# Drugs and Devices for Atrial Fibrillation – Left Atrial Appendage Occlusion (LAAO) in Patients with Medical Failure

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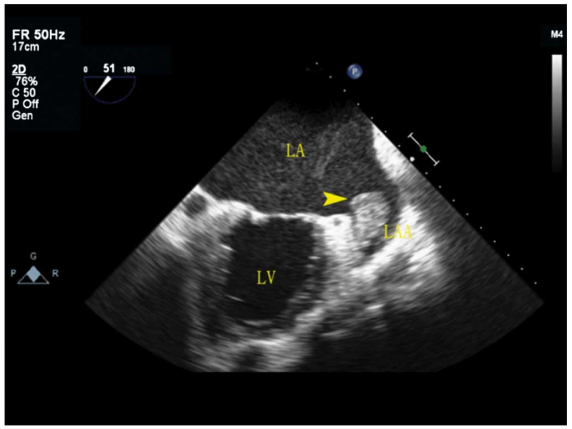
Beth Israel Lahey Health
Beth Israel Deaconess Medical Center

# Disclosures

Principal investigator for Medtronic and Cordis

Consulting for Cordis

# Why Atrial Fibrillation Matters in Stroke




## Thrombus Location

*Non-Rheumatic Atrial Fibrillation*

| Setting | N | Appendage | (%) | LA Body | (%) | Ref. |
|---|---|---|---|---|---|---|
| TEE | 317 | 66 | 21% | 1 | 0.3% | Stoddard; JACC '95 |
| TEE | 233 | 34 | 15% | 1 | 0.4% | Manning; Circ '94 |
| Autopsy | 506 | 35 | 7% | 12 | 2.4% | Aberg; Acta Med Scan '69 |
| TEE | 52 | 2 | 4% | 2 | 3.8% | Tsai; JFMA, '90 |
| TEE | 48 | 12 | 25% | 1 | 2.1% | Klein; Int J Card Imag '93 |
| TEE & Operation | 171 | 8 | 5% | 3 | 1.8% | Manning; Circ '94 |
| SPAF III TEE | 359 | 19 | 5% | 1 | 0.3% | Klein; Circ '94 |
| TEE | 272 | 19 | 7% | 0 | 0.0% | Leung; JACC '94 |
| TEE | 60 | 6 | 10% | 0 | 0.0% | Hart; Stroke '94 |
| **TOTAL** | **2018** | **201** | **10%** | **21** | **1.0%** | |

**90% in LAA**

*Blackshear & Odell Ann Thor Surg 61:755, 1996*

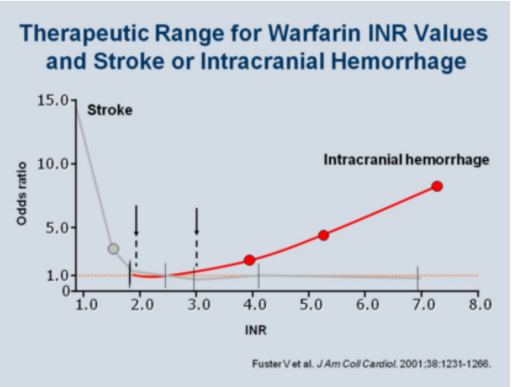
- AF significantly ↑ the risk of stroke
  - ~5%/year risk on average when not AC, can go up to 20%/y
- Up to 30% of ESUS cases may be from occult AF
- Majority of thrombus originate from LAA
- AF-related strokes carry high mortality and disability
- OAC lowers the thromboembolic risk by 2/3

Ruff C.T. et al. Lancet. 2014

# Anticoagulants: The Cornerstone

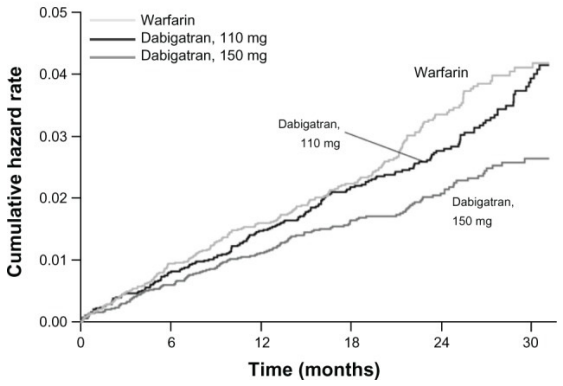
- **DOACs (Direct Oral Anticoagulant) are first-line therapy** in non-valvular AF

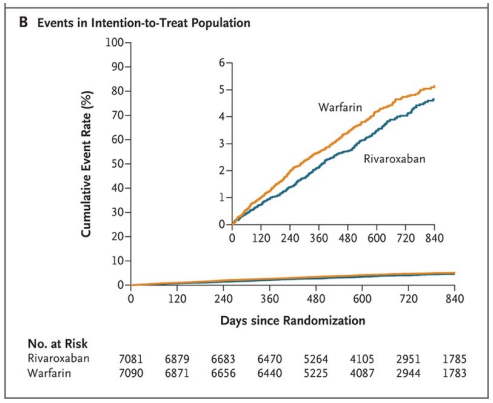
- Warfarin
  - Narrow therapeutic window
  - Numerous factors affecting maintenance dose (food and medications)
  - Needs close monitoring and dose adjustments

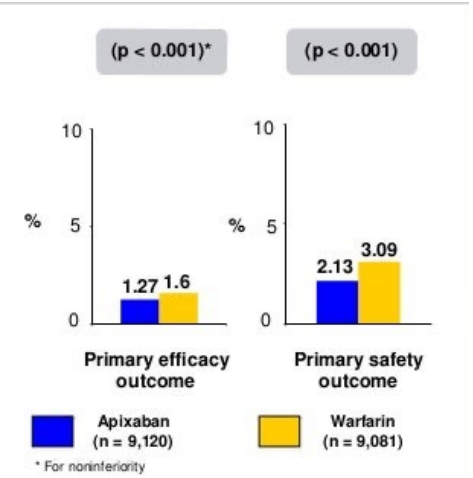


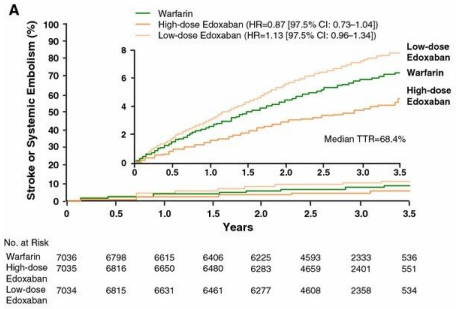

# DOACs

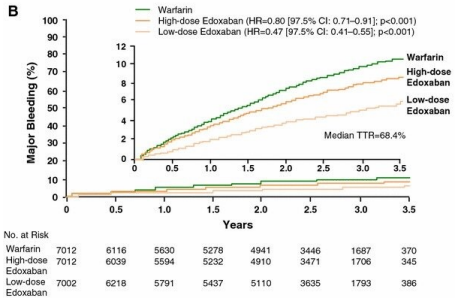
- All DOAC better or non-inferior to warfarin for stroke prevention
- All DOAC ↓ IC bleed
- All DOAC except Apixaban ↑ GI bleed



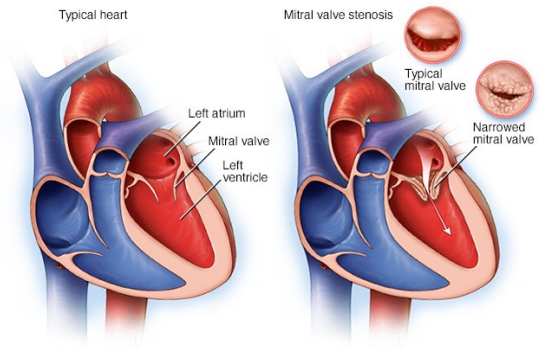
# Key Information on DOACs

- Renal function requires dose adjustment in most!

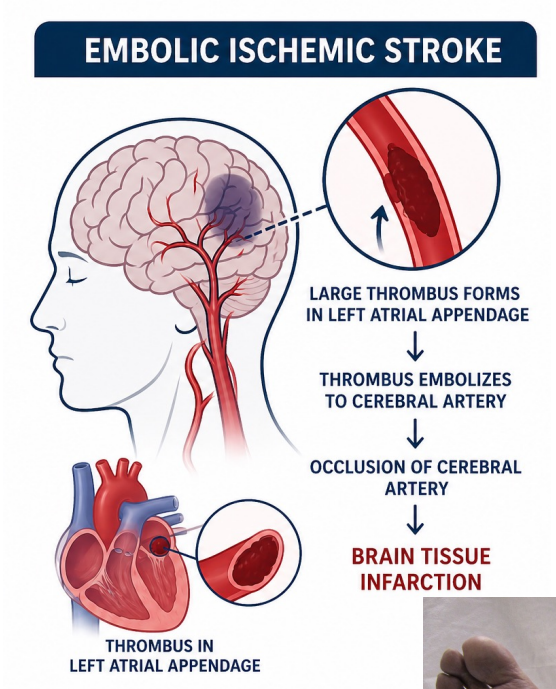
| | Dabigatran | Rivaroxaban | Apixaban | Edoxaban |
|---|---|---|---|---|
| *Dosing* | 150mg BID | 20mg daily | 5 mg BID | 60mg daily |
| *Reduced dosing* | 75mg BID<br>for CrCl 15-30mL | 15mg daily<br>for CrCl 15-50mL | 2.5 mg BID<br>if 2/3 +: ≥80yo;<br>≤ 60kg or Cr ≥1.5 | 30mg daily<br>for CrCl 15-50mL<br>or ≤ 60kg |
| *Mechanism of action* | Direct factor IIa (thombin) inhibitor | Direct factor Xa inhibitor | Direct factor Xa inhibitor | Direct factor Xa inhibitor |
| *Food interactions* | none | *Needs to be taken with food* | none | none |
| *Cutoff Cr Cl for use* | >30 | >15 | >15-30 | >30 |
| *Antidote* | Idarucizumab | Andexanet alfa<br>prothrombin complex concentrate (PCC) | | |

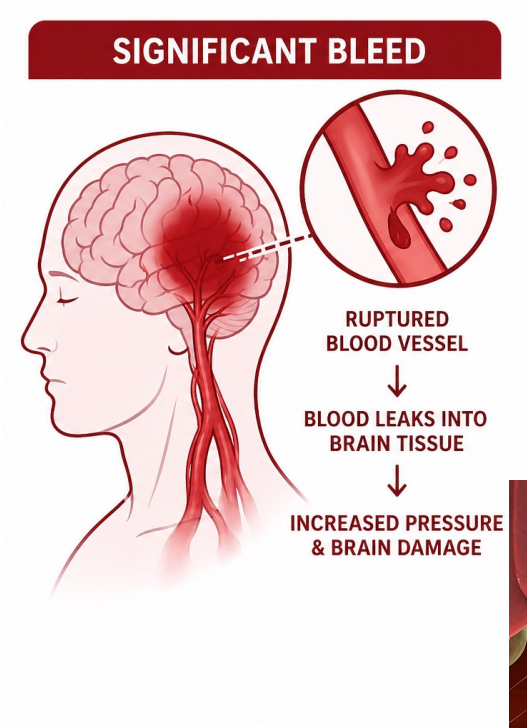
# Special Scenarios in Anticoagulation

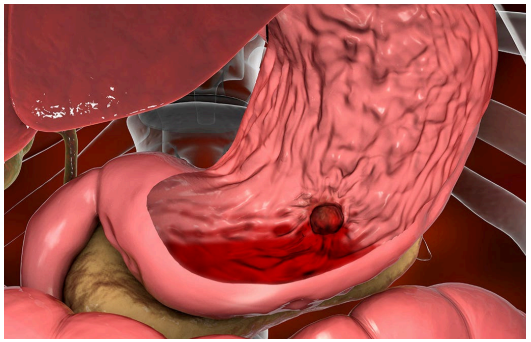
- Warfarin should be used
  - Valvular AF (moderate to severe mitral stenosis)
  - H/o mechanical heart valve
  - Advanced renal failure and hemodialysis
  - Antiphospholipid syndrome
  - When DOAC are cost prohibitive



# Medical Failure



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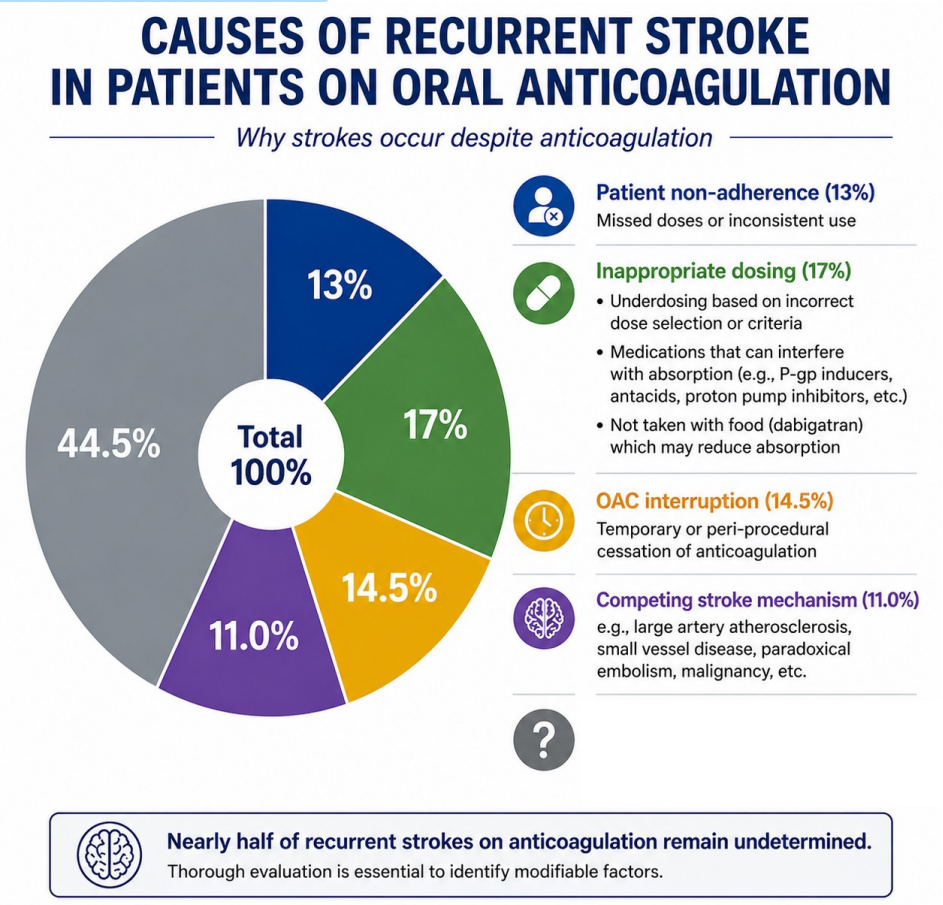
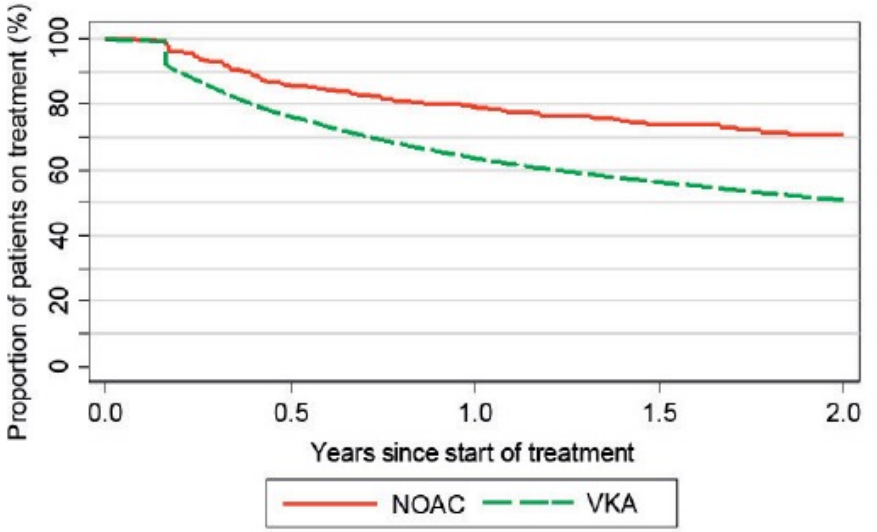
# High Rate of Recurrent Stroke despite OAC




Dube, M-C. et al. Canadian Journal of Neurological Sciences. 2024.

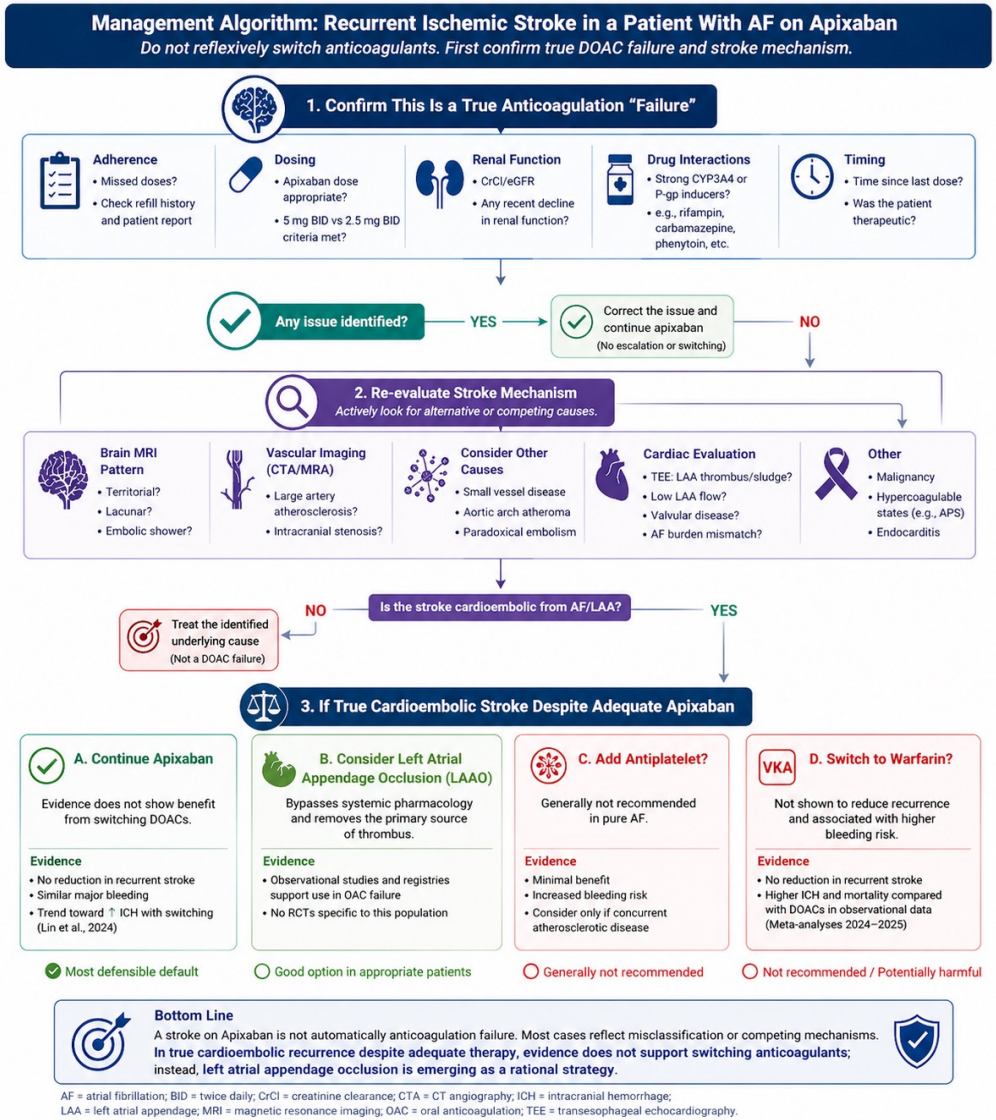
# Non-Adherence with OAC

**~30% of NOAC patients stop taking any drug at 2 years**



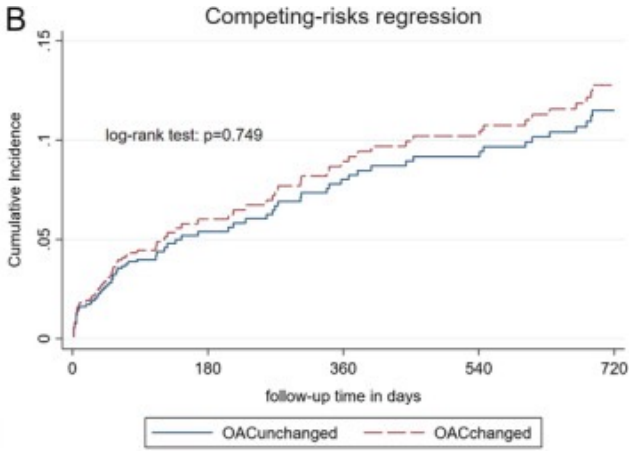

| | | | | | |
|---|---|---|---|---|---|
| NOAC | 914 | 651 | 342 | 139 | 41 |
| VKA | 12307 | 8453 | 5762 | 3915 | 2506 |

Martinez C, et al. Thromb Haemost. 2015 Dec 22;115(1):31-9.

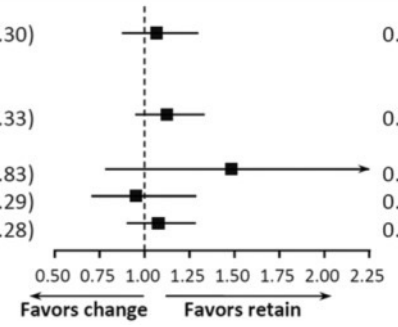

Management Algorithm: Recurrent Ischemic Stroke in a Patient With AF on Apixaban
Do not reflexively switch anticoagulants. First confirm true DOAC failure and stroke mechanism.
1. Confirm This Is a True Anticoagulation "Failure"
Adherence
• Missed doses?
• Check refill history and patient report
Dosing
• Apixaban dose appropriate?
• 5 mg BID vs 2.5 mg BID criteria met?
Renal Function
• CrCl/eGFR
• Any recent decline in renal function?
Drug Interactions
• Strong CYP3A4 or P-gp inducers?
• e.g., rifampin, carbamazepine, phenytoin, etc.
Timing
• Time since last dose?
• Was the patient therapeutic?
Any issue identified?
YES
Correct the issue and continue apixaban
(No escalation or switching)
NO
2. Re-evaluate Stroke Mechanism
Actively look for alternative or competing causes.
Brain MRI Pattern
• Territorial?
• Lacunar?
• Embolic shower?
Vascular Imaging (CTA/MRA)
• Large artery atherosclerosis?
• Intracranial stenosis?
Consider Other Causes
• Small vessel disease
• Aortic arch atheroma
• Paradoxical embolism
Cardiac Evaluation
• TEE: LAA thrombus/sludge?
• Low LAA flow?
• Valvular disease?
• AF burden mismatch?
Other
• Malignancy
• Hypercoagulable states (e.g., APS)
• Endocarditis
Is the stroke cardioembolic from AF/LAA?
NO
Treat the identified underlying cause
(Not a DOAC failure)
YES
3. If True Cardioembolic Stroke Despite Adequate Apixaban
A. Continue Apixaban
Evidence does not show benefit from switching DOACs.
Evidence
• No reduction in recurrent stroke
• Similar major bleeding
• Trend toward ↑ ICH with switching (Lin et al., 2024)
Most defensible default
B. Consider Left Atrial Appendage Occlusion (LAAO)
Bypasses systemic pharmacology and removes the primary source of thrombus.
Evidence
• Observational studies and registries support use in OAC failure
• No RCTs specific to this population
Good option in appropriate patients
C. Add Antiplatelet?
Generally not recommended in pure AF.
Evidence
• Minimal benefit
• Increased bleeding risk
• Consider only if concurrent atherosclerotic disease
Generally not recommended
VKA
D. Switch to Warfarin?
Not shown to reduce recurrence and associated with higher bleeding risk.
Evidence
• No reduction in recurrent stroke
• Higher ICH and mortality compared with DOACs in observational data (Meta-analyses 2024–2025)
Not recommended / Potentially harmful
Bottom Line
A stroke on Apixaban is not automatically anticoagulation failure. Most cases reflect misclassification or competing mechanisms.
In true cardioembolic recurrence despite adequate therapy, evidence does not support switching anticoagulants; instead, left atrial appendage occlusion is emerging as a rational strategy.
AF = atrial fibrillation; BID = twice daily; CrCl = creatinine clearance; CTA = CT angiography; ICH = intracranial hemorrhage;
LAA = left atrial appendage; MRI = magnetic resonance imaging; OAC = oral anticoagulation; TEE = transesophageal echocardiography.

# DOAC → DOAC

| Strategy | Effect on recurrence |
|---|---|
| Continue same DOAC | baseline |
| Switch DOAC → DOAC | ≈ no change, signal for ↑ bleeding |
| Switch DOAC → warfarin | Worse (↑ stroke, ↑ ICH, ↑ mortality) |
| Add antiplatelet | no clear benefit, ↑ bleeding |



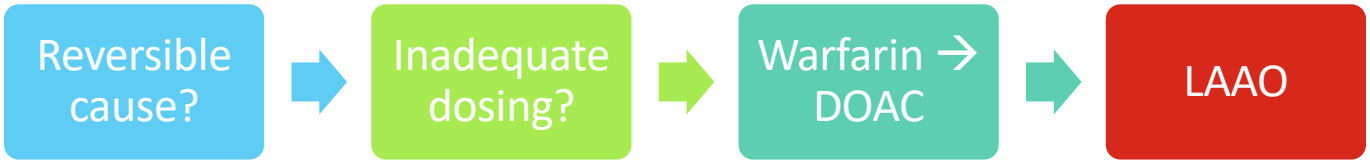

| Outcomes | IPTW aHR (95% CI) | *P* value |
|---|---|---|
| **Primary outcome** | | |
| Recurrent IS and TIA | 1.07 (0.87–1.30) | 0.530 |
| **Secondary outcome** | | |
| Effectiveness | | |
| STE | 1.13 (0.95–1.33) | 0.175 |
| Safety | | |
| Intracranial hemorrhage | 1.49 (0.78–2.83) | 0.229 |
| Major bleeding | 0.95 (0.70–1.29) | 0.748 |
| **All-cause death** | 1.08 (0.90–1.28) | 0.418 |



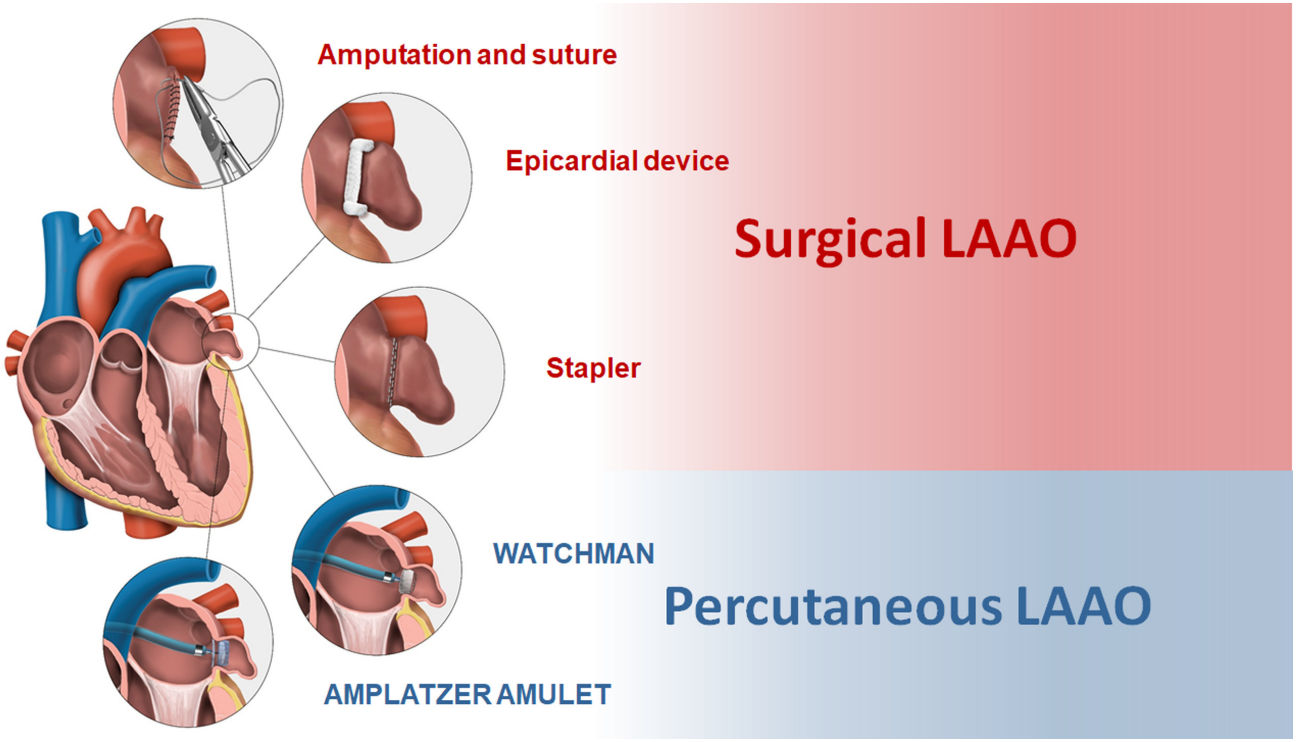

Lin et al. JAHA 2024. Seiffge et al. Ann Neurol 2020. Romoli et al. Neurology 2025.

# Bleeding Event

- Major bleeding:
  - Intracranial hemorrhage
  - Recurrent GI bleeding
- High-risk substrates:
  - Cerebral amyloid angiopathy
  - Frequent falls / frailty
- Inability to take long term anticoagulation



# Left Atrial Appendage (LAA) Closure Devices

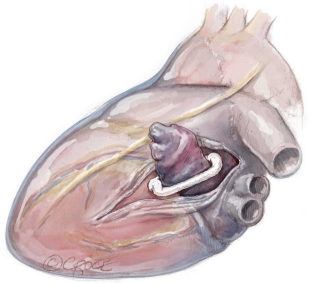


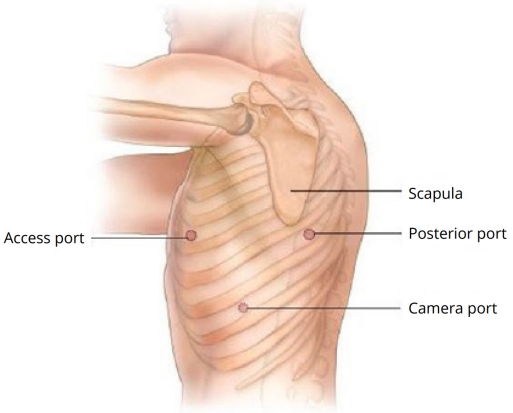
# LAA Exclusion at the time of Surgery

**Recommendations for Cardiac Surgery—LAA Exclusion/Excision**
**Referenced studies that support the recommendations are summarized in the Online Data Supplement.**

| COR | LOE | Recommendations |
|---|---|---|
| 1 | A | 1. In patients with AF undergoing cardiac surgery with a $CHA_2DS_2$-VASc score ≥2 or equivalent stroke risk, surgical LAA exclusion, in addition to continued anti-coagulation, is indicated to reduce the risk of stroke and systemic embolism.[1–3] |
| 1 | A | 2. In patients with AF undergoing cardiac surgery and LAA exclusion, a surgical technique resulting in absence of flow across the suture line and a stump of <1 cm as determined by intraoperative trans-esophageal echocardiography should be used.[1,4,5] |
| 2b | A | 3. In patients with AF undergoing cardiac surgery with $CHA_2DS_2$-VASc score ≥2 or equivalent stroke risk, the benefit of surgical LAA exclusion in the absence of continued anticoagulation to reduce the risk of stroke and systemic embolism is uncertain.[1–3] |

# AtriClip PRO-V (AtriCure)

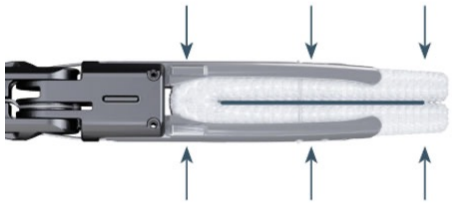





- >650,000 devices implanted globally
- >10 y follow up clinical data (>20y for safety)
- CE marked and FDA approval (only surgical device)

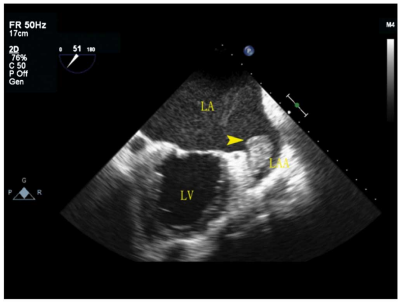
- Median sternotomy/thoracotomy or thoracoscopic access
- 97% successful left atrial appendage (LAA) exclusion
  - No residual leak
  - <1cm residual LAA neck
  - No device migration or complication
  - No intracardiac thrombus, stroke/TIA

- No nickel (titanium alloy)
- Continuous dynamic closing pressure of the LAA as it atrophies
- Leads to electrical isolation of LAA within minutes (less Afib)



- Anticoagulation recommended for ≥ 2 months post

# LAA: Target for Device-Based Prevention




- LAAO is an alternative for patients who are not good candidate for long-term anticoagulants (but can tolerate short term anticoagulation)

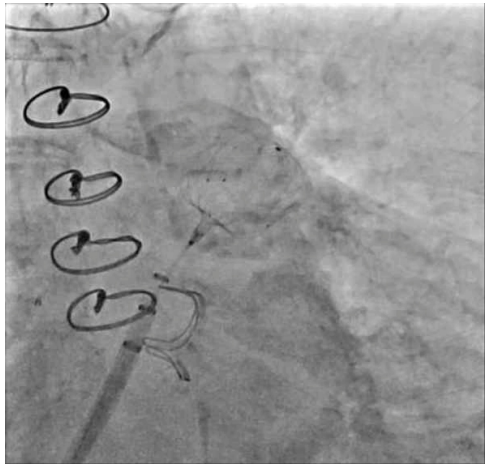
## Candidates for LAA Occlusion

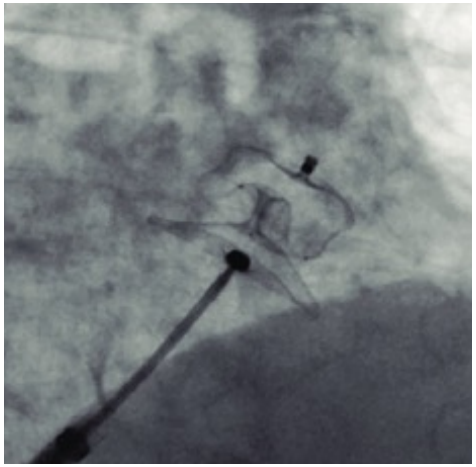
$CHA_2DS_2$-VASc ≥3 or $CHADS_2$ score ≥2

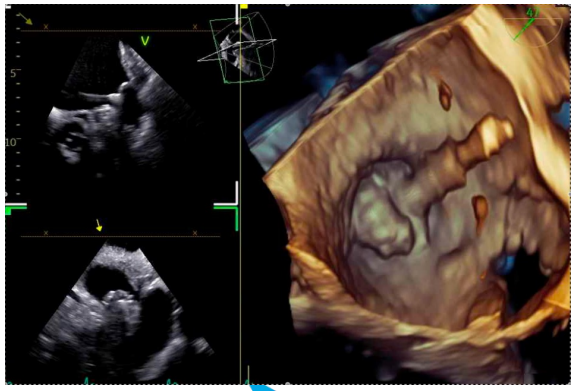
**AND** rationale for alternate therapy:

- Major bleeding episode or recurrent bleeding while on OAC
- Poor adherence, difficulty to maintain in a therapeutic range
- High fall risk, h/o falls
- Recurrent ischemic stroke despite OAC (belt-suspender approach)
- Occupation or lifestyle placing the patient at high risk of major bleeding secondary to trauma

# LAA Occlusion Procedure



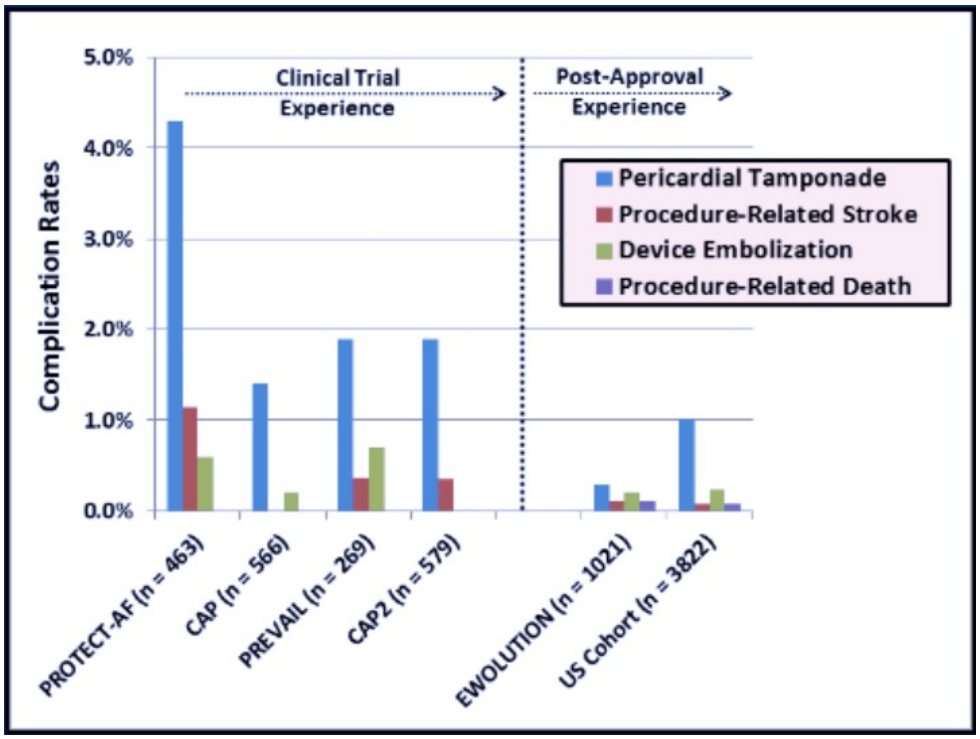




- Done in a cath lab / EP lab
- ~1h procedure
- General anesthesia → TEE guidance needed
- Femoral venous access → transseptal puncture
- Heparin with ACT ~250
- Intracardiac echo (ICE) imaging guidance
  - Avoids need for GA
  - Can be done when TEE is not possible
  - LAA measurements tend to be underestimated (requires pre-procedural imaging with CTA)

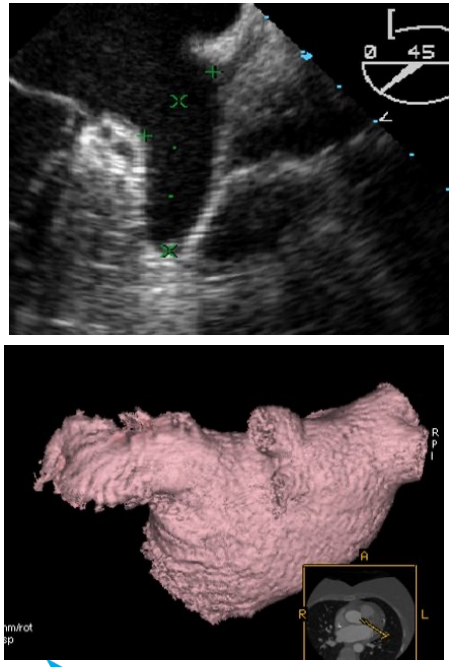
# Percutaneous LAAO

- Overall safe procedure
- Successful (>97%)
- Low rate of complications:
  - Bleeding
  - Pericardial effusion/tamponade ~1%
  - Stroke <0.1%
  - Device embolization 0.1%
  - Death <0.1%
  - Esophageal injury
  - Other anesthesia related complications

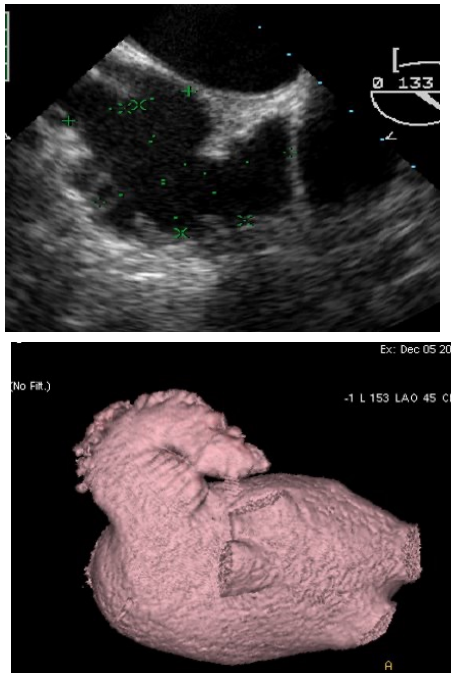


# LAA Morphology

**Wind Sock Type**
one dominant deep lobe of is the primary structure

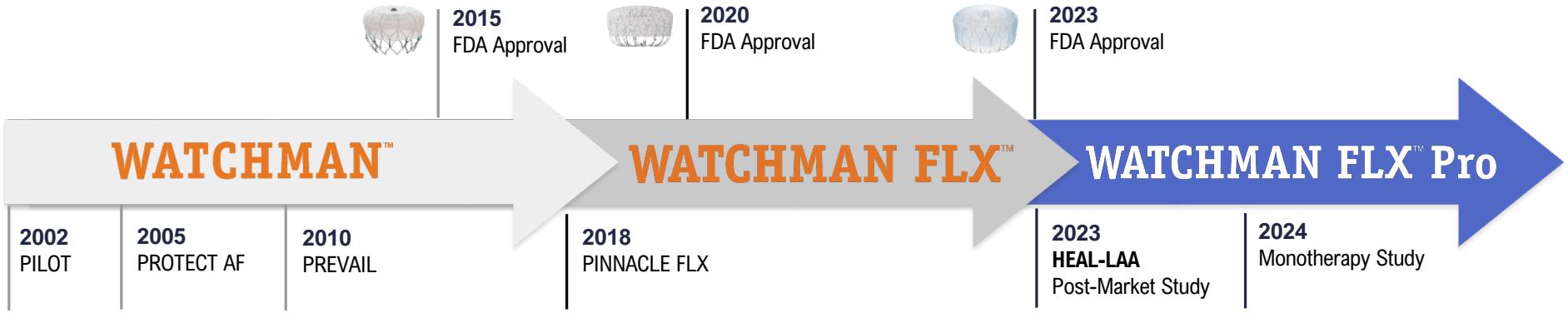


**Chicken Wing Type**
a sharp bend in the dominant lobe



**Broccoli Type**
limited length with complex internal trabeculations.

# Watchman Device




**500,000+**
Patients treated

**20 years**
Clinical & Real-World Experience

**10+**
Clinical Trials

***WATCHMAN is the most studied, most implanted LAAC device in the world***

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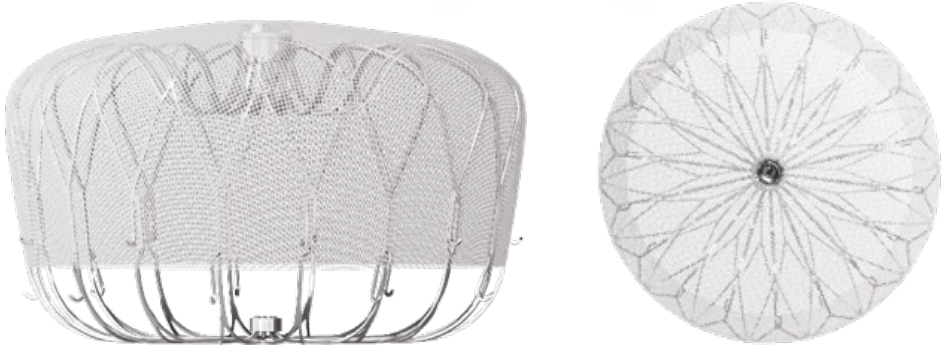
Kar, S., et al, Circulation, 2021.

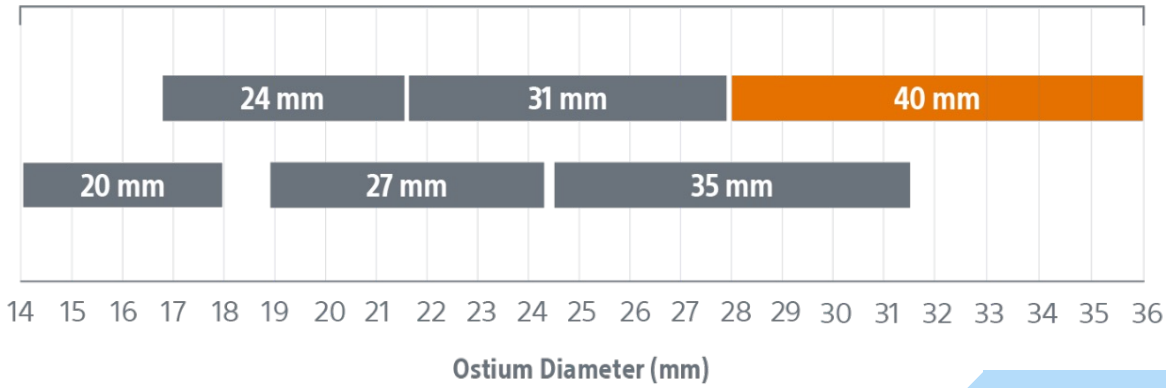
# Watchman FLX Pro Device

- Self-expanding nitinol frame with Polyethylene Terephthalate (PET) that extends to 2/3rd of device
- 2 rows of anchors
- 18 struts frame for increased conformability

- Fits most anatomy
  - 6 sizes (20-40mm)
  - Full recapture and reposition
  - >97% success rate
  - Very low adverse event rates (<1%)

- May not work for very shallow LAA or proximal lobes
- MR Conditional device






Watchman FLX IFU

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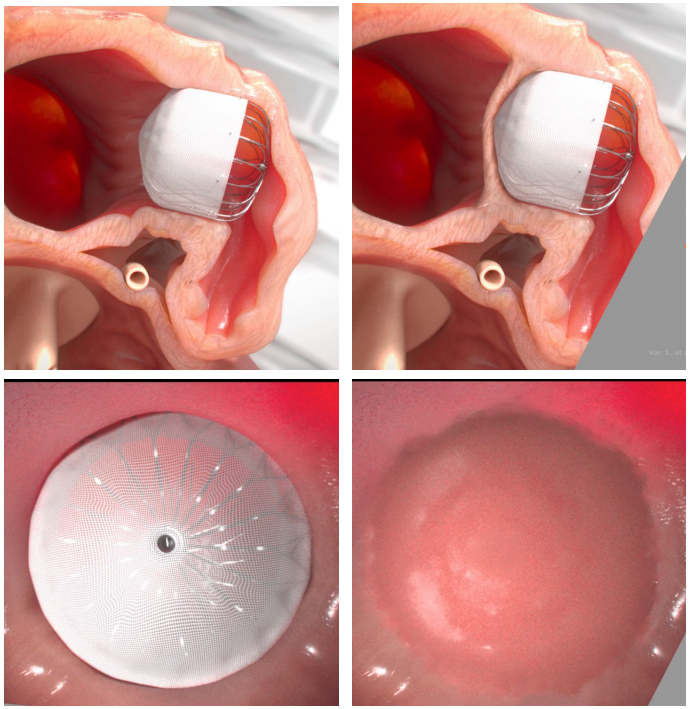
# Watchman FLX Pro

- HEMOCAOT technology (faster endothelization)
  - Reduces devices related thrombus (~2-4% @ 12mo)
  - Improved seal (90% Complete Seal at 12 mo)

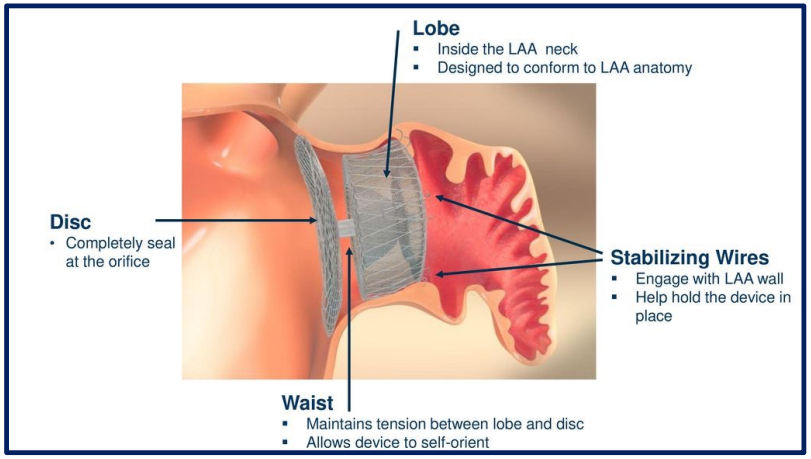
- Endothelization at 45 days*
  - 96.2% off anticoagulation at 45 days



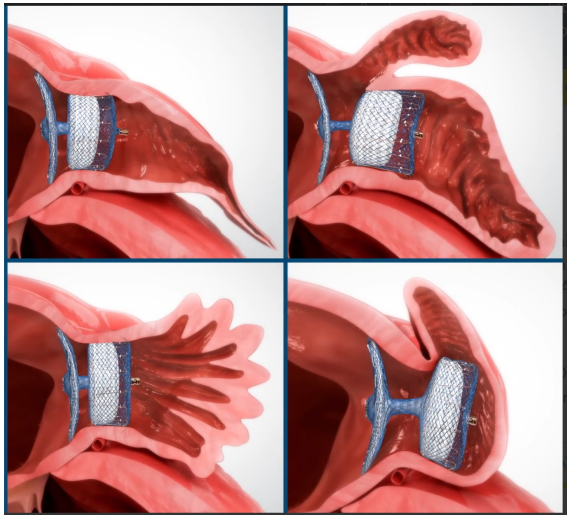
Kar, S., et al, Circulation, 2021

# Watchman NG – Pivotal Trial starting in 2026

# Amplatzer™ Amulet™ Device




- Dual Seal technology
- Self-expanding nitinol plug
  - Lobe and disc, connected by a central waist
- Can be used for all LAA shapes
- 8 sizes (16 mm - 34 mm)
  - 99% success rate
  - 99% effective closure
  - Recapturable and repositionable
- Slightly higher peri-procedural complications (pericardial effusion) compared to Watchman FLX
- MR conditional device



# Amulet 360

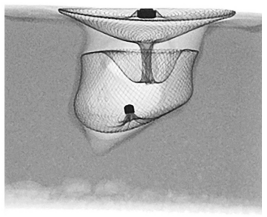
- Veritas Trial presented in 2026

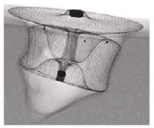
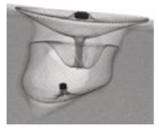
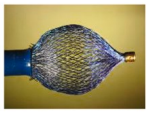
**0%**
Primary Safety Endpoint*
p < 0.0001 (performance goal: 3.75%)

**100%**
Primary Effectiveness Endpoint*
p < 0.0001 (performance goal: 96.6%)

**100%**
Clinically relevant closure (no PDL > 3mm identified

**93.9%**
Complete closure (0 mm leak) identified



| | Current generation dual-seal LAAO device | Next generation dual-seal LAAO device |
|---|---|---|
| Increased conformability in the lobe |  |  |
| Redesigned anchors |  |  |
| Dual rows of shorter anchors |  |  |
| Inverted distal end screw |  |  |

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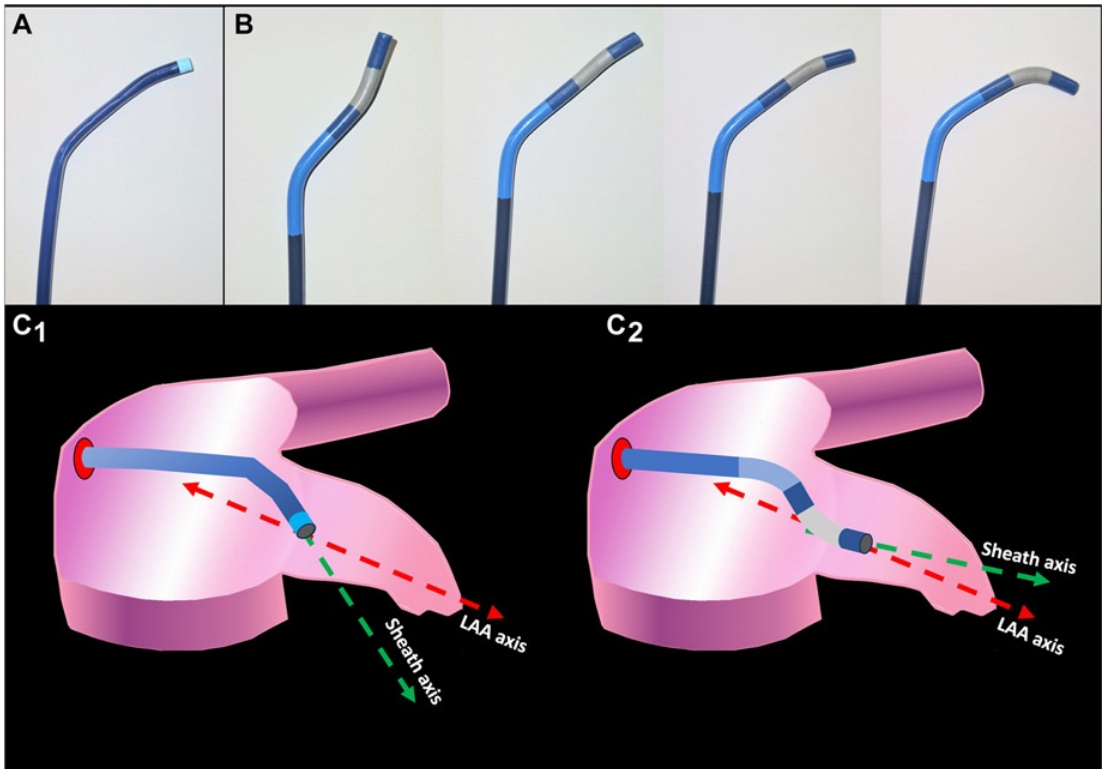
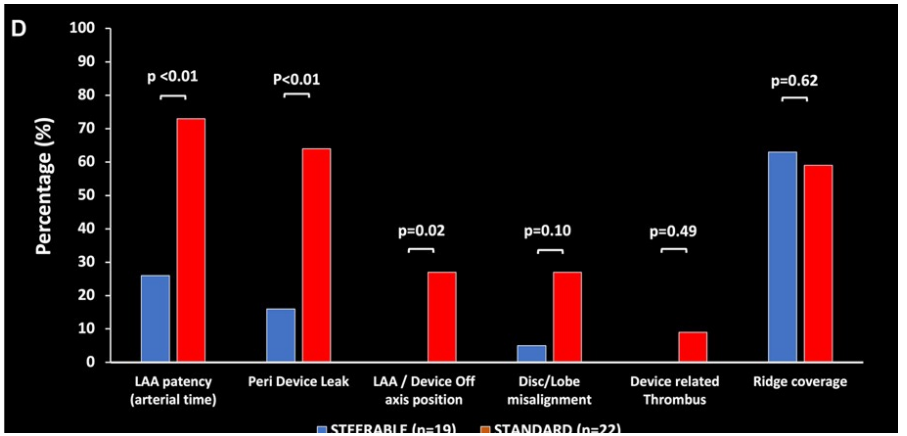
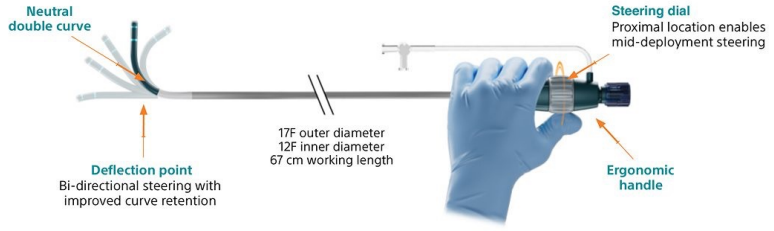
# Steerable Delivery Catheters

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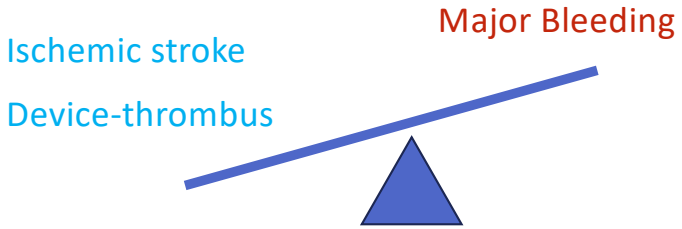
Amabile N et al. JSAI 2024

# Post-LAAO Management

- 3h of bedrest
- Same day discharge
- No cardioversion for 30 days → risk of device embolization
- Endocarditis prophylaxis for 6 months prior to dental work
- Follow-up imaging at 30-**45** days and 1y



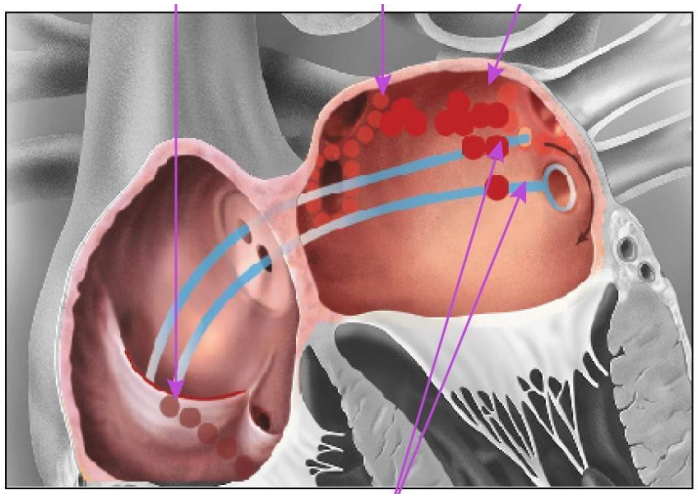

| | 0 - 45 days ** | >45 days |
|---|---|---|
| Acceptable bleeding risk | NOAC (warfarin) +/- ASA | Aspirin 81mg |
| Very high bleeding risk | NOAC alone | |
| Bleeding episode on NOAC | Apixaban 2.5 mg BID | |
| Cerebral amyloid angiopathy | Apixaban 2.5 mg BID | n/a |
| Belt-suspender LAAO | NOAC (warfarin) + ASA | NOAC (warfarin) |

** On TEE, if leak 1-3mm, patients remain on OAC until complete seal is documented

# Concurrent LAAO + PVI

- AF ablation can be considered in patients who need an AF ablation
  - Rhythm control is preferred in patient with systolic HF and most patients <70 years of age
  - Ablation reduced mortality/hospitalization in HF, but no significant stroke reduction

- OPTION trial demonstrated that post AF ablation
  - Non-inferiority to continued anticoagulation
  - Superiority for bleeding



# 2025 SCAI/HRS guidelines

JSCAI
The official journal of the Society for Cardiovascular Angiography & Interventions

**Standards and Guidelines**

2025 SCAI/HRS Clinical Practice Guidelines on Transcatheter Left Atrial Appendage Occlusion

Andrew M. Goldsweig, MD, MS, FSCAI [a,*], Michael Glikson, MD [b], Jacqueline Joza, MD [c], Clifford J. Kavinsky, MD, PhD, MSCAI [d], Omar Khalique, MD, FSCAI [e], Dhanunjaya Lakkireddy, MD [f], G. Burkhard Mackensen, MD, PhD, FSCAI [g], Gerald V. Naccarelli, MD [h], Devi G. Nair, MD [i], Jacqueline Saw, MD, FSCAI [j], Rahul Prakash Sharma, MD, FSCAI [k], Matthew Sherwood, MD, FSCAI [l], Molly Szerlip, MD, FSCAI [m], Yngve Falck-Ytter, MD [n,t], Rebecca L. Morgan, PhD, MPH [n,q,s], Chelsea Armah, MPH [o], Scott Firestone, MS [o], Angela Fix, MPH, MWC [p], Emily Senerth, MS, MPH [q], Christopher R. Ellis, MD [r]

## Recommendations

1. In adults with nonvalvular atrial fibrillation (NVAF) and contraindication to oral anticoagulation (OAC), should LAAO be performed rather than no therapy?
   - 1.1 For patients with NVAF and contraindication to OAC, the SCAI/HRS guideline panel suggests LAAO over no therapy (neither OAC nor LAAO) (conditional recommendation, very low certainty evidence).

     *Remarks*: Many patients with contraindications to OAC (eg, bleeding history or bleeding risk) would reasonably choose to reduce their stroke risk by selecting LAAO over no therapy. Patients who value avoiding possible procedure-related adverse events more than a possible reduction in risk of stroke would reasonably choose no therapy. Clinicians should discuss with patients the procedural risk of LAAO vs the ongoing risk of thromboembolic events associated with no treatment. LAAO may be inappropriate for patients with less than 1 year of quality life expectancy.
2. In adults with NVAF, should LAAO be performed rather than OAC?
   - 2.1 For patients with NVAF who have decided to pursue stroke prevention treatment, the SCAI/HRS guideline panel suggests OAC or LAAO as treatment options.

     *Remarks:* While most patients are offered stroke prevention with OAC, those with elevated bleeding risk, prior bleeding complications, or strong preferences to avoid long-term anticoagulation would reasonably choose LAAO over OAC. LAAO may be inappropriate for patients with less than 1 year of quality life expectancy.

# LAAO Patient Selection: CHAMPION-AF

3,000 pts | 141 sites | 16 countries | Mean $CHA_2DS_2$-VASc 3.5 | Mean HAS-BLED 1.3

68.9% paroxysmal AF | 47.8% prior ablation | **98.8% procedural success** | **Effective closure at 4mo 98.6%**

## Primary Efficacy: Non-Inferiority MET (P < 0.001)

*CV death + stroke + systemic embolism at 3 years*

| WATCHMAN FLX | DOAC | Difference | 95% CI | NI margin |
|---|---|---|---|---|
| 5.7% | 4.8% | 0.9% | -0.8 to 2.6% | 4.8% |

**Note: More ischemic strokes in LAAO arm (45 vs 27) : 3.2% vs 2.0%** — hemorrhagic stroke same for both 0.4%

## Primary Safety: Superiority ACHIEVED (P < 0.001)

*Non-procedural bleeding at 3 years*

| WATCHMAN FLX | DOAC | P |
|---|---|---|
| 10.9% | 19.0% | <0.001 |

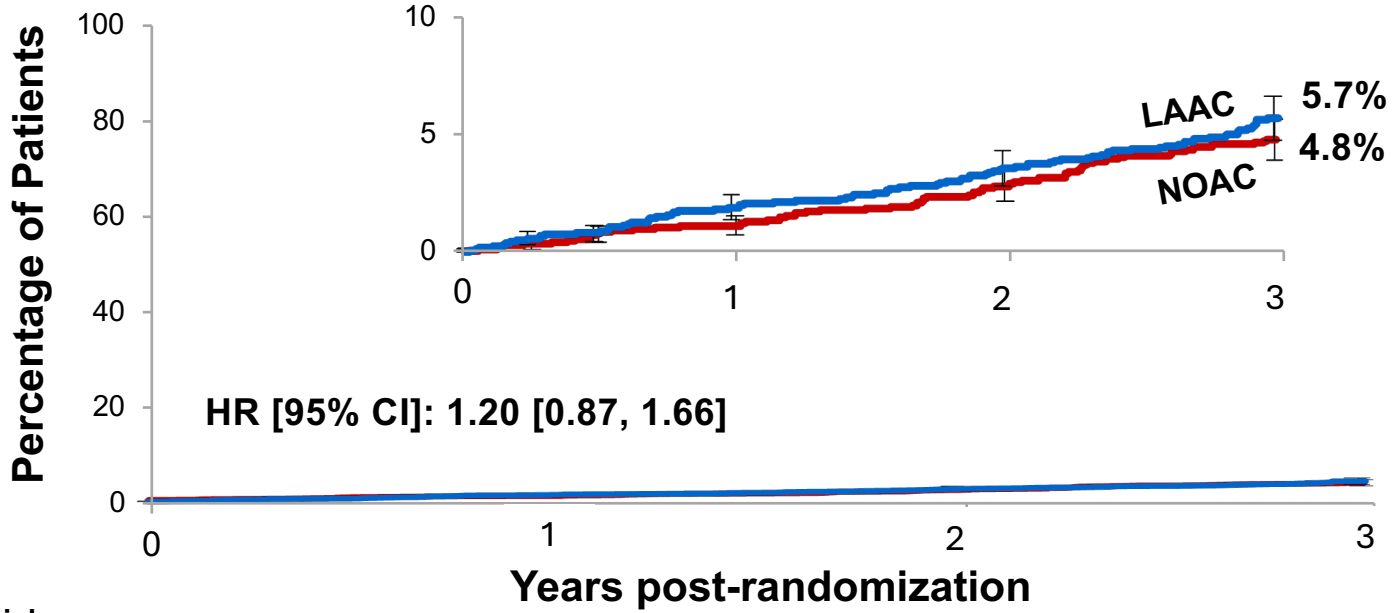
**BUT: Overall ISTH major bleeding (incl. procedural): LAAO 83 vs 87 in DOAC— essentially equal**

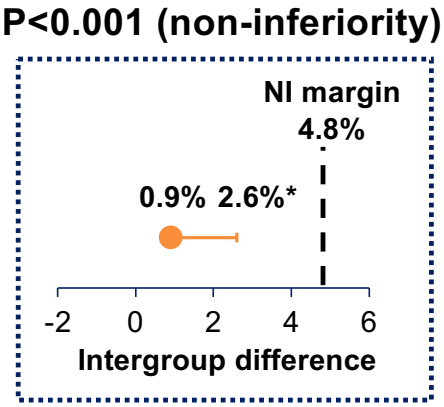


*Doshi SK, Kar S, et al. N Engl J Med. 2026*

# Primary Efficacy Endpoint

## Cardiovascular death, stroke or systemic embolism



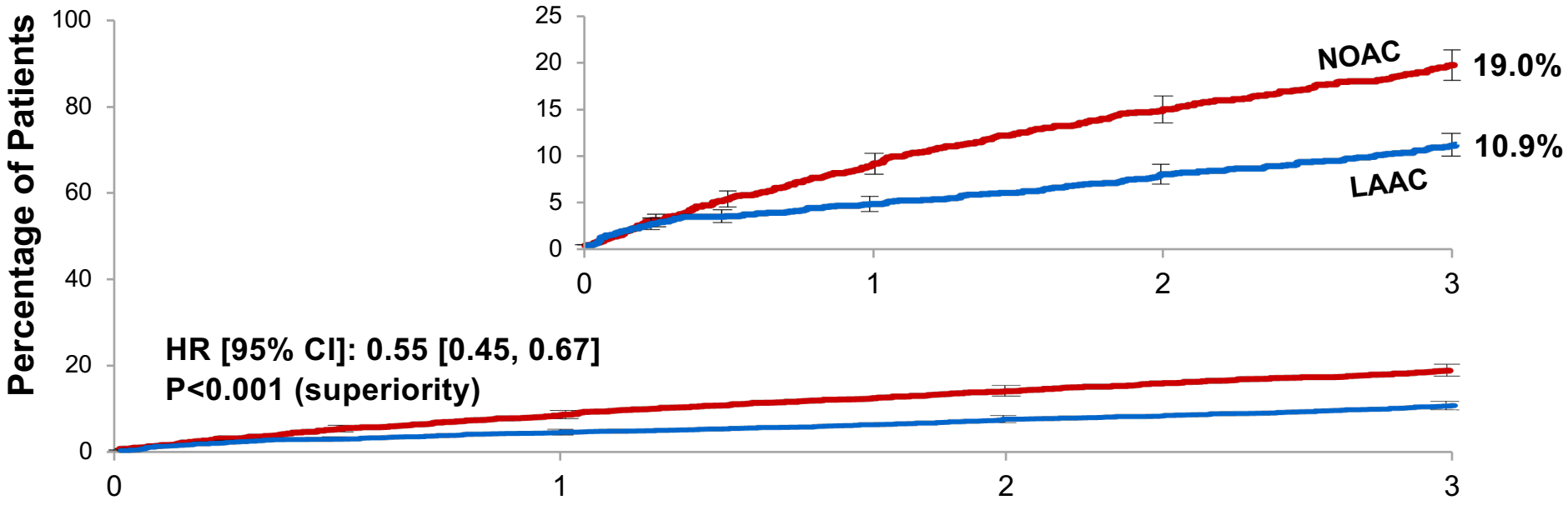

| No. at risk | | | | |
|---|---|---|---|---|
| LAAC | 1499 | 1430 | 1395 | 1326 |
| NOAC | 1501 | 1394 | 1344 | 1254 |

***1-sided 97.5% Z upper confidence bound = 2.6%**
**KM Event Rate ± 1.5 SE**

Doshi S, Kar S et al. N Engl J Med 2026

# Primary Safety Endpoint

## Non-procedural bleeding*




| No. at risk | | | | |
|---|---|---|---|---|
| LAAC | 1499 | 1392 | 1349 | 1252 |
| NOAC | 1501 | 1330 | 1236 | 1093 |

***ISTH major and modified clinically relevant non-major**

**KM Event Rate ± 1.5 SE; log-rank *P* value**

Doshi S, Kar S et al. N Engl J Med 2026

# CHAMPION-AF: My Take-Away Points

- ✓ Watchman device continues to be safe and effective
- ✓ Low bleeding risk patients have a significant cumulative bleeding risk over time
- ✓ Small increase in ischemic stroke in the LAAO arm (~0.3%/year)
- ✓ Small peri-device leak (>0 to ≤3mm) were frequent = 20.3%
- ✓ DOAC post implant should remain the preferred regimen
- ✓ LAAO can now be considered as a first-line alternative to DOAC therapy in select patients

# CLOSURE-AF: Patient Selection Is Key

## CLOSURE-AF (High-Risk)

- 912 pts, single country trial
- Mean age 78 yrs
- Various devices, some older
- "physician directed best medical therapy"

- Mean $CHA_2DS_2$-VASc of 5.2
- Mean HAS-BLED of 3.0

- 80% discharged on DAPT
- 56% of implanted devices have an outdated safety profile (WM 2.5, Amulet, LAmbre)
- **Procedural complications 6%**

**LAAO did NOT meet NI**
HR 1.28 (95% CI: 1.01–1.62)

## CHAMPION-AF (Lower-Risk)

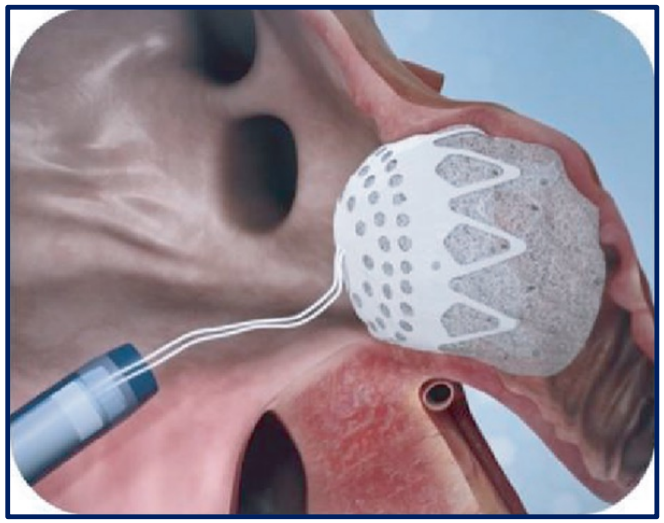
- 3,000 pts, international trial
- Mean age 71.7 yrs
- Watchman FLX

- Mean $CHA_2DS_2$-VASc of 3.5
- Mean HAS-BLED of 1.3

- 85% discharged on DOAC
- **Low procedural complications 1.1%**

**LAAO met NI**
**Non-procedural bleeding superiority**

# Device for LAA Occlusion – Clinical trial resumed



**Conformal Device (Conformal Medical)**

- self-expanding cylindrical nitinol frame
- covered with a polyurethane–carbonate matrix foam
- atraumatic distal end

# LAAOS -4 Trial

- 4000 patients
- 127 sites
- H/o atrial fibrillation with a history of ischemic stroke or systemic embolism
- CHA2DS2-VASc stroke risk score of ≥ 4
- Randomized to watchman + DOAC  vs DOAC alone
- Evaluate if LAAO will help reduce recurrent ischemic stroke

# Take Home Points

1. AF-related stroke can be significantly lowered with OAC
2. DOACs are the mainstay therapy
3. 90% of thrombus comes from the LAA, making it a target for stroke reduction
4. LAA occlusion offers non-pharmacologic alternative for select patients
5. Consideration as first line therapy in select patients (CHAMPION AF)
6. LAAO can be considered in addition to anticoagulation for failed medical therapy