAGUE-17 Trial



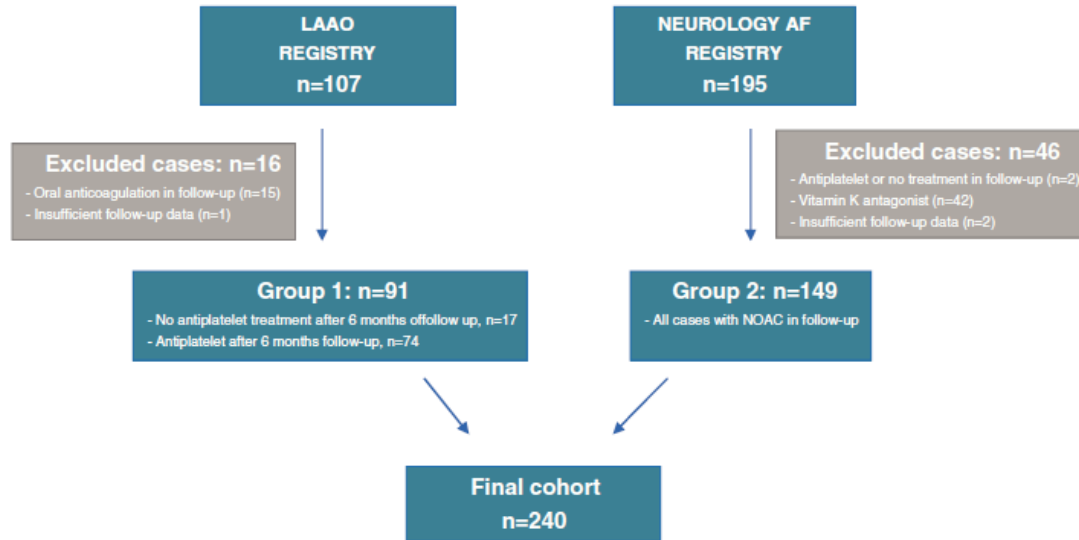
- 402 High-Risk AF Pts → Randomized
CHA₂DS₂-VASc = 4.7 ± 1.5
HAS-BLED = 3.1 ± 0.9
- Follow-up: 20.8 ± 10.8 mo (695 pt-year)



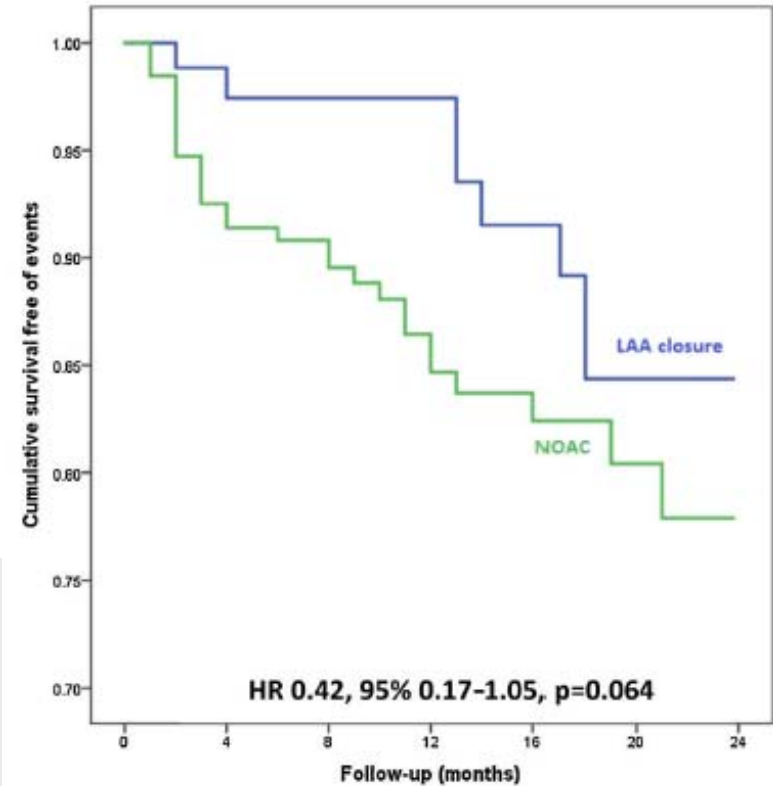
	sHR (95% CI)	p value
Primary Endpoint		
mITT	0.84 (0.53-1.31)	0.44
Per Protocol	0.82 (0.52-1.30)	0.40
On-Treatment	0.79 (0.49-1.25)	0.31
All-Stroke/TIA	1.00 (0.40-2.51)	0.99
CV Death	0.75 (0.34-1.62)	0.46
Major + NMCR Bleeding		
All	0.81 (0.44-1.52)	0.51
Nonprocedural	0.53 (0.26-1.06)	0.07

Osmancik P et al. *J Am Coll Cardiol* 2020;75:3122-3135

LAAO vs. NOAC from observational study



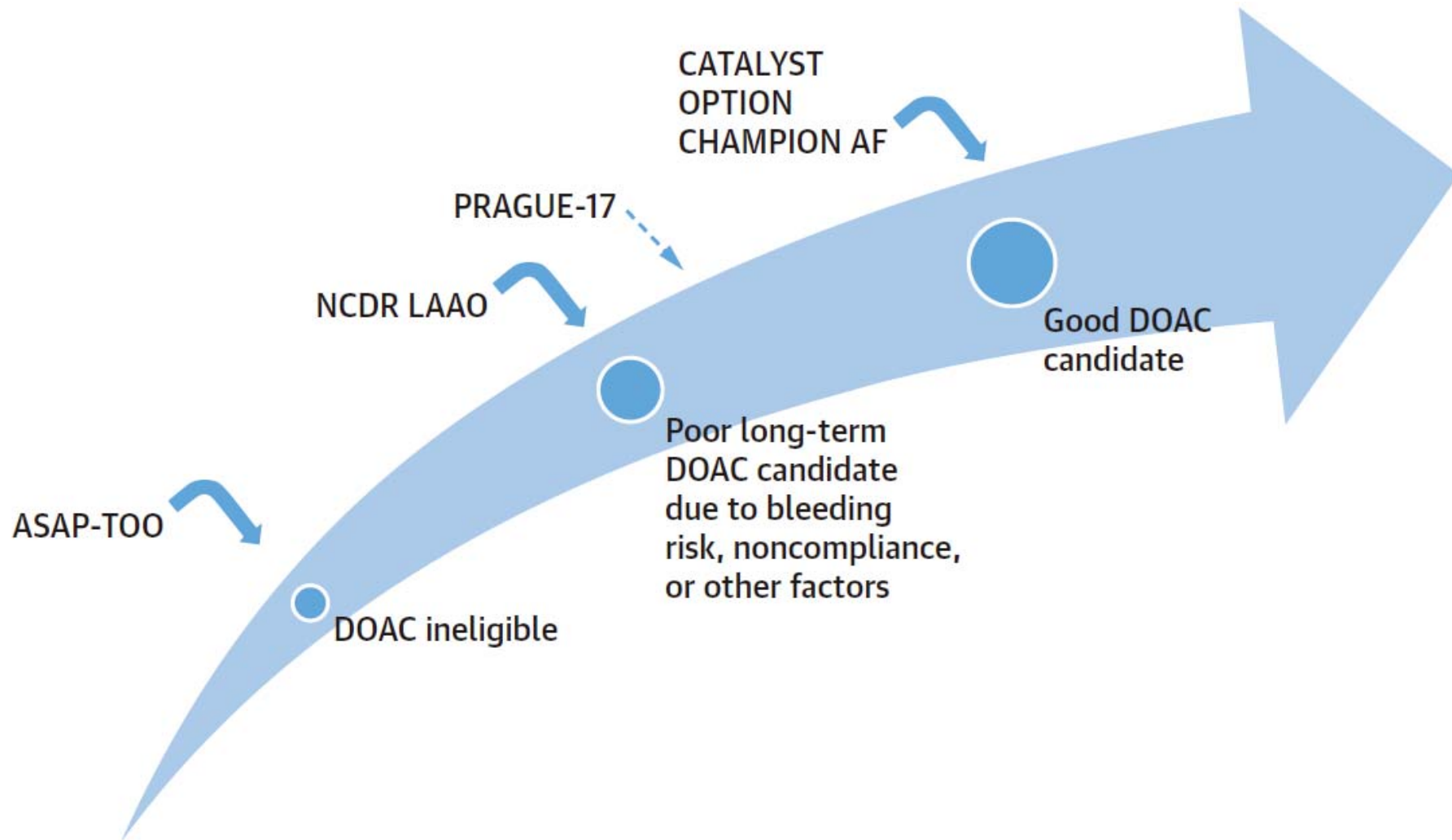
	HR	95% CI	p
Age	1.027	0.976-1.080	0.307
Type of AF (permanent)	0.150	0.033-0.682	0.014
History of carotid disease	0.171	0.052-0.561	0.004
Male gender	1.948	0.851-4.460	0.115
HAS-BLED score	3.613	1.694-7.707	0.001
CHA ₂ DS ₂ -VASc score	1.006	0.729-1.388	0.971
LAAO versus NOAC	0.419	0.167-1.052	0.064



- ✓ A prospective, single-center, non-randomized cohort study
- ✓ Primary outcome: composite of death, stroke and major bleeding

Paiva L et al. Rev Port Cardiol 2021;40:357-365

Ongoing or Planned RCTs and Registries of LAAO



Ongoing RCT comparing LAAO vs. NOAC : CATALYST Trial (NCT04226547)

Clinical trial of atrial fibrillation patients comparing left atrial appendage occlusion therapy to non-vitamin K antagonists

Design:

- Prospective, randomized, multicenter active control worldwide trial.

Primary Endpoints:

- Composite of ischemic stroke, systemic embolism, or CV mortality (non-inferiority)
- Major or clinically relevant non-major bleeding (non-inferiority)
- Major or clinically relevant non-major bleeding, excluding procedure related events (superiority)

Expected enrollment timeline

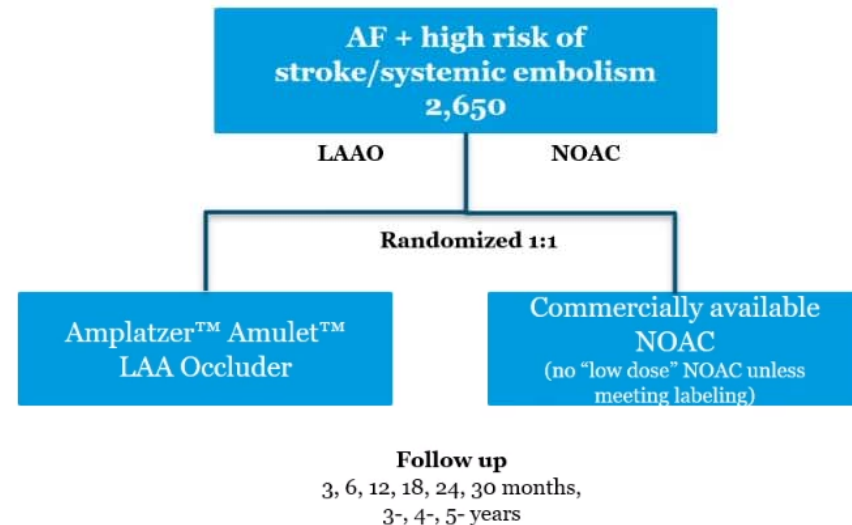
- July 2020 - August 2024

Total length of study

- 9 years

Steering Committee

- Chair: Vivek Reddy, MD
- Co-Chairs: Stephan Windecker, MD PhD & Elaine Hylek, MD



INTRODUCING
THE CATALYST TRIAL

Summary of RCTs Comparing LAAO with NOACs

Study Name	N	Key Inclusion Criteria	Intervention Arm	Control Arm	Primary Endpoint	Follow-Up	Sponsor
CATALYST (NCT04226547)	2,650	Patients with NVAF who are at high risk for stroke (CHA ₂ DS ₂ -VASc ≥3, and who are also suitable for DOAC	LAAO with Amulet	DOAC	1. Composite of ischemic stroke, SE, or CV death (NI) 2. Major bleeding or clinically relevant non-major bleeding excluding procedural bleeding (S) 3. Composite ischemic stroke/SE (NI)	2 yrs 3 yrs*	Abbott Medical Devices
CLOSURE-AF (NCT03463317)	1,512	Patients NVAF who are at high risk of stroke (CHA ₂ DS ₂ -VASc ≥2), and at risk of bleeding or have contraindication to OAC	CE-mark/ approved LAAO device	DOAC or VKA	Composite of stroke, SE, BARC type 3-5 bleeding, CV or unexplained death	2 yrs	Charite University Germany
CHAMPION-AF†	3,000	Patients with NVAF who are at high risk of stroke (CHA ₂ DS ₂ -VASc ≥2 for men, ≥3 for women), and are suitable for DOAC	LAAO with Watchman/FLX	DOAC	1. Composite of ischemic stroke, SE, or CV death (NI) 2. Nonprocedural bleeding (ISTH major bleeding and clinically relevant non-major bleeding) (S)	3 yrs	Boston Scientific
OCCLUSION-AF (NCT03642509)	750	Patients with NVAF who have neuroimaging-confirmed ischemic stroke or TIA within the past 6 months, and who are also eligible for DOAC	LAAO with Amulet or Watchman	DOAC	Composite of stroke, SE, major bleeding, and all-cause mortality	5 yrs	University of Aarhus Denmark
OPTION (NCT03795298)	1,600	Patients NVAF who are at high risk of stroke (CHA ₂ DS ₂ -VASc ≥2 for men, ≥3 for women), are suitable for DOAC, and who will undergo either concomitant or sequential catheter ablation for AF	LAAO WITH Watchman/FLX	DOAC	1. Stroke, all-cause death, and SE (NI) 2. Nonprocedural bleeding (ISTH major bleeding and clinically relevant nonmajor bleeding) (S)	3 yrs	Boston Scientific

Summary

- **OACs are the cornerstone** of SPAF. However, they are frequently underused or discontinued because of **adverse effects** and **nonadherence**.
- **LAAO** has emerged as a **feasible alternative to OAC** in patients who are not ideal candidates for long-term anticoagulation.
- **Ongoing RCTs comparing LAAO and NOACs** are being conducted involving AF patients and relative or absolute contraindication for long-term OAC.
- **LAAO** can be utilized as **second line therapy in patients with high risk of bleeding or recurrent stroke** under standard anticoagulation.

Thank you for your attention!

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