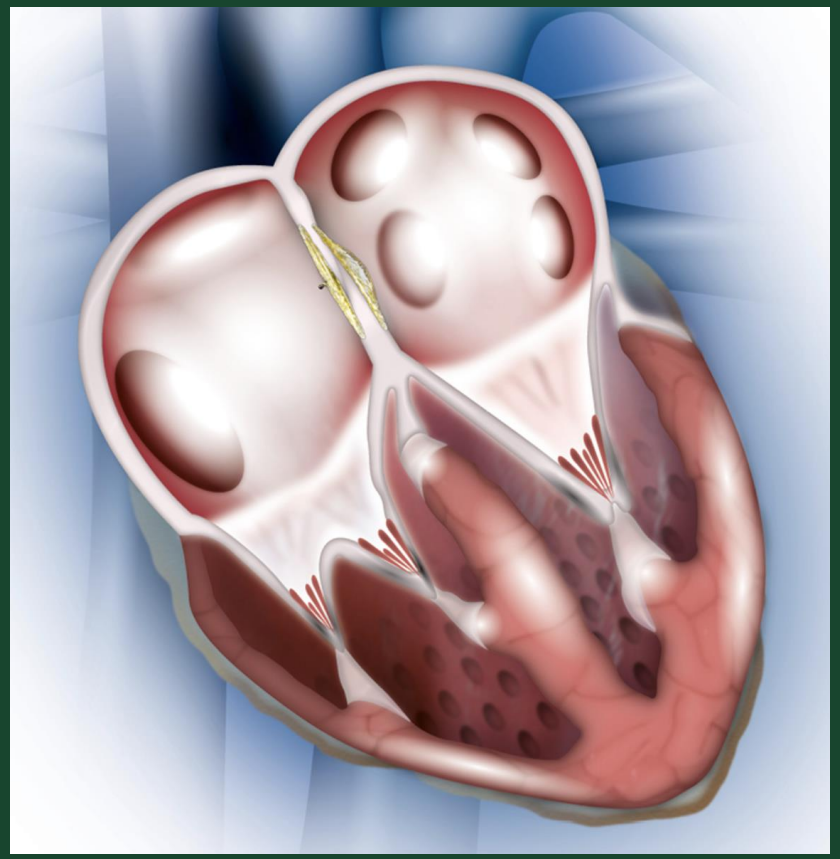
Fermeture de FOP post AVC



Charles Dussault, MD MPH FRCPC
Cardiologue électrophysiologiste
Université de Sherbrooke

Conflits d'intérêt

- **Consultant / conférencier**
  - Alliance BMS/Pfizer
  - Amgen
  - Bayer
  - Boeringher-Ingelheim
  - Medtronic
  - Novartis
  - Servier

- **Bourse de recherche**
  - Johnson & Johnson

Objectifs

- Connaître les données récentes en matière de FOP et de maladie neurovasculaire
- Connaître les données récentes en matière de FA et de maladie neurovasculaire
- Intégrer ces données à la pratique clinique

Constats

- 20-25% de FOP dans la population générale
  - **50% des patients AVC crypto.**
- FOP et AVC crypto: risque de récidive de 3,8%.
- Lignes directrices contemporaines dépassées (ACC/AHA)
  - Basé sur études de 2012-2013.

Première vague d'études randomisées

CLOSURE I, 2012

- **Starflex+ Tx médical** (ASA, AVK, les deux) vs. **Tx médical**

- **909 patients**
  - 18-60 ans
  - AVC-ICT crypto (incluant lacunaires)
  - FOP confirmé (pas de gradation)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 21, 2013 VOL. 368 NO. 12

Percutaneous Closure of Patent Foramen Ovale in Cryptogenic Embolism

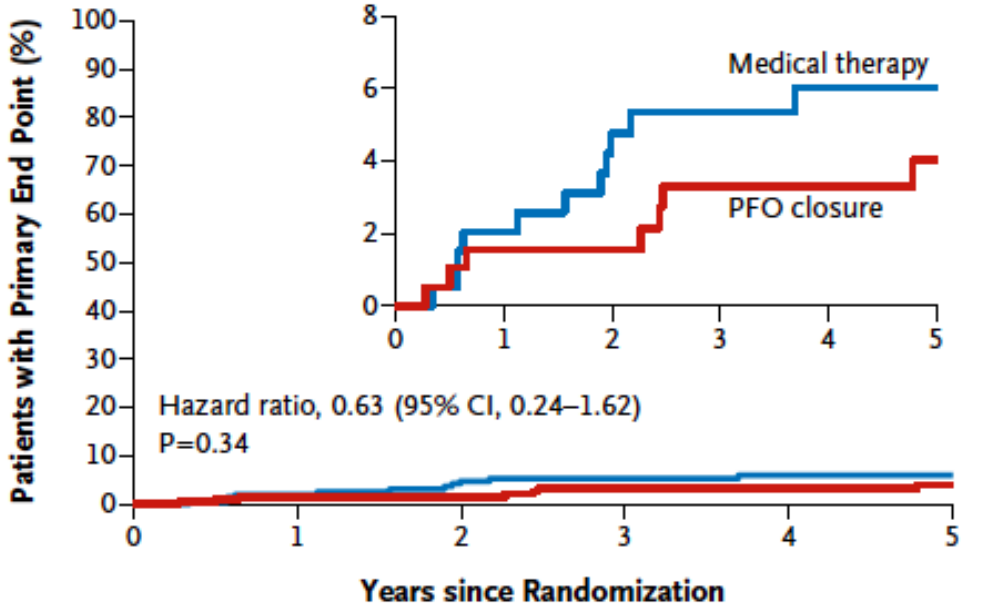
Bernhard Meier, M.D., Bindu Kalesan, Ph.D., Heinrich P. Mattle, M.D., Ahmed A. Khattab, M.D., David Hildick-Smith, M.D., Dariusz Dudek, M.D., Grethe Andersen, M.D., Reda Ibrahim, M.D., Gerhard Schuler, M.D., Antony S. Walton, M.D., Andreas Wahl, M.D., Stephan Windecker, M.D., and Peter Jüni, M.D., for the PC Trial Investigators*

PC, 2013

- **414 patients**
  - Moins de 60 ans
  - AVC crypto ou ICT avec imagerie + ou embolie périphérique
  - FOP prouvé

- Fermeture+ Tx médical (ASA, Plavix) vs. Tx médical.

PC, 2013



No. at Risk

Medical therapy	210	185	170	159	131	90
PFO closure	204	186	181	163	142	110

Figure 1. Kaplan–Meier Cumulative Estimates of the Rate of the Primary End Point.

PFO denotes patent foramen ovale.

Manque de puissance

ORIGINAL ARTICLE

Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke

John D. Carroll, M.D., Jeffrey L. Saver, M.D., David E. Thaler, M.D., Ph.D., Richard W. Smalling, M.D., Ph.D., Scott Berry, Ph.D., Lee A. MacDonald, M.D., David S. Marks, M.D., and David L. Tirschwell, M.D., for the RESPECT Investigators*

- Devis similaire PC sans embolies périphériques
- 980 patients

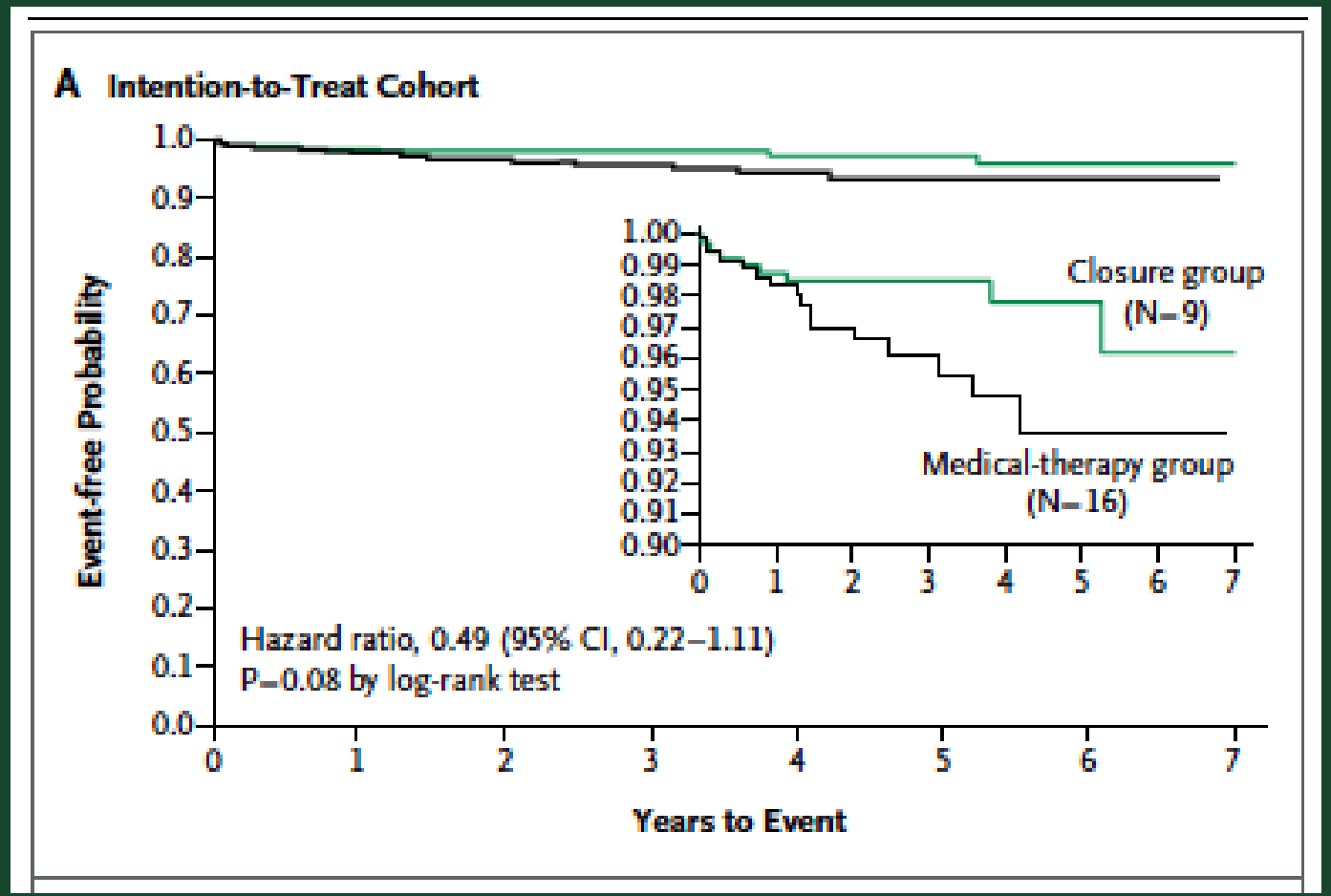
Table 1. Characteristics of the Patients at Baseline.*

Characteristic	PFO Closure Group (N=499)	Medical-Therapy Group (N=481)	All Patients (N=980)
Age — yr	45.7±9.7	46.2±10.0	45.9±9.9
Male sex — no. (%)	268 (53.7)	268 (55.7)	536 (54.7)
Time from index stroke to randomization — days	130±70	130±69	130±70
Medical history — no./total no. (%)			
Diabetes mellitus	33/499 (6.6)	41/481 (8.5)	74/980 (7.6)
Hypertension	160/499 (32.1)	153/481 (31.8)	313/980 (31.9)
Smoking status			
Current smoker	75/499 (15.0)	55/481 (11.4)	130/980 (13.3)
Former smoker	134/499 (26.9)	143/481 (29.7)	277/980 (28.3)
Hypercholesterolemia	196/499 (39.3)	195/481 (40.5)	391/980 (39.9)
Coronary artery disease	19/499 (3.8)	9/481 (1.9)	28/980 (2.9)
Myocardial infarction	5/499 (1.0)	2/481 (0.4)	7/980 (0.7)
Peripheral vascular disease	5/499 (1.0)	1/481 (0.2)	6/980 (0.6)
Previous transient ischemic attack	58/499 (11.6)	61/481 (12.7)	119/980 (12.1)
Previous stroke	53/498 (10.6)	51/481 (10.6)	104/979 (10.6)
Family history of stroke	136/495 (27.5)	109/480 (22.7)	245/975 (25.1)
Migraine	195/499 (39.1)	186/481 (38.7)	381/980 (38.9)
Deep-vein thrombosis	20/499 (4.0)	15/481 (3.1)	35/980 (3.6)
Congestive heart failure	3/499 (0.6)	0	3/980 (0.3)
Chronic obstructive pulmonary disease	4/499 (0.8)	7/481 (1.5)	11/980 (1.1)
Birth control or hormone-replacement medications	41/499 (8.2)	51/481 (10.6)	92/980 (9.4)
Substantial right-to-left shunt — no./total no. (%)†	247/499 (49.5)	231/481 (48.0)	478/980 (48.8)
Atrial septal aneurysm — no./total no. (%)	180/499 (36.1)	170/481 (35.3)	350/980 (35.7)

* Plus–minus values are means ±SD. There were no significant differences between the two groups in any of the characteristics listed.

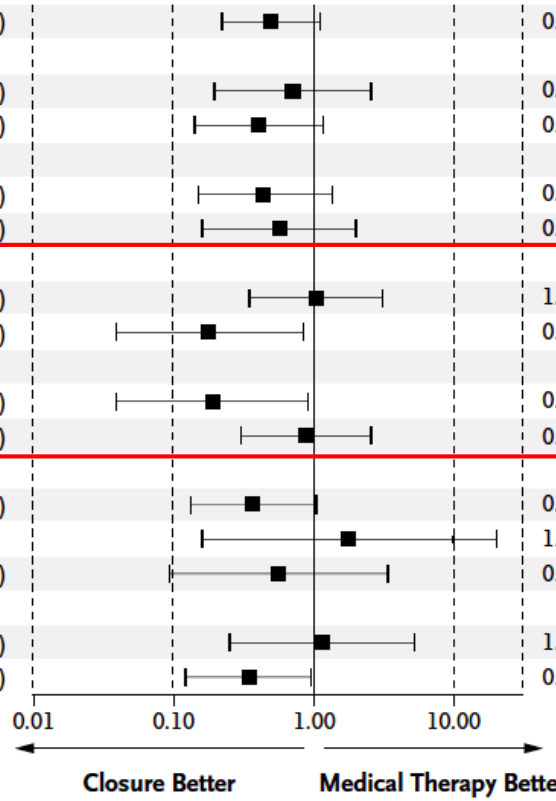
† A substantial shunt refers to a shunt size of grade 3. Grades ranged from 1 to 3, with higher grades indicating a larger size.

RESPECT, 2013 (suivi 2,6 ans)

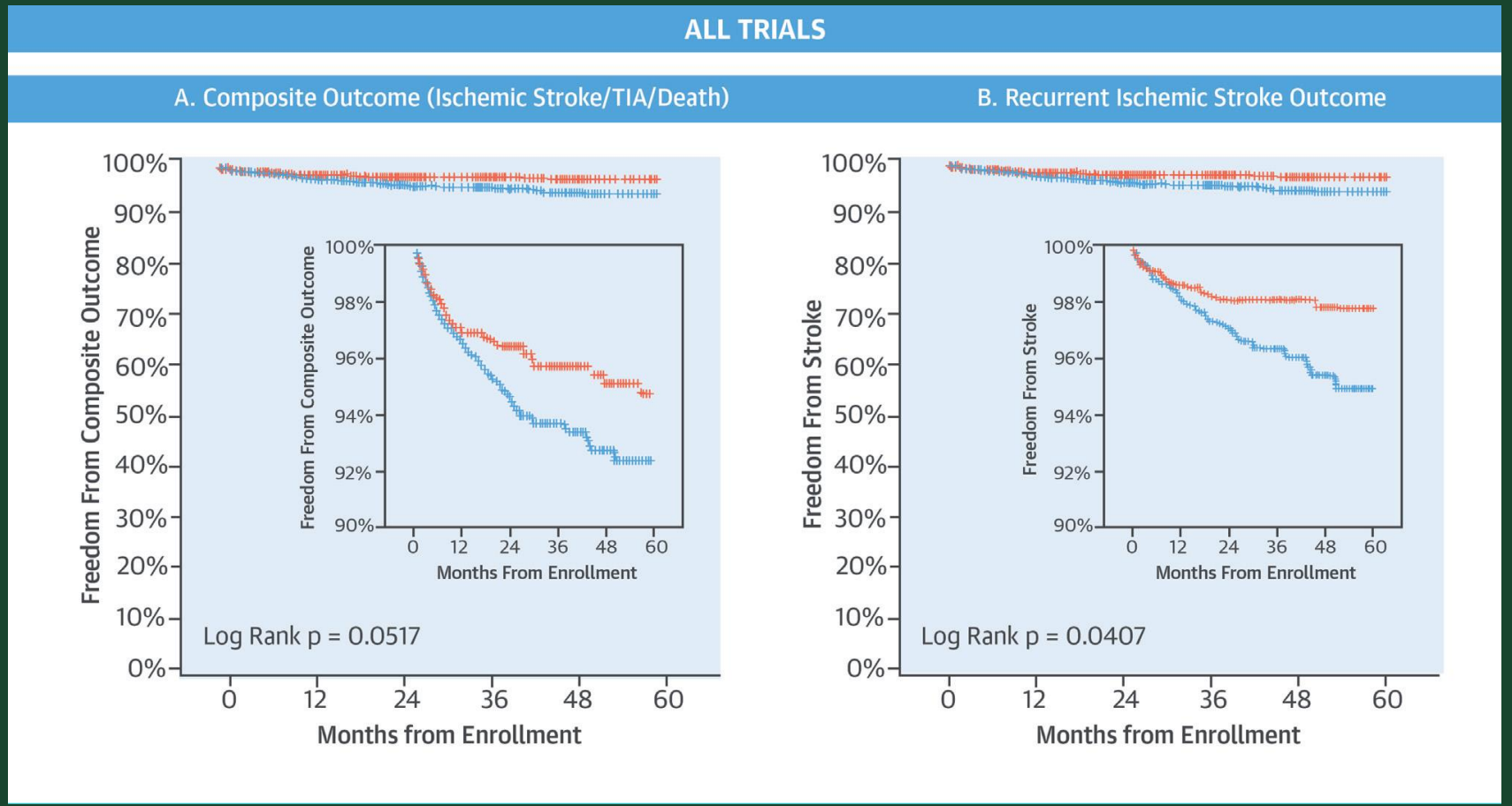


RESPECT, 2013

Subgroup	Closure Group	Medical-Therapy Group	Hazard Ratio (95% CI)	P Value by Log-Rank Test	P Value for Interaction
	no. of patients/total no. (%)				
Overall	9/499 (1.8)	16/481 (3.3)	0.49 (0.22–1.11)	0.08	
Age					0.52
18–45 yr	4/230 (1.7)	5/210 (2.4)	0.70 (0.19–2.60)	0.59	
46–60 yr	5/262 (1.9)	11/266 (4.1)	0.41 (0.14–1.17)	0.08	
Sex					0.73
Male	5/268 (1.9)	10/268 (3.7)	0.45 (0.15–1.31)	0.13	
Female	4/231 (1.7)	6/213 (2.8)	0.57 (0.16–2.02)	0.38	
Shunt size					0.07
None, trace, or moderate	7/247 (2.8)	6/244 (2.5)	1.03 (0.35–3.08)	0.95	
Substantial	2/247 (0.8)	10/231 (4.3)	0.18 (0.04–0.81)	0.01	
Atrial septal aneurysm					0.10
Present	2/180 (1.1)	9/169 (5.3)	0.19 (0.04–0.87)	0.02	
Absent	7/319 (2.2)	7/312 (2.2)	0.89 (0.31–2.54)	0.83	
Index infarct topography					0.39
Superficial	5/280 (1.8)	12/269 (4.5)	0.37 (0.13–1.04)	0.05	
Small deep	2/57 (3.5)	1/70 (1.4)	1.76 (0.16–19.93)	0.64	
Other	2/157 (1.3)	3/139 (2.2)	0.56 (0.09–3.34)	0.52	
Planned medical regimen					0.20
Anticoagulant	4/132 (3.0)	3/121 (2.5)	1.14 (0.26–5.10)	0.86	
Antiplatelet	5/367 (1.4)	13/359 (3.6)	0.34 (0.12–0.94)	0.03	



Méta-analyse (closure 1, PC, Respect)



Encore plus significatif pour l'Amplatzer

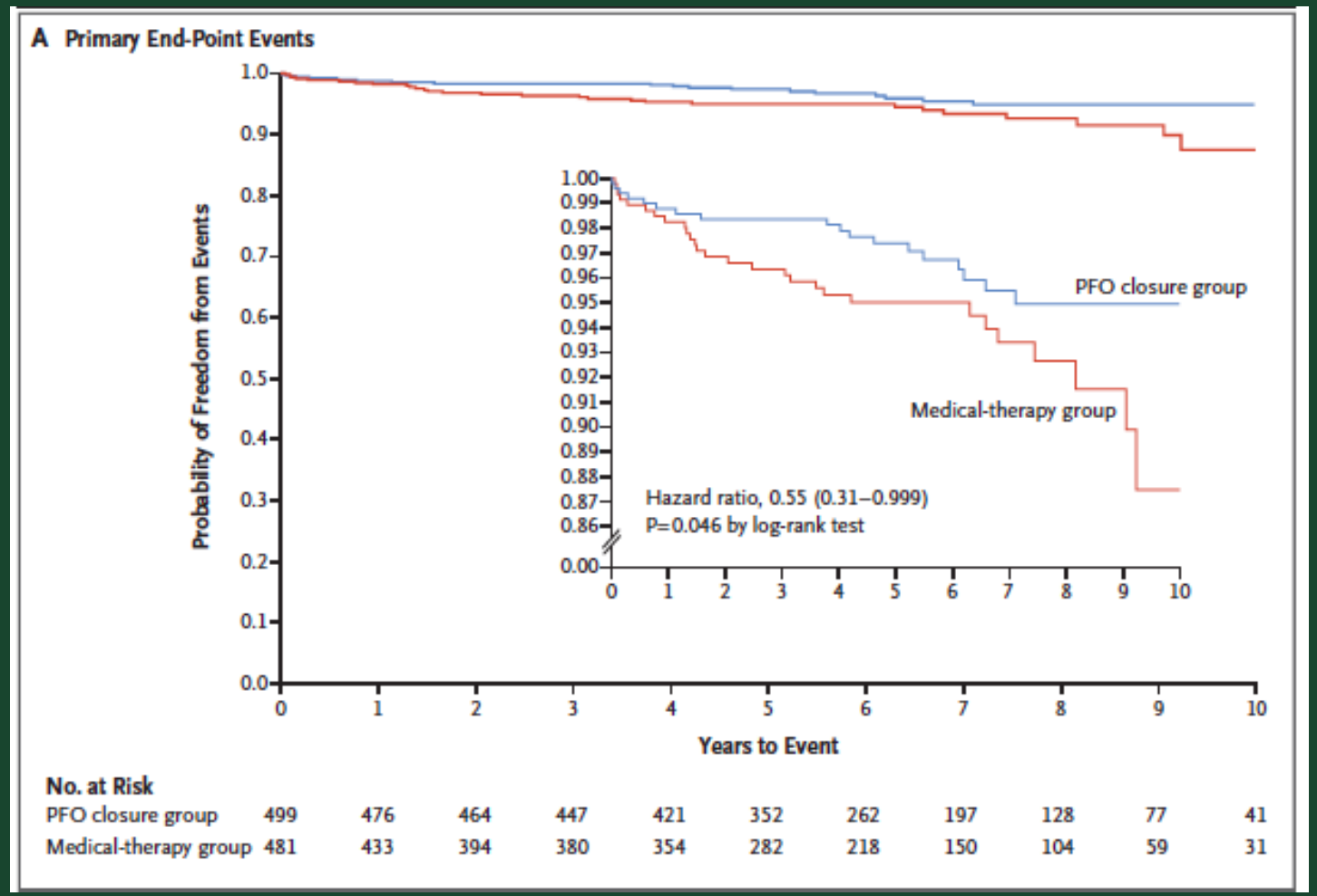
RESPECT, 2017

ORIGINAL ARTICLE

Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke

Jeffrey L. Saver, M.D., John D. Carroll, M.D., David E. Thaler, M.D., Ph.D., Richard W. Smalling, M.D., Ph.D., Lee A. MacDonald, M.D., David S. Marks, M.D., and David L. Tirschwell, M.D., for the RESPECT Investigators*

RESPECT – Issue 1aire



5688 patients année

Suivi médian 5.9 ans

NNT pour prévenir un AVC à 5 ans = 42

RESPECT – Sous-groupes

Subgroup	PFO Closure Group	Medical-Therapy Group	Hazard Ratio (95% CI)	P Value by Log-Rank Test	P Value for Interaction
	no. of patients with event/total no. (%)				
Overall	18/499 (3.6)	28/481 (5.8)	0.55 (0.30–1.00)	0.046	
Age					0.78
18–45 yr	6/230 (2.6)	10/210 (4.8)	0.49 (0.18–1.35)	0.16	
46–60 yr	12/262 (4.6)	18/266 (6.8)	0.59 (0.28–1.23)	0.16	
Sex					1.00
Male	10/268 (3.7)	16/268 (6.0)	0.56 (0.25–1.23)	0.14	
Female	8/231 (3.5)	12/213 (5.6)	0.55 (0.22–1.34)	0.18	
Shunt size					0.04
None, trace or moderate	13/247 (5.3)	12/244 (4.9)	0.96 (0.44–2.11)	0.93	
Substantial	5/247 (2.0)	16/231 (6.9)	0.26 (0.10–0.71)	0.005	
Atrial septal aneurysm					0.04
Present	3/179 (1.7)	13/170 (7.6)	0.20 (0.06–0.70)	0.005	
Absent	15/320 (4.7)	15/311 (4.8)	0.86 (0.42–1.76)	0.68	
Index infarct topography					0.21
Superficial	9/280 (3.2)	18/269 (6.7)	0.43 (0.19–0.96)	0.03	
Small deep	4/57 (7.0)	2/70 (2.9)	2.25 (0.41–12.32)	0.34	
Other	5/157 (3.2)	8/140 (5.7)	0.48 (0.16–1.48)	0.19	
Planned medical regimen					0.07
Anticoagulant	8/132 (6.1)	5/121 (4.1)	1.32 (0.43–4.03)	0.63	
Antiplatelet	10/367 (2.7)	23/360 (6.4)	0.38 (0.18–0.79)	0.007	

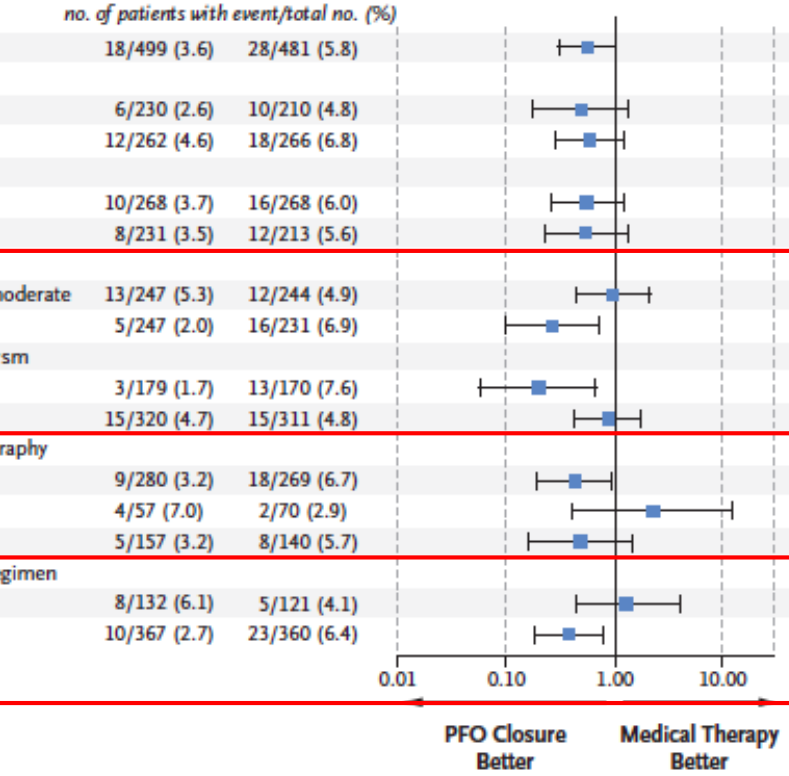


Figure 2. Rate of Recurrent Ischemic Stroke According to Subgroup.

Potential heterogeneity of the treatment effect was noted with respect to three baseline characteristics (threshold for significant interaction, P=0.10), with a suggestion of greater risk reductions with PFO closure than with medical therapy alone among patients with an atrial septal aneurysm, among patients with a substantial shunt size, and among patients whose planned medical regimen was antiplatelet therapy rather than anticoagulant therapy if they were to be randomly assigned to the medical-therapy group. A substantial shunt refers to a shunt size of grade 3. Grades ranged from 1 to 3, with higher grades indicating a larger size.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 14, 2017 VOL. 377 NO. 11

Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke

J.-L. Mas, G. Derumeaux, B. Guillon, E. Massardier, H. Hosseini, L. Mechtouff, C. Arquizan, Y. Béjot, F. Vuillier, O. Detante, C. Guidoux, S. Canaple, C. Vaduva, N. Dequatre-Ponchelle, I. Sibon, P. Garnier, A. Ferrier, S. Timsit, E. Robinet-Borgomano, D. Sablot, J.-C. Lacour, M. Zuber, P. Favrole, J.-F. Pinel, M. Apoil, P. Reiner, C. Lefebvre, P. Guérin, C. Piot, R. Rossi, J.-L. Dubois-Randé, J.-C. Eicher, N. Meneveau, J.-R. Lusson, B. Bertrand, J.-M. Schleich, F. Godart, J.-B. Thambo, L. Leborgne, P. Michel, L. Pierard, G. Turc, M. Barthelet, A. Charles-Nelson, C. Weimar, T. Moulin, J.-M. Juliard, and G. Chatellier, for the CLOSE Investigators*

CLOSE – Sélection des patients

- 16 – 60 ans
- AVC cryptogénique 6 derniers mois
- FOP à haut risque
- Dispositif: choix opérateur

Critères haut risque

- **Anévrysme**: incursion+10mm à l'ETO
- **Shunt** : +30 bulles OG en 3 cycles

CLOSE – Randomisation

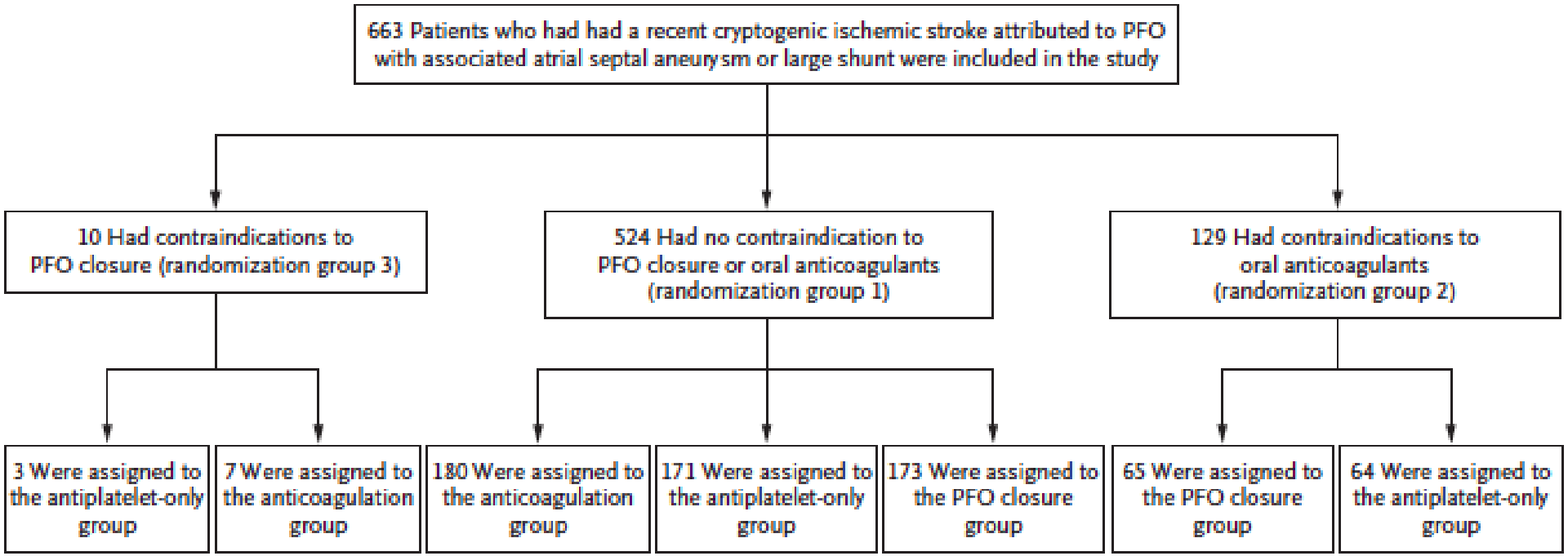
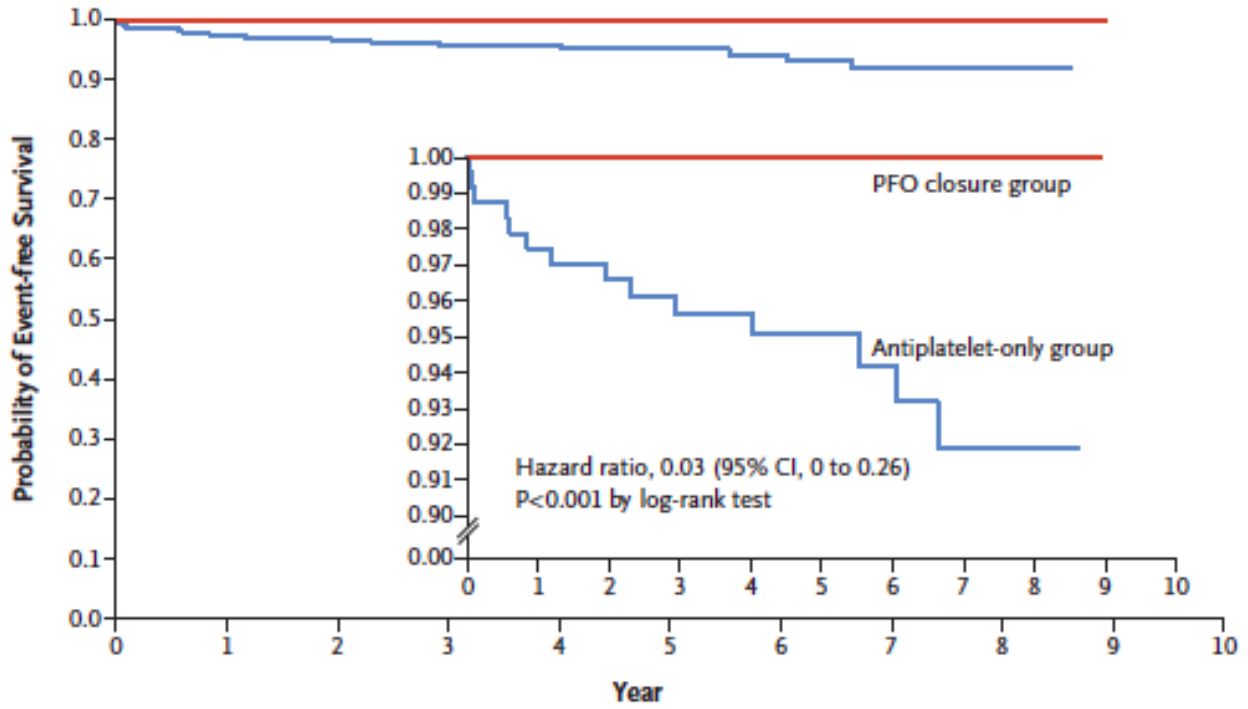


Figure 1. Randomization of Patients.

Of the 664 patients initially enrolled, 1 patient withdrew consent soon after randomization. According to French law, data concerning this patient cannot be used. Therefore, data from only 663 patients are presented. The patent foramen ovale (PFO) closure group comprised patients assigned to transcatheter PFO closure plus long-term antiplatelet therapy; the antiplatelet-only group, patients assigned to antiplatelet therapy alone; and the anticoagulation group, patients assigned to oral anticoagulation.

CLOSE – Issue 1aire



No. at Risk											
PFO closure group	238	238	232	200	179	141	99	64	20	0	0
Antiplatelet-only group	235	229	223	198	160	130	96	55	19	0	0

Figure 2. Kaplan–Meier Cumulative Estimates of Probability of Stroke in the PFO Closure Group versus the Antiplatelet-Only Group.

The analysis was performed in the intention-to-treat cohort, which included all patients who were randomly assigned to a treatment. The inset shows the same data on an enlarged y axis.

NNT pour prévenir un AVC à 5 ans = 20

FA (aigu seulement)

CLOSE - Complications

Table 3. Procedural Complications and Serious Adverse Events.*

Complication or Event	Randomization Groups 1 and 2			Randomization Groups 1 and 3		
	PFO Closure Group (N=238)	Antiplatelet-Only Group (N=235)	P Value	Anticoagulant Group (N=187)	Antiplatelet-Only Group (N=174)	P Value
	no. of patients (%)			*no. of patients (%)*		
Major or fatal device-related or procedure-related complication†	14 (5.9)	NA	NA	NA	NA	NA
Major or fatal bleeding complication	2 (0.8)	5 (2.1)	0.28	10 (5.3)	4 (2.3)	0.18
Atrial fibrillation or flutter‡	11 (4.6)§	2 (0.9)	0.02	0	2 (1.1)	0.23
Death	0	0	NA	1 (0.5)¶	0	0.65
At least one serious adverse event	85 (35.7)	78 (33.2)	0.56	62 (33.2)	59 (33.9)	0.88

* Definitions of major or fatal device-related or procedure-related complications, definitions of major or fatal bleeding complications, and a full list of serious adverse events are provided in the Supplementary Appendix.
† Major or fatal device-related or procedure-related complications in the PFO closure group are listed for those that occurred within 30 days after the procedure and included atrial fibrillation (9 patients), atrial flutter (1 patient), supraventricular tachycardia (2 patients), air embolism (1 patient), and hyperthermia resulting in prolongation of hospitalization (1 patient).
‡ Atrial fibrillation or flutter was classified as cases that required treatment for more than 1 month.
§ In 10 patients, atrial fibrillation or flutter occurred within 30 days after the procedure.
¶ The one death was due to pancreatic cancer.

ORIGINAL ARTICLE

Patent Foramen Ovale Closure or Antiplatelet Therapy for Cryptogenic Stroke

Lars Søndergaard, M.D., Scott E. Kasner, M.D., John F. Rhodes, M.D., Grethe Andersen, M.D., D.M.Sc., Helle K. Iversen, M.D., D.M.Sc., Jens E. Nielsen-Kudsk, M.D., D.M.Sc., Magnus Settergren, M.D., Ph.D., Christina Sjöstrand, M.D., Ph.D., Risto O. Roine, M.D., David Hildick-Smith, M.D., J. David Spence, M.D., and Lars Thomassen, M.D., for the Gore REDUCE Clinical Study Investigators*

REDUCE – Résumé

- 18-59 ans suivis 2 – 5 ans
- AVC crypto. dans les 180 jours
- FOP avec shunt D-G
- AVC lacunaires exclus
- IRM 0 et 24 mois

REDUCE - Résultats

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	PFO Closure Group (N=441)	Antiplatelet-Only Group (N=223)
Age — yr	45.4±9.3	44.8±9.6
Days from qualifying event to randomization	100±52	101±53
Male sex — no. (%)	261 (59.2)	138 (61.9)
Medical history — no. (%)		
Current smoking	63 (14.3)	25 (11.2)
Hypertension	112 (25.4)	58 (26.0)
Diabetes mellitus	18 (4.1)	10 (4.5)
Stroke or TIA before the index event	62 (14.1)	23 (10.3)
Previous stroke	42 (9.5)	13 (5.8)
Previous TIA	26 (5.9)	11 (4.9)
Index event — no. (%)		
Ischemic stroke with symptoms lasting ≥24 hr	402 (91.2)	199 (89.2)
Ischemic stroke symptoms lasting <24 hr, with imaging confirmation of infarct	39 (8.8)	24 (10.8)
Patent foramen ovale shunt size — no./total no. (%)†		
Small	77/425 (18.1)	43/216 (19.9)
Moderate	166/425 (39.1)	94/216 (43.5)
Large	182/425 (42.8)	79/216 (36.6)
Atrial septal aneurysm — no./total no. (%)	86/422 (20.4)	NA‡

- 664 patients
- Âge moyen 45,2 ans
- Shunt modéré-large 81%
- Durée médiane de suivi 3,2 ans
- Tx antiplaquett. similaire

REDUCE – Issues cliniques

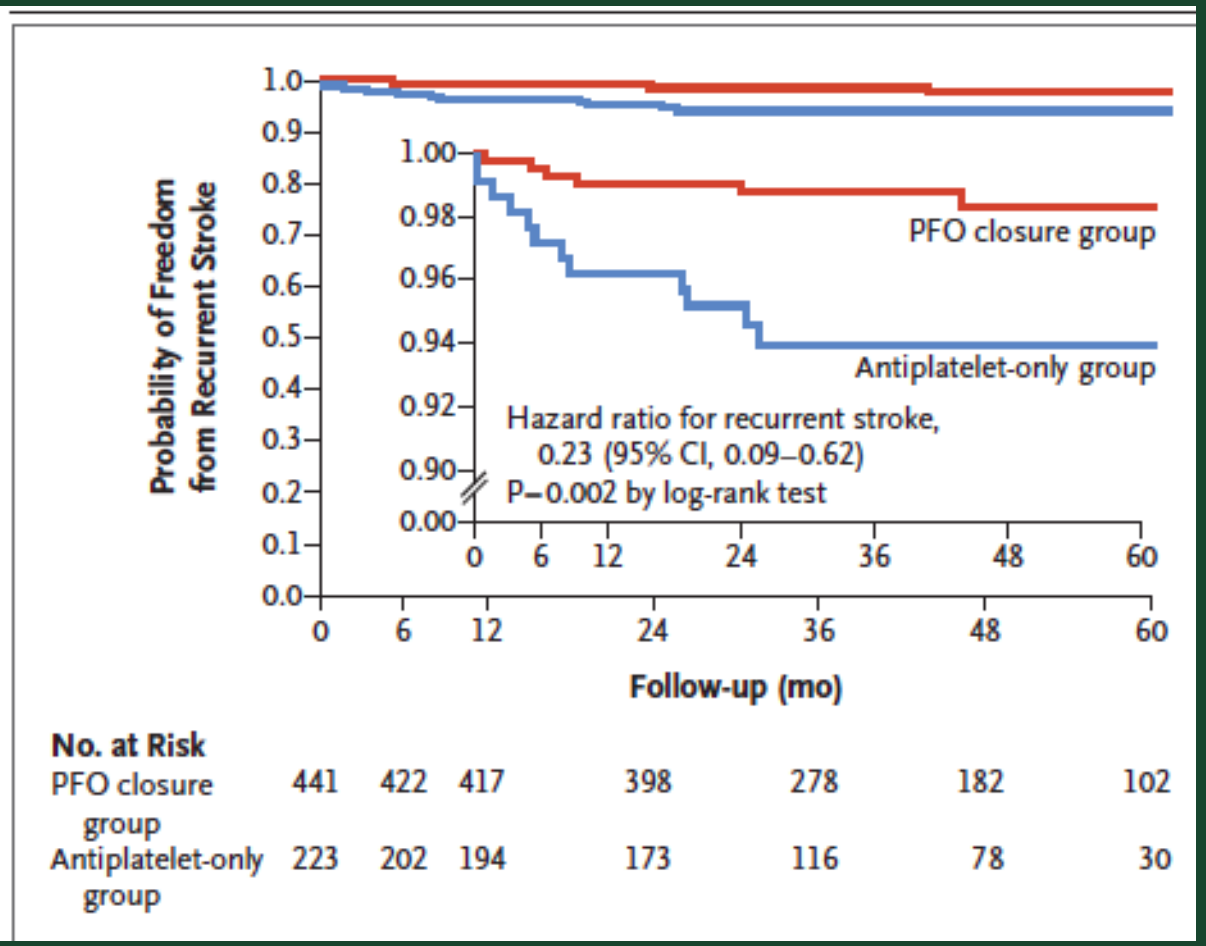


Table 2. Coprimary End Points of Freedom from Clinical Ischemic Stroke and Incidence of New Brain Infarction.*

End Point	PFO Closure Group	Antiplatelet-Only Group	Effect Size	P Value
	no. of patients/total no. (%)			
Clinical ischemic stroke†	6/441 (1.4)	12/223 (5.4)	0.23 (0.09–0.62)‡	0.002§
New brain infarction¶	22/383 (5.7)	20/177 (11.3)	0.51 (0.29–0.91)‖	0.04**
Recurrent clinical ischemic stroke	5/383 (1.3)	12/177 (6.8)	0.19 (0.07–0.54)‖	0.005**
Silent brain infarction only	17/383 (4.4)	8/177 (4.5)	0.98 (0.43–2.23)‖	0.97**

⬆ **FA (aigu seulement)**

Perspective

- Comment peut-on expliquer 3 nouvelles études démontrant une diminution de la récidive d'AVC avec la fermeture du FOP, alors que nous en avions 3 autres démontrant le contraire en 2012-2013?
- Critères des sélection plus serrés.
  - AVC lacunaire dans CLOSURE I.

Perspective

- Étude RESPECT s'est positivée avec un suivi médian passant de 2,1 à 5,9 ans.
  - Pas seulement expliqué par un suivi plus long, comme le démontre l'étude PC qui était négative avec un suivi respectable de 4 ans…
- Critères de sélection très serrés de CLOSE ont permis une absence de récidive d'AVC dans le groupe fermeture.
- REDUCE : étude mitoyenne avec critères un peu moins serrés.

Cryptogenic Stroke and High-Risk Patent Foramen Ovale

The DEFENSE-PFO Trial

Pil Hyung Lee, MD,[a] Jae-Kwan Song, MD, PhD,[a] Jong S. Kim, MD, PhD,[b] Ran Heo, MD,[a] Sahmin Lee, MD,[a] Dae-Hee Kim, MD, PhD,[a] Jong-Min Song, MD, PhD,[a] Duk-Hyun Kang, MD, PhD,[a] Sun U. Kwon, MD, PhD,[b] Dong-Wha Kang, MD, PhD,[b] Dongwhane Lee, MD,[b] Hyuk Sung Kwon, MD,[b] Sung-Cheol Yun, PhD,[c] Byung Joo Sun, MD, PhD,[d] Jae-Hyeong Park, MD, PhD,[d] Jae-Hwan Lee, MD, PhD,[d] Hye Seon Jeong, MD, PhD,[e] Hee-Jung Song, MD, PhD,[e] Jei Kim, MD, PhD,[e] Seung-Jung Park, MD, PhD[a]

DEFENSE – Sélection de patients

- AVC ischémique x 6 mois sans cause identifiable
  - Amplatzer (DAPT x 6 mois) vs Tx Medical (choix MD)

- Évaluation extensive standardisée de l'AVC pour s'assurer de l'absence de cause autre.

- FOP jugés à haut risque
  - Anevrysme septum interauriculaire
  - Taille du FOP plus de 2 mm

DEFENSE - Résultats

TABLE 2 Changes in Antiplatelet or Anticoagulation Therapy During Follow-Up

	PFO Closure Group (N = 60)	Medication-Only Group (N = 60)	p Value
At 30 days			
Single-antiplatelet therapy	10.0 (6/60)	16.7 (10/60)	0.42
Dual-antiplatelet therapy	75.0 (45/60)	58.3 (35/60)	0.08
Warfarin	15.0 (9/60)	25.0 (15/60)	0.25
At 6 months			
Single-antiplatelet therapy	34.6 (18/52)	25.0 (13/52)	0.39
Dual-antiplatelet therapy	57.7 (30/52)	51.9 (27/52)	0.69
Warfarin	7.7 (4/52)	23.1 (12/52)	0.05
At 12 months			
Single-antiplatelet therapy	42.6 (20/47)	37.0 (17/46)	0.67
Dual-antiplatelet therapy	34.0 (16/47)	41.3 (19/46)	0.53
Warfarin	6.4 (3/47)	21.7 (10/46)	0.04
No antiplatelet therapy or warfarin	17.0 (8/47)	0.0 (0/46)	0.006

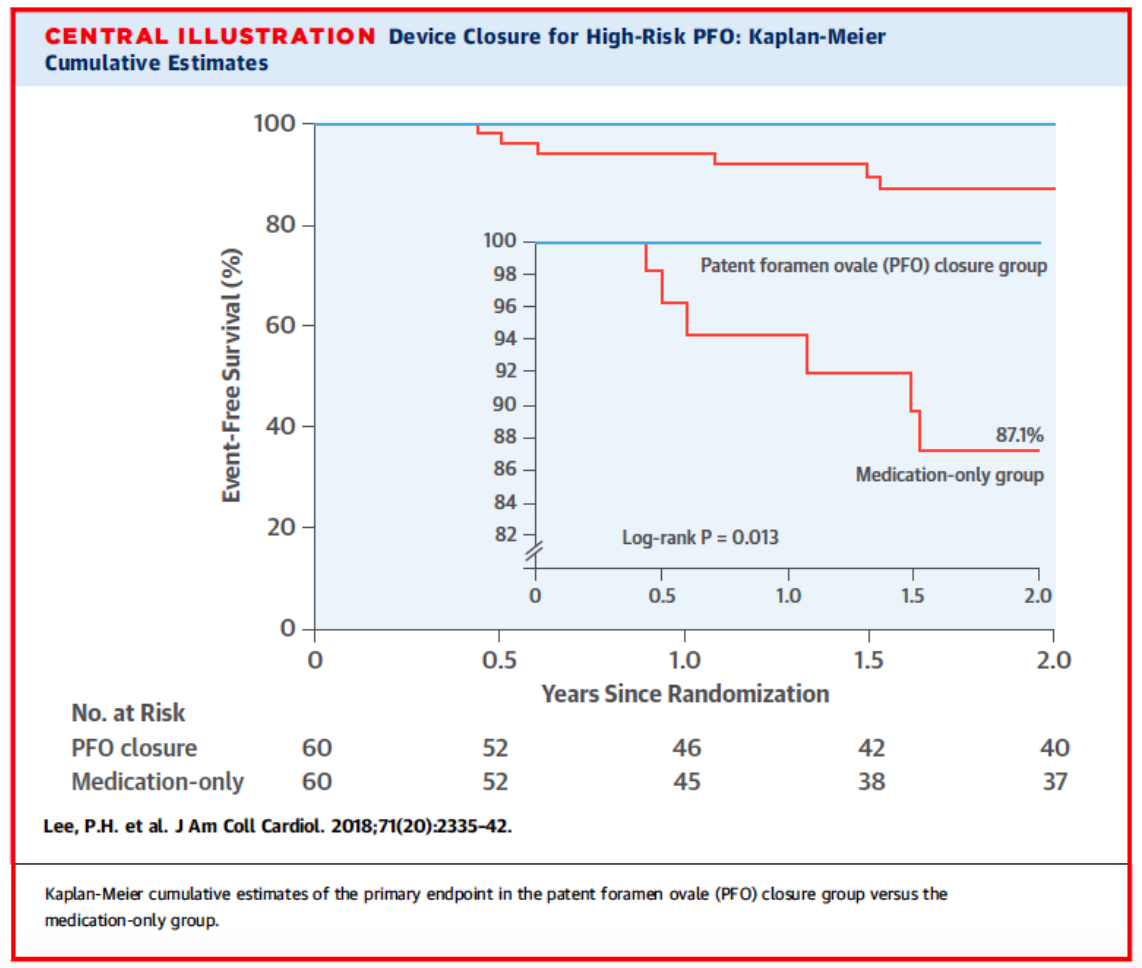
Values are % (n/N).
PFO = patent foramen ovale.

TABLE 1 Baseline Characteristics of the Patients

	PFO Closure Group (N = 60)	Medication-Only Group (N = 60)	p Value
Age, yrs	49 ± 15	54 ± 12	0.06
Male	33 (55.0)	34 (56.7)	>0.99
Medical history			
Hypertension	12 (20.0)	17 (28.3)	0.39
Diabetes	6 (10.0)	8 (13.3)	0.78
Current smoker	10 (16.7)	16 (26.7)	0.27
Hypercholesterolemia	18 (30.0)	25 (41.7)	0.25
Qualifying event			0.28
Anterior circulatory territory	28 (46.7)	34 (56.7)	
Multiple territories	0 (0.0)	2 (3.3)	
Modified Rankin scale			0.74
0 or 1	47 (78.3)	45 (75.0)	
2 or 3	13 (21.7)	15 (25.0)	
Morphologic characteristics of PFO			
Shunt at rest			
No shunt	25 (41.7)	26 (43.3)	0.25
Left-to-right shunt	31 (51.7)	34 (56.7)	
Right-to-left shunt	3 (5.0)	0 (0.0)	
Bidirectional shunt	1 (1.7)	0 (0.0)	
PFO size, mm	3.2 ± 1.5	3.2 ± 1.1	0.85
Atrial septal aneurysm	5 (8.3)	8 (13.3)	0.56
Atrial septal hypermobility	28 (46.7)	27 (45.0)	>0.99

Values are mean ± SD or n (%).
PFO = patent foramen ovale.

DEFENSE – Issue 1aire



NNT à 2 ans = 10

CLOSE & DEFENSE : 900 patients avec 0 AVC jusqu'à maintenant!

Méta-analyses incluant les études modernes

Mojadidi et al, 2017

FIGURE 2 Recurrent Stroke and Atrial Fibrillation/Flutter Outcomes in Cryptogenic Stroke Patients Randomized to PFO Closure or Medical Therapy

A Recurrent Stroke

Study or Subgroup	Device Events	Device Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
CLOSE (40)	0	238	14	235	6.1%	0.03 [0.00-0.57]	2017
RESPECT (27)	18	499	28	481	32.2%	0.62 [0.35-1.11]	2017
REDUCE (41)	6	441	12	223	24.1%	0.25 [0.10-0.66]	2017
PC (23)	1	204	5	210	9.5%	0.21 [0.02-1.75]	2013
CLOSURE I (20)	12	447	13	462	28.0%	0.95 [0.44-2.07]	2012
Total (95% CI)		**1829**		**1611**	**100.0%**	**0.42 [0.20-0.91]**	
Total events	37		72				

Heterogeneity: $Tau^2 = 0.38$; $Chi^2 = 9.72$, df = 4 (P = 0.05); $I^2 = 59\%$

Test for overall effect: Z = 2.22 (P = 0.03)

Risk Ratio M-H, Random, 95% CI

0.001 0.1 1 10 1000

Favors [Device] Favors [Control]

B Atrial Fibrillation/Flutter

Study or Subgroup	Device Events	Device Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
CLOSE (40)	11	238	2	235	19.0%	5.43 [1.22-24.24]	2017
RESPECT (27)	7	499	4	481	25.5%	1.69 [0.50-5.73]	2017
REDUCE (41)	29	441	1	223	12.0%	14.66 [2.01-106.95]	2017
PC (23)	6	204	2	210	17.3%	3.09 [0.63-15.12]	2013
CLOSURE I (20)	23	447	3	462	26.2%	7.92 [2.40-26.21]	2012
Total (95% CI)		**1829**		**1611**	**100.0%**	**4.55 [2.16-9.60]**	
Total events	76		12				

Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 5.33$, df = 4 (P = 0.26); $I^2 = 25\%$

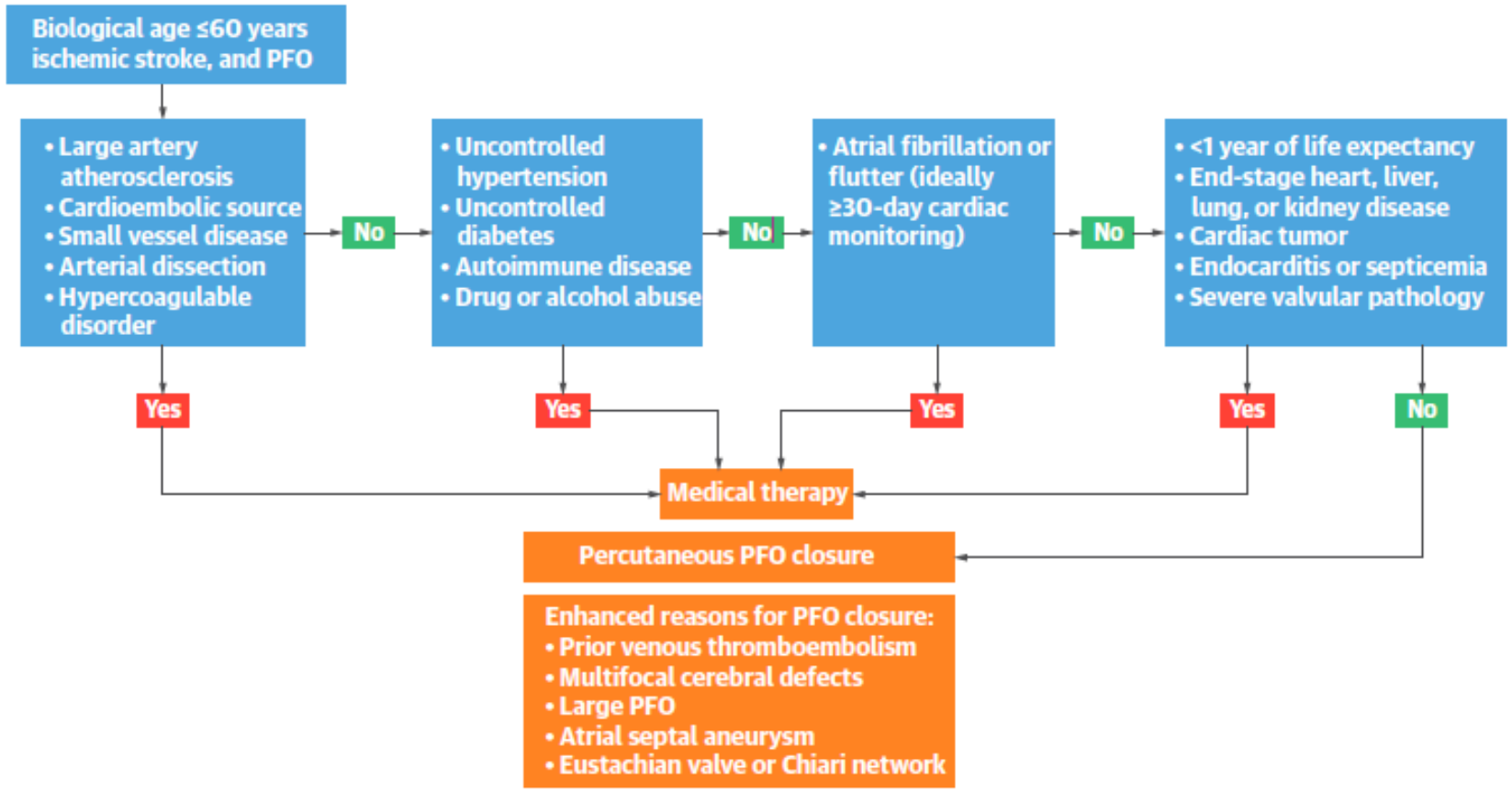
Test for overall effect: Z = 3.98 (P < 0.0001)

Risk Ratio M-H, Random, 95% CI

0.001 0.1 1 10 1000

Favors [Device] Favors [Control]

CENTRAL ILLUSTRATION Evidence-Based Algorithm for PFO Closure in Ischemic Stroke Patients for Highest Clinical Yield, Based on Randomized Trials



Mojadidi, M.K. et al. J Am Coll Cardiol. 2018;71(9):1035–43.

Patients can expect the greatest benefit from percutaneous PFO closure if they have no other cardiovascular stroke causes on imaging/laboratory analyses, no uncontrolled risk factors, no atrial fibrillation or flutter, and no poor prognostic markers. PFO = patent foramen ovale.

Mise à jour Guidelines canadiennes d'AVC 2017…

9.1 Patent Foramen Ovale (PFO) ***(Revised 2017)***

i. Patients with a recent ischemic stroke or TIA attributed to a PFO should have an evaluation by clinicians with stroke and cardiovascular expertise [Evidence Level C].

ii. For carefully-selected patients with a recent ischemic stroke or TIA attributed to a PFO, PFO device closure plus long-term antiplatelet therapy is recommended over long-term antithrombotic therapy alone **provided all** the following criteria are met [Evidence Level A]:

   a. Age 18–60 years;
   b. The diagnosis of the index stroke event is confirmed by imaging as a nonlacunar embolic ischemic stroke or a TIA with positive neuroimaging or cortical symptoms;
   c. The patient has been evaluated by a neurologist or clinician with stroke expertise, and the PFO is felt to be the most likely cause for the index stroke event following a thorough etiological evaluation to exclude alternate etiologies.

iii. For patients requiring long-term anticoagulation, the decision regarding PFO closure remains unclear, and decisions should be based on individual patient characteristics and risk versus benefit profile [Evidence C].

iv. For patients with a recent ischemic stroke or TIA attributed to a PFO who do no undergo PFO closure and are aged 60 years or younger, either antiplatelet or anticoagulant therapy is recommended for secondary stroke prevention, unless there is a separate evidence-based indication for chronic anticoagulant therapy [Evidence Level B].

v. There is insufficient evidence to make a recommendation regarding the comparative effectiveness of PFO closure vs. anti-coagulant therapy.

Conclusion

- Fermeture de FOP semble prévenir la récidive d'AVC
- Résultats initiaux négatifs: device / AVC non-paradoxaux
- Sélection des patients de la plus haute importance
  - Caractéristiques du FOP (critères haut risque)
  - Exclusion des causes alternatives d'AVC
- Plusieurs questions demeurent sans réponse

Question de soulever la controverse …

Patient ≥ 60 ans ???

FOP à faible risque

Monitoring FA … 24 heures ou 30 jours ?

Patients avec autre indication d'anticoagulothérapie ?

Anticoagulation vs fermeture du FOP ?

Prévention primaire ?

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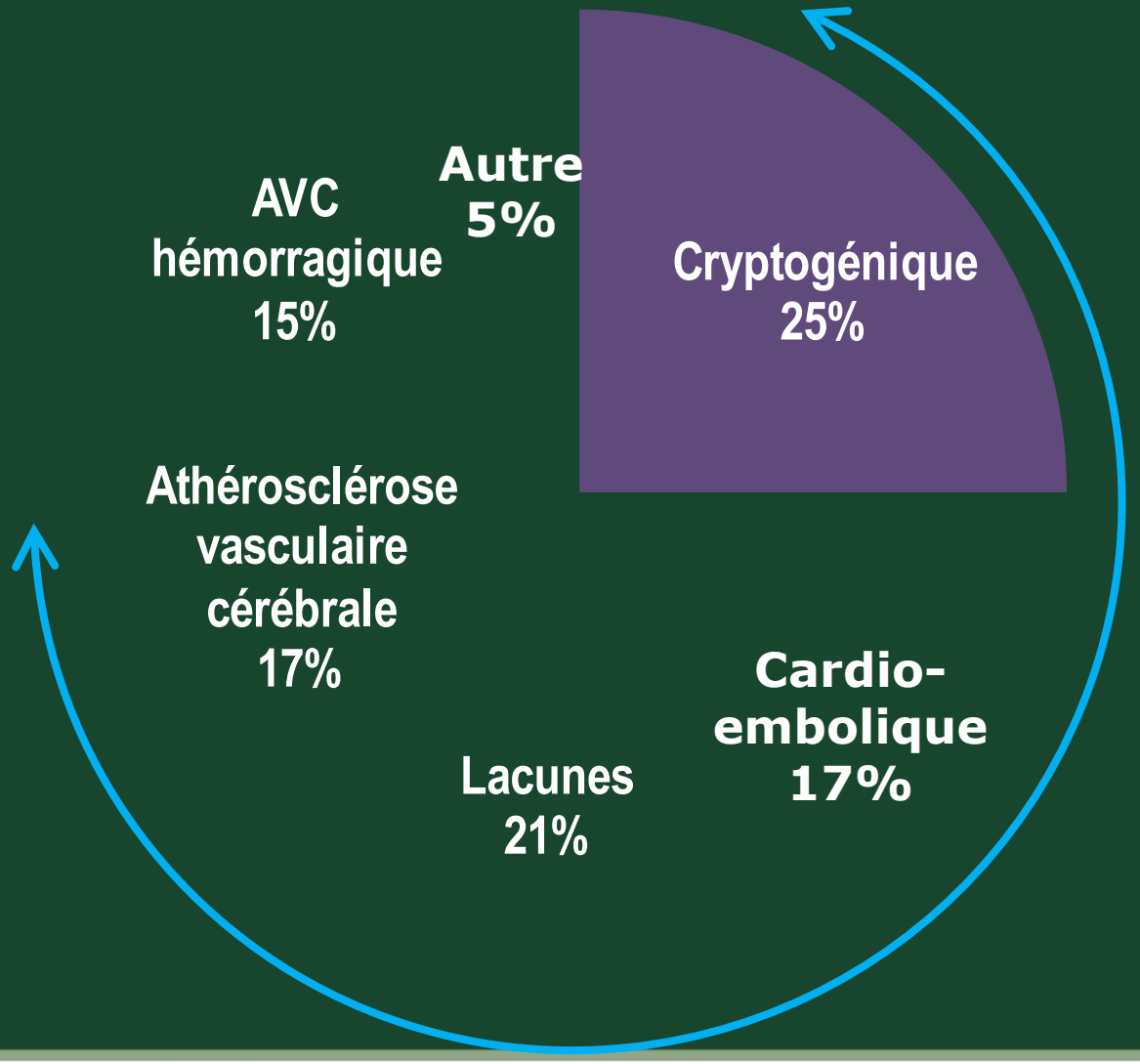
FA subclinique

Détection post AVC cryptogénique

AVC cryptogénique



AVC ischémique 85%

AVC cryptogénique

- 20-40% des AVC n'ont pas de cause identifiée
  - FA bien reconnue comme cause d'AVC
  - Jusqu'à 50% des AVC cryptogéniques pourraient être 2nd à FA
  - L'anticoagulation prévient les récidives d'AVC et diminue la mortalité en présence FA
- Holter 24h: diagnostic pour FA dans 2-6% du temps

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cryptogenic Stroke and Underlying Atrial Fibrillation

Tommaso Sanna, M.D., Hans-Christoph Diener, M.D., Ph.D., Rod S. Passman, M.D., M.S.C.E., Vincenzo Di Lazzaro, M.D., Richard A. Bernstein, M.D., Ph.D., Carlos A. Morillo, M.D., Marilyn Mollman Rymer, M.D., Vincent Thijs, M.D., Ph.D., Tyson Rogers, M.S., Frank Beckers, Ph.D., Kate Lindborg, Ph.D., and Johannes Brachmann, M.D., for the CRYSTAL AF Investigators*

Sanna et et al. NEJM 2014

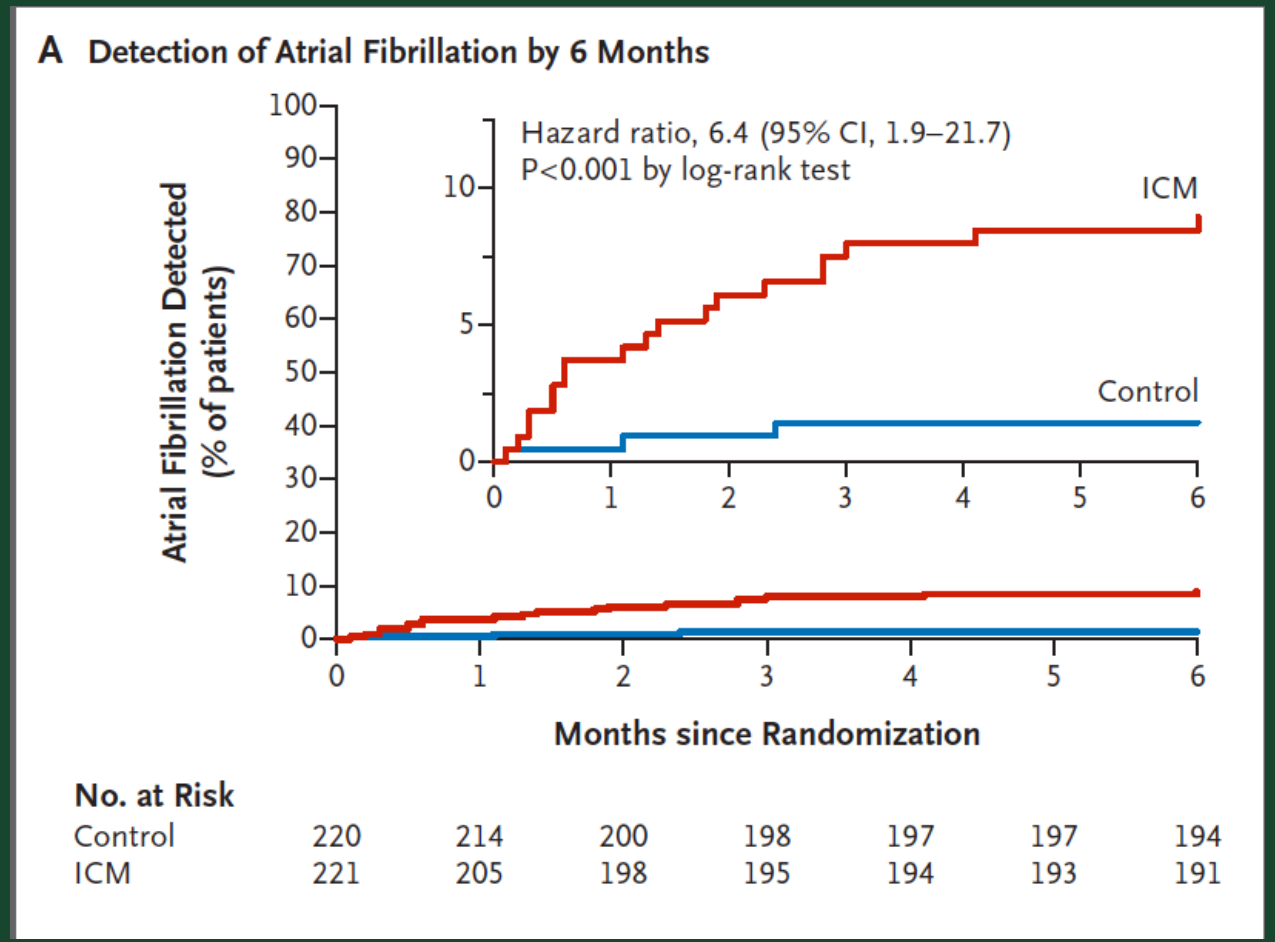
CRISTAL-AF

- Étude randomisée contrôlée
- 441 patients > 400 ana avec AVC cryptogénique
  - AVC < 90 jours sans FA au Holter de 24 heures
- Monitoring à long terme (REVEAL XT) vs monitoring conventionnel
- Issue primaire: survenue de FA à 6 mois
- Issue secondaire: survenue de FA à 12 mois
- Durée FA: 30 secondes
- Suivi 12 mois

Sanna et et al. NEJM 2014

CRISTAL-AF

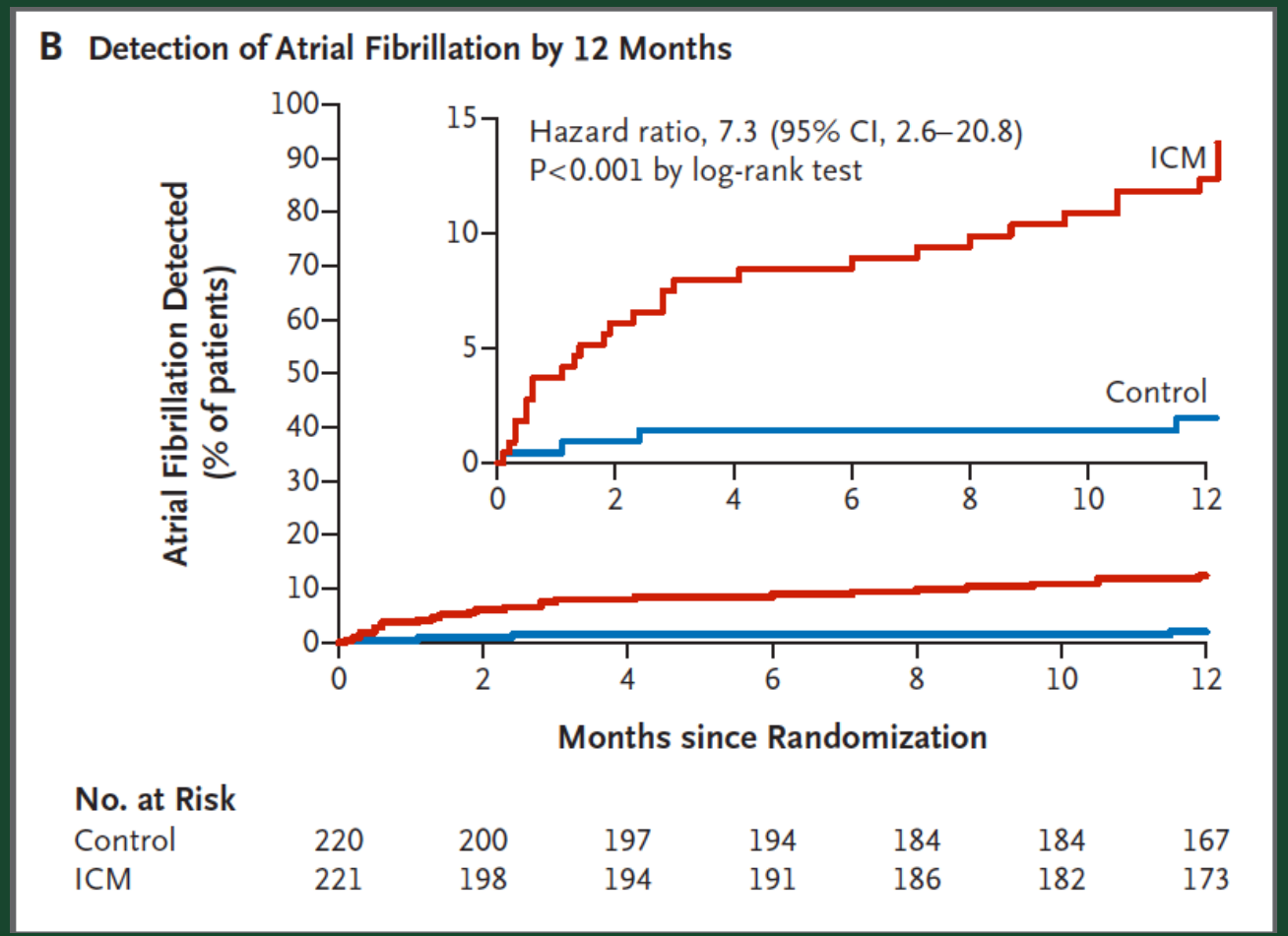
Issue primaire: FA détectée à 6 mois



Sanna et et al. NEJM 2014

CRISTAL-AF

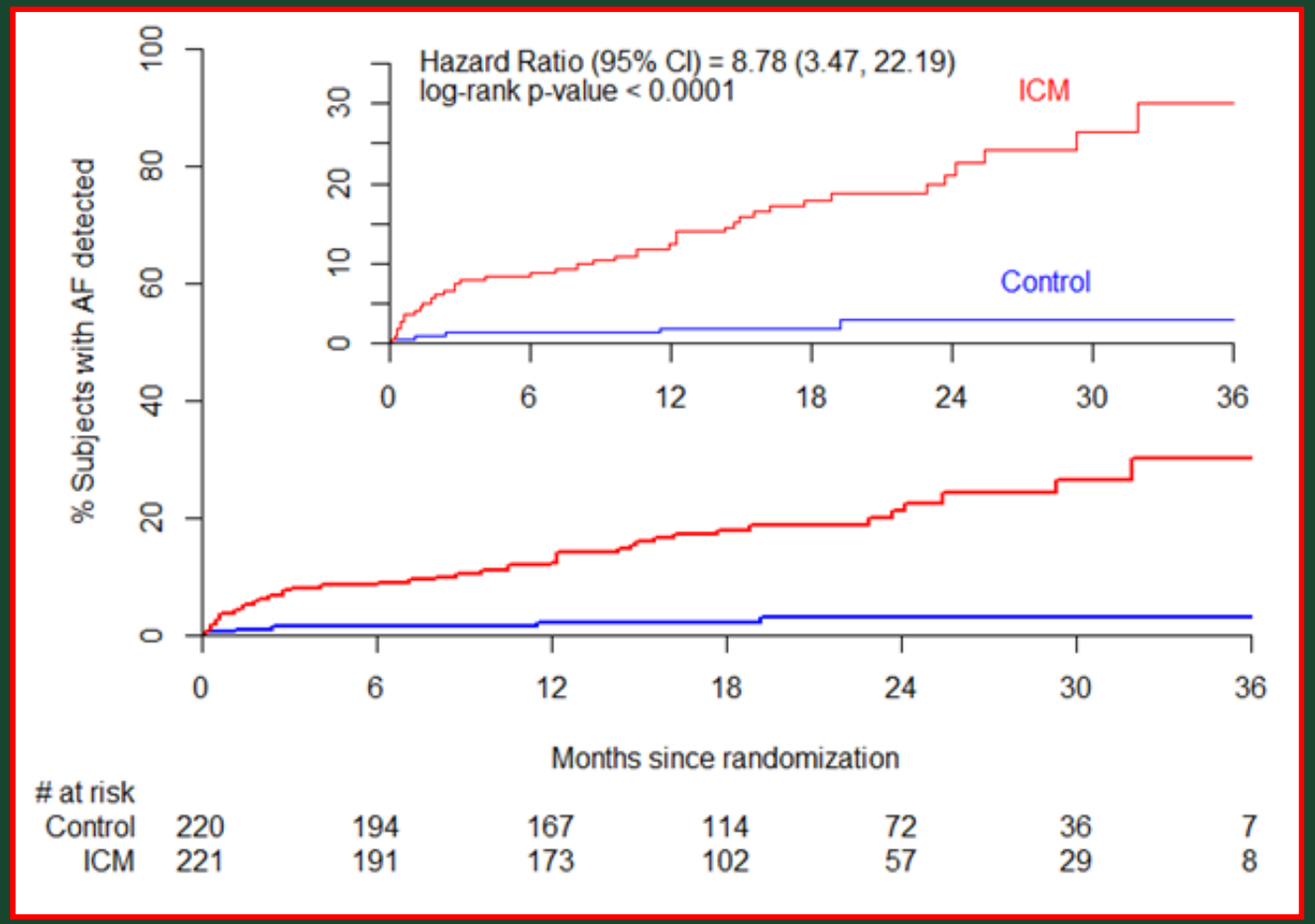
Issue secondaire: FA détectée à 12 mois



Sanna et et al. NEJM 2014

CRISTAL-AF

Résultats à 3 ans



Brachman et al Circ EP 2016

CRISTAL-AF

Conclusion

- Plus de détection de FA dans le groupe monitoring continu
- NNI pour trouver 1 épisode de FA
  - **14 à 6 mois**
  - **1 0 à 12 mois**
- Manque de puissance pour démontrer effet sur récidive d'AVC

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 26, 2014 VOL. 370 NO. 26

Atrial Fibrillation in Patients with Cryptogenic Stroke

David J. Gladstone, M.D., Ph.D., Melanie Spring, M.D., Paul Dorian, M.D., Val Panzov, M.D., Kevin E. Thorpe, M.Math., Judith Hall, M.Sc., Haris Vaid, B.Sc., Martin O'Donnell, M.B., Ph.D., Andreas Laupacis, M.D., Robert Côté, M.D., Mukul Sharma, M.D., John A. Blakely, M.D., Ashfaq Shuaib, M.D., Vladimir Hachinski, M.D., D.Sc., Shelagh B. Coutts, M.B., Ch.B., M.D., Demetrios J. Sahlas, M.D., Phil Teal, M.D., Samuel Yip, M.D., J. David Spence, M.D., Brian Buck, M.D., Steve Verreault, M.D., Leanne K. Casaubon, M.D., Andrew Penn, M.D., Daniel Selchen, M.D., Albert Jin, M.D., David Howse, M.D., Manu Mehdiratta, M.D., Karl Boyle, M.B., B.Ch., Richard Aviv, M.B., Ch.B., Moira K. Kapral, M.D., and Muhammad Mamdani, Pharm.D., M.P.H., for the EMBRACE Investigators and Coordinators*

Gladstone et et al. NEJM 2014

EMBRACE

- Étude randomisée contrôlée
- 572 patients ≥ 55 ans avec AVC cryptogénique
  - AVC < 6 mois sans FA détectée au Holter
- Monitoring de 30 jours vs monitoring conventionnel
- Issue 1^{aire}: incidence FA ≥ 30 secondes à 90 jours

Gladstone et et al. NEJM 2014

EMBRACE

Table 2. Detection of Atrial Fibrillation in the Two Monitoring Groups.

Outcome	Intervention Group (N=286)	Control Group (N=285)	Absolute Difference (95% CI)	P Value
	number/total number (percent)		*percentage points*	
Primary outcome: detection of atrial fibrillation with duration ≥30 sec within 90 days†	45/280 (16.1)	9/277 (3.2)	12.9 (8.0–17.6)	<0.001
Secondary outcomes‡				
Detection of atrial fibrillation with duration ≥30 sec	44/284 (15.5)	7/277 (2.5)	13.0 (8.4–17.6)	<0.001
Detection of atrial fibrillation with duration ≥2.5 min	28/284 (9.9)	7/277 (2.5)	7.4 (3.4–11.3)	<0.001
Detection of atrial fibrillation of any duration	56/284 (19.7)	13/277 (4.7)	15.0 (9.8–20.3)	<0.001

Gladstone et et al. NEJM 2014

EMBRACE

- Conclusion
  - Le monitoring de 30 jours permet de détecter beaucoup plus d'épisodes de FA que le monitoring conventionnel
  - Manque de puissance pour démontrer effet sur récidive d'AVC

Gladstone et et al. NEJM 2014

Monitoring long terme

- Jeunes patients
- Bonne qualité de vie
- ESA +++
- Atriopathie (dilatation OG)
- Élévation BNP ?

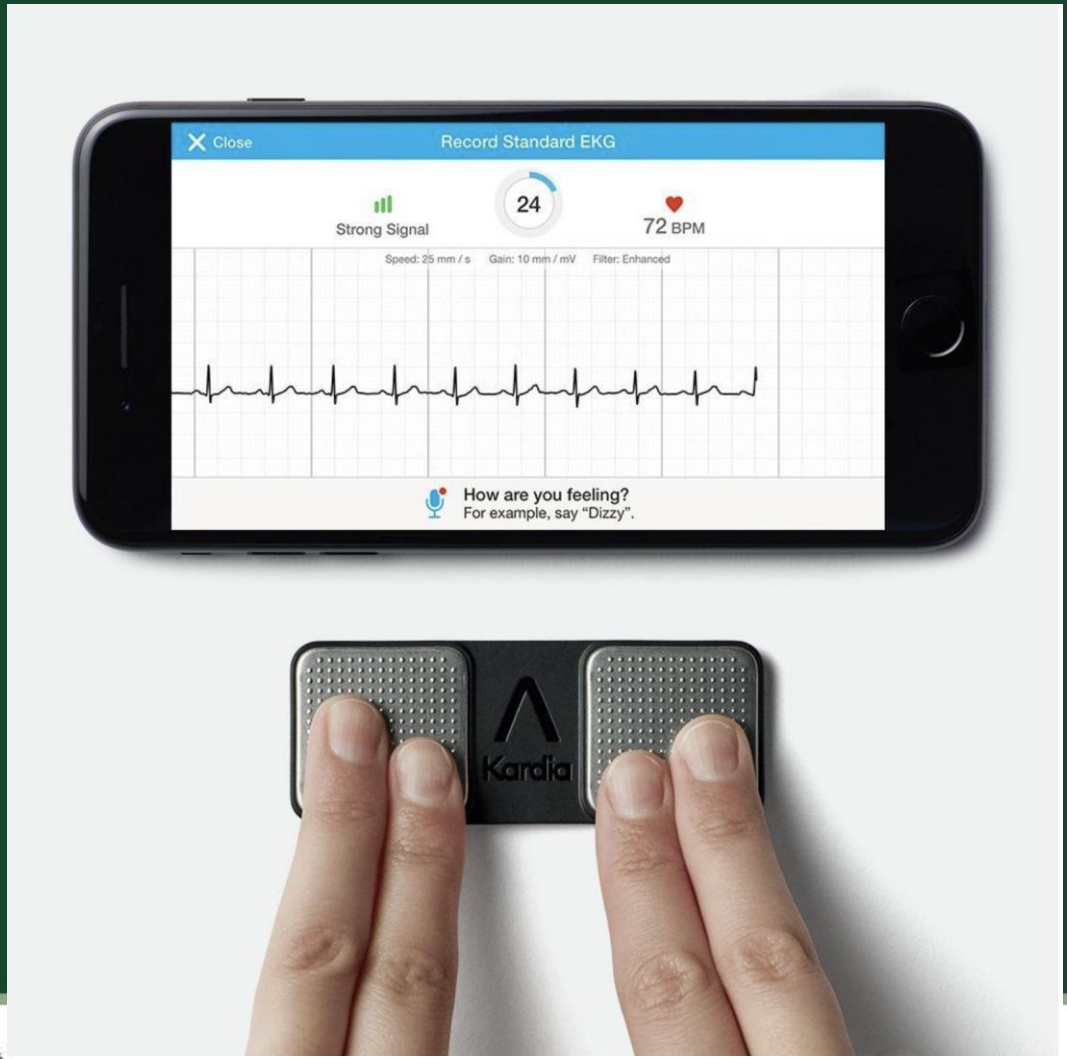
Gladstone et et al. NEJM 2014

Canadian Stroke Best Practices

iii. Patients with suspected transient ischemic attack or ischemic stroke should have a 12-lead ECG to assess cardiac rhythm and identify atrial fibrillation or flutter or evidence of structural heart disease (e.g. myocardial infarction, left ventricular hypertrophy) [Evidence Level B].

iv. For patients being investigated for an acute embolic ischemic stroke or TIA, ECG monitoring for more than 24 hours is recommended as part of the initial stroke work-up to detect paroxysmal atrial fibrillation in patients who would be potential candidates for anticoagulant therapy [Evidence Level A].

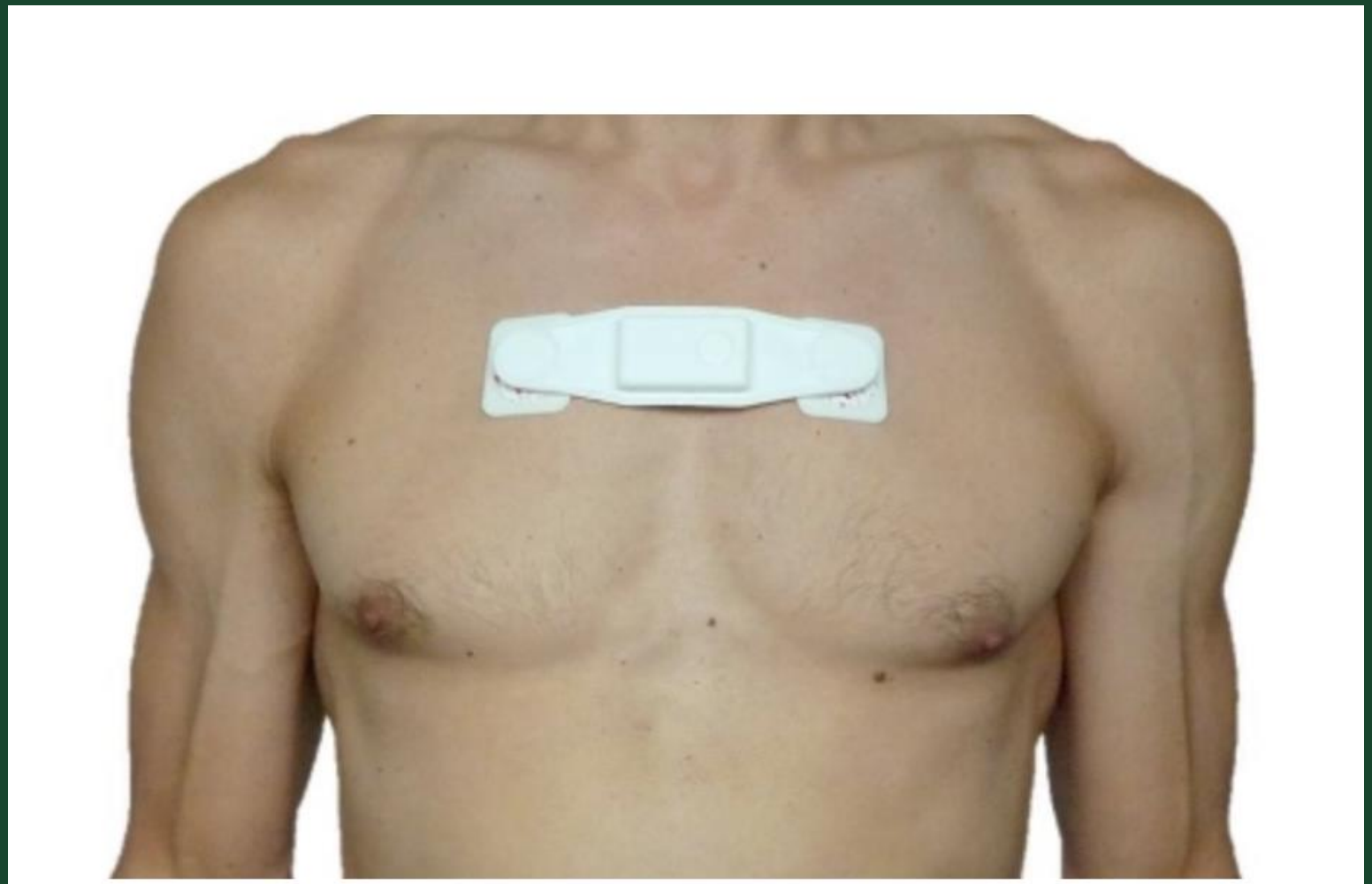
Alivecor-Kardia



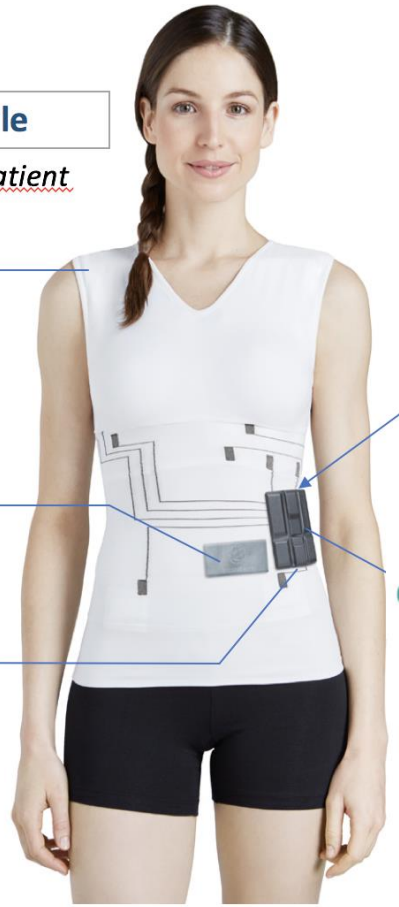
Spyder Flash

- Monitor up to 40 days
- 1 st day continuous ECG
- Pre-event and post-event:
- All RR intervals recorded
- ECG holter quality:
- 1 alkaline or lithium AAA battery
- Communication: Audio modulation
- ECG patient cable: 1 or 2 channels
- Recording stored on a Sorin SD card
- Weight: 50 g w/o battery
- Dimensions: 75 X 50 X 19.5 mm

CardioStat



Cardioskin overview



Smart textile

For patient

Cardioskin textile 15-lead ECG

Close-fitting T-shirt

Embedded electrodes

Multiple size for all genders

Washable (30 times)

Cardioskin Battery

***30 hours** of autonomy*

Removable from the shirt (snap buttons)

Cardioskin Recorder

***Unlimited record for patients with wifi connection** - 14 days storage without*

Flat and flexible

Removable from the shirt (snap buttons)

Cardioskin App

For patient

Launch the record

***Report an event** /symptom to the Cloud*

Cardioskin Cloud

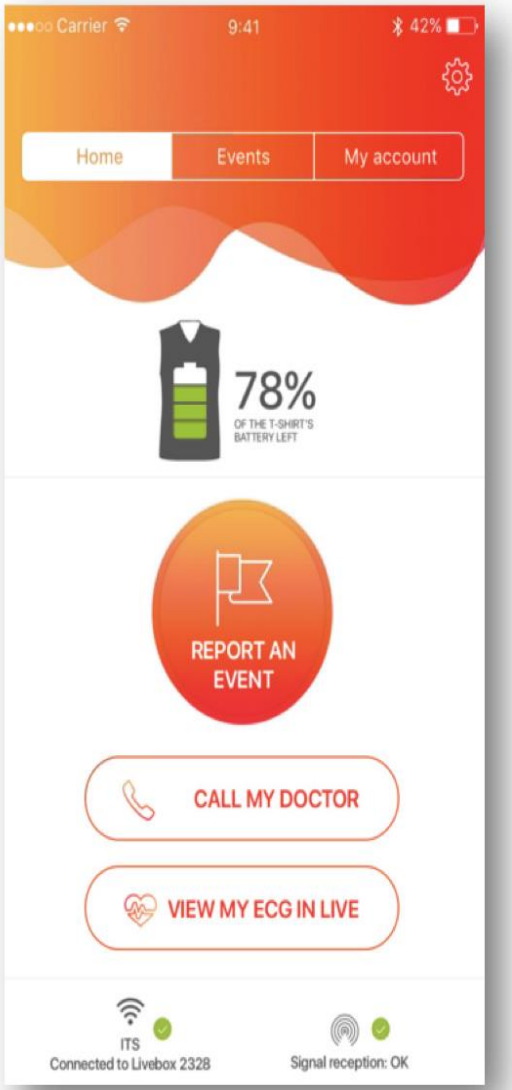
For physician

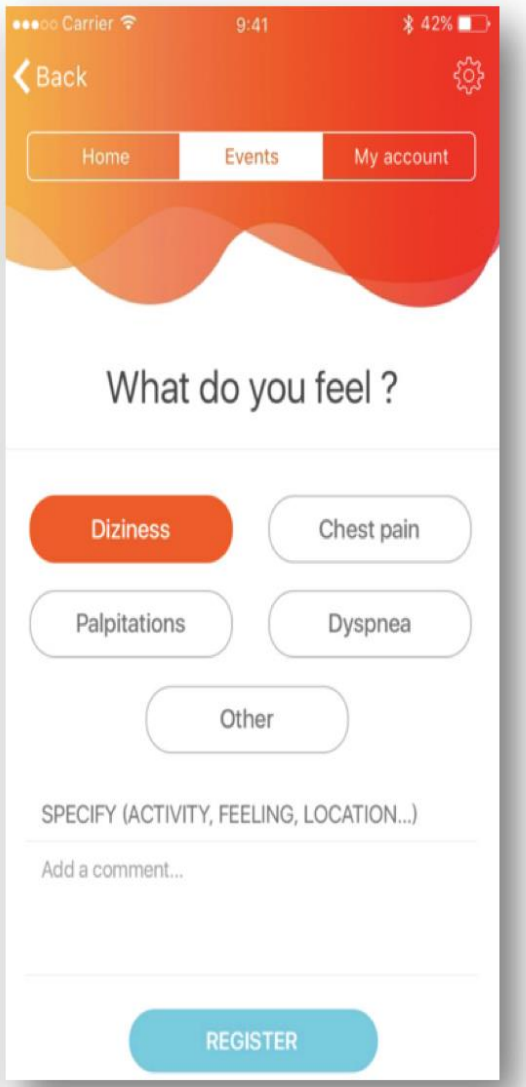
Allows to prescribe a recording

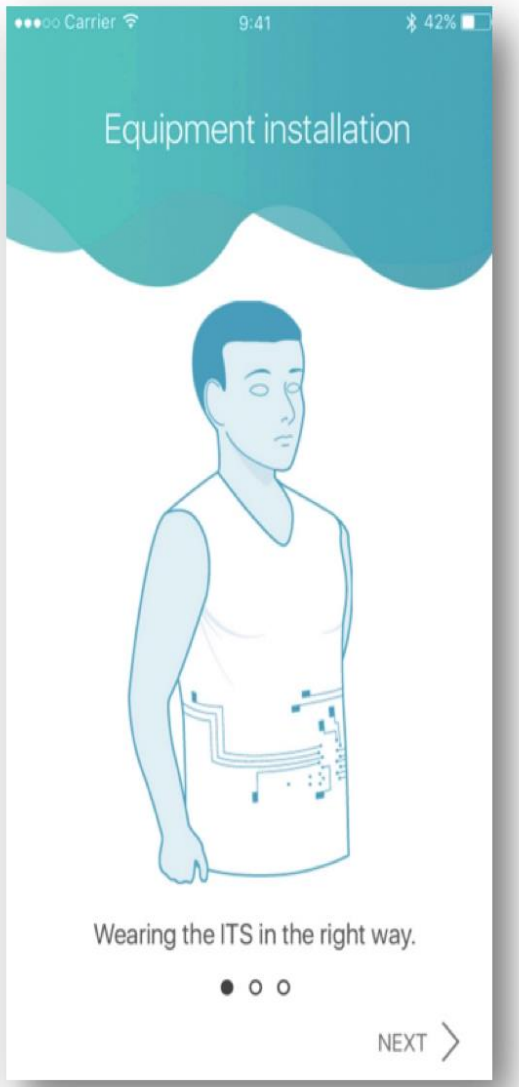
*Contains the **analysis platform**, **powered by AI***

Optional: review of all data by a Cardioskin cardiologist

Cardioskin® App







Conclusion

- Le mécanisme des AVC et leur relation temporelle avec la FA est complexe
- Le Holter de 24h manque de sensibilité pour détecter la FA post AVC cryptogénique
- Le monitoring d’au moins 30 jours devient de plus en plus fréquent
- Sélection des patients pour moniteur implantable a améliorer