# NACO post-AVC : POUR

Sylvain Lanthier MD OD CSPQ

Professeur agrégé, Faculté de Médecine, Université de Montréal

Programme Neurovasculaire, Hôpital du Sacré-Cœur de Montréal

# Conflits d'interêt potentiels

| | |
|---|---|
| Conférences | AZ, Bayer, BI, BMS, Pfizer, Sanofi, Servier |
| Fonds de recherche | Fondation des Gouverneurs de l'Espoir, Pfizer, Shire Human Genetics |
| Comités aviseurs | AZ, Bayer, BI, BMS, Covidien, Pfizer, Sanofi, Servier |

**Approche propose majoritairement basée sur mon simple avis**

# Les causes d'AVC sont variées

Artériolosclérose (lacunaire; 20%)

Cause indéterminée (20%)

Athéromatose cervicale (20%) et intracrânienne (5%)

Causes inhabituelle (5%)

Athéromatose aortique (5%)

Cardiopathies emboligènes (25%)

# Cause ⟶ prévention secondaire


**AVC lacunaire = aPlt + FR athéro**

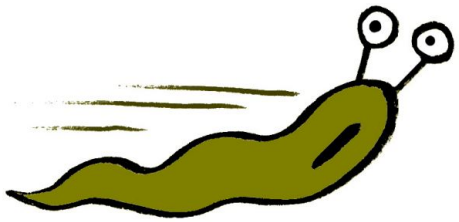
**AVC athéro = aPlt + FR athéro + endartériectomie**

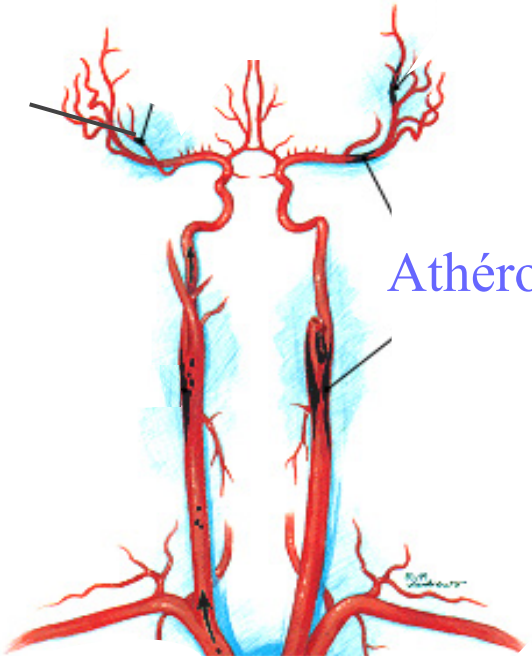
**Cardioembo = Anticoag + FR associés**

**Cause inhabituelle = tx causal + antithrombo varié**

# Investigation étiologique

Artériolosclérose (lacunaire; 20%)





Cause indéterminée (20%)

Athéromatose cervicale (20%) et intracrânienne (5%)

Imagerie cérébrale
Imagerie vasculaire
Echocardio

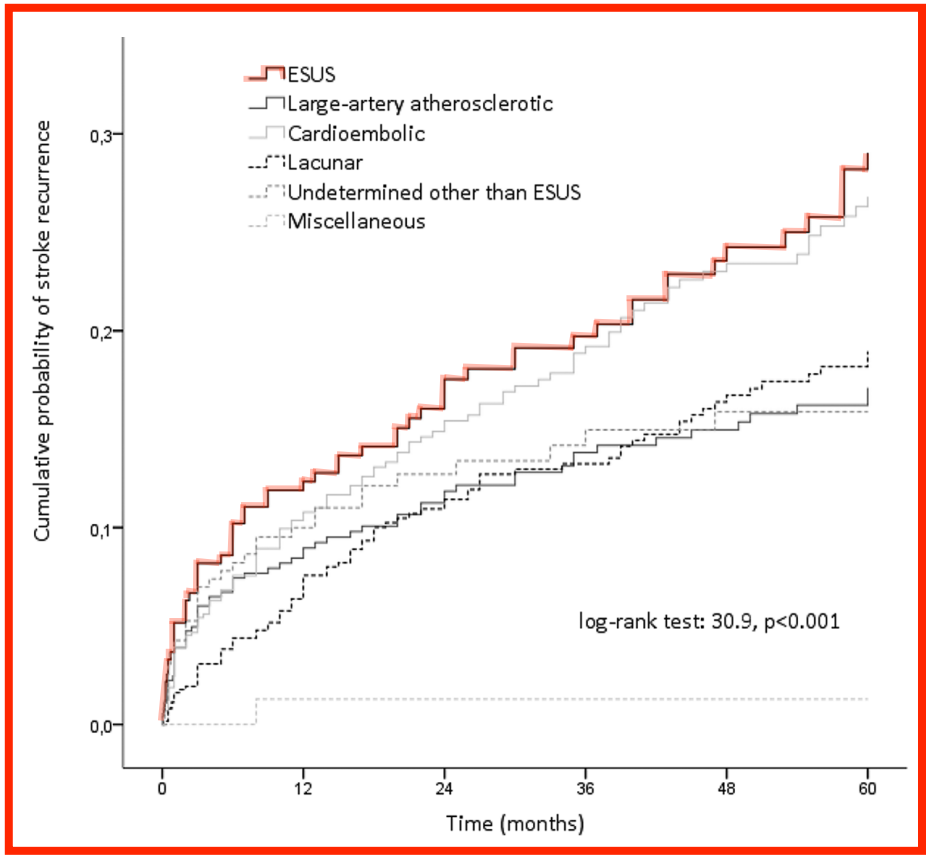
Wow! Wow! Pas si vite monsieur Gérard!

Athéromatose aortique (5%)

Cardiopathies emboligènes (25%)

Petit problème : ÇA FINIT PLUS !!!

# Pendant ce temps…

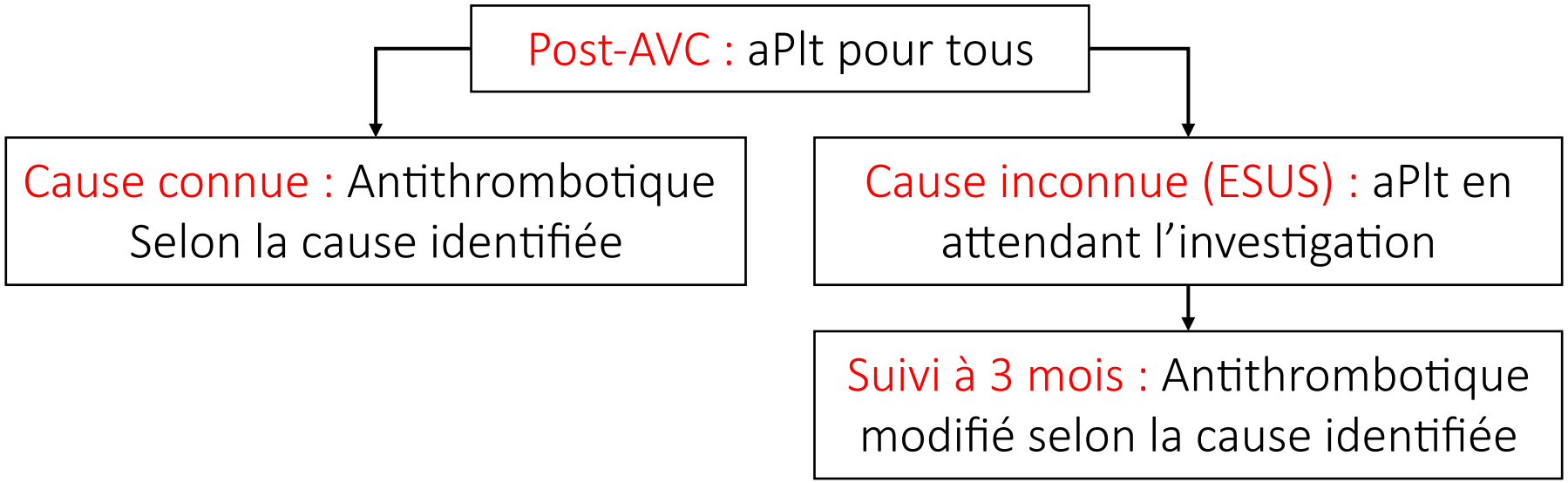



## AVC récidivant

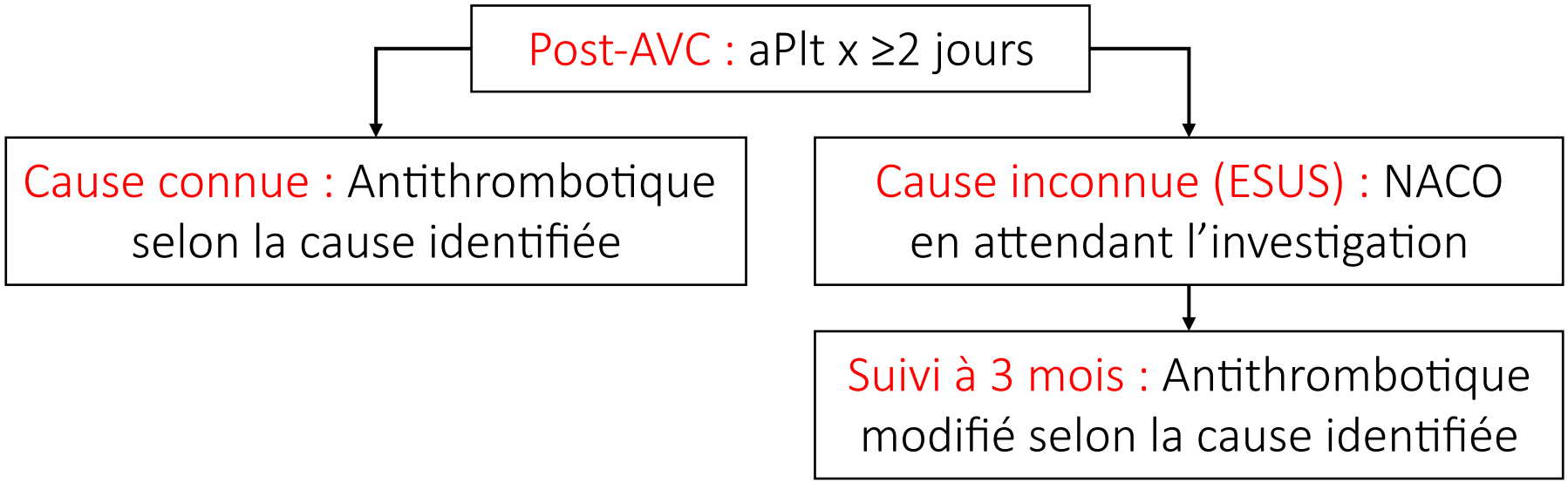
- Élevé
- Max dès les premiers jours
- Comparable à cardioembolique
- Différent des non-cardio

Ntaios G et al. Stroke 2015;46:2087

# Approche actuelle



# Approche basée sur l'évidence en attendant les études



## Causes cardiaque d'ESUS (88,2%)

| | |
|---|---|
| Mitral valve | |
| Myxomatous valvulopathy with prolapse | 5 (1.8%) |
| Mitral annular calcification | 8 (2.9%) |
| Aortic valve | |
| Aortic valve stenosis | 3 (1.1%) |
| Calcific aortic valve | 12 (4.4%) |
| Non-atrial fibrillation atrial dysrhythmias and stasis | |
| Atrial asystole and sick-sinus syndrome | 3 (1.1%) |
| Atrial high-rate episodes | 7 (2.6%) |
| Atrial appendage stasis with reduced flow velocities or spontaneous echodensities | 6 (2.2%) |
| Atrial structural abnormalities | |
| Atrial septal aneurysm | 10 (3.6%) |
| Chiari network | 0 |
| Left ventricle | |
| Moderate systolic or diastolic dysfunction (global or regional) | 42 15.4%) |
| Ventricular noncompaction | 12 (4.4%) |
| Endomyocardial fibrosis | 1 (0.4%) |
| Covert paroxysmal atrial fibrillation (detected during follow-up) | |
| Atrial fibrillation detected on stroke recurrence | 30 (11.0%) |
| Atrial fibrillation detected on monitoring during follow-up | 50 (18.3%) |
| Atrial fibrillation not confirmed but strongly suspected | 38 (13.9%) |
| Paradoxical embolism | |
| Patent foramen ovale | 11 (4.0%) |
| Atrial septal defect | 3 (1.1%) |

## Causes non-cardiaques d'ESUS (15,1%)

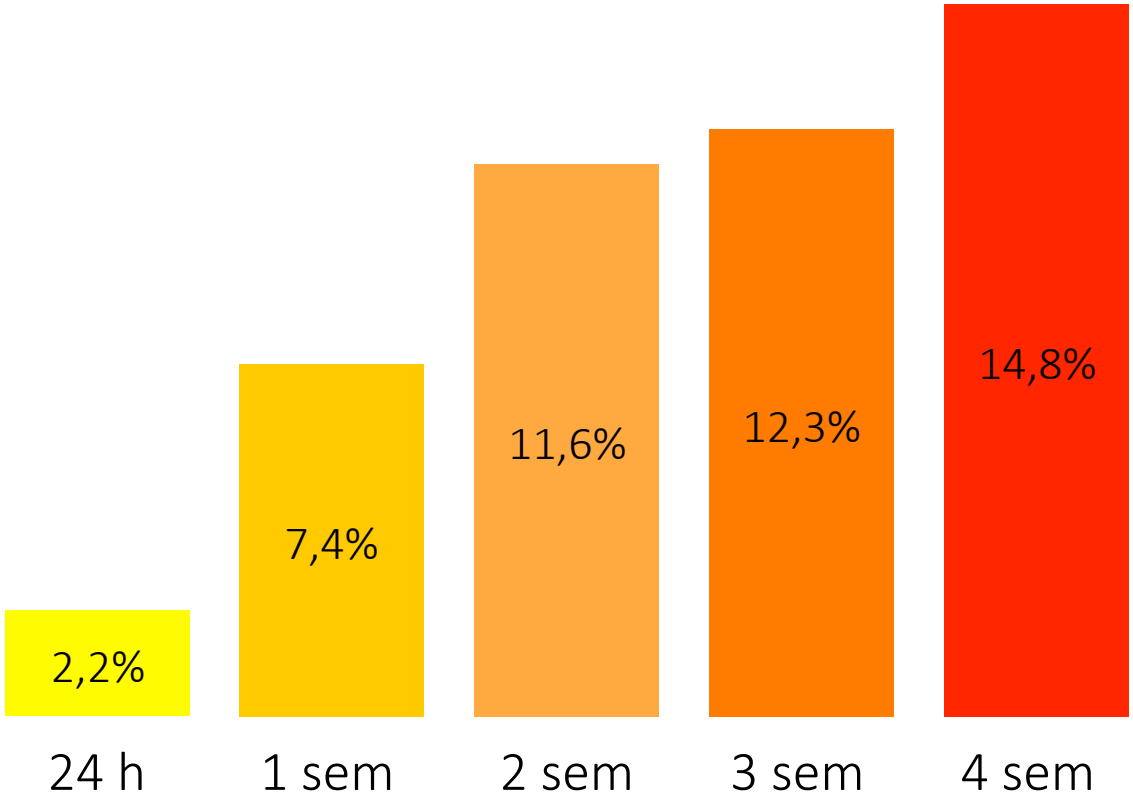
| | |
|---|---|
| Cancer-associated | |
| Covert nonbacterial thrombotic endocarditis | 1 (0.4%) |
| Tumor emboli from occult cancer | 2 (0.8%) |
| Arteriogenic emboli | |
| Aortic arch atherosclerotic plaques | 9 (3.3%) |
| Cerebral artery nonstenotic plaques with ulceration | 29 (10.6%) |

# Focus sur les NACO dans la FA

| | |
|---|---|
| Mitral valve | |
| Myxomatous valvulopathy with prolapse | 5 (1.8%) |
| Mitral annular calcification | 8 (2.9%) |
| Aortic valve | |
| Aortic valve stenosis | 3 (1.1%) |
| Calcific aortic valve | 12 (4.4%) |
| Non-atrial fibrillation atrial dysrhythmias and stasis | |
| Atrial asystole and sick-sinus syndrome | 3 (1.1%) |
| Atrial high-rate episodes | 7 (2.6%) |
| Atrial appendage stasis with reduced flow velocities or spontaneous echodensities | 6 (2.2%) |
| Atrial structural abnormalities | |
| Atrial septal aneurysm | 10 (3.6%) |
| Chiari network | 0 |
| Left ventricle | |
| Moderate systolic or diastolic dysfunction (global or regional) | 42 15.4%) |
| Ventricular noncompaction | 12 (4.4%) |
| Endomyocardial fibrosis | 1 (0.4%) |
| Covert paroxysmal atrial fibrillation (detected during follow-up) | |
| Atrial fibrillation detected on stroke recurrence | 30 (11.0%) |
| Atrial fibrillation detected on monitoring during follow-up | 50 (18.3%) |
| Atrial fibrillation not confirmed but strongly suspected | 38 (13.9%) |
| Paradoxical embolism | |
| Patent foramen ovale | 11 (4.0%) |
| Atrial septal defect | 3 (1.1%) |
| Cancer-associated | |
| Covert nonbacterial thrombotic endocarditis | 1 (0.4%) |
| Tumor emboli from occult cancer | 2 (0.8%) |
| Arteriogenic emboli | |
| Aortic arch atherosclerotic plaques | 9 (3.3%) |
| Cerebral artery nonstenotic plaques with ulceration | 29 (10.6%) |

FA = 43,2% des ESUS !

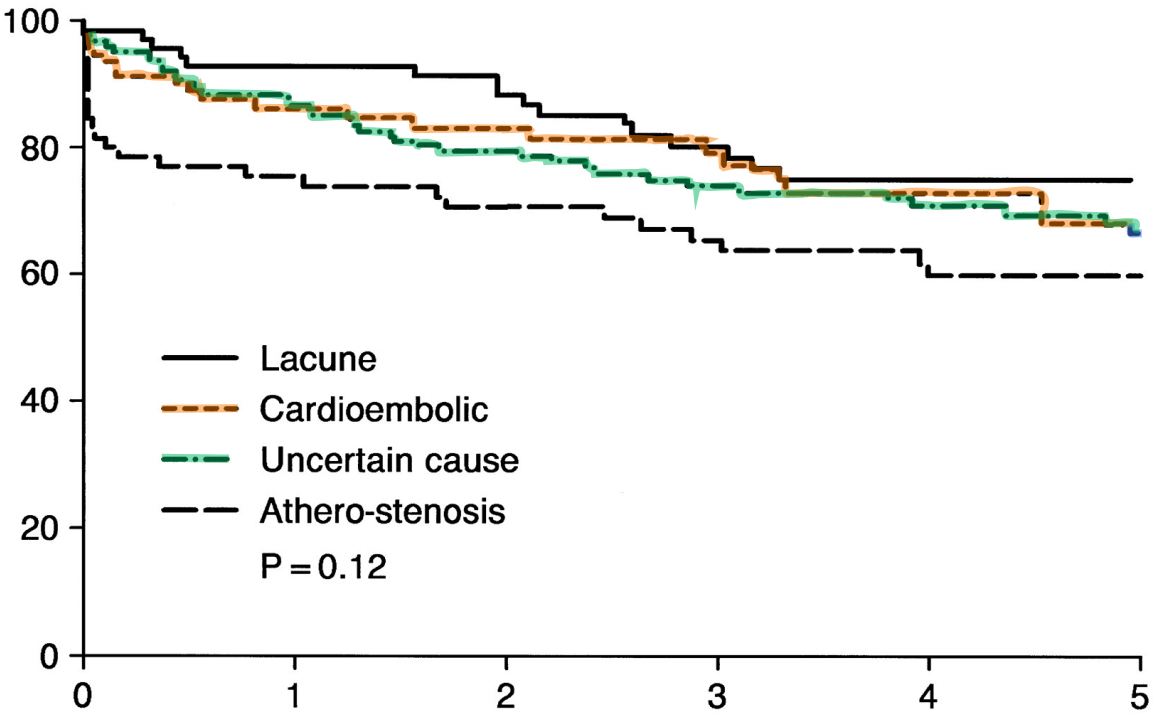
# Après un premier Holter : FA = 15% des ESUS




Gladstone et al. NEJM 2014;370:2467 (EMBRACE)

# Risque de récidive dans la FA

| | ESUS avec FA |
|---|---|
| Sem. 1-3 | 4,3% |
| Sem. 4-13 | 4,3% |
| Récidive à 3 mois | 8,6% |




Survie sans AVC récidivant (%)

Années après l'AVC

Petty et al. Stroke 2000;31:1062

| | ESUS avec FA |
|---|---|
| Sem. 1-3 | 4,3% |
| Sem. 4-13 | 4,3% |
| Récidive à 3 mois [1] | 8,6% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : **Warfarin** | 4,3% → **1,5%** |

Warfarin dans la FA : RRR=64% [1]

Hart RG et al. Ann Intern Med 2007;146:857

| | ESUS avec FA |
|---|---|
| Sem. 1-3 | 4,3% |
| Sem. 4-13 | 4,3% |
| Récidive à 3 mois [1] | 8,6% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 1,5% → 2,2% |

AAS + clopido dans la FA : RR=1,44 vs Warfarin

ACTIVE writing committee. Lancet 2006;367:1903

| | ESUS avec FA |
|---|---|
| Sem. 1-3 | 4,3% |
| Sem. 4-13 | 4,3% |
| Récidive à 3 mois | 8,6% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 2,2% |
| Sem. 4-13 : **1 aPlt** | 4,3% → **3,4%** |

AAS dans la FA : RRR=22%

Hart RG et al. Ann Intern Med 2007;146:857

| | ESUS avec FA |
|---|---|
| Sem. 1-3 | 4,3% |
| Sem. 4-13 | 4,3% |
| Récidive à 3 mois [1] | 8,6% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 2,2% |
| Sem. 4-13 : 1 aPlt | 4,3% → 3,4% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 2,2% |
| Sem. 4-13 : **Anticoag.** | 4,3% → **1,5%** |

Warfarin dans la FA : RRR=64%

Hart RG et al. Ann Intern Med 2007;146:857

| | ESUS avec FA |
|---|---|
| Sem. 1-3 | 4,3% |
| Sem. 4-13 | 4,3% |
| Récidive à 3 mois [1] | 8,6% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 2,2% |
| Sem. 4-13 : 1 aPlt | 4,3% → 3,4% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 2,2% |
| Sem. 4-13 : NACO | 4,3% → 1,5% |

NACO ≥ Warfarin dans la FA : RRR=64%

1. Connolly SJ et al. NEJM 2009;361:1139 3. Giugliano RP et al. NEJM 2013
2. Patel MR et al. NEJM 2011;365:883 4. Granger CB et al. NEJM 2011;365:981

| | ESUS avec FA |
|---|---|
| Sem. 1-3 | 4,3% |
| Sem. 4-13 | 4,3% |
| Récidive à 3 mois [1] | 8,6% |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 2,2% |
| Sem. 4-13 : 1 aPlt | 4,3% → **3,4%** |

| | ESUS avec FA |
|---|---|
| Sem. 1-3 : 2 aPlt | 2,2% |
| Sem. 4-13 : NACO | 4,3% → **1,5%** |

RRR = 55,9% !!!

RRA = 1,9% !!!

NNT = 53 patients avec FA masquée traités x 10 sem.

FA masquée : 43,2% des ESUS !!!

# Averroes : Apixaban vs AAS dans la FA

- RR=0,45
- 3,4% ⟶ 1,5%

| Outcome | Apixaban (N=2808) | | Aspirin (N=2791) | | Hazard Ratio with Apixaban (95% CI) | P Value |
|---|---|---|---|---|---|---|
| | *no. of patients with first event* | %/yr | *no. of patients with first event* | %/yr | | |
| Bleeding event | | | | | | |
| Major | 44 | 1.4 | 39 | 1.2 | 1.13 (0.74–1.75) | 0.57 |
| Intracranial | 11 | 0.4 | 13 | 0.4 | 0.85 (0.38–1.90) | 0.69 |
| Subdural‡ | 4 | 0.1 | 2 | 0.1 | — | — |
| Other intracranial, excluding hemorrhagic stroke and subdural‡ | 1 | <0.1 | 2 | 0.1 | — | — |
| Extracranial or unclassified | 33 | 1.1 | 27 | 0.9 | 1.23 (0.74–2.05) | 0.42 |
| Gastrointestinal | 12 | 0.4 | 14 | 0.4 | 0.86 (0.40–1.86) | 0.71 |
| Non-gastrointestinal | 20 | 0.6 | 13 | 0.4 | 1.55 (0.77–3.12) | 0.22 |
| Fatal | 4 | 0.1 | 6 | 0.2 | 0.67 (0.19–2.37) | 0.53 |
| Clinically relevant nonmajor | 96 | 3.1 | 84 | 2.7 | 1.15 (0.86–1.54) | 0.35 |
| Minor | 188 | 6.3 | 153 | 5.0 | 1.24 (1.00–1.53) | 0.05 |

Aucune différence statistiquement significative

NACO = AAS

Connolly SJ et al. NEJM 2011;364:806

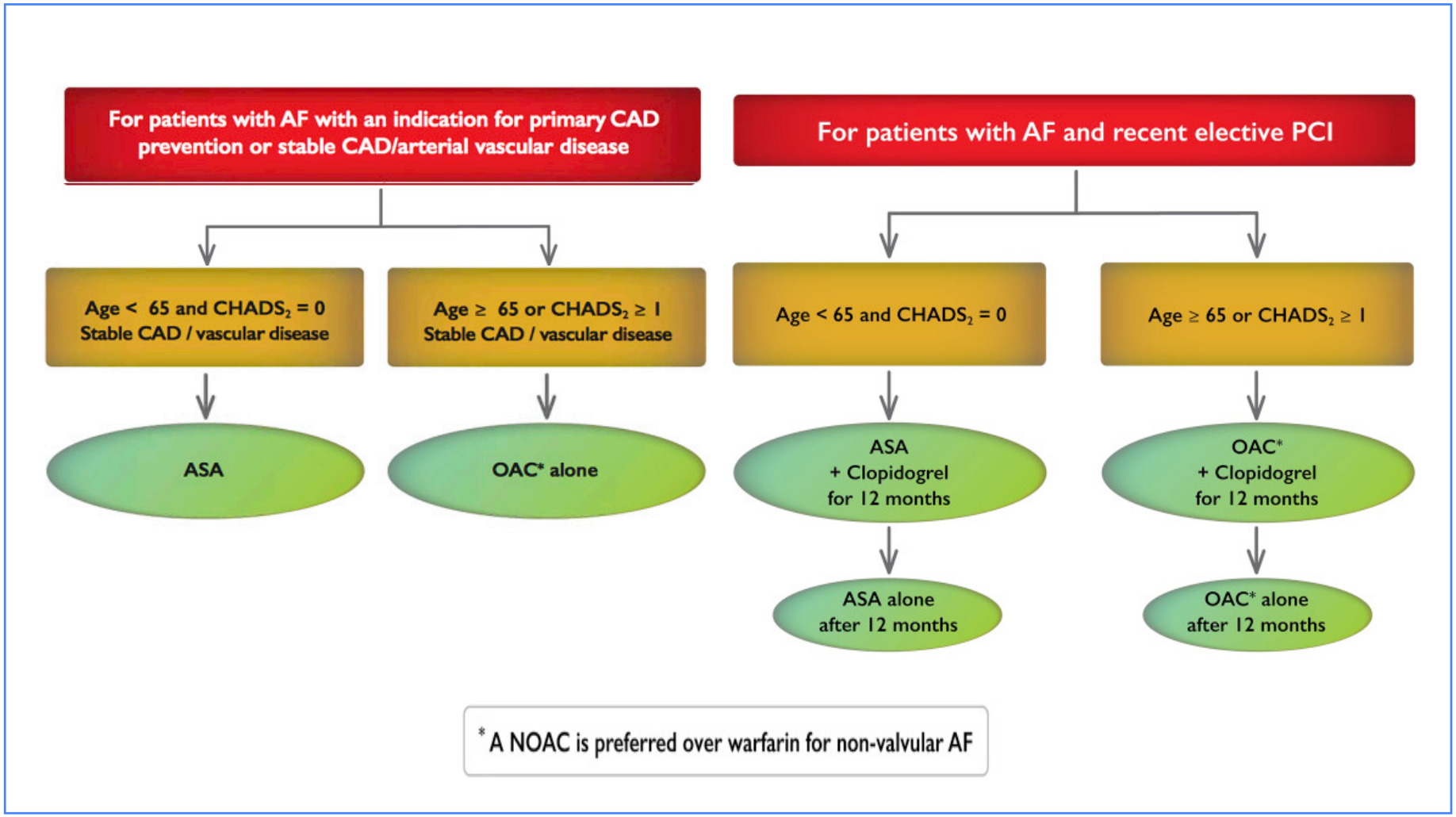
# Études en cours NACO vs aPlt dans le ESUS :

- Navigate-ESUS (Rivaroxaban)
- Respect-ESUS (Dabigatran)

# Focus sur les NACO dans l'athéro

| | |
|---|---|
| Mitral valve | |
| Myxomatous valvulopathy with prolapse | 5 (1.8%) |
| Mitral annular calcification | 8 (2.9%) |
| Aortic valve | |
| Aortic valve stenosis | |
| Calcific aortic valve | 12 (4.4%) |
| Non-atrial fibrillation atrial dysrhythmias and stasis | |
| Atrial asystole and sick-sinus syndrome | 3 (1.1%) |
| Atrial high-rate episodes | 7 (2.6%) |
| Atrial appendage stasis with reduced flow velocities or spontaneous echodensities | 6 (2.2%) |
| Atrial structural abnormalities | |
| Atrial septal aneurysm | 10 (3.6%) |
| Chiari network | 0 |
| Left ventricle | |
| Moderate systolic or diastolic dysfunction (global or regional) | 42 15.4%) |
| Ventricular noncompaction | 12 (4.4%) |
| Endomyocardial fibrosis | 1 (0.4%) |
| Covert paroxysmal atrial fibrillation (detected during follow-up) | |
| Atrial fibrillation detected on stroke recurrence | 30 (11.0%) |
| Atrial fibrillation detected on monitoring during follow-up | 50 (18.3%) |
| Atrial fibrillation not confirmed but strongly suspected | 38 (13.9%) |
| Paradoxical embolism | |
| Patent foramen ovale | 11 (4.0%) |
| Atrial septal defect | 3 (1.1%) |
| Cancer-associated | |
| Covert nonbacterial thrombotic endocarditis | 1 (0.4%) |
| Tumor emboli from occult cancer | 2 (0.8%) |
| Arteriogenic emboli | |
| Aortic arch atherosclerotic plaques | 9 (3.3%) |
| Cerebral artery nonstenotic plaques with ulceration | 29 (10.6%) |

# Lignes directrices SCC : NACO seul (aPlt cessé) dans la FA chez le coronarien stable ou 1 an après PCI




Macle L et al. *Can J Cardiol 2016;32:1170-1185*

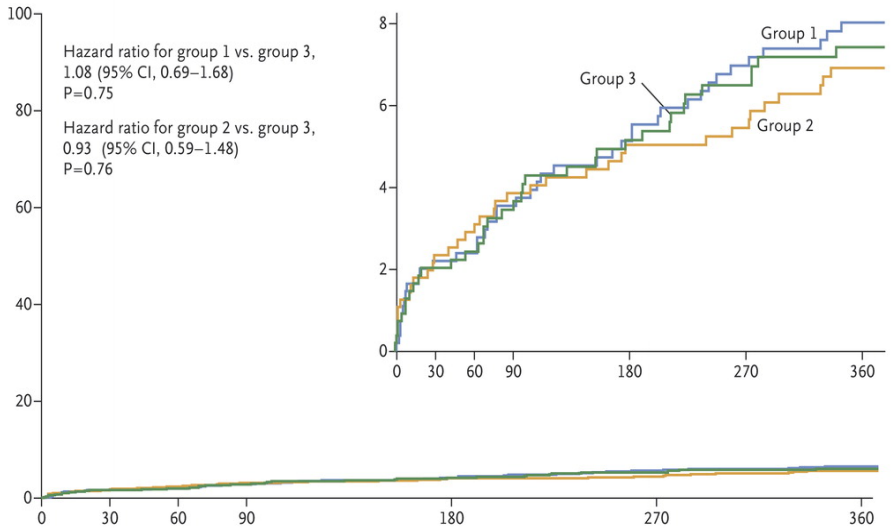
# NACO chez le coronarien instable

## Riva + 2 aPlt = option efficace et sécuritaire

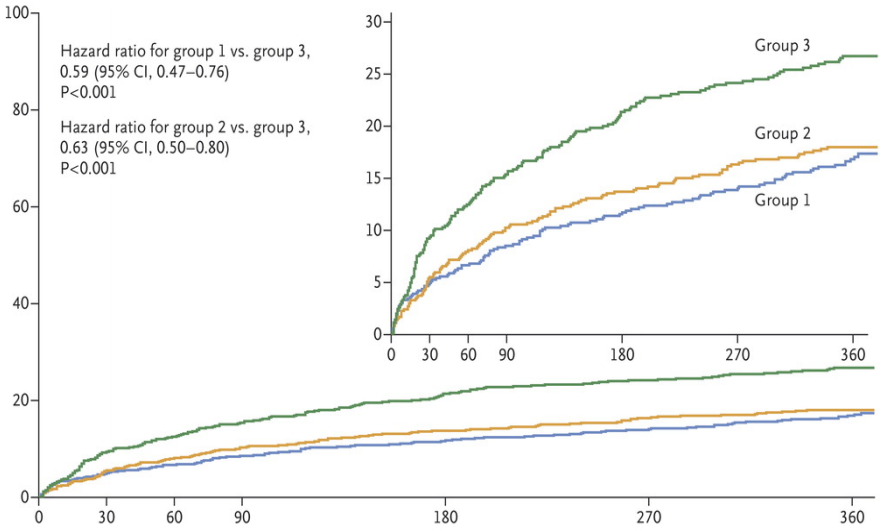
**PIONEER AF-PCI : Individus avec FA subissant un PCI-stent**

- Groupe 1 : Warfarin + 2 aPlt
- Groupe 2 : Riva 2,5 bid + 2 aPlt
- Groupe 3 : Riva 15 die + 1 aPlt

Risque cumulatif d'événements cardiovasc. majeurs (%)




Risque cumulatif de saignements majeurs (%)



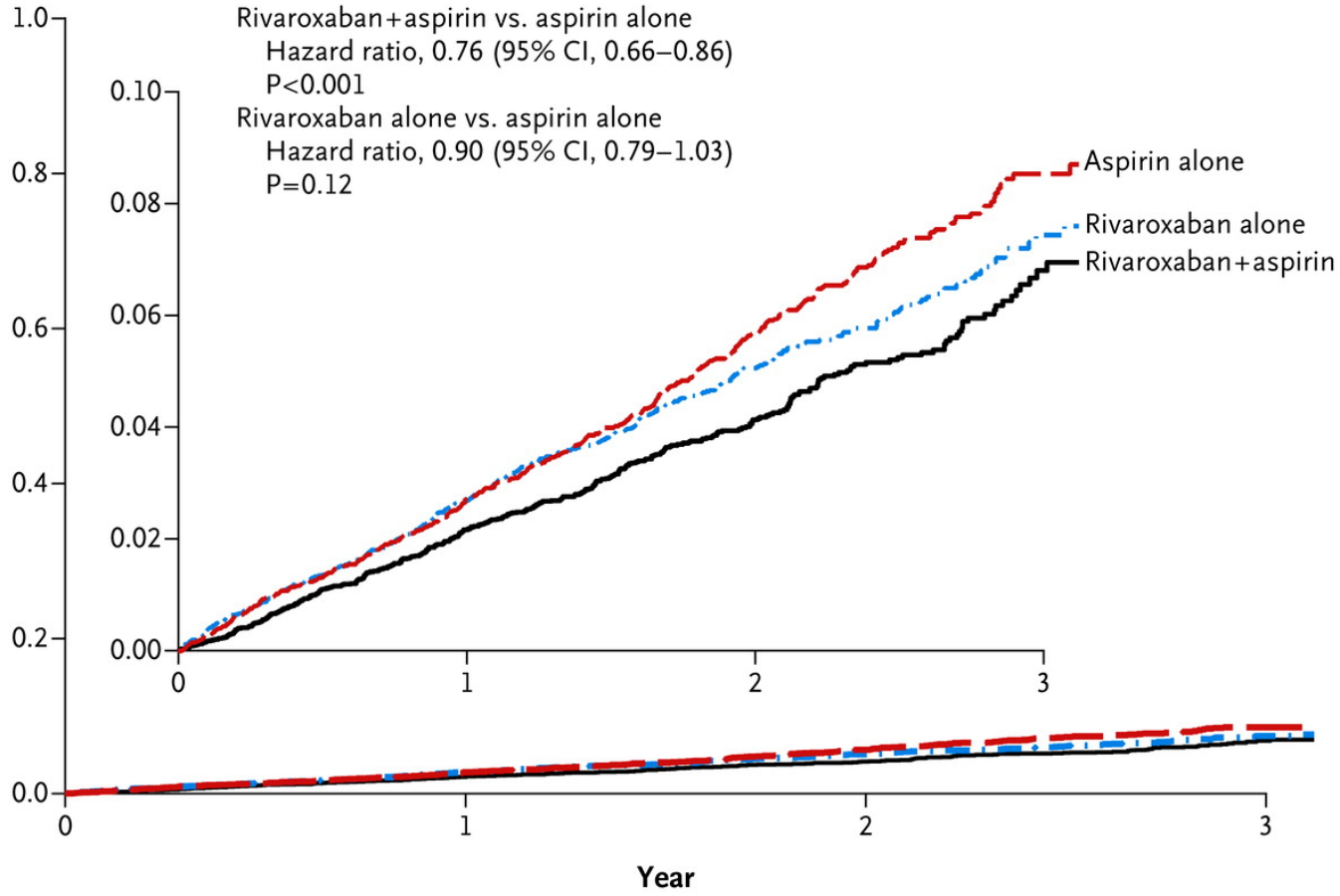

Gibson CM et al. NEJM 2016;375:2423

# NACO dans l'athéromatose stable (carotidienne, coronarienne ou MI) sans FA

COMPASS :

- Groupe 1 : AAS
- Groupe 2 : Riva 5 bid
- Groupe 3 : Riva 2,5 bid + AAS

Risque cumulatif de décès cardiovasc., AVC ou IM (%)




Eikelboom JW et al. NEJM 2017 (COMPASS; ahead of print)

# COMPASS

| Outcome | Rivaroxaban plus Aspirin (N=9152) | Rivaroxaban Alone (N=9117) | Aspirin Alone (N=9126) | Rivaroxaban plus Aspirin vs. Aspirin Alone | | Rivaroxaban Alone vs. Aspirin Alone | |
|---|---|---|---|---|---|---|---|
| | | | | Hazard Ratio (95% CI) | P Value | Hazard Ratio (95% CI) | P Value |
| | *number (percent)* | | | | | | |
| Major and minor bleeding | | | | | | | |
| Major bleeding | 288 (3.1) | 255 (2.8) | 170 (1.9) | 1.70 (1.40–2.05) | <0.001 | 1.51 (1.25–1.84) | <0.001 |
| Fatal bleeding† | 15 (0.2) | 14 (0.2) | 10 (0.1) | 1.49 (0.67–3.33) | 0.32 | 1.40 (0.62–3.15) | 0.41 |
| Nonfatal symptomatic ICH† | 21 (0.2) | 32 (0.4) | 19 (0.2) | 1.10 (0.59–2.04) | 0.77 | 1.69 (0.96–2.98) | 0.07 |
| Nonfatal, non-ICH, symptomatic bleeding into critical organ† | 42 (0.5) | 45 (0.5) | 29 (0.3) | 1.43 (0.89–2.29) | 0.14 | 1.57 (0.98–2.50) | 0.06 |
| Other major bleeding† | 210 (2.3) | 164 (1.8) | 112 (1.2) | 1.88 (1.49–2.36) | <0.001 | 1.47 (1.16–1.87) | 0.001 |
| Fatal bleeding or symptomatic ICH | 36 (0.4) | 46 (0.5) | 29 (0.3) | 1.23 (0.76–2.01) | 0.40 | 1.59 (1.00–2.53) | 0.05 |
| Fatal bleeding or symptomatic bleeding into critical organ | 78 (0.9) | 91 (1.0) | 58 (0.6) | 1.34 (0.95–1.88) | 0.09 | 1.58 (1.13–2.19) | 0.006 |
| Major bleeding according to ISTH criteria | 206 (2.3) | 175 (1.9) | 116 (1.3) | 1.78 (1.41–2.23) | <0.001 | 1.52 (1.20–1.92) | <0.001 |
| Transfusion within 48 hr after bleeding | 87 (1.0) | 66 (0.7) | 44 (0.5) | 1.97 (1.37–2.83) | <0.001 | 1.50 (1.03–2.20) | 0.03 |
| Minor bleeding | 838 (9.2) | 741 (8.1) | 503 (5.5) | 1.70 (1.52–1.90) | <0.001 | 1.50 (1.34–1.68) | <0.001 |
| Site of major bleeding | | | | | | | |
| Gastrointestinal | 140 (1.5) | 91 (1.0) | 65 (0.7) | 2.15 (1.60–2.89) | <0.001 | 1.40 (1.02–1.93) | 0.04 |
| Intracranial | 28 (0.3) | 43 (0.5) | 24 (0.3) | 1.16 (0.67–2.00) | 0.60 | 1.80 (1.09–2.96) | 0.02 |
| Skin or injection site | 28 (0.3) | 28 (0.3) | 12 (0.1) | 2.31 (1.18–4.54) | 0.01 | 2.34 (1.19–4.60) | 0.01 |
| Urinary | 13 (0.1) | 30 (0.3) | 21 (0.2) | 0.61 (0.31–1.23) | 0.16 | 1.43 (0.82–2.50) | 0.20 |
| Net-clinical-benefit outcome: CV death, stroke, myocardial infarction, fatal bleeding, or symptomatic bleeding into critical organ | 431 (4.7) | 504 (5.5) | 534 (5.9) | 0.80 (0.70–0.91) | <0.001 | 0.94 (0.84–1.07) | 0.36 |

Eikelboom JW et al. NEJM 2017 (COMPASS; ahead of print)

Désavantage pour rivaroxaban et anticipé et edoxaban pourrait disparaître avec dabigatran 110 bid ou apixaban

| | AVC et embolie systémique | AVC ischémique | Saignements majeurs | | | Mortalité totale |
|---|---|---|---|---|---|---|
| | | | Total | GI | Intra-crânien | |
| Dabigatran 150 BID | 0,66 | 0,76 | 0,93 | 1,50 | 0,40 | 0.88 |
| Dabigatran 110 BID | 0,91 | 1,11 | 0,80 | 1,10 | 0,31 | 0.91 |
| Apixaban 5 BID | 0,79 | 0,92 | 0,69 | 0,89 | 0,42 | 0.89 |
| Rivaroxaban 20 die c repas | 0,88 | 0,94 | 1,04 | 1,46 | 0,67 | 0.92 |
| Edoxaban 60 die | 0,87 | 1,00 | 0,80 | 1,23 | 0,47 | 0,92 |


1. Connolly SJ et al. NEJM 2009;361:1139
2. Patel MR et al. NEJM 2011;365:883
3. Granger CB et al. NEJM 2011;365:981
4. Giugliano RP et al. NEJM 2013

Saignements intracrâniens – incidence annuelle = 0,23-0,50%

- Dabigatran 110 bid : 0,23%
- Dabigatran 150 bid : 0,30%
- Apixaban : 0,33%
- Rivaroxaban : 0,50%
- Edoxaban : 0,39%

1. Connolly SJ et al. NEJM 2009;361:1139 3. Granger CB et al. NEJM 2011;365:981
2. Patel MR et al. NEJM 2011;365:883 4. Giugliano RP et al. NEJM 2013

# Focus sur les NACO dans le FOP

| | |
|---|---|
| Mitral valve | |
| Myxomatous valvulopathy with prolapse | 5 (1.8%) |
| Mitral annular calcification | 8 (2.9%) |
| Aortic valve | |
| Aortic valve stenosis | 3 (1.1%) |
| Calcific aortic valve | 12 (4.4%) |
| Non-atrial fibrillation atrial dysrhythmias and stasis | |
| Atrial asystole and sick-sinus syndrome | 3 (1.1%) |
| Atrial high-rate episodes | 7 (2.6%) |
| Atrial appendage stasis with reduced flow velocities or spontaneous echodensities | 6 (2.2%) |
| Atrial structural abnormalities | |
| Atrial septal aneurysm | 10 (3.6%) |
| Chiari network | 0 |
| Left ventricle | |
| Moderate systolic or diastolic dysfunction (global or regional) | 42 15.4%) |
| Ventricular noncompaction | 12 (4.4%) |
| Endomyocardial fibrosis | 1 (0.4%) |
| Covert paroxysmal atrial fibrillation (detected during follow-up) | |
| Atrial fibrillation detected on stroke recurrence | 30 (11.0%) |
| Atrial fibrillation detected on monitoring during follow-up | 50 (18.3%) |
| Atrial fibrillation not confirmed but strongly suspected | 38 (13.9%) |
| Paradoxical embolism | |
| Patent foramen ovale | 11 (4.0%) |
| Atrial septal defect | 3 (1.1%) |
| Cancer-associated | |
| Covert nonbacterial thrombotic endocarditis | 1 (0.4%) |
| Tumor emboli from occult cancer | 2 (0.8%) |
| Arteriogenic emboli | |
| Aortic arch atherosclerotic plaques | 9 (3.3%) |
| Cerebral artery nonstenotic plaques with ulceration | 29 (10.6%) |

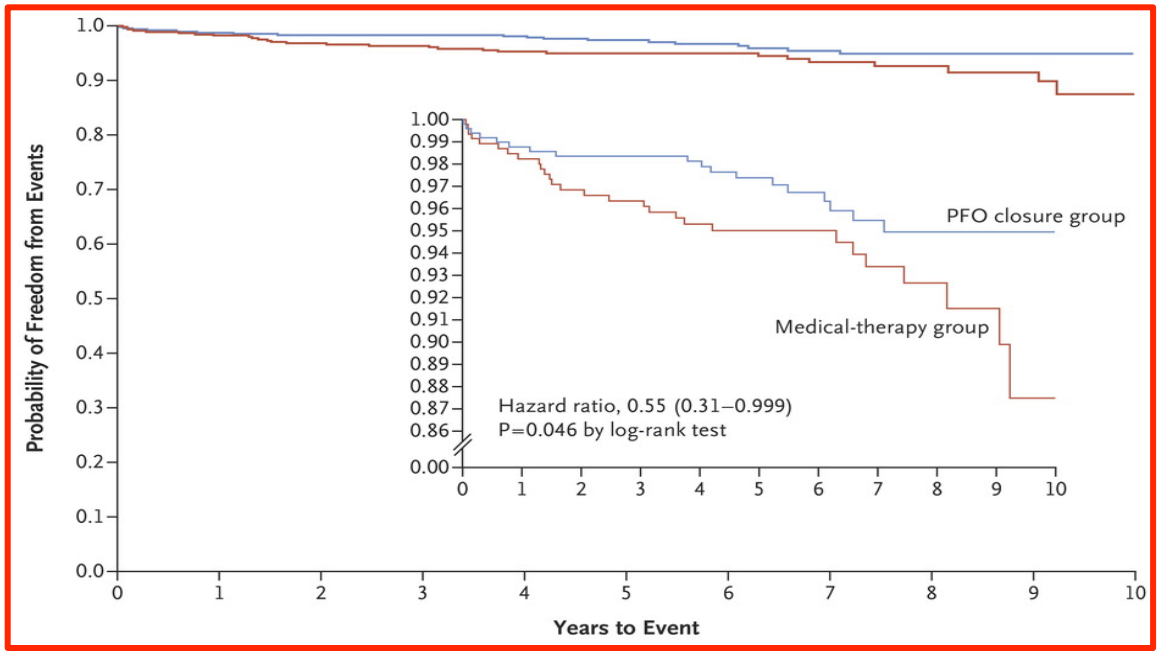
FOP : 50% des ESUS du jeune

# RESPECT

FOP → R

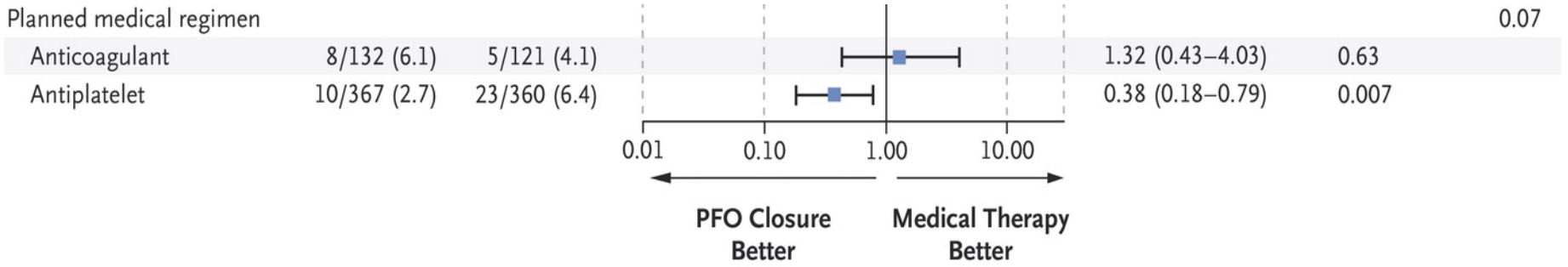
- Antithrombotique au choix (AAS, clopido, Aggrenox, anticoag.)
- Fermeture AAS-clopido x 1 mois AAS x 5 mois
  Discrétionnaire

AVC ischémique ou décès précoce




Saver JL et al. NEJM 2017;377:1022

## AVC ischémque ou décès : Anticoag = Fermeture du FOP !!!




## TEV : Anticoag > Fermeture du FOP !!!

| Événements (% pts-années) | Fermeture | Médical (aPlt ou anticoag) | HR (95%CI) | *P*-stat. |
|---|---|---|---|---|
| Embolie pulm. | 0,41 | 0,11 | 3,48 (0,98-12,34) | P=0.04 |
| TPP | 0,16 | 0,04 | 4,44 (0,52-38,05) | P=0.14 |

Saver JL et al. NEJM 2017;377:1022

# Autres causes

| | |
|---|---|
| Mitral valve | |
| Myxomatous valvulopathy with prolapse | 5 (1.8%) |
| Mitral annular calcification | 8 (2.9%) |
| Aortic valve | |
| Aortic valve stenosis | 3 (1.1%) |
| Calcific aortic valve | 12 (4.4%) |
| Non-atrial fibrillation atrial dysrhythmias and stasis | |
| Atrial asystole and sick-sinus syndrome | 3 (1.1%) |
| Atrial high-rate episodes | 7 (2.6%) |
| Atrial appendage stasis with reduced flow velocities or spontaneous echodensities | 6 (2.2%) |
| Atrial structural abnormalities | |
| Atrial septal aneurysm | 10 (3.6%) |
| Chiari network | 0 |
| Left ventricle | |
| Moderate systolic or diastolic dysfunction (global or regional) | 42 15.4%) |
| Ventricular noncompaction | 12 (4.4%) |
| Endomyocardial fibrosis | 1 (0.4%) |
| Covert paroxysmal atrial fibrillation (detected during follow-up) | |
| Atrial fibrillation detected on stroke recurrence | 30 (11.0%) |
| Atrial fibrillation detected on monitoring during follow-up | 50 (18.3%) |
| Atrial fibrillation not confirmed but strongly suspected | 38 (13.9%) |
| Paradoxical embolism | |
| Patent foramen ovale | 11 (4.0%) |
| Atrial septal defect | 3 (1.1%) |
| Cancer-associated | |
| Covert nonbacterial thrombotic endocarditis | 1 (0.4%) |
| Tumor emboli from occult cancer | 2 (0.8%) |
| Arteriogenic emboli | |
| Aortic arch atherosclerotic plaques | 9 (3.3%) |
| Cerebral artery nonstenotic plaques with ulceration | 29 (10.6%) |

# Conclusion

Il est temps de sortir de la préhistoire…

- NACO dans le ESUS : Sécuritaires et équivalents ou souvent supérieurs aux antiplaquettaires
- Imprudent de rester avec AAS (RRR = 22-25%)

# Ne manquez pas à Montréal