

**Protection thrombo-
embolique mécanique
en FA**



Mise à jour sur la fermeture de l'appendice auriculaire gauche



**CENTRE CARDIOVASCULAIRE
DU CHUM**

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Directeur Médical, Unité des Soins Intensifs Cardiaques
Centre Hospitalier de l'Université de Montréal - CHUM**



CHUM
Centre hospitalier
de l'Université de Montréal

Divulgations

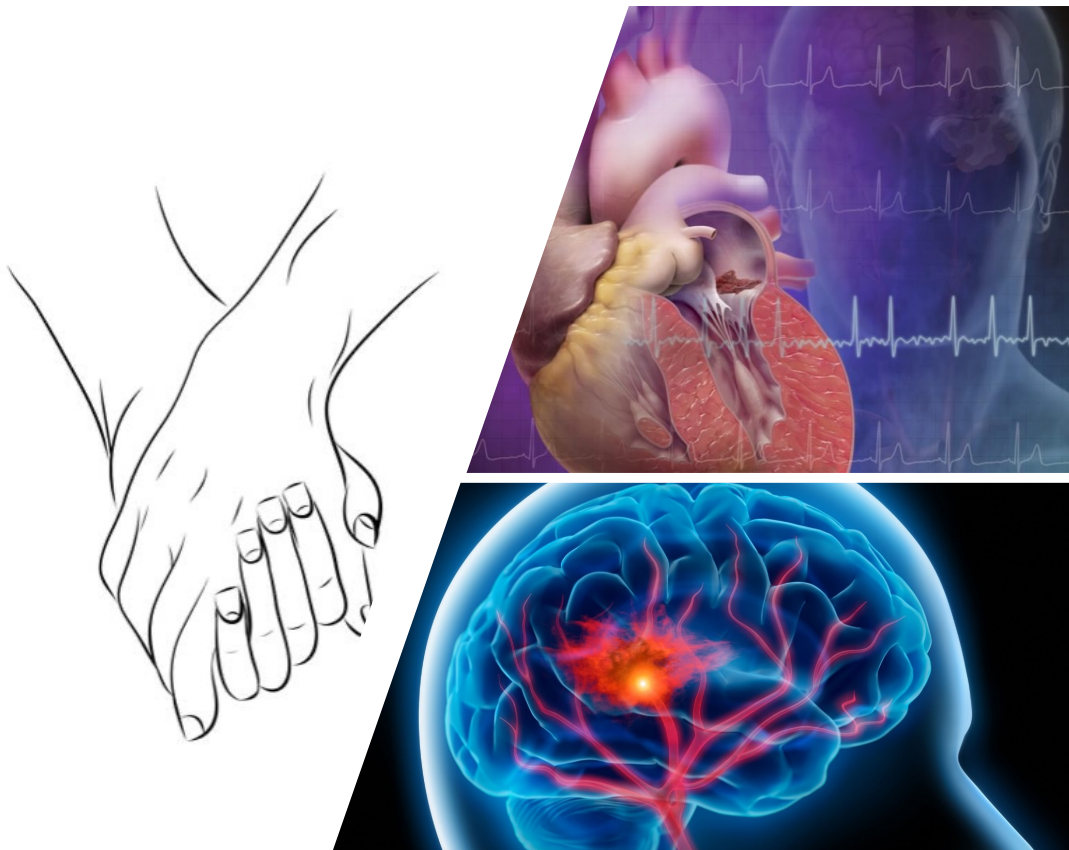
Consultant et conférencier : Boston Scientific

Proctor et conférencier : Abbott

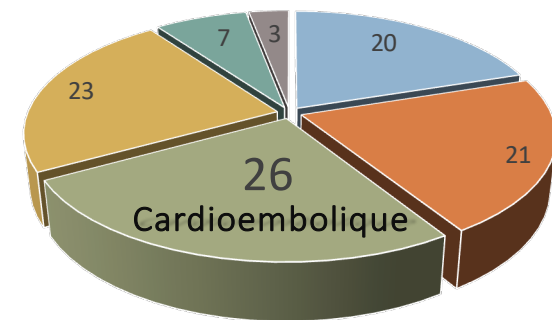
Objectifs

- Revoir la littérature récente concernant la fermeture transcathéter de l'appendice auriculaire gauche (FAAG) en FA
- Discuter des risques et bénéfices de l'intervention
- Identifier les patients susceptibles de bénéficier d'une référence pour évaluation leur candidature à la procédure

AVC ischémiques cardioemboliques



Étiologie des AVC ischémiques



- Lacunaires
- Gros vaisseaux
- Cardioembolique
- Cryptogénique
- Multiple
- Autres

Survie suite à AVC cardioembolique

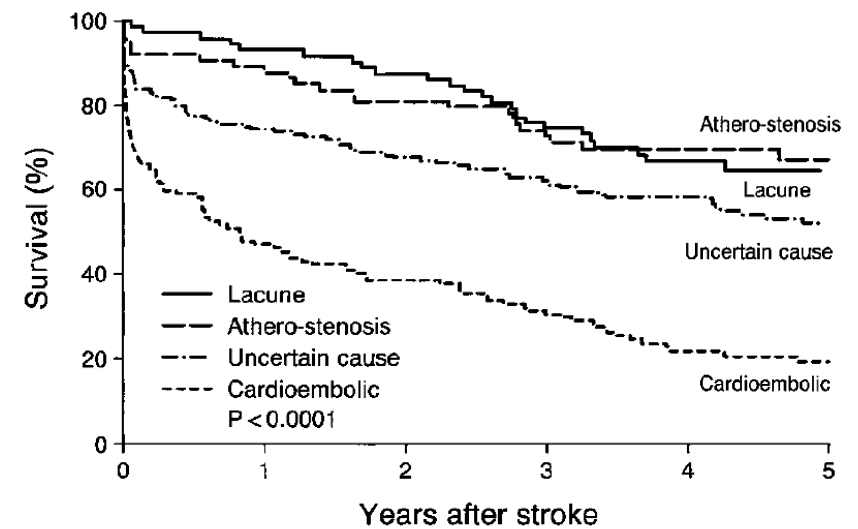
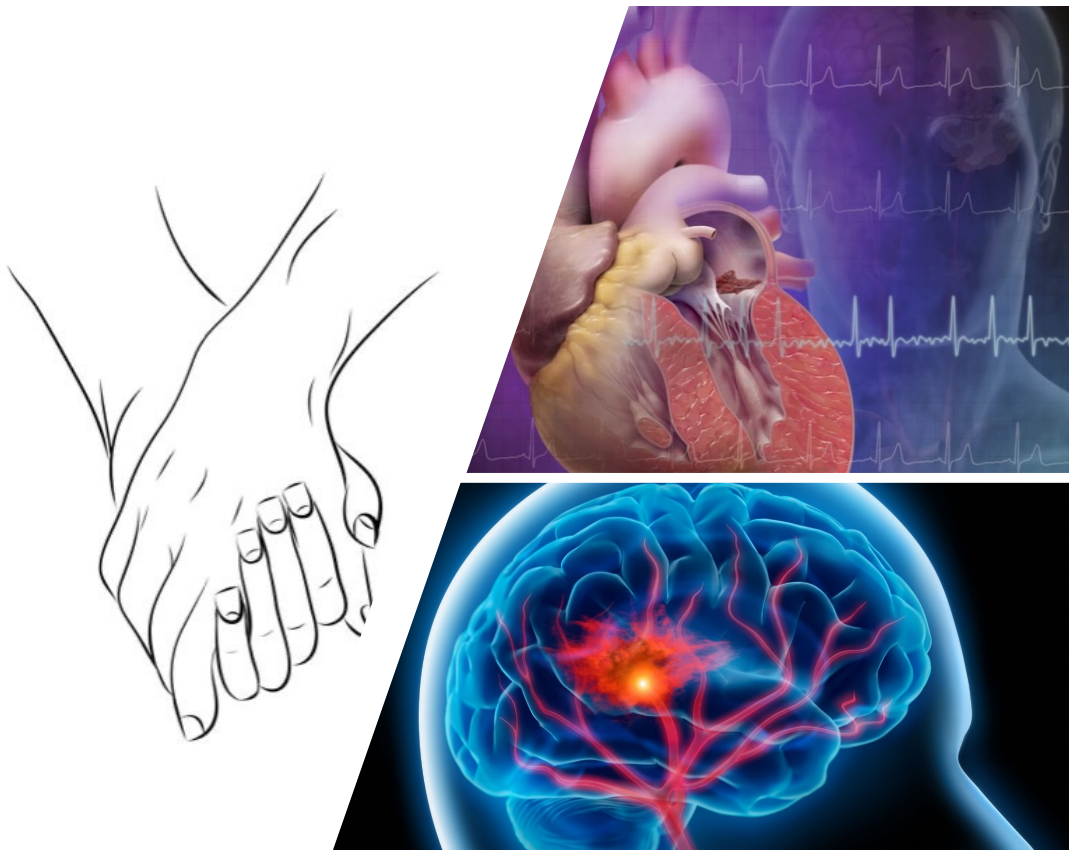


Figure 2. Observed percentage surviving (Kaplan-Meier estimates) after incident ischemic stroke among 442 residents of Rochester, Minnesota, 1985 to 1989, with common ischemic stroke subtypes.

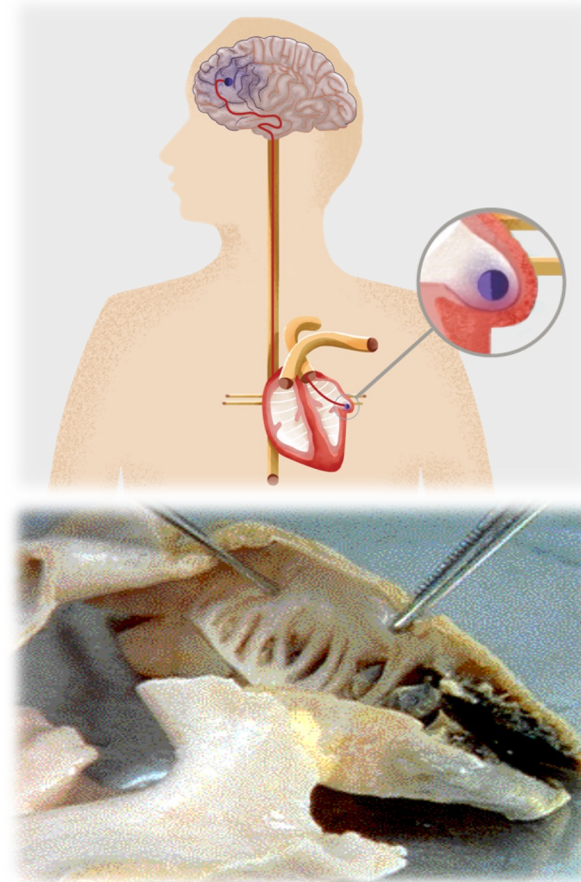
FA et AVC

Responsable du
1/4 des AVC
ischémiques

En FA non
valvulaire, **90%**
des thrombus se
forment dans
l'AAG

Prévalence de FA
et poids
étiologique
augmentent avec
âge

Tolérance aux
anticoagulants
variable



L'évolution des outils



RIVAROXABAN (XARELTO; BAYER)

Usual dose: 20mg od with food. **Bioavailability:** 66% (without food), almost 100% (with food). **Peak plasma level:** 2-4 hrs. **Half-life:** 5-9 hrs (young), 11-13 hrs (elderly). **Renal excretion:** 36%. **Liver metabolism:** yes.

Interactions: Use with strong inhibitors of both CYP3A4 and P-gp, such as azole-antimycotics or HIV protease inhibitors, is not recommended. Co-administration with dronedarone and strong CYP3A4 inducers should be avoided.



DABIGATRAN ETEXILATE (PRADAXA; BOEHRINGER INGELHEIM)

Usual dose: 150mg bid. **Bioavailability:** 3-7%. **Peak plasma level:** 2hrs. **Half-life:** 12-17hrs. **Renal excretion:** 80%. **Liver metabolism:** no.

Interactions: Use with strong P-gp inhibitors ketoconazole, cyclosporine, itraconazole and dronedarone is contraindicated. Use with P-gp inhibitor verapamil requires dose reduction. Use with P-gp inducers should be avoided.



APIXABAN

(ELIQUIS; BRISTOL-MYERS SQUIBB-PFIZER)

Usual dose: 5mg bid. **Bioavailability:** 60%. **Peak plasma level:** 1-4 hrs. **Half-life:** 12 hrs. **Renal excretion:** 27%. **Liver metabolism:** yes.

Interactions: Use with strong inhibitors of CYP3A4 or P-glycoprotein (P-gp) is not recommended. Use with strong inducers of CYP3A4 and P-gp requires caution.

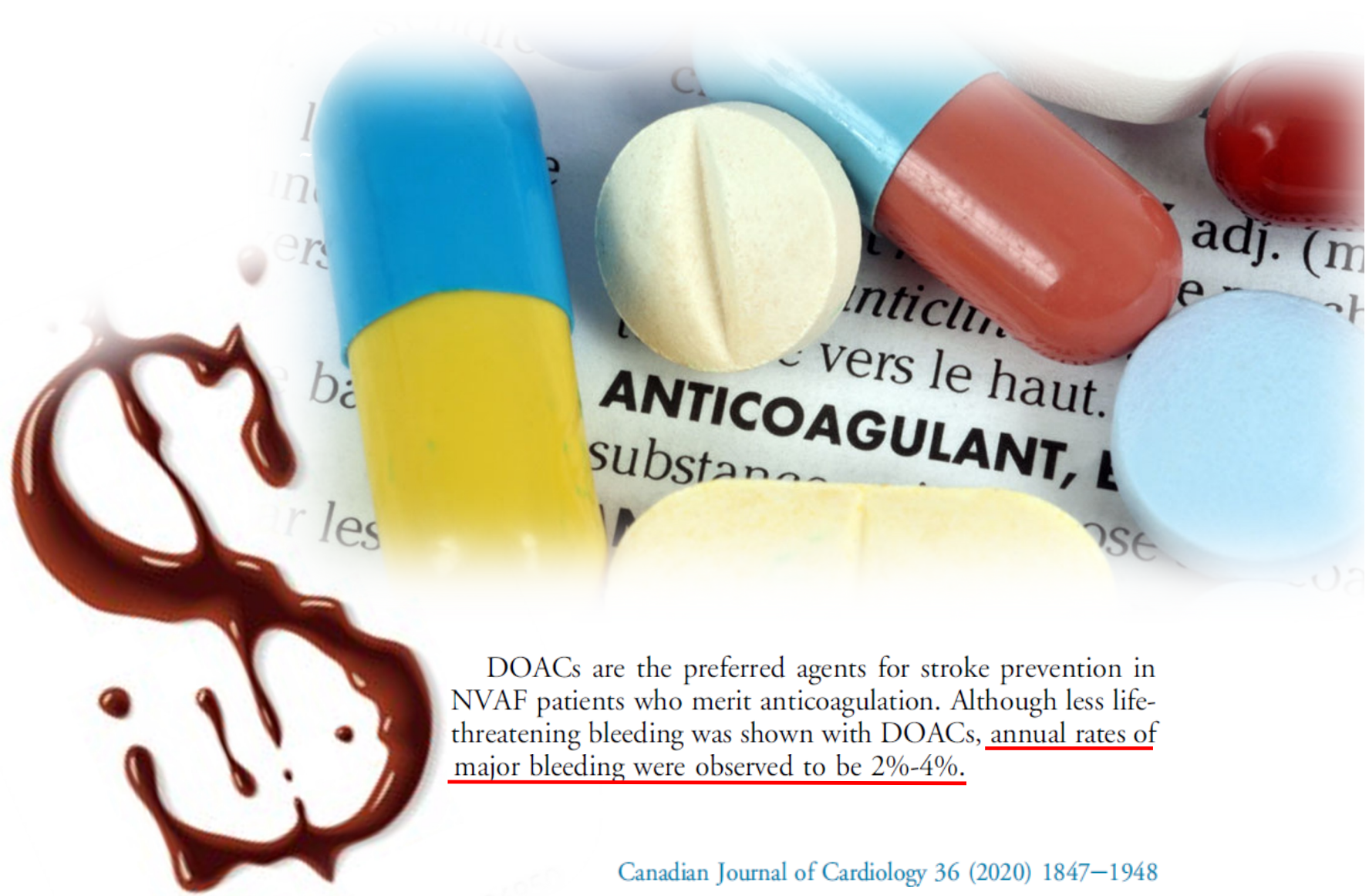


EDOxabAN (LIXIANA; DAIICHI SANKYO UK)

Usual dose: 60 mg od. **Bioavailability:** 62%. **Peak plasma level:** 1-2 hrs. **Half-life:** 10-14 hrs. **Renal excretion:** 50%. **Liver metabolism:** minimal.

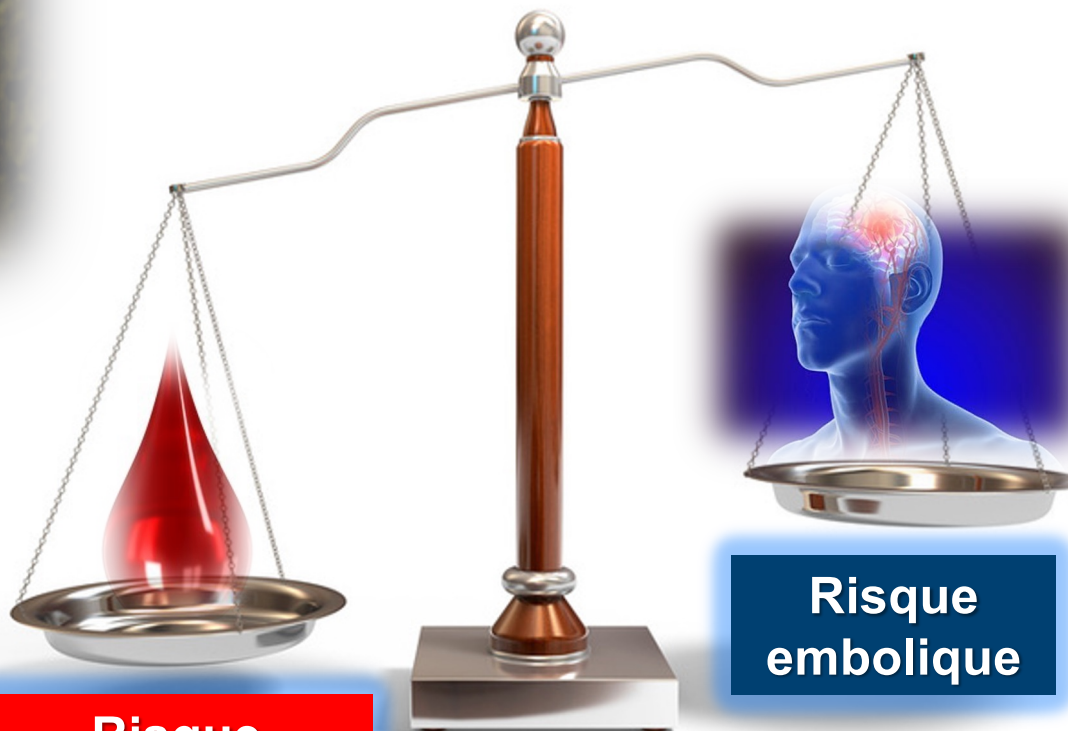
Interactions: Use with the P-gp inhibitors ciclosporin, dronedarone, erythromycin or ketoconazole requires dose reduction to 30mg once daily. Use with caution concomitantly with P-gp inducers (e.g. rifampicin).





DOACs are the preferred agents for stroke prevention in NVAF patients who merit anticoagulation. Although less life-threatening bleeding was shown with DOACs, annual rates of major bleeding were observed to be 2%-4%.

ENTRE L'ARBRE ET L'ÉCORCE



**Risque
hémorragique**

**Risque
embolique**

Dilemme thérapeutique post-saignement sous anticoagulant



Élevé ≥ 3

CHADS ₂ acronym for risk of stroke		Risk factors	
Feature	Score	Letter	Points
(Congestive) Heart failure	1	C	+1
Hypertension	1	H	+1
Aged ≥ 65 years	1	A ₂	+2
Diabetes mellitus	1	D	+1
Stroke/ TIA	2	S ₂	+2
		V	+1
		A	+1
		S	+1

Letter	Clinical characteristic ^a	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Prochaine étape?

Réduire dose NACO?

Changer NACO?

Changer pour Coumadin?

Changer pour ASA?

Rien et tolérer risque embolique?

Bleeding while on OAC

Initiate OAC as soon as possible after the cause of bleeding has been identified and corrected⁸
Re-evaluate concomitant medications which may contribute to bleeding (e.g. ASA, NSAIDs)

62. We recommend that anticoagulant therapy should be recommenced in patients at high risk of stroke as soon as possible after the cause of bleeding has been identified and corrected (Strong Recommendation; Moderate-Quality Evidence).

Values and preferences. This recommendation places a relatively high value on the recognition that OAC discontinuation after a bleeding event is associated with a significant increase in the risk of stroke and all-cause mortality.

Approche des cliniciens du CHUM



Brouillard et al. *Real-world management strategies of anticoagulated atrial fibrillation patients following a clinically significant bleeding episode*

Cohorte 01-2017 à 12-2019

N = 252 patients avec FA non valvulaire anticoagulée admis pour saignement entre le 1er Janvier 2017 et le 31 décembre 2019

14% décès intrahospitaliers

Décès per-hospitalisation: 33
Autre indication d'ACO: 24
Saignement péri-procédure: 53
Quitte contre avis medical: 2

Cohorte analysée
N=140 patients

Approche des cliniciens du CHUM



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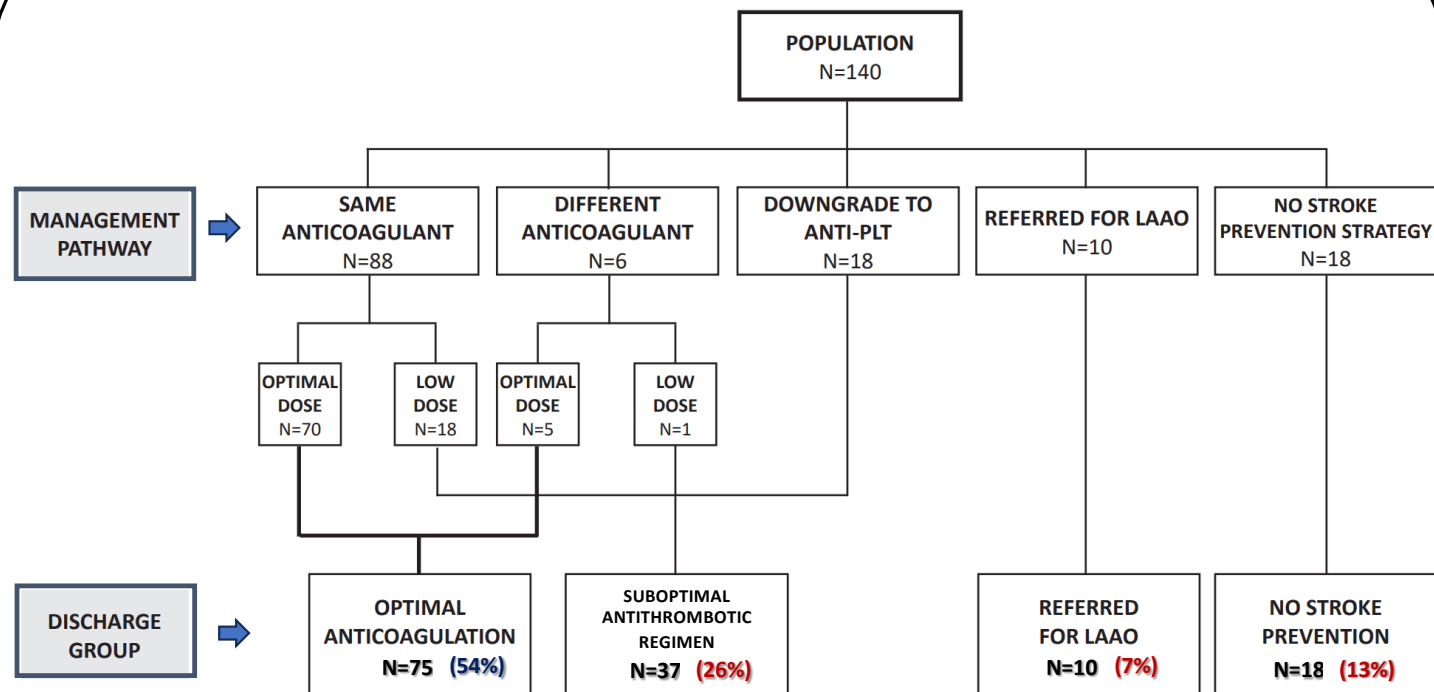
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Cohorte analysée
N=140 patients

Stratégie de protection embolique retenue au congé



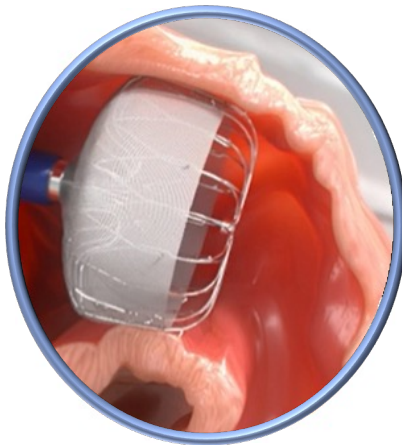
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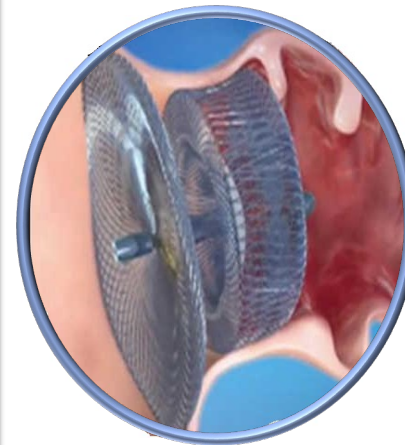
Issue clinique	Anticoagulation optimale N = 75	Thérapie anti- thrombotique sous optimale N = 37	Aucune prévention thromboembolique N = 18	P
Mortalité toute cause	19 (25.3)	11 (29.7)	7 (38.9)	0.71
Réadmission pour saignement	26 (34.7)	10 (27)	0 (0)	0.01
Réadmission pour événement thromboembolique	0 (0)	1 (2.7)	3 (16.7)	0.06

Besoin clinique



Patients avec FA non-valvulaire, indication de protection thrombo-embolique et:

- ✓ Saignements récidivants sous anticoagulant
- ✓ ATCD de saignement majeur
- ✓ Haut risque de saignement
- ✓ AVC sous anticoagulant (auricule malin)
- ✓ Chez qui anti-plt privilégiés
- ✓ Préférence du patient



Occlusion AAG: rationnelle

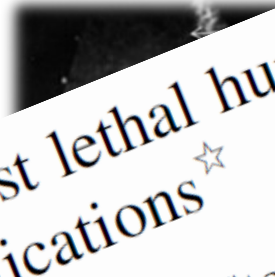
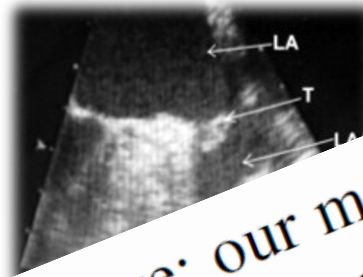
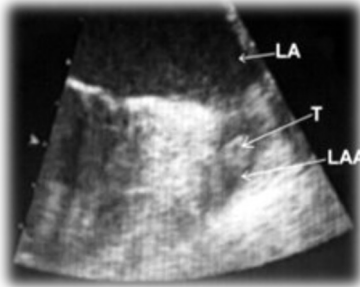


TABLE 1. Review of Published Literature on the Frequency and Site of Thrombus in the Nonrheumatic Atrial Appendage

Study	No. of Patients	LA (%)	LAA (%)	LA + LAA (%)
W. Dudley Johnson ^{a,*}	35	12 (34.3)	23 (65.7)	35 (100.0)
A.K. Ganjoo ^b	47	2 (4.3)	45 (95.7)	47 (100.0)
Christopher D. Stone ^c	13	1 (7.7)	12 (92.3)	13 (100.0)
Ramahalli C. Srivayas ^a	171	8 (4.7)	163 (95.3)	171 (100.0)
Mary Howard ^{a,d}	549	67 (12.2)	482 (87.8)	549 (100.0)
Other studies	272	19 (7.0)	253 (93.0)	272 (100.0)
TEE	60	6 (10.0)	54 (90.0)	60 (100.0)
Total	2208	249 (11.3)	1959 (88.7)	2208 (100.0)

The left atrial appendage: our most lethal human attachment! Surgical implications

Sur 2208 patients en FA, 12.6% ont du thrombus dans l'OG qui est retrouvé 90% du temps (249/278) dans l'auricule gauche

Occlusion AAG: littérature

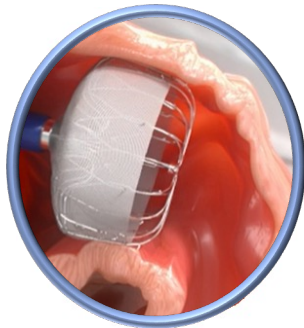


Table 9. WATCHMAN studies.

Study details			Patient details				Efficacy				Safety				
First author and dates of publication	RCT or registry	Number of patients with device	Mean age	Mean CHADS ₂ /CHADS ₂ -VASC score	% ineligible for OAC	Mean FU (months)	Implant success	Major leak	All stroke	Ischaemic stroke/SE	SAE in first 7 days	Effusion+	Embolisation	Procedure-related stroke	Procedure-related death
Holmes 2009 ¹⁰⁶ Reddy 2014 ¹⁰⁷	MRCT	463	71.7±8.8	2.2±1.2/3.4	0	18±10 45±20	88.0%	8% at 6-month TOE	2.3/100 patient years 1.5/100 patient years	2.5/100 patient years 1.6/100 patient years	7.7%	4.1%	0.6%	0.9%	0
Holmes 2014 ¹⁰⁸	MRCT	269	74±4	2.6±1.0/ 3.8±1.2	0	11.8±5.8	95.1%		2.3% patients during FU	2.3% patients during FU	4.2%	1.9%	0.7%	0.4%	0
Reddy 2017 ⁶	Meta-analysis of 2 RCTs	732	72.6±8.4	2.3±1.1/ 3.6±1.4	0	4,343 patient years	95.4%		1.77 per 100 patient years	1.6 per 100 patient years					
Reddy 2011 ⁹⁸	MReg	460	74±8	2.2±1.2	0		95.0%				3.7%	2.2%	0	0	0
Reddy 2013 ¹⁰⁹	MReg	150	72.5±7.4	2.8±1.2/ 4.4±1.7	100%	14.4±8.6	95.0%		2.3 per 100 patient years	1.7 per 100 patient years		1.3%	1.3%	0	0
Boersma 2016 ¹¹² , 2017 ⁹⁵	MReg	1,021	73±9	2.8±1.3/ 4.5±1.6	62%	12 months	98.5%	0.7%	Ischaemic stroke 1.1% per year	Ischaemic stroke/TIA/ SE=1.5% per year	2.8%	0.4%	0.2%	0.1%	0.1%
Reddy 2017 ¹¹³	MReg	3,822					95.6%					1%	0.24	0.08%	0.08%

+ needing intervention (drainage or surgery). FU: follow-up; MReg: multicentre registry; (M)RCT: (multicentre) randomised controlled trial

Occlusion AAG: littérature

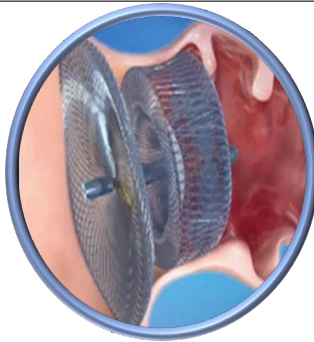


Table 10. AMPLATZER studies.

Study details				Patient details				Efficacy				Safety				
First author and dates of publication	RCT or registry	Device	Number of patients with device	Mean age	Mean CHADS ₂ /CHADS ₂ -VASC score	% ineligible for OAC	Mean FU (months)	Implant success	Major leak	All stroke	Ischaemic stroke / SE / TIA	SAE in first 7 days	Effusion+	Embolisation	Procedure-related stroke	Procedure-related death
Nietlispach 2013 ⁷²	SReg	ACP+Nded Dev.	152	72±10	3.4±1.7	76%	32 (up to 120)	96.1% 99.2% in ACP group	0.7%	0.5%/year		7.2% overall, 3.3% in ACP	2.6%	3.9%; 0.8% in ACP group	0.7%	0.0%
Tzikas 2016 ¹¹⁴	MReg	ACP	1,047	7±8	2.8±1.3/ 4.5±1.6	73%	13	97.3%	1.9%		Stroke or TIA 2.3% per year	5%	0.5%	0.8%	0.9%	0.8%
Lopez-Minguez 2015 ¹¹⁵	MReg	ACP	167	74.7±8.6	3/4	100%	22±8.3	94.6%	8.2%	–	Stroke or TIA 2.4% per year	5.4%	1.2%	0.6%	0	0
Urena 2013 ¹²⁹	MReg	ACP	52	74±8	3/–	100%	20±5	98.1%	0	1 ischaemic stroke and 1 TIA during FU		5.8%	1.9%	1.9%	0	0
Berti 2017 ¹¹⁸	MReg	ACP+Am	613	75.1±8.0	–/4.2±1.5	84.5%	20	95.4%	0.5%	1.8 per 100 patient years	Stroke or TIA 2.45% per year	6.2%		0.7%		0
Landmesser 2017 ⁹⁷ and 2018 ¹¹⁶	MReg	Am	1,088	75±8.5	–/4.2±1.6	83%	12	99.0%	1.8%	2.9% per year		3.6%	1.2%	0.1%	0.4%	0.2%
Kleinecke 2017 ¹¹⁷	SReg	Am	50	76.1±8.3	–/5.2±1.8	24%	12	98.0%	0	6 ischaemic strokes per 100 patient years		8%	4%	2.0%	0	0
Nielsen-Kudsk 2017 ¹¹⁹	MReg (ICH patients)	ACP+Am	151	72±8.7	–/3.9	100%	6	97.7%	–	17 (vs 81) ischaemic strokes per 1,000 patient years 116 (vs 95) recurrent ICH per 1,000 patient years		4%	0.7%	0.7%	0.7%	0

ACP: AMPLATZER Cardiac Plug; AM: Amulet; FU: follow-up; ICH: intracranial haemorrhage; MRCT: multicentre randomised controlled trial; MReg: multicentre registry; Nded Dev.: non-dedicated devices for LAAO (AMPLATZER PFO, ASD, VSD Occluder); OAC: oral anticoagulation; SAE: serious adverse event; SReg: single-centre registry; TIA: transient ischaemic attack

Occlusion AAG: recommandations



2020 ESC guidelines for the diagnosis and management of AF

2019 AHA/ACC/HRS focused update on the management of patients with AF

Percutaneous LAA occlusion	May be considered in patients with AF and contraindications for long term OAC therapy COR: IIb LOE: B	May be considered in patients with AF and contraindications for long term OAC therapy COR: IIb LOE: B-NR
Surgical LAA occlusion/exclusion	Surgical occlusion or exclusion of the LAA may be considered in patients with AF undergoing cardiac surgery. COR: IIb LOE: C	Surgical occlusion of the LAA may be considered in patients with AF undergoing cardiac surgery. COR: IIb LOE: B-NR

Canadian Journal of Cardiology 36 (2020) 1847–1948

Society Guidelines

The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines Management of Atrial Fibrillation

We suggest that percutaneous LAAO be considered for stroke prevention in patients with NVAf who are at moderate to high risk of stroke and have absolute contraindications to OAC (Weak Recommendation; Low-Quality Evidence).

- ✓ Saignements intracrâniens non-traumatiques à haut risque de récurrence
- ✓ Saignements récidivants sans cause réversible a/n pulmonaire, génito-urinaire, GI, rétropéritonéal, intraoculaire, de varices œsophagiennes
- ✓ Télangiectasie hémorragique héréditaire (syndrome Osler-Weber-Rendu)

Left Atrial Appendage Closure Versus Direct Oral Anticoagulants in High-Risk Patients With Atrial Fibrillation

PRAGUE-17

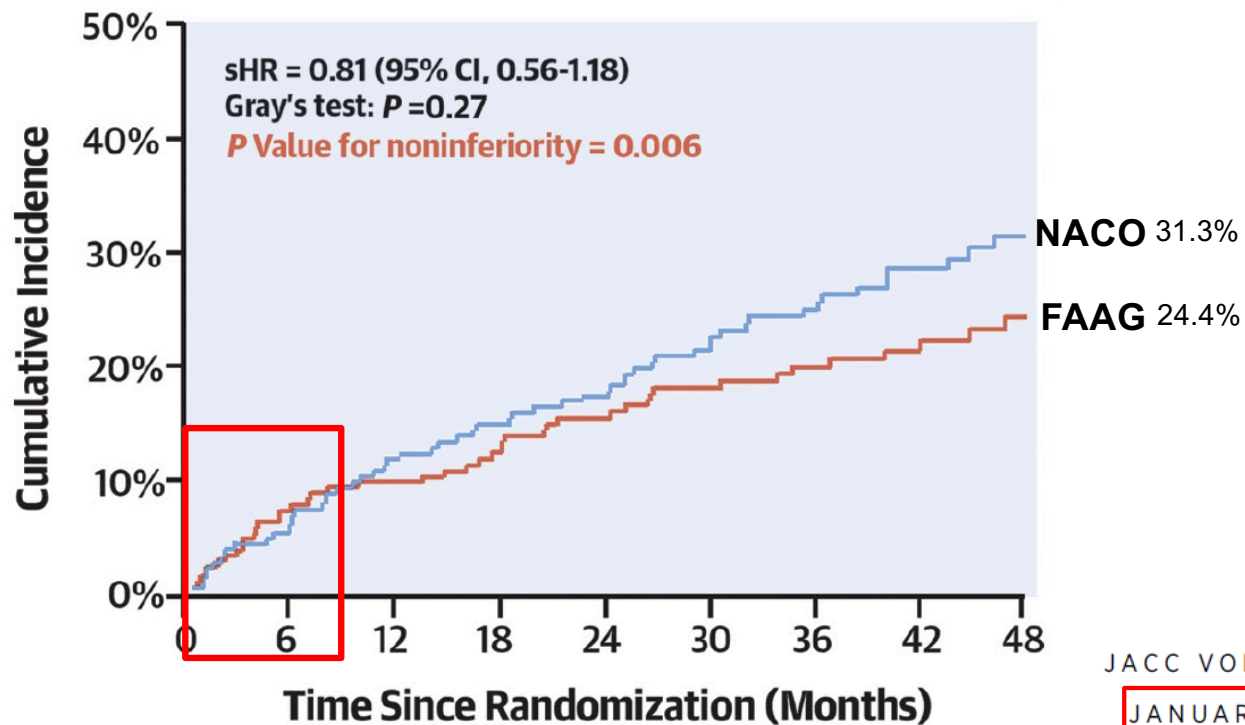
JACC VOL. 75, NO. 25, 2020

JUNE 30, 2020:3122-35

- ✓ Étude randomisée-contrôlée Occlusion AG (61% Amulet vs 36% WM) vs NOAC (96% Apixaban)
- ✓ 402 patients (73a, CHADSVASC 4.7, HAS-BLED 3) avec FA non-valvulaire + indication d'anticoagulation ET l'un des scénarios suivants:
 - Hx de saignement nécessitant intervention ou hospitalisation (n=192)
 - Profil embolique et hémorragique à risque (CHADSVASC ≥ 3 + HAS-BLED ≥ 2) (n=112)
 - Événement cardioembolique sous anticoagulant (n=142)

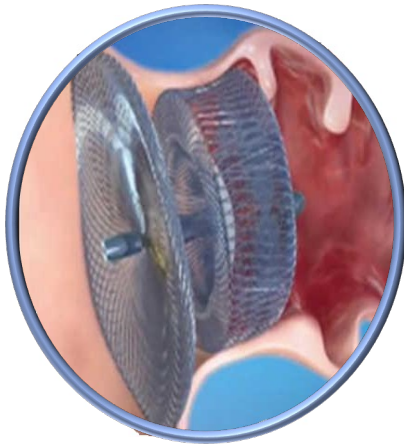
4-Year Outcomes After Left Atrial Appendage Closure Versus Nonwarfarin Oral Anticoagulation for Atrial Fibrillation PRAGUE-17

Primary Endpoint
Stroke, TIA, SE, CV Death, Bleeding or Complications



JACC VOL. 79, NO. 1, 2022

JANUARY 4/11, 2022:1-14



Clinical Outcomes Associated With Left Atrial Appendage Occlusion Versus Direct Oral Anticoagulation in Atrial Fibrillation

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 14, NO. 1, 2021

JANUARY 11, 2021:69-78

pairage par score de propension

Amulet vs NACO

N=1071

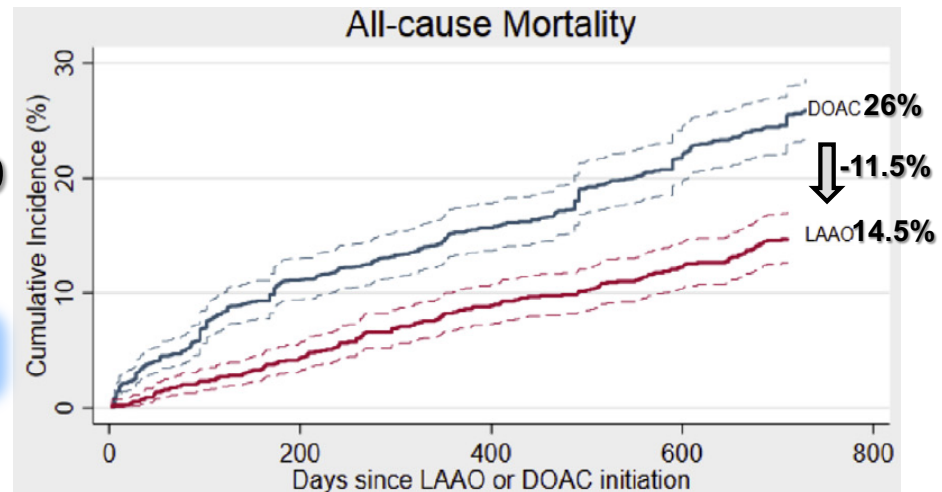
N=1184

Bénéfice significatif sur mortalité toute cause

Mortalité toute cause ↓ 47%

HR 0.53 (95%CI 0.43-0.64)

Suivi à 2 ans





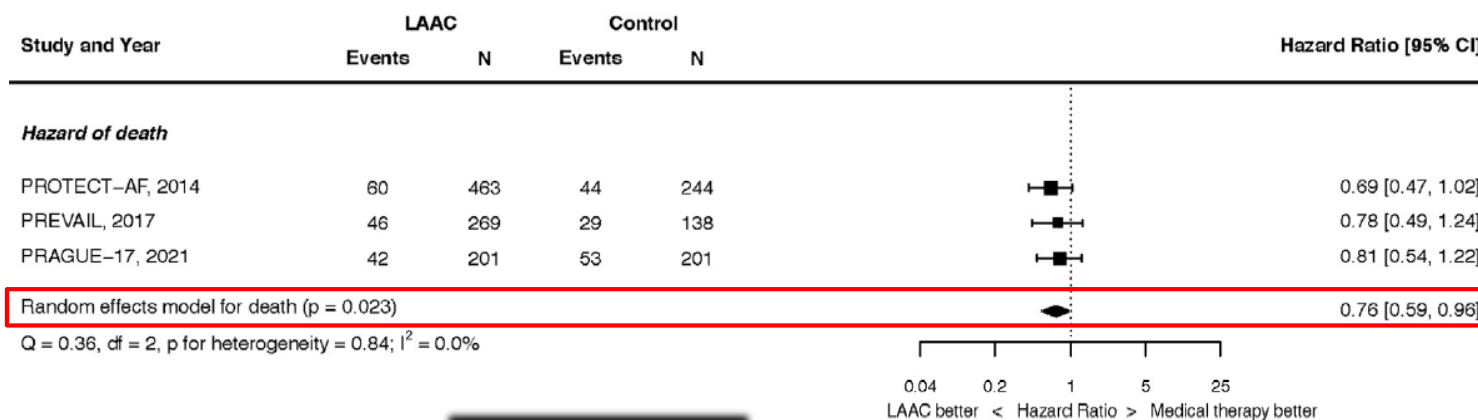
Long-Term Outcomes of Randomized Controlled Trials Comparing Percutaneous Left Atrial Appendage Closure to Oral Anticoagulation for Nonvalvular Atrial Fibrillation: A Meta-Analysis

Yousif Ahmad, MRCP, PhD

Structural Heart Accepted 17 August 2022

Meta-analyse des 3 études randomisées PROTECT-AF et PREVAIL (FAAG WM vs Coumadin) PRAGUE-17 (FAAG vs Apixaban)

Bénéfice significatif sur mortalité toute cause



Mortalité toute cause ↓ **24%**
HR 0.76 (95%CI 0.59-0.96)

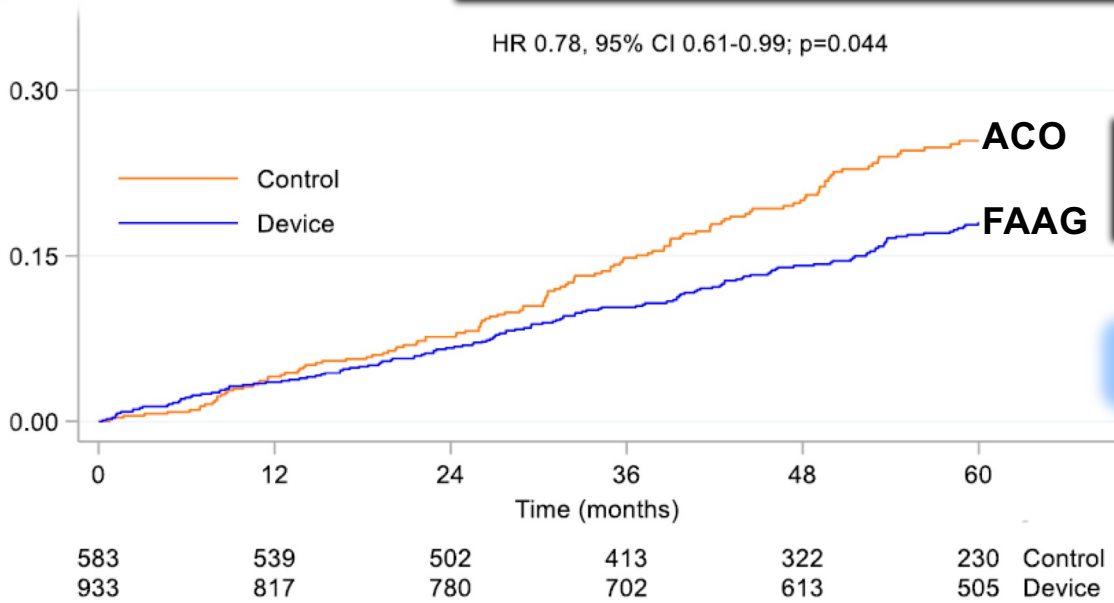
Suivi à ~4 ans



Percutaneous left atrial appendage closure versus oral anticoagulation for non-valvular atrial fibrillation: an individual patient data meta-analysis of randomized controlled trials Yousif Ahmad

CRF
TCT 10-2023

933 FAAG vs 201 NACO + 382 VKA



Mortalité toute cause ↓ 22%
HR 0.78 (95%CI 0.61-0.99)

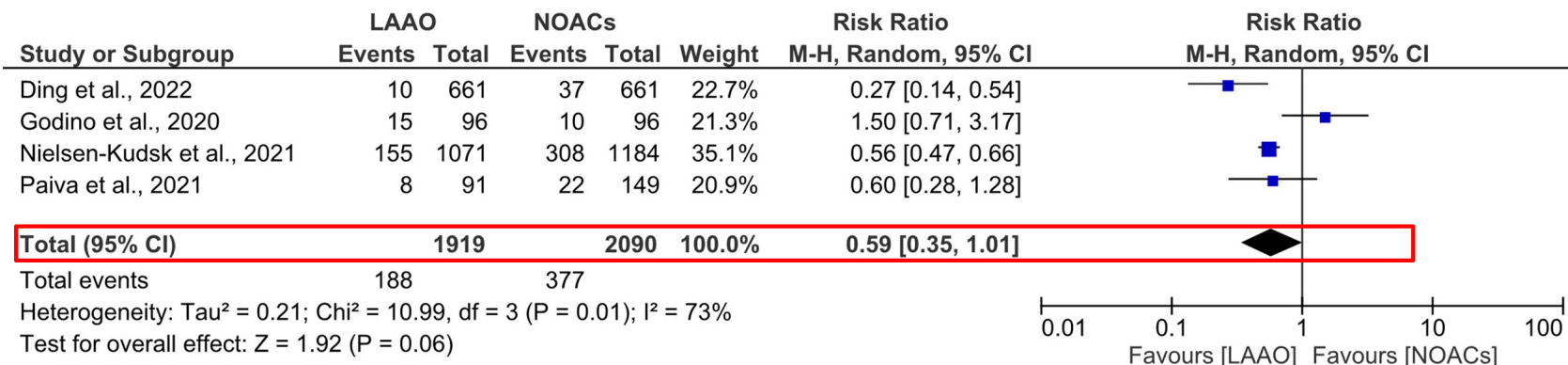
Suivi à 5 ans



Head-to-head comparison between left atrial appendage occlusion and non-vitamin K oral anticoagulants in non-valvular atrial fibrillation patients: A systematic review and meta-analysis study

Waranugraha et al. *Trends in Cardiovascular Medicine*, ePub 02-2023

**5 études (1 RCT, 4 cohortes avec score de propension)
2021 FAAG vs 2291 NACO**



**Mortalité
toute cause**

↓ 41%

Suivi à 1.5-2 ans

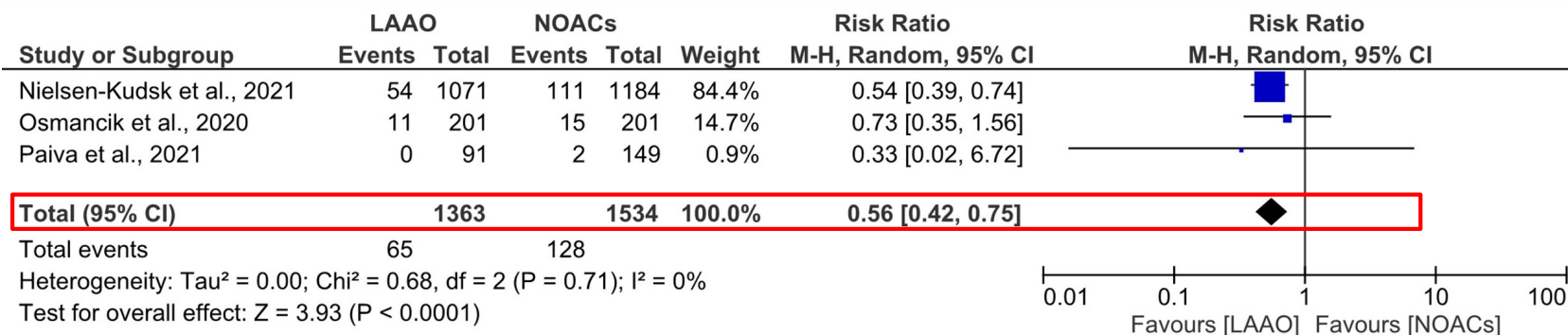
HR 0.59 (95%CI 0.35-1.01) p=0.06



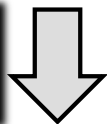
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Waranugraha et al. *Trends in Cardiovascular Medicine*, ePub 02-2023

**5 études (1 RCT, 4 cohortes avec score de propension)
2021 FAAG vs 2291 NACO**



**Mortalité
cardiovasc**



44%

Suivi à 1.5-2 ans

HR 0.56 (95%CI 0.42-0.75) p<0.01



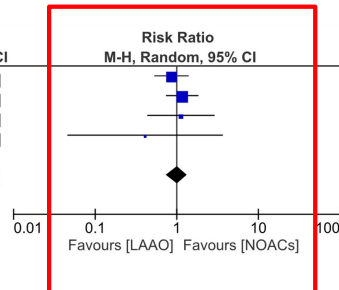
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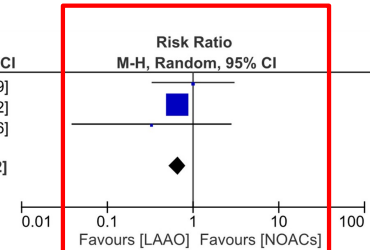
(A) Stroke or transient ischemic attack

Study or Subgroup	LAAO		NOACs		Weight	Risk Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
Ding et al., 2022	31	661	36	661	41.3%	0.86 [0.54, 1.37]
Nielsen-Kudsk et al., 2021	39	1071	37	1184	46.3%	1.17 [0.75, 1.81]
Osmancik et al., 2020	9	201	8	201	10.4%	1.13 [0.44, 2.86]
Paiva et al., 2021	1	91	4	149	1.9%	0.41 [0.05, 3.61]
Total (95% CI)		2024		2195	100.0%	1.00 [0.74, 1.36]
Total events	80		85			
Heterogeneity: Tau ² = 0.00; Chi ² = 1.56, df = 3 (P = 0.67); I ² = 0%						
Test for overall effect: Z = 0.03 (P = 0.98)						



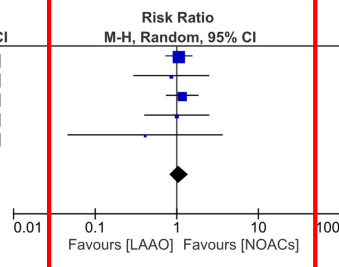
(A) Major bleeding

Study or Subgroup	LAAO		NOACs		Weight	Risk Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
Godino et al., 2020	6	96	6	96	3.9%	1.00 [0.33, 2.99]
Nielsen-Kudsk et al., 2021	108	1071	183	1184	95.0%	0.65 [0.52, 0.82]
Paiva et al., 2021	1	91	5	149	1.0%	0.33 [0.04, 2.76]
Total (95% CI)		1258		1429	100.0%	0.66 [0.53, 0.82]
Total events	115		194			
Heterogeneity: Tau ² = 0.00; Chi ² = 0.98, df = 2 (P = 0.61); I ² = 0%						
Test for overall effect: Z = 3.76 (P = 0.0002)						



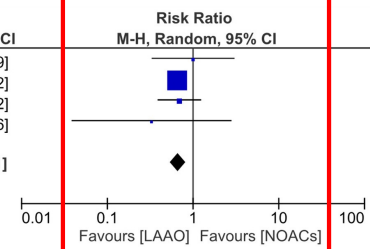
(B) Stroke or thromboembolic events

Study or Subgroup	LAAO		NOACs		Weight	Risk Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
Ding et al., 2022	54	661	51	661	49.9%	1.06 [0.73, 1.53]
Godino et al., 2020	6	96	7	96	6.1%	0.86 [0.30, 2.46]
Nielsen-Kudsk et al., 2021	39	1071	37	1184	34.4%	1.17 [0.75, 1.81]
Osmancik et al., 2020	9	201	9	201	8.2%	1.00 [0.41, 2.47]
Paiva et al., 2021	1	91	4	149	1.4%	0.41 [0.05, 3.61]
Total (95% CI)		2120		2291	100.0%	1.06 [0.82, 1.37]
Total events	109		108			
Heterogeneity: Tau ² = 0.00; Chi ² = 1.08, df = 4 (P = 0.90); I ² = 0%						
Test for overall effect: Z = 0.45 (P = 0.66)						



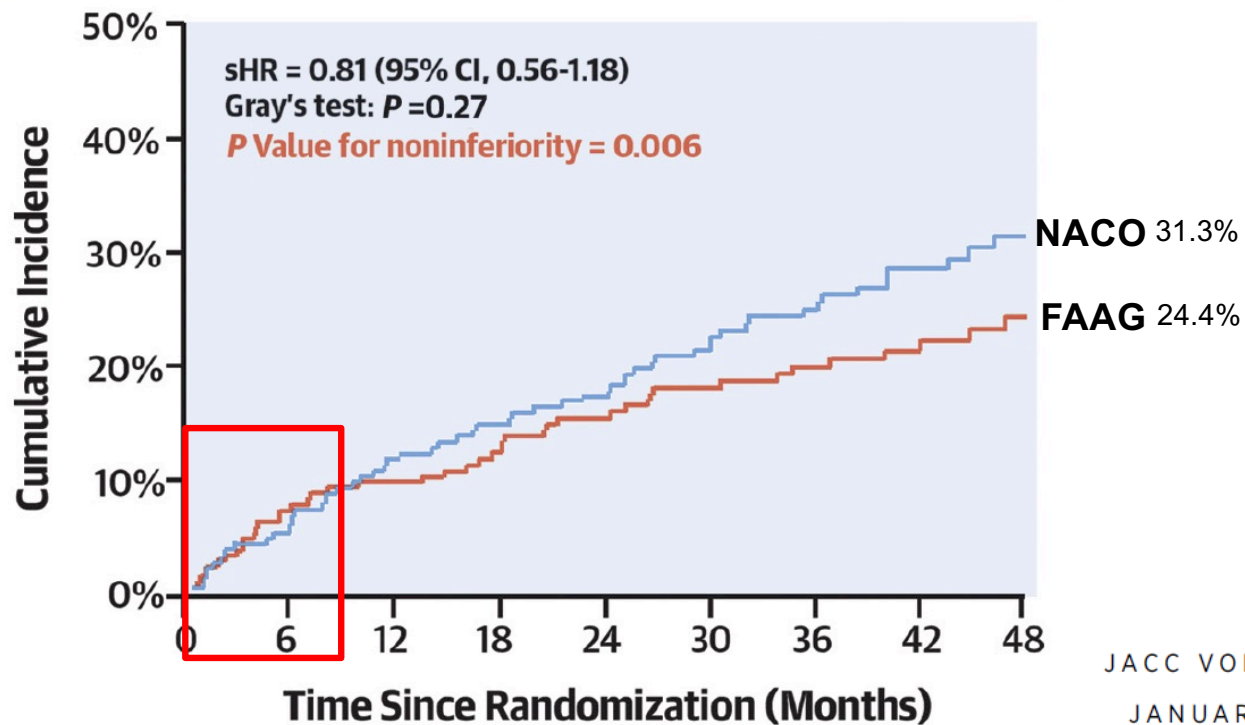
(B) Major or non-major bleeding

Study or Subgroup	LAAO		NOACs		Weight	Risk Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
Godino et al., 2020	6	96	6	96	3.4%	1.00 [0.33, 2.99]
Nielsen-Kudsk et al., 2021	108	1071	183	1184	82.9%	0.65 [0.52, 0.82]
Osmancik et al., 2020	18	201	26	201	12.8%	0.69 [0.39, 1.22]
Paiva et al., 2021	1	91	5	149	0.9%	0.33 [0.04, 2.76]
Total (95% CI)		1459		1630	100.0%	0.66 [0.54, 0.81]
Total events	133		220			
Heterogeneity: Tau ² = 0.00; Chi ² = 1.00, df = 3 (P = 0.80); I ² = 0%						
Test for overall effect: Z = 3.97 (P < 0.0001)						

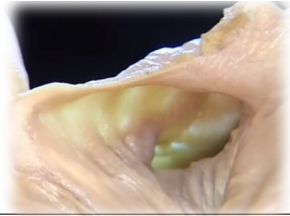


4-Year Outcomes After Left Atrial Appendage Closure Versus Nonwarfarin Oral Anticoagulation for Atrial Fibrillation PRAGUE-17

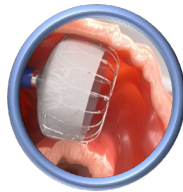
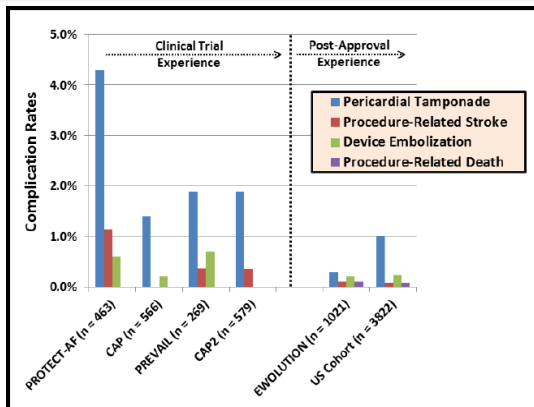
Primary Endpoint
Stroke, TIA, SE, CV Death, Bleeding or Complications



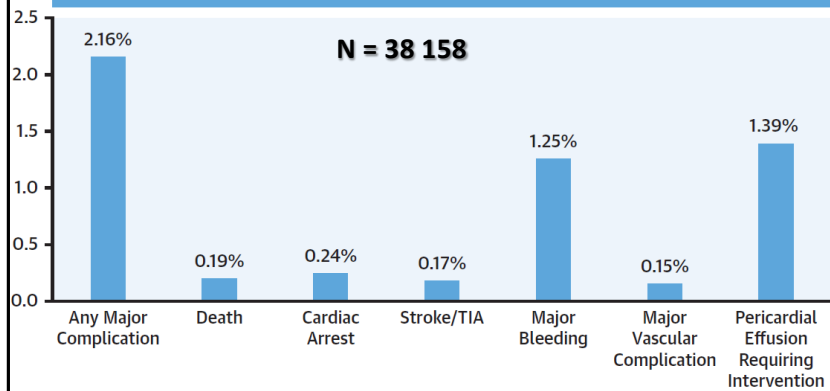
Occlusion AAG: complications péri-procédurales



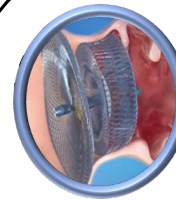
Expérience Watchman



In-Hospital Adverse Event Rates in the NCDR LAO Registry

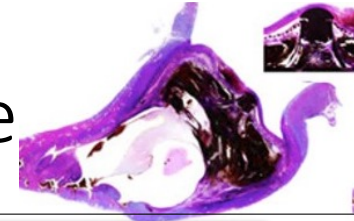


Expérience ACP/Amulet



	ACP registry N = 1047	Amulet registry N = 1074
Mortalité	0.75%	0.3%
AVC	0.86%	0.3%
Tamponnade	1.24%	0.5%
Embolisation	0.67%	0.1%
Saignement majeur	1.24%	0.9%
Autres	0.5%	0.7%
Total	5.26%	2.7%

Occlusion AAG: complications suivi court terme



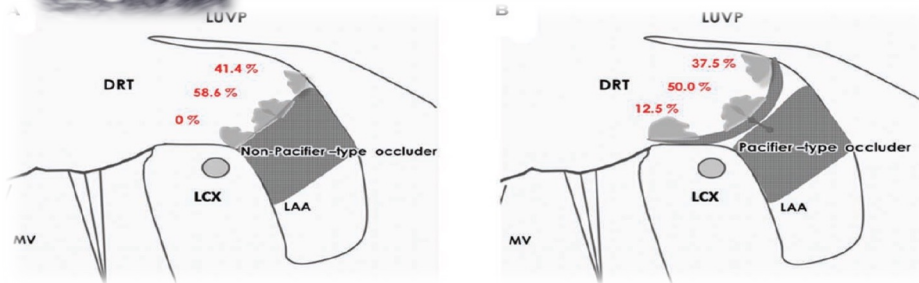
Thromboses de dispositif



Device-Related Thrombus After Left Atrial Appendage Closure

Data on Thrombus Characteristics, Treatment Strategies, and Clinical Outcomes From the EUROC-DRT-Registry

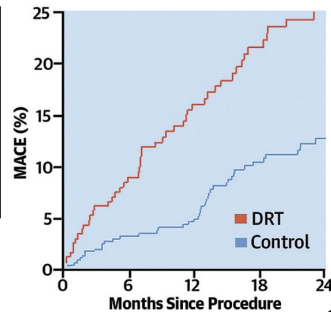
Sedaghat et al *Circ Cardiovasc Interv.* 2021;14:e010195. May 2021



Incidence 1.5% ad 15%, découverte parfois tardive (>6m)

Major Risk Factors	
• Iatrogenic pericardial effusion	1 major risk factor
• Hypercoagulable state	
OR	
Minor Risk Factors	
• Deep LAAO implant (>10mm from pulmonary ridge)	2 minor risk factors
• Renal insufficiency	
• Non-paroxysmal AF	

Simard et al. *JACC* 2021;78(4):297-313.

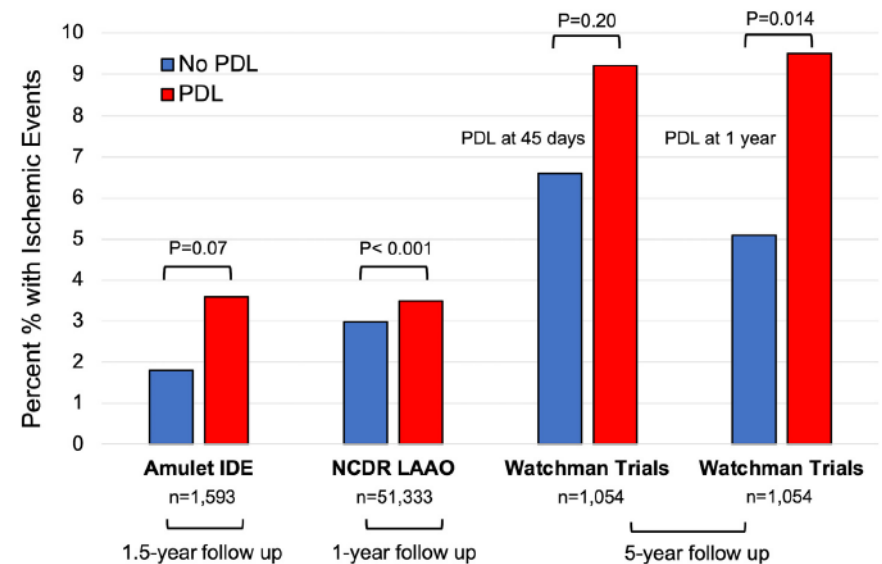


Fuites péri-dispositif

Peridevice Leak After Left Atrial Appendage Occlusion

Incidence, Mechanisms, Clinical Impact, and Management

FIGURE 4 Summary of Recent Studies Documenting an Association of PDL With Ischemic Events

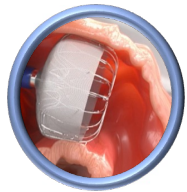


JACC: CARDIOVASCULAR INTERVENTIONS VOL. 16, NO. 6, 2023

MARCH 27, 2023:627-642

Occlusion AAG: régime anti-thrombotique post-intervention

L'histoire est en cours d'écriture...



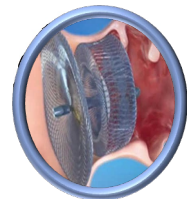
PROTECT-AF et PREVAIL
45 jours de coumadin
DTAP ad 6 mois
ASA seule



ASAP WATCHMAN
DTAP x 6 mois



WATCHMAN ASAP-TOO
DTAP x 3 mois



ACP registry
Durée moyenne de la DTAP 3.8 mois



Amulet registry
STAP – 31.3%
DTAP – 45.6%

En pratique...

DTAP 3 mois



ASA long cours

Occlusion AAG: régime anti-thrombotique post-intervention

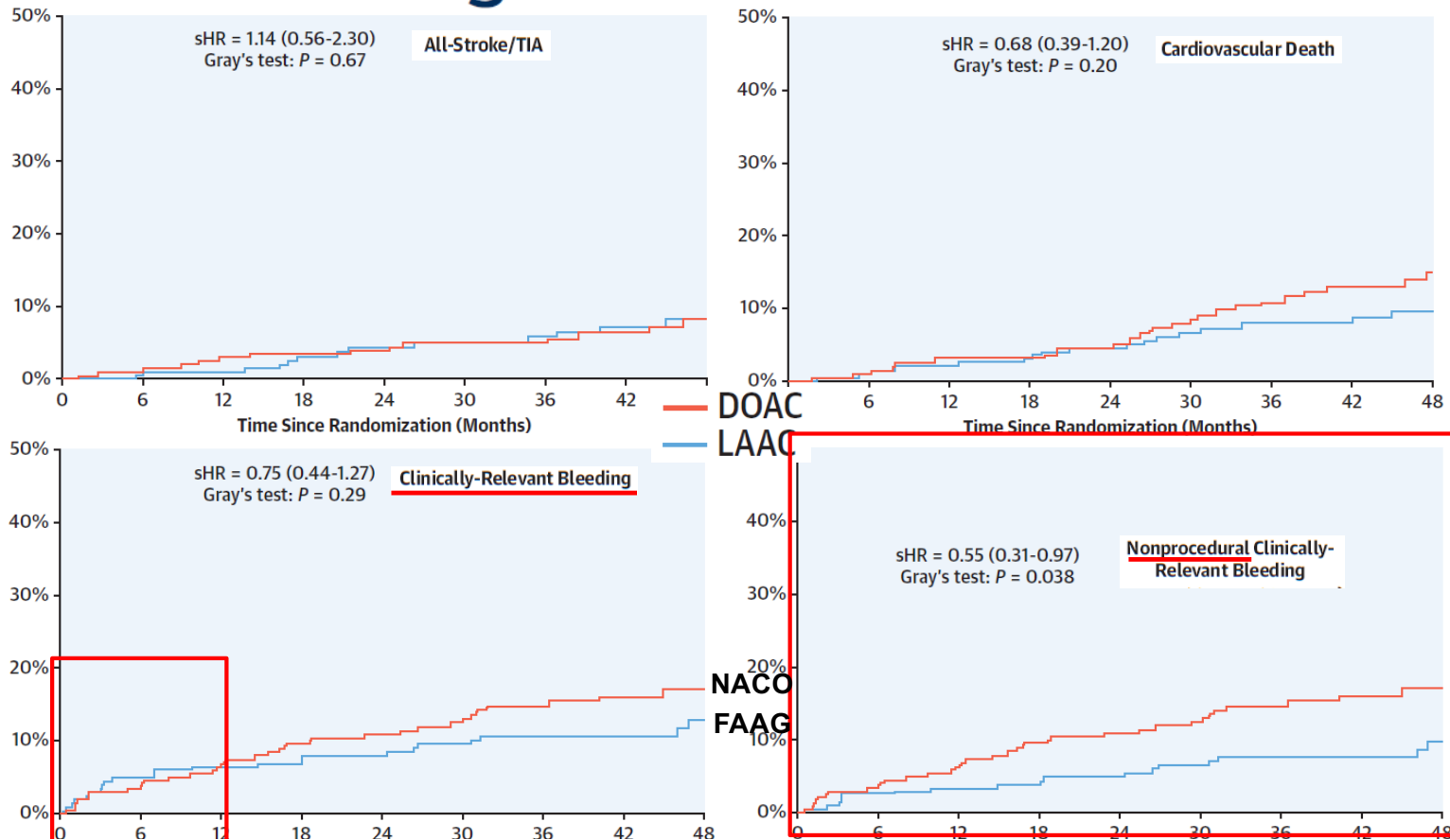


L'histoire est en cours d'écriture...

Study acronym	NCT/EuroCT number	Study design	Intervention	n	Target population	Main outcomes
ADALA (Antithrombotic therapy after left atrial appendage occlusion: double antiplatelet therapy versus apixaban)	2018-001013-32	Randomised trial	DAPT vs apixaban (5/2.5 mg bid)	160	LAAO closure (no specific device)	Combined of efficacy (thromboembolic events and device thrombosis) and safety (major bleeding incidence) at 3 months
ANDES (Short-term anticoagulation versus antiplatelet therapy for preventing device thrombosis following left atrial appendage closure)	NCT03568890	Randomised trial	DAPT vs any approved NOAC	350	LAAO with the WATCHMAN or ACP/Amulet devices	Device thrombosis as evaluated by TOE at 2 months
APPROACH (A multicentre study of apixaban)	NCT04550637	Prospective, observational	Apixaban (5 mg bid) for 3 months following LAAC	200	LAAO (no specified device)	All-cause death, stroke, transient ischaemic attack, systemic embolism at 6 months
ASPIRIN-LAAO (Aspirin discontinuation after left atrial appendage occlusion in atrial fibrillation)	NCT03821883	Randomised trial	Aspirin discontinuation vs continuation at the sixth month after LAAO	1,120	LAAO with the WATCHMAN device	Stroke, systemic embolism, acute coronary syndrome, cardiovascular/unexplained death, major bleeding, coronary/peripheral revascularisation at 2 years
DEA-LAA (Efficacy of short-term dabigatran etexilate followed by aspirin monotherapy after LAA (left atrial appendage) device closure)	NCT03539055	Prospective, observational	Dabigatran 75 or 150 mg BID x 90 days plus ASA 81 mg daily	100	LAAO with the WATCHMAN device	Device-related thrombosis at 90 days (as evaluated by TOE or CT)
FADE-DRT (Efficacy of different anti-thrombotic strategies on device-related thrombosis prevention after percutaneous left atrial appendage occlusion)	NCT04502017	Randomised trial	DAPT, half-dose DOAC or clopidogrel in combination with ASA on the basis of CYP2C19 genotype or half-dose DOAC	360	LAAO (no specified device)	Composite of stroke, systemic embolism, and device-related thrombosis; incidence of major bleeding events at 1 year

4-Year Outcomes After Left Atrial Appendage Closure Versus Nonwarfarin Oral Anticoagulation for Atrial Fibrillation

PRAGUE-17





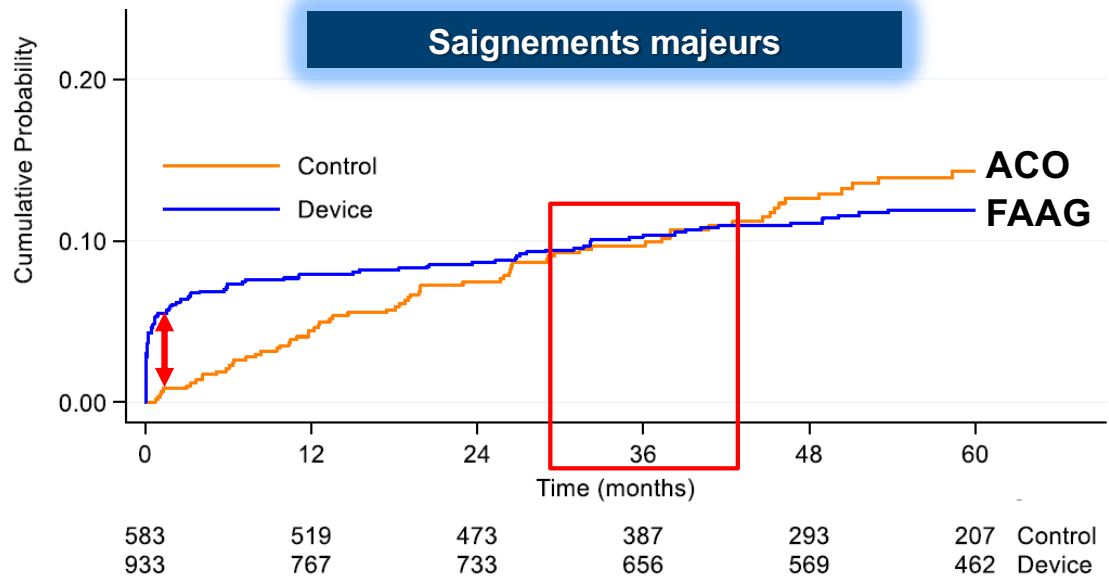
Percutaneous left atrial appendage closure versus oral anticoagulation for non-valvular atrial fibrillation: an individual patient data meta-analysis of randomized controlled trials

Yousif Ahmad

CRF
TCT 10-2023

933 FAAG vs 201 NACO + 382 VKA

Saignements majeurs



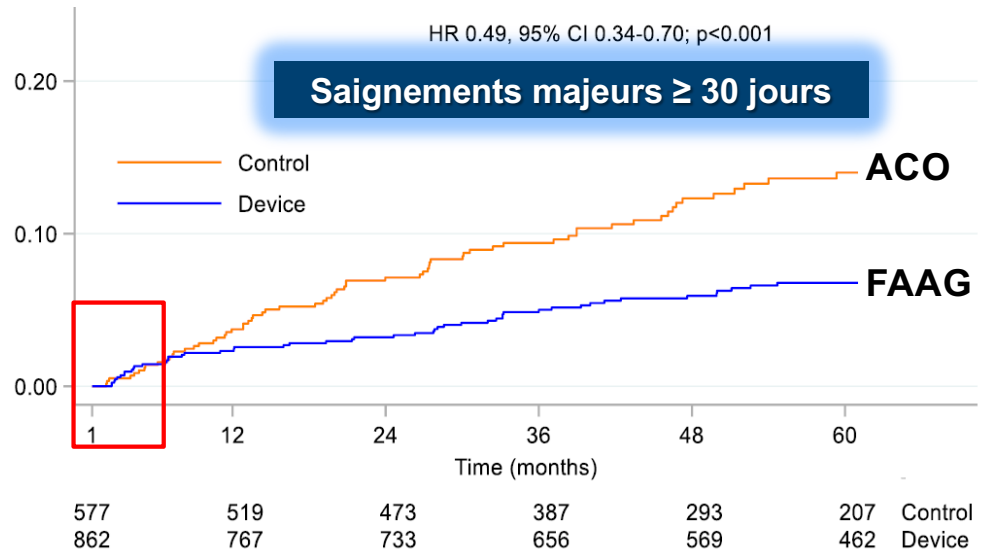
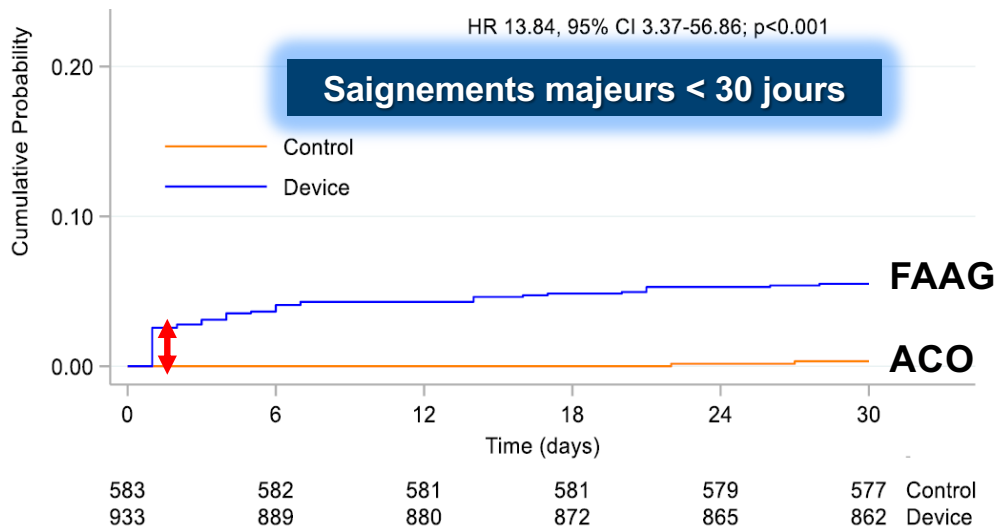


Percutaneous left atrial appendage closure versus oral anticoagulation for non-valvular atrial fibrillation: an individual patient data meta-analysis of randomized controlled trials

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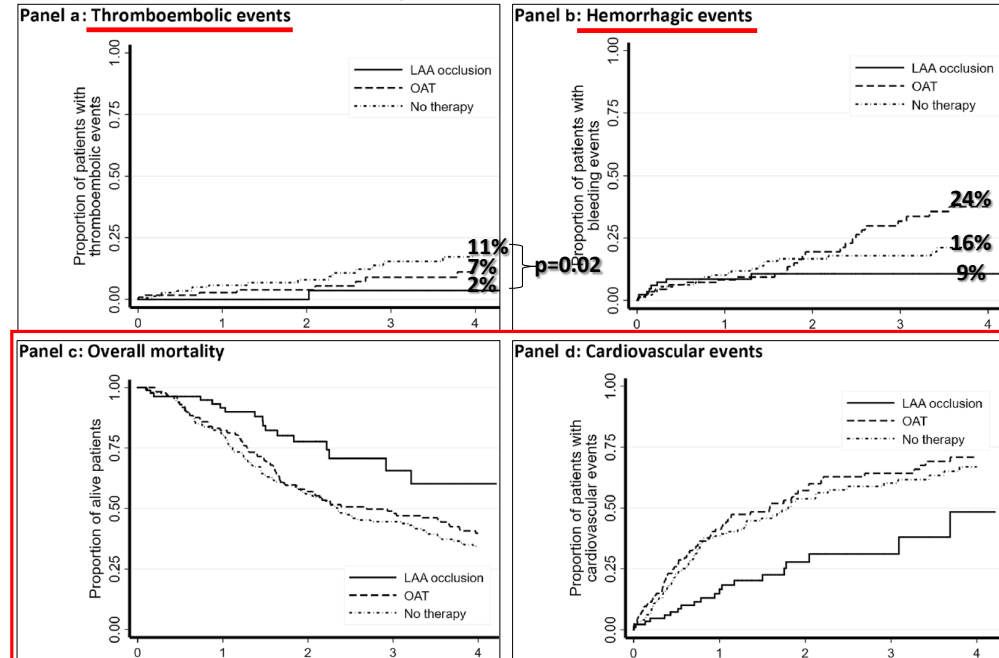


Occlusion AAG dans population spécifique: insuffisants rénaux dialysés



Outcomes on safety and efficacy of left atrial appendage occlusion in end stage renal disease patients undergoing dialysis

	LAA occlusion N=92		Cohort	
			OAT N=114	No therapy N=148
Age, N (%)				
Yrs (median [IQR])	74 [76,80]	76 [71,80]	76 [69, 82]	
>= 75 yrs	42 (45.7)	64 (56.1)	85 (57.4)	
CHA2DS2VASc				
Score (median [IQR])	4 [3, 5]	4 [4, 5]	5 [3, 6]	
HASBLED				
Score (median [IQR])	4[4, 5]	4 [3, 5]	4[4, 5]	
Comorbidities, N (%)				
Hypertension	82 (89.1)	95 (83.3)	131 (88.5)	
Diabetes mellitus	33 (35.9)	36 (31.6)	50 (33.8)	
Dyslipidemia	49 (53.3)	45 (39.5)	41 (27.7)	
Peripheral artery disease	50 (54.3)	83 (72.8)	101 (68.2)	
Ischaemic heart disease	43 (46.7)	56 (49.1)	75 (50.7)	
Heart failure	32 (34.8)	49 (43.0)	54 (36.5)	
Ischaemic stroke	9 (9.8)	12 (11.4)	9 (6.7)	



Occlusion AAG dans population spécifique: sécurité chez patients âgés



Comparison of Efficacy and Safety of Left Atrial Appendage Occlusion in Patients Aged <75 to ≥75 Years

Am J Cardiol 2016;117:84–90

Variable	Age (years) (n = 828)		P value
	< 75 (n = 376)	≥ 75 (n = 452)	
	Death	1 (0.27%)	
Stroke	4 (1.1%)	3 (0.7%)	0.53
Major bleeding	3 (0.8%)	6 (1.3%)	0.46
Device embolization	2 (0.5%)	4 (0.9%)	0.55
Pericardial effusion	8 (2.1%)	13 (2.9%)	0.49
Cardiac tamponade	2 (0.5%)	10 (2.2%)	0.04
Major adverse events	12 (3.2%)	23 (5.1%)	0.17

Outcomes of Percutaneous Left Atrial Appendage Occlusion in the Elderly

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 14, NO. 24, 2021
DECEMBER 27, 2021:2749–2756

TABLE 1 In-Hospital Outcomes of ≥80 Years of Age Versus <80 Years of Age With Propensity Score Matching

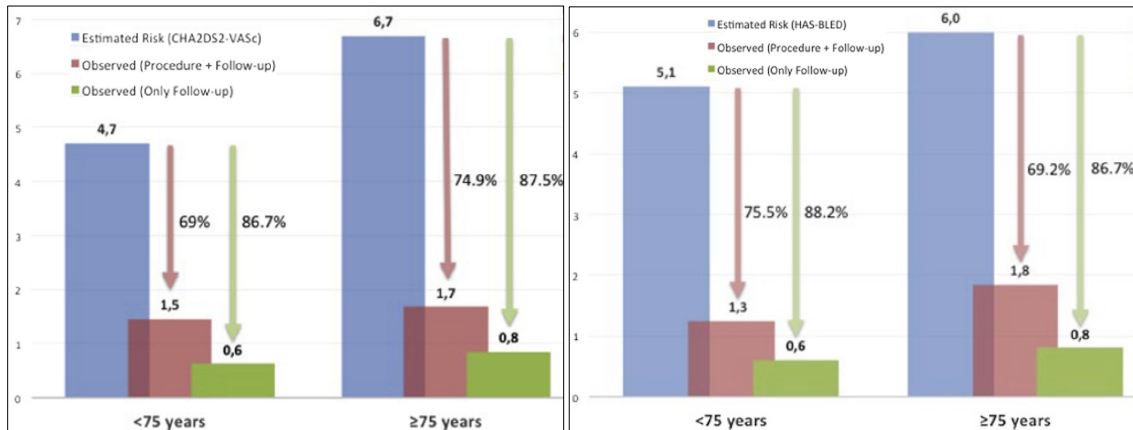
	Age <80 y (n = 11,712)	Age ≥ 80 y (n = 11,684)	OR (95% CI)	P Value
In-hospital mortality	23 (0.2)	35 (0.3)	1.52 (0.90 to 2.58)	0.11
Stroke/TIA	92 (0.8)	154 (1.3)	1.68 (1.30 to 2.18)	<0.001
Systemic embolization	5 (0.04)	18 (0.2)	3.61 (1.34 to 9.73)	0.007
Vascular complication	62 (0.5)	63 (0.5)	1.01 (0.71 to 1.22)	0.92
Pericardial tamponade requiring pericardiocentesis	75 (0.6)	124 (1.1)	1.66 (1.24 to 2.20)	<0.01
AKI	318 (2.7)	316 (2.7)	0.99 (0.85 to 1.15)	0.96
Bleeding/transfusion	453 (3.9)	532 (4.6)	1.18 (1.04 to 1.34)	0.009

Occlusion AAG dans population spécifique: efficacité chez patients âgés



Comparison of Efficacy and Safety of Left Atrial Appendage Occlusion in Patients Aged <75 to ≥75 Years

Am J Cardiol 2016;117:84–90



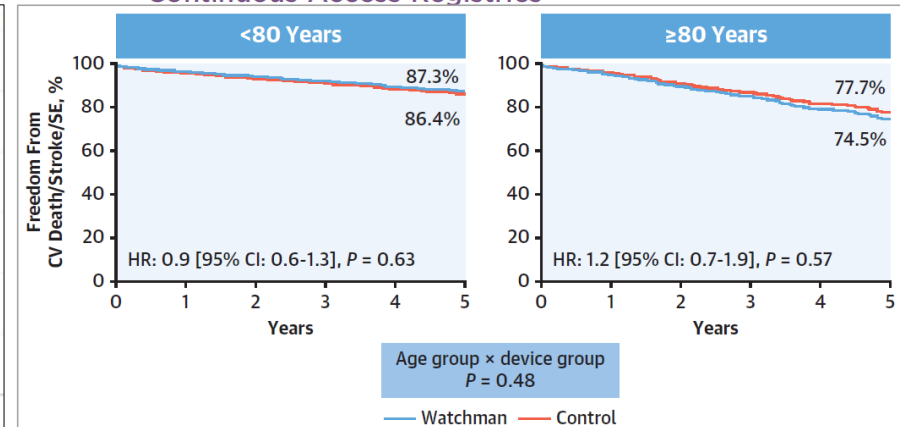
Prévention des AVC

Prévention des saignements

Left Atrial Appendage Occlusion in the Elderly

JACC: CLINICAL ELECTROPHYSIOLOGY VOL. 9, NO. 5, 2023
MAY 2023:669-676

Insights From PROTECT-AF, PREVAIL, and Continuous Access Registries



Chez des patients jugés éligibles à l'anticoagulation, FAAG offre protection équivalente au Coumadin

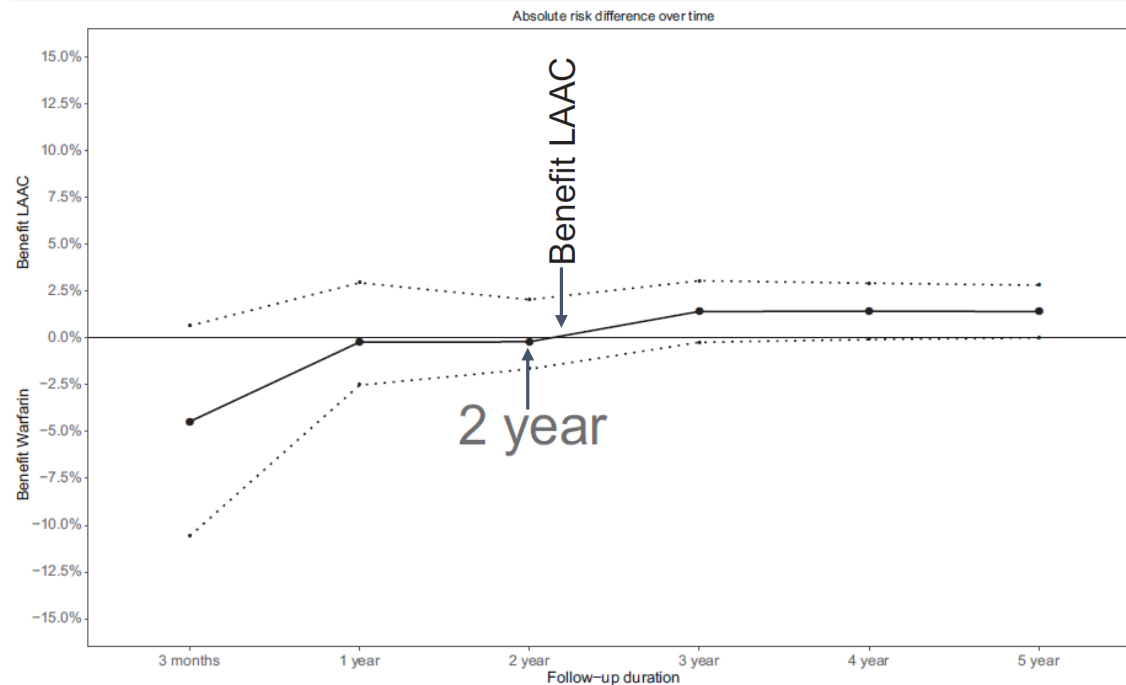
Occlusion AAG dans population spécifique: patients âgés – pronostic vital > 2a désirable



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 *J Am Heart Assoc.* 2019;8:e013525.

Tom F. Brouwer, MD, PhD; William Whang, MD; Kenji Kuroki, MD, PhD; Jonathan L. Halperin, MD; Vivek Y. Reddy, MD

FAAG vs Coumadin



Clinical Commissioning Policy: Left Atrial Appendage Occlusion for patients with atrial fibrillation and relative or absolute contraindications to anticoagulation (Adults)

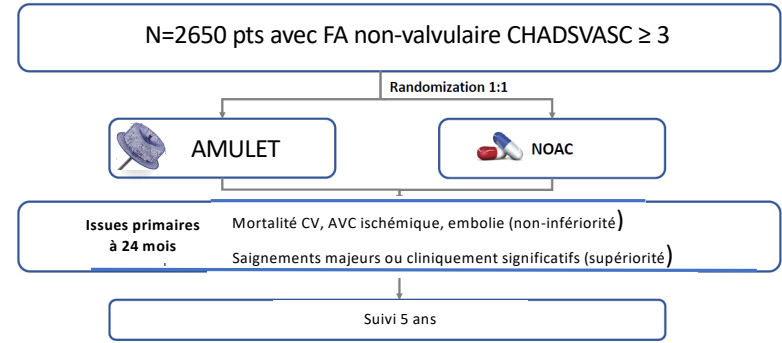
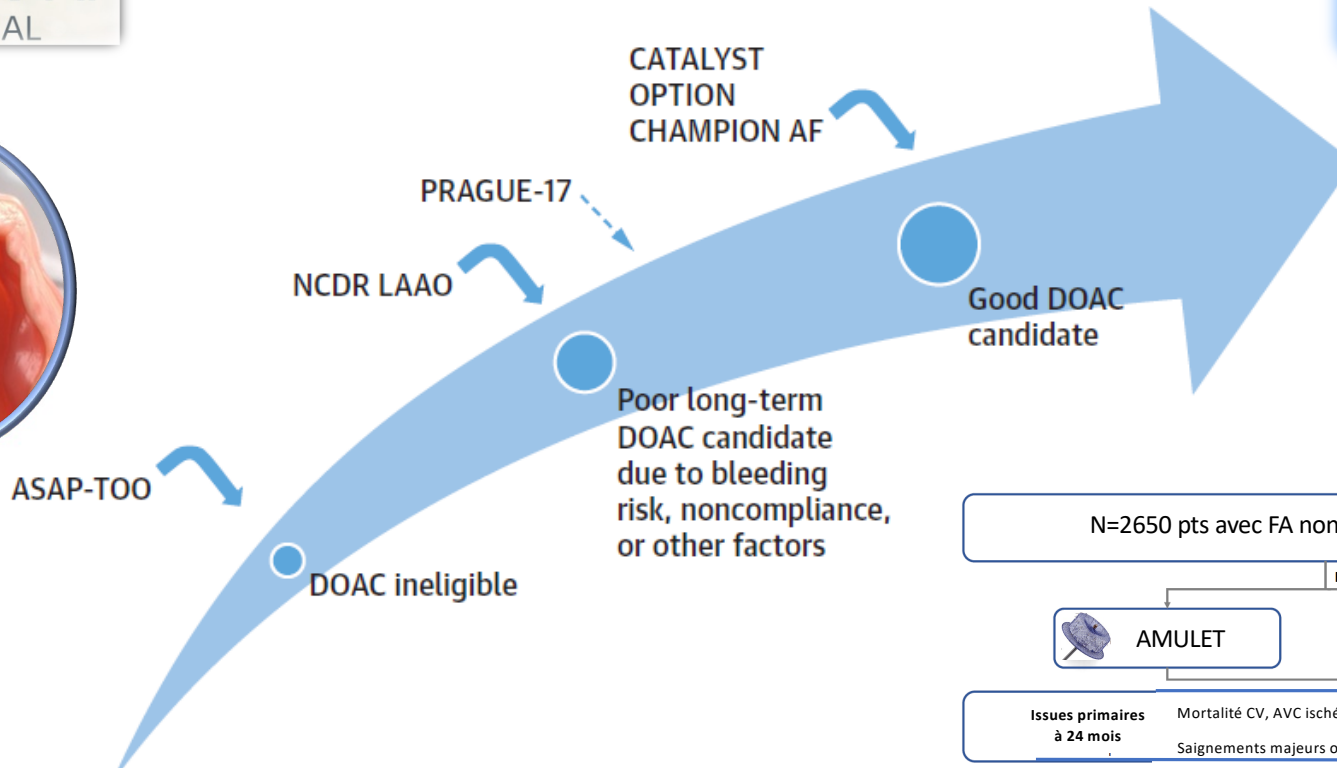
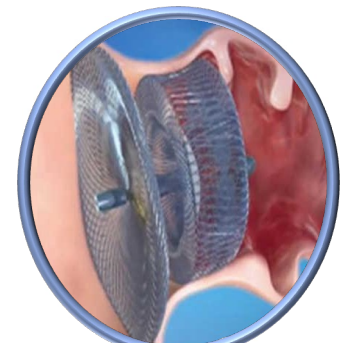
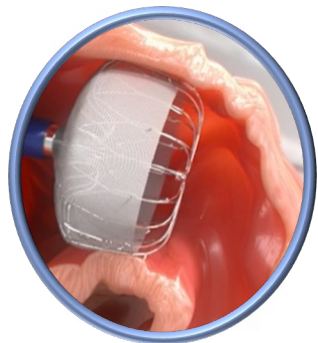
Prepared by NHS England Specialised Services Clinical Reference Group for Cardiac Services

First published: July 2018

Exclusion criteria:

- Life expectancy less than 3 years.
- Left atrial appendage thrombus visualised.
- Valvular atrial fibrillation (i.e rheumatic mitral stenosis, mechanical mitral valve).
- Other indications for long-term or lifelong OAC—mechanical prosthetic valve, pulmonary embolism and deep vein thrombosis, thrombi in the left atrium or ventricle.
- Contraindications for trans-septal catheterisation—left atrial thrombus or tumour, active infection.
- Patients clinically eligible and suitable for oral anticoagulants.
- Low risk for stroke $CHA_2DS_2-VASc < 2$.

Occlusion AAG dans population spécifique: candidats aux NACO

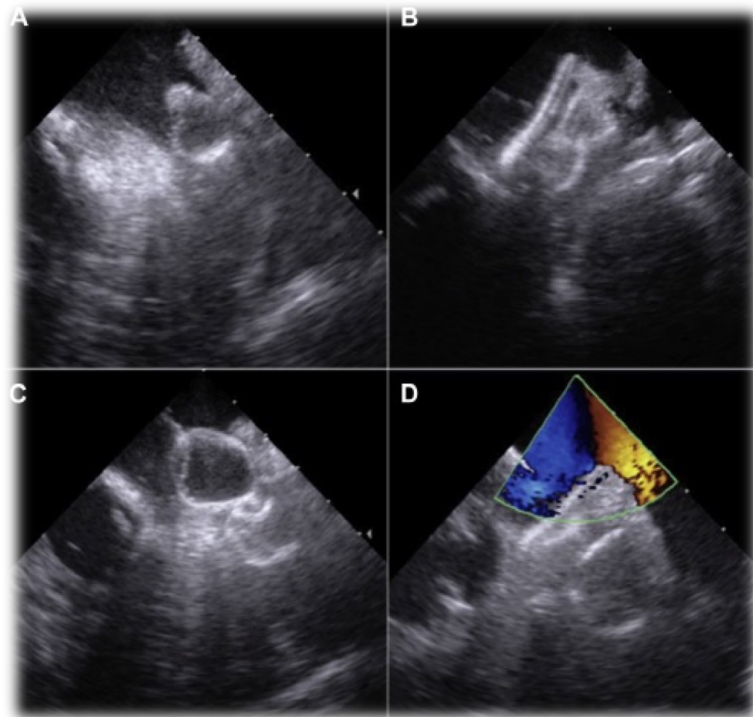


Price MJ, Saw J. JACC 2020;75(25):3136-39.

Occlusion AAG au CHUM: guidance ICE

Transcatheter Left Atrial Appendage Closure Using Intracardiac Echocardiographic Guidance From the Left Atrium

Masson et al. *Canadian Journal of Cardiology* 31 (2015) 1497.e7–1497.



Comparaison ETO vs ICE

ETO

Confort opérateur

Acquisition images par expert

Interprétation en direct par expert

Reproductible

Anesthésie générale

ICE

Autonomie

Logistique de planification

Roulement entre les procédures

Coûts globaux

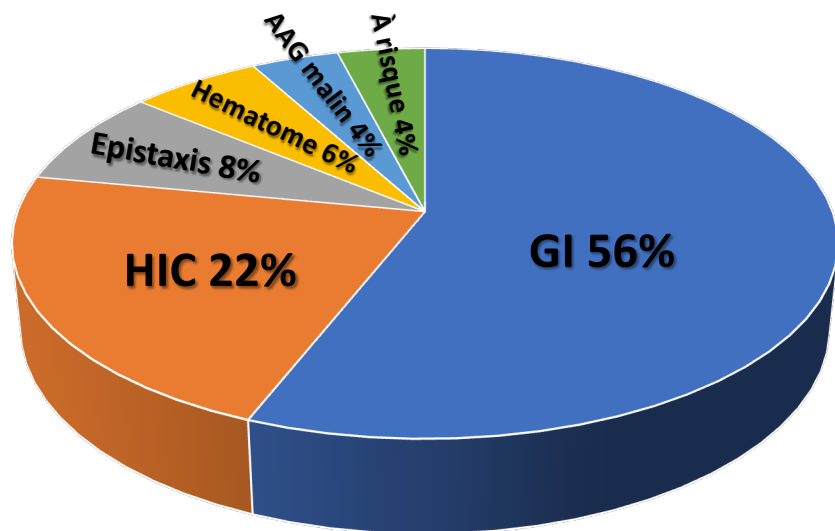
Courbe apprentissage

2^e accès veineux

Occlusion AAG au CHUM: population

Échantillon 50 patients consécutifs 2021-2022

Indication



■ GI ■ Intracrânien ■ Epistaxis ■ Hématome ■ AVC sous ACO ■ Risque élevé

Profil clinique

	NCDR registry	PRAGUE-17	CHUM
n	38 158	201	50
Âge	76	73	74
Ancien AVC/ICT	30%	36%	20%
CHADSVASC	4.6±1.5	4.7±1.5	4.0±1.4
HASBLED	3.0±1.1	3.1±0.9	2.6±0.7

Occlusion AAG au CHUM: procédure



Échantillon 50 patients consécutifs 2021-2022

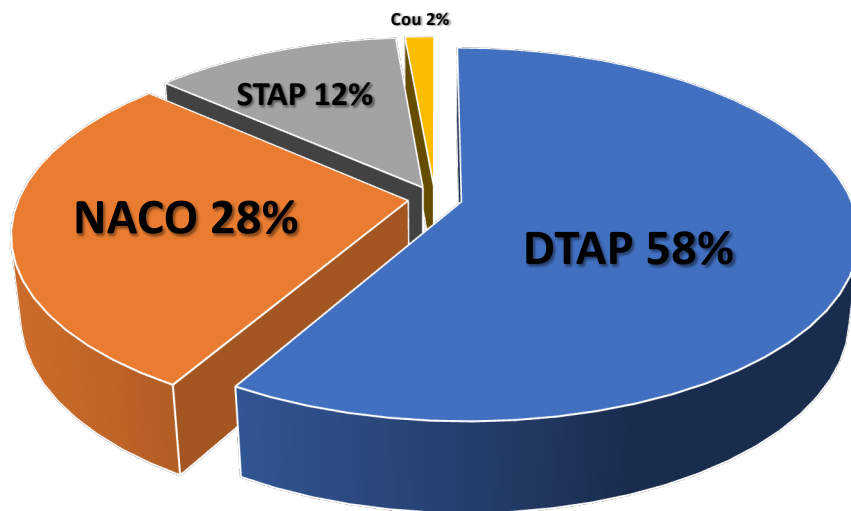
N	50
Durée, moy	68 +/- 19 min
Colorant, moy	82 +/- 37 cc
Nombre de déploiements, médiane	2
Changement taille	4/50
Succès procédural	100%
Complication intra-hospitalisation	3/50*
Durée de séjour, médiane	1 (1-4)

*1 AVC, 1 tamponnade, 1 péricardite

Occlusion AAG au CHUM: suivi 3 mois

Échantillon 50 patients consécutifs 2021-2022

Régime anti-thrombotique



■ DTAP ■ NACO ■ STAP ■ Coumadin

Évolution 3 mois (n=39)

Clinique

0 décès

2 ré-admissions
HB 60 ss NACO
EH

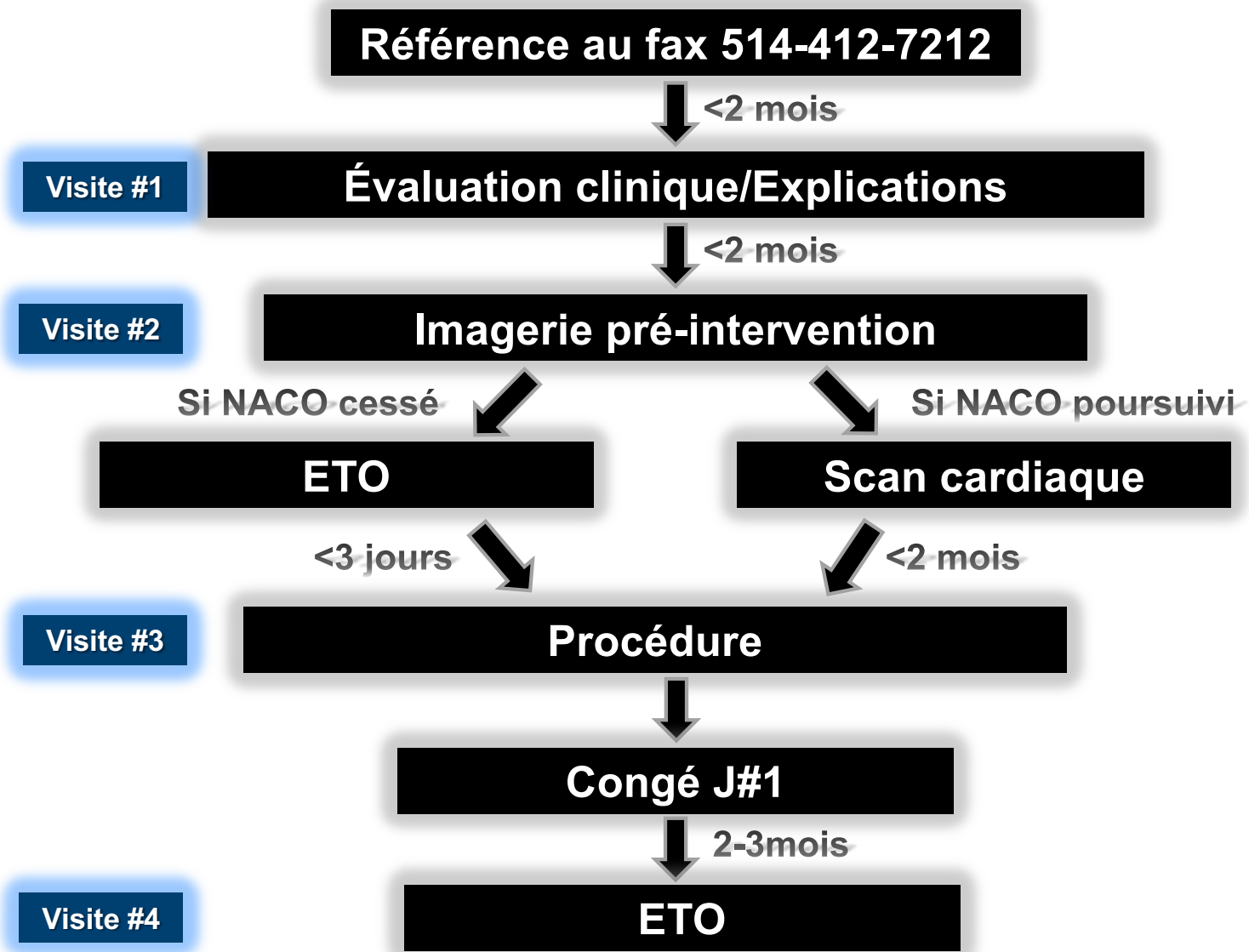
ETO

0 thrombose

0 fuite > 5mm

29 occlusions
complètes

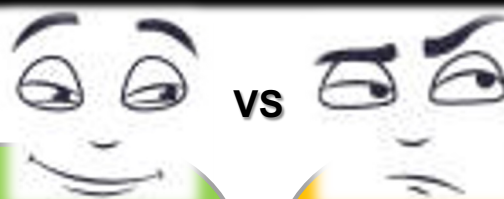
10 fuites ≤ 3mm





Occlusion auricule gauche

MESSAGES CLÉS



Alternative mécanique attrayante pour la prévention des AVCs chez les patients avec FA non valvulaire

- ✓ Efficacité similaire aux NACO
- ✓ Profil de sécurité qui s'améliore avec l'expérience des opérateurs et l'évolution des dispositifs
- ✓ Le bénéfice clinique net semble s'accroître avec le temps
- ✓ Signaux de bénéfices sur mortalité de plus en plus présents
- ✓ Résultats chez patients candidats aux NACO, moins vulnérables à la procédure seront déterminants

Les données restent insuffisantes à ce stade pour justifier la magnitude de l'adoption clinique

- ✓ Marges de non-infériorité utilisées étaient favorables à la procédure
- ✓ Non-infériorité non-atteinte dans 1/3 (PREVAIL) des études randomisées
- ✓ Taux de complications non-négligeable pour procédure préventive
- ✓ Ad 15% des patients reçoivent encore un anti-thrombotique (Coumadin ou NACO ou Clopidogrel) 1a post (thrombus, fuites)

D'ici à ce que...

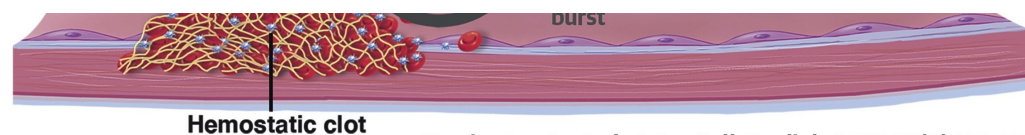
Réduction thrombose pathologique tout

November 19, 2023

Not intended for U.S. and UK Media

OCEANIC-AF study stopped early due to lack of efficacy

Independent Data Monitoring Committee (IDMC) recommends stopping the OCEANIC-AF study due to an inferior efficacy of asundexian versus the control arm / OCEANIC-AF is one trial which evaluates asundexian versus apixaban in patients with atrial fibrillation at risk for stroke within the overall OCEANIC phase III program // IDMC recommends continuing the OCEANIC-STROKE phase III as planned



Harrington J, et al. J Am Coll Cardiol. 2023;81(8):771-779.

Ma perspective

Alternative mécanique démontrée, à utiliser en partenariat avec le patient en fonction de son profil de risque (embolique et hémorragique), de sa tolérance au risque, de son pronostic et de ses préférences à moyen/long terme

Objectifs

- Revoir la littérature récente concernant la fermeture transcathéter de l'appendice auriculaire gauche (FAAG) en FA
- Discuter des risques et bénéfices de l'intervention
- Identifier les patients susceptibles de bénéficier d'une référence pour évaluation leur candidature à la procédure

Merci de votre
attention

Question ou
commentaires?

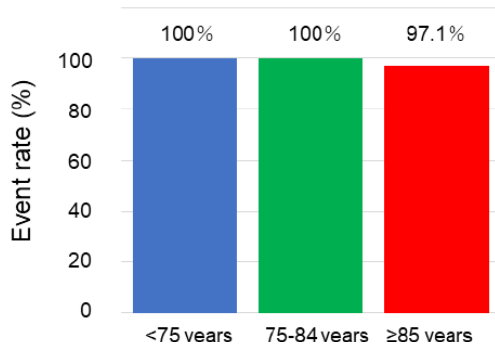




Mid-Term Feasibility of Percutaneous Left Atrial Appendage Occlusion in Elderly Patients with Non-Valvular Atrial Fibrillation

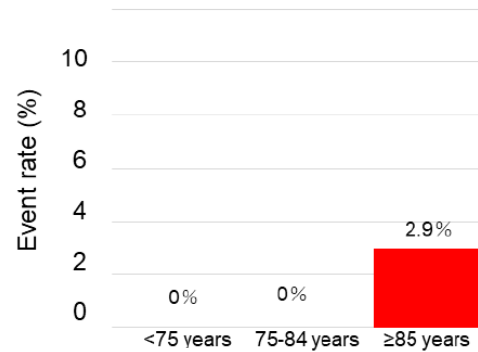
A

Implant success

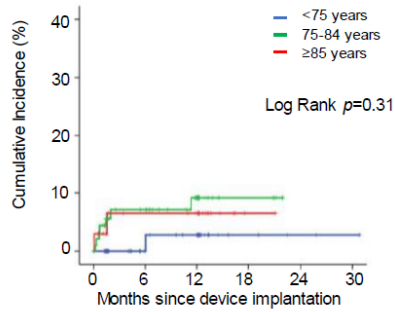


B

Major procedure related adverse events

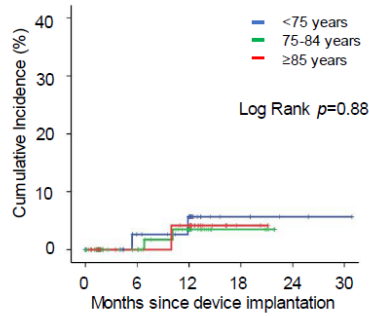


Any bleeding events

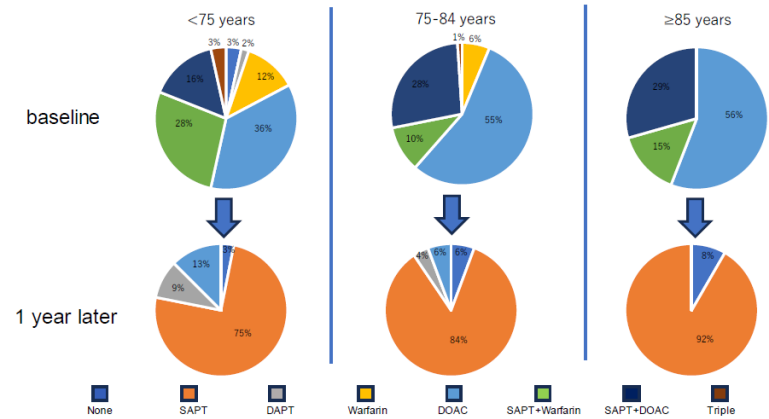


No at Risk	0	6	12	18	24	30
<75 years	58	34	28	4	2	1
75-84 years	96	56	35	5	0	0
≥85 years	34	22	20	1	0	0

Stroke or TIA or Systemic embolic events



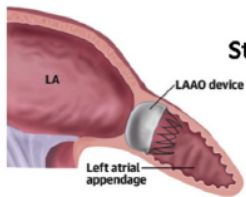
No at Risk	0	6	12	18	24	30
<75 years	58	34	28	3	2	1
75-84 years	96	56	41	6	0	0
≥85 years	34	23	20	3	0	0



Original Article

Long-term Clinical Outcomes in Contemporary Patients Undergoing Left Atrial Appendage Occlusion Procedures in Ontario, Canada

Sheldon M. Singh, MD,^{a,b} Feng Qui, MSc,^c and Harindra C. Wijeyesundera, MD^{a,b,c,d}



Patients: 549 LAAO patients
Study period: April 1st 2013 and Mar 31st 2022
Location: Ontario, Canada

Stroke rate: 1.1/100 patient-years
Bleeding rate: 4.0/100 patient-years
Re-hospitalization rate: 43/100 patient-years
All-cause mortality rate: 11/100 patient-years

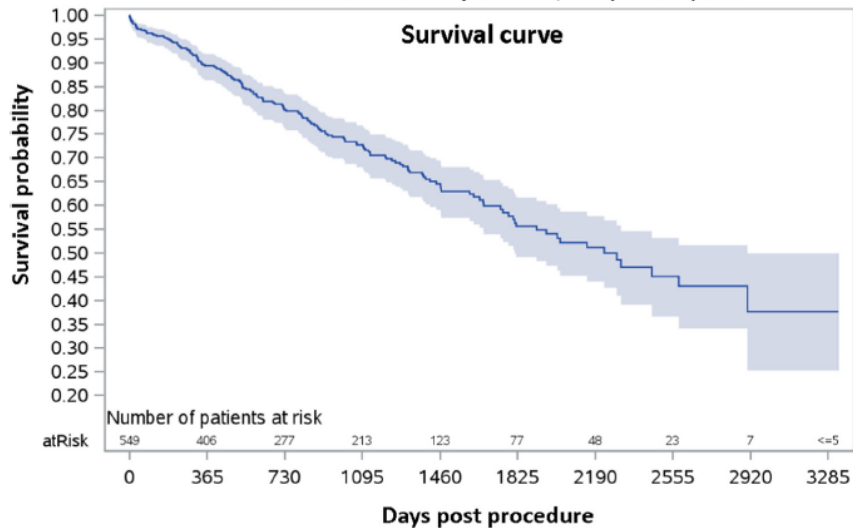
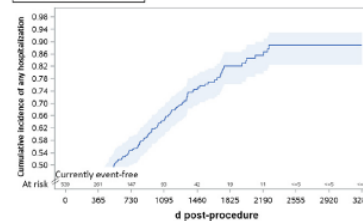


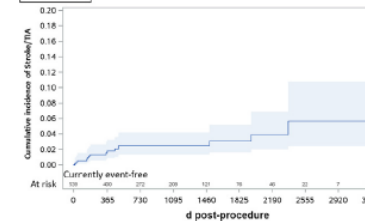
Table 2. Complications

Variable	Within 7 d	Within 30 d
Death	6 (1.15)	12 (2.2)
Stroke and/or TIA	< 6	< 6
Any bleeding	7 (1.3)	18 (3.3)
Pericardial effusion requiring drainage	8 (1.4)	8 (1.4)
Any rehospitalization	18 (3.3)	58 (11)

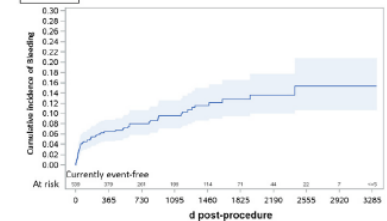
Any re-hospitalization



Stroke/TIA



Bleeding

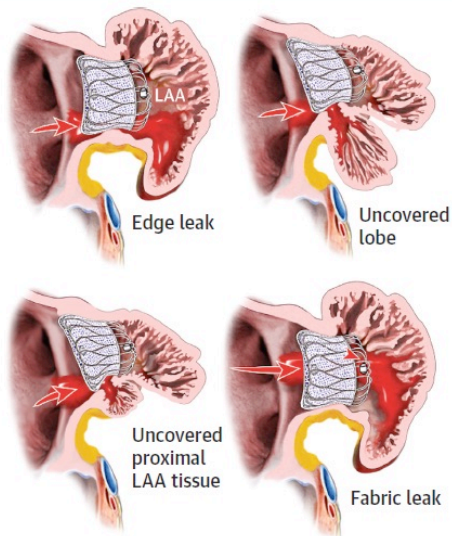


Peridevice Leak After Left Atrial Appendage Occlusion

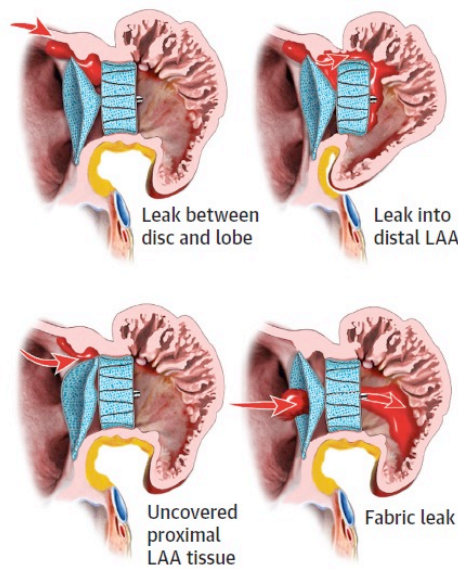
Incidence, Mechanisms, Clinical Impact, and Management

CENTRAL ILLUSTRATION Residual Leaks Following LAA Occlusion

Mechanism of Leak With Plug Occluders

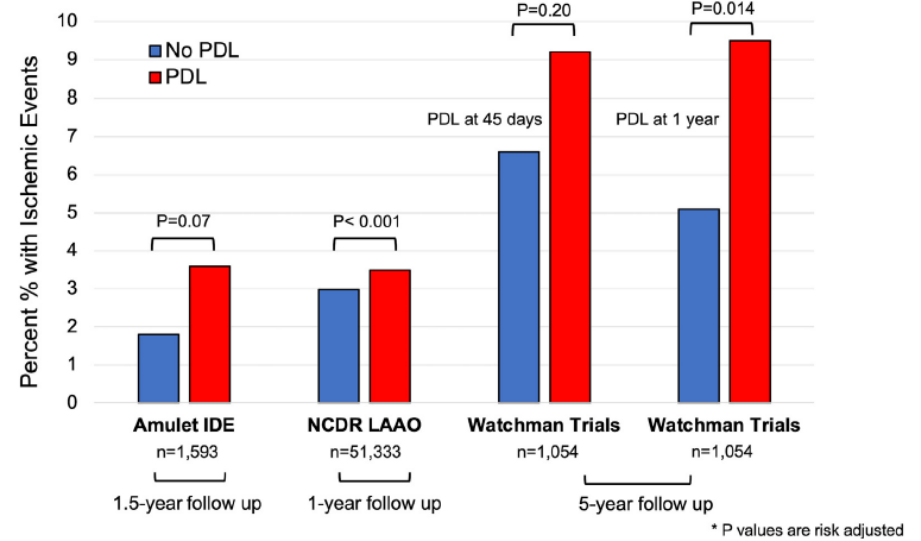


Mechanism of Leak With Lobe-and-Disc Occluders



Alkhouli M, et al. J Am Coll Cardiol Intv. 2023;16(6):627-642.

FIGURE 4 Summary of Recent Studies Documenting an Association of PDL With Ischemic Events



Peridevice Leak After Left Atrial Appendage Occlusion

Incidence, Mechanisms, Clinical Impact, and Management

FIGURE 7 Interventional Strategies for Peridevice Leak Closure

Device Leak Treatment

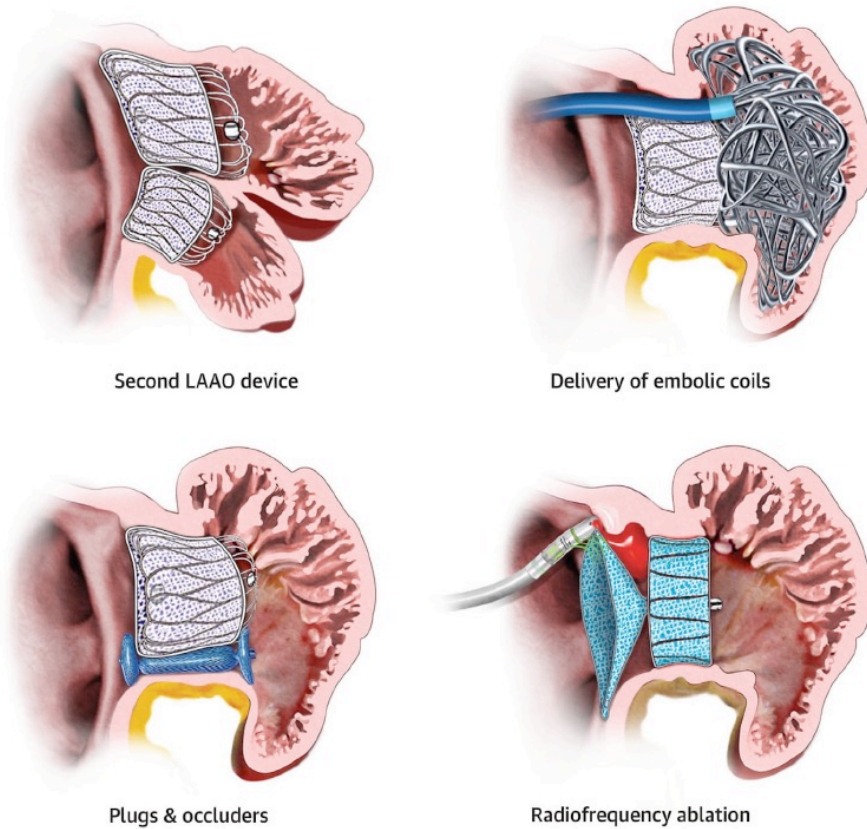
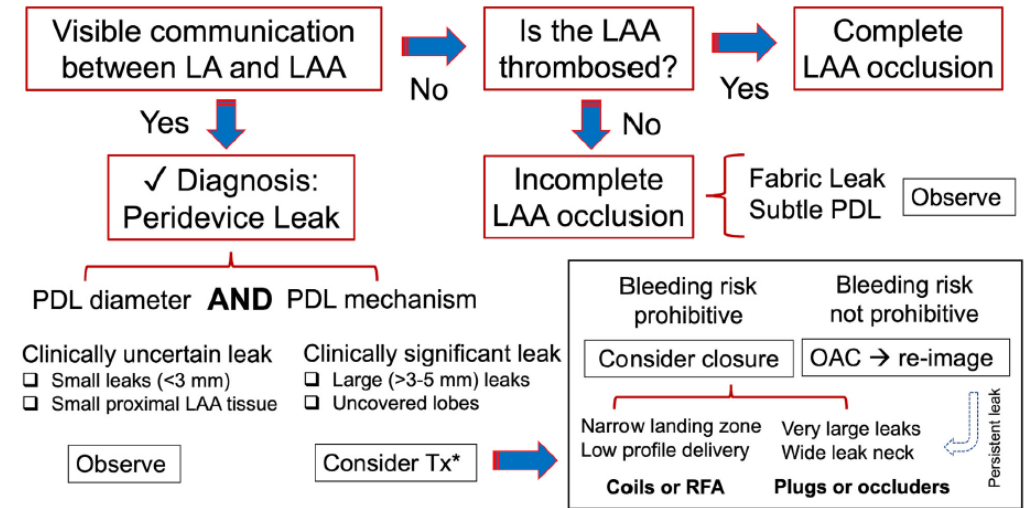


FIGURE 10 Proposed Algorithm for the Diagnosis and Management of PDLs

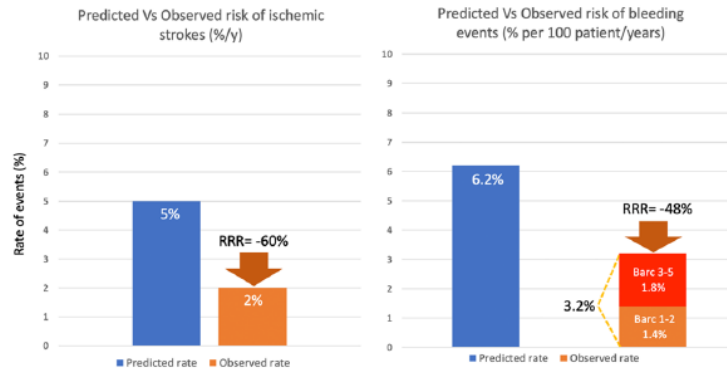


Clinical outcomes of left atrial appendage occlusion in patients with previous intracranial or gastrointestinal bleeding: Insights from the LOGIC (Left atrial appendage Occlusion in patients with Gastrointestinal or IntraCranial bleeding) International Multicenter Registry

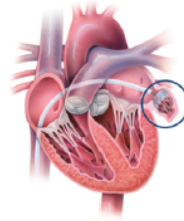
NVAF - Anticoagulation contraindicated for intracranial bleeding



N= 270



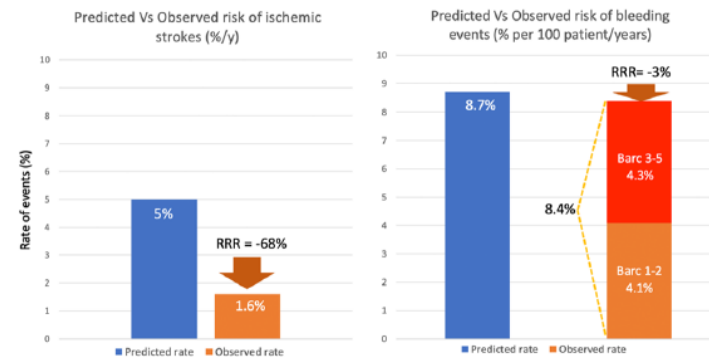
Left Atrial Appendage Occlusion



NVAF - Anticoagulation contraindicated for gastrointestinal bleeding



N= 358



Bleeding events at 12 months = Adjusted HR for GI group 2.39 (CI 95%1.02-5.63) p=0.047

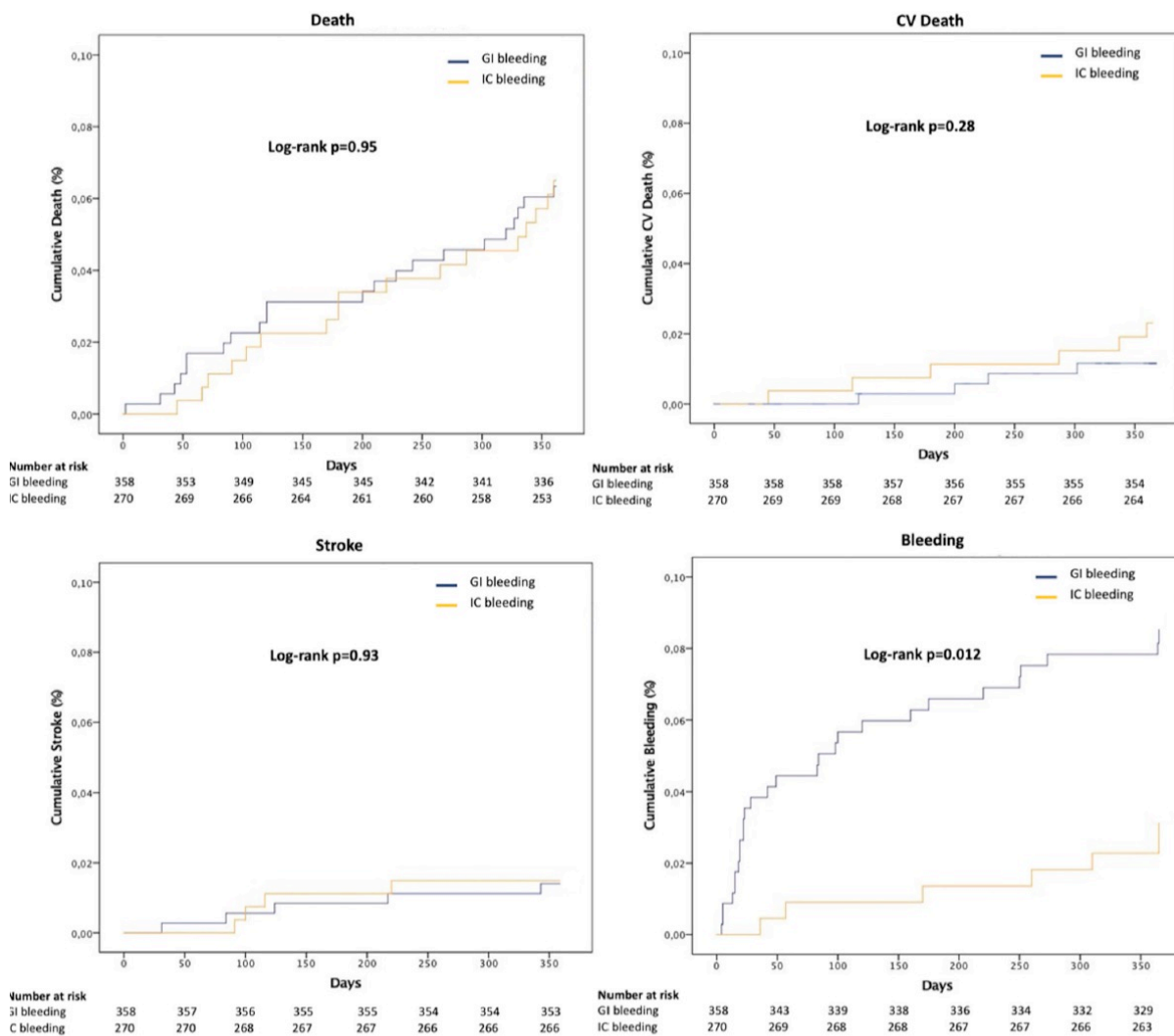


TABLE 3 Antithrombotic regimen at discharge and at 12 months.

	GI bleeding (n = 358)	IC bleeding (n = 270)	p Value
<i>Antithrombotic therapy at discharge</i>			
None	44/357 (12.3)	33/269 (12.2)	0.969
SAPT (%)	51/357 (14.3)	68/269 (25.2)	0.001
DAPT (%)	163/357 (45.7)	107/269 (39.6)	0.131
VKA (%)	24/357 (6.7)	5/269 (1.9)	0.004
DOAC (%)	21/357 (5.9)	12/269 (4.4)	0.425
AC + SAPT (%)	37/357 (10.4)	32/269 (11.9)	0.556
LMWH alone (%)	17/357 (4.8)	13/269 (4.8)	0.989
<i>Antithrombotic therapy at 12 months</i>			
None	58/315 (18.4)	42/237 (17.7)	0.835
SAPT (%)	197/315 (62.5)	155/237 (65.4)	0.489
DAPT (%)	36/315 (11.4)	20/237 (8.4)	0.249
VKA (%)	4/315 (1.3)	3/237 (1.3)	0.997
DOAC (%)	15/315 (4.8)	16/237 (6.8)	0.315
AC + SAPT (%)	3/315 (1)	0/237 (0)	0.132
LMWH alone (%)	2/315 (0.6)	1/237 (0.4)	0.736

FIGURE 2 Kaplan-Meier estimates curves for all-cause death, cardiovascular death, bleeding events and stroke events). [Color figure can be viewed at wileyonlinelibrary.com]

Impact of Device Implant Depth After Left Atrial Appendage Occlusion

CENTRAL ILLUSTRATION Study Overview and Findings

