Approach & Management of AF
What should be changed since 2023?

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Declaration

- I have no disclosure.

Outline

- Introduction
- Approach & management of AF
- What's new in 2023?
- Available evidence for clinical practice
- What should be changed in 2023?
- Conclusion

Introduction

- Most common & medically significant cardiac arrhythmia
- Increasing morbidity, mortality & medical expense, significant negative impact on public health
- Deeper understanding of mechanisms of AF, successfully applying knowledge to clinical practice, utilizing development of technologies improve AF management
- Principal goals of AF Mx : to improve the quality of life (symptom control) & to prevent associated morbidity & mortality (prevention of thromboembolism)

Approach & Management of AF

Components of integrated AF Management

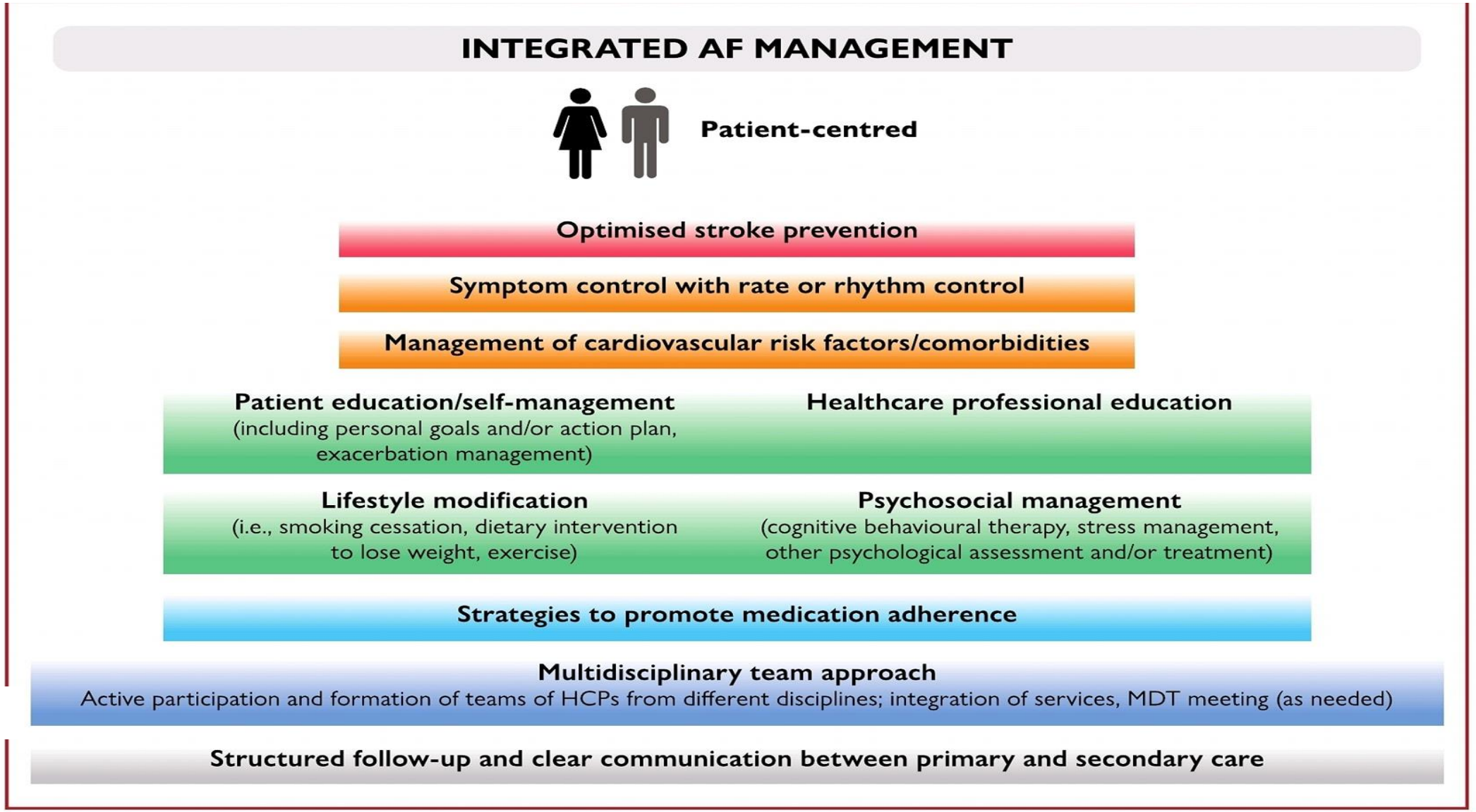
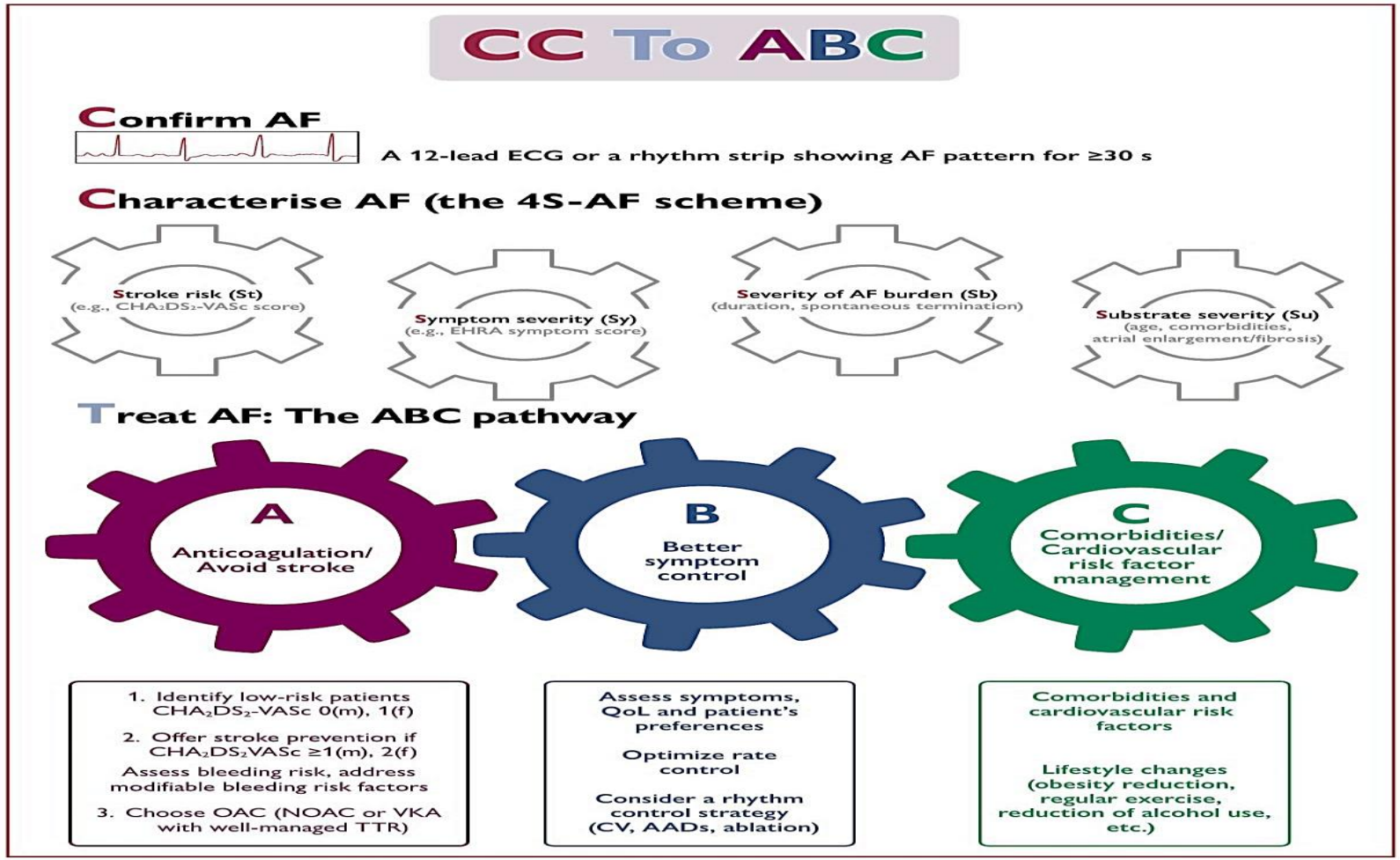


Figure 10 Components of integrated AF management. AF = atrial fibrillation; HCP = healthcare professional; MDT = multidisciplinary team.

Guideline for Management of AF (ESC 2020)



Central Illustration Management of AF. AAD = antiarrhythmic drug; AF = atrial fibrillation; ECG = electrocardiogram; EHRA = European Heart Rhythm Association; CHA_2DS_2-VASc = Congestive HF, Hypertension, Age ≥75 years, diabetes mellitus, Stroke, Vascular disease, Age 65 - 74 years, Sex category (female); CV = cardioversion; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulant; TTR = time in therapeutic range; VKA = vitamin K antagonist.

CV risk factors & Concomitant diseases: Detection & Management

Reduction of mortality and morbidity
Primary prevention of AF

- Life-style modification
- AF risk factors modification
- Treatment of underlying conditions

Reduction of mortality and morbidity
Symptomatic improvement
Secondary prevention of AF

- Life-style modification
- AF risk factors modification
- Treatment of underlying conditions

- Stroke modification
- Rate control
- AAD therapy
- Cardioversion
- Catheter ablation
- Surgery

AF risk factors

Modifiable	Partially modifiable or non-modifiable
Hypertension	HF, CAD, VHD, COPD
Diabetes mellitus	Aging
Obesity	Genetics
OSA	
Alcohol	
Dyslipidaemia	
Physical activity	
Smoking	

LA remodeling

Reversible
- Electrical
- Biochemical
- Inflammation

Non-reversible
- Fibrosis
- Scaring
- Dilatation

AF development and progression

Paroxysmal → Persistent → Permanent

AF outcomes
- Mortality
- Stroke/systemic TE
- Symptoms and quality of life
- Heart failure
- Dementia
- Myocardial infarction
- Hospitalization and health care costs

What's new in 2023 ?

Catheter Ablation of AF

- Widespread acceptance as an initial treatment producing better CV outcomes & quality of life than AAD
- Can be associated with severe complications, dependent on types of AF, its complexity, PVI alone or more ablation, patient's comorbidities, experience of the performing centers
- RF ablation in conjunction with an Electro-Anatomical Mapping (EAM) is a gold standard
- Alternative energy sources for PVI : balloon based ablation; Cryo & Pulsed Field ablation are highlighted during 2023.

Balloon based PVI (Cryo-Balloon)

- An alternative ablation tool for PVI, single shot modality
- As second Gold Standard in current guidelines
- Easy to learn, over the wire strategy, safe
- Low incidence of major complications, most common phrenic nerve palsy, avoidable phrenic nerve pacing with monitoring of compound motor action potential
- Non-inferiority of CB ablation vs RF ablation in terms of efficacy & safety (FIRE and ICE trial)
- Recent analyses encourage the application of CB ablation for persistent AF

Initial rhythm control with Cryoablation vs AAD in patients (n-303) with PAF, 3 yr follow-up

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 12, 2023 VOL. 388 NO. 2

Progression of Atrial Fibrillation after Cryoablation or Drug Therapy

J.G. Andrade, M.W. Deyell, L. Macle, G.A. Wells, M. Bennett, V. Essebag, J. Champagne, J.-F. Roux, D. Yung, A. Skanes, Y. Khaykin, C. Morillo, U. Jolly, P. Novak, E. Lockwood, G. Amit, P. Angaran, J. Sapp, S. Wardell, S. Lauck, J. Cadrin-Tourigny, S. Kochhäuser, and A. Verma, for the EARLY-AF Investigators*

Table 1. Main End Points of Interest.*

End Point	Ablation Group (N = 154)	Antiarrhythmic Drug Group (N = 149)	Hazard Ratio (95% CI)
	number (percent)		
Progression to persistent atrial fibrillation from 91 days after treatment initiation to final follow-up	3 (1.9)	11 (7.4)	0.25 (0.09–0.70)
Recurrence of any atrial tachyarrhythmia			
From 91 days to 12 mo after treatment initiation†	66 (42.9)	101 (67.8)	0.48 (0.35–0.66)
From 91 days to 36 mo after treatment initiation	87 (56.5)	115 (77.2)	0.51 (0.38–0.67)

* Observed data are shown in the trial-group columns. The hazard ratio is a model-based effect estimate and was calculated with a Cox regression analysis. Because the statistical analysis plan did not include a provision for correcting for multiplicity when conducting tests for secondary or other outcomes, results are reported as point estimates and 95% confidence intervals. The widths of the confidence intervals have not been adjusted for multiplicity, so the intervals should not be used to infer definitive treatment effects for secondary outcomes.

† Data were previously reported by Andrade et al.[11]

Lower incidence of Persistent AF or Recurrence AT over 3 yr with Cryo-abalation

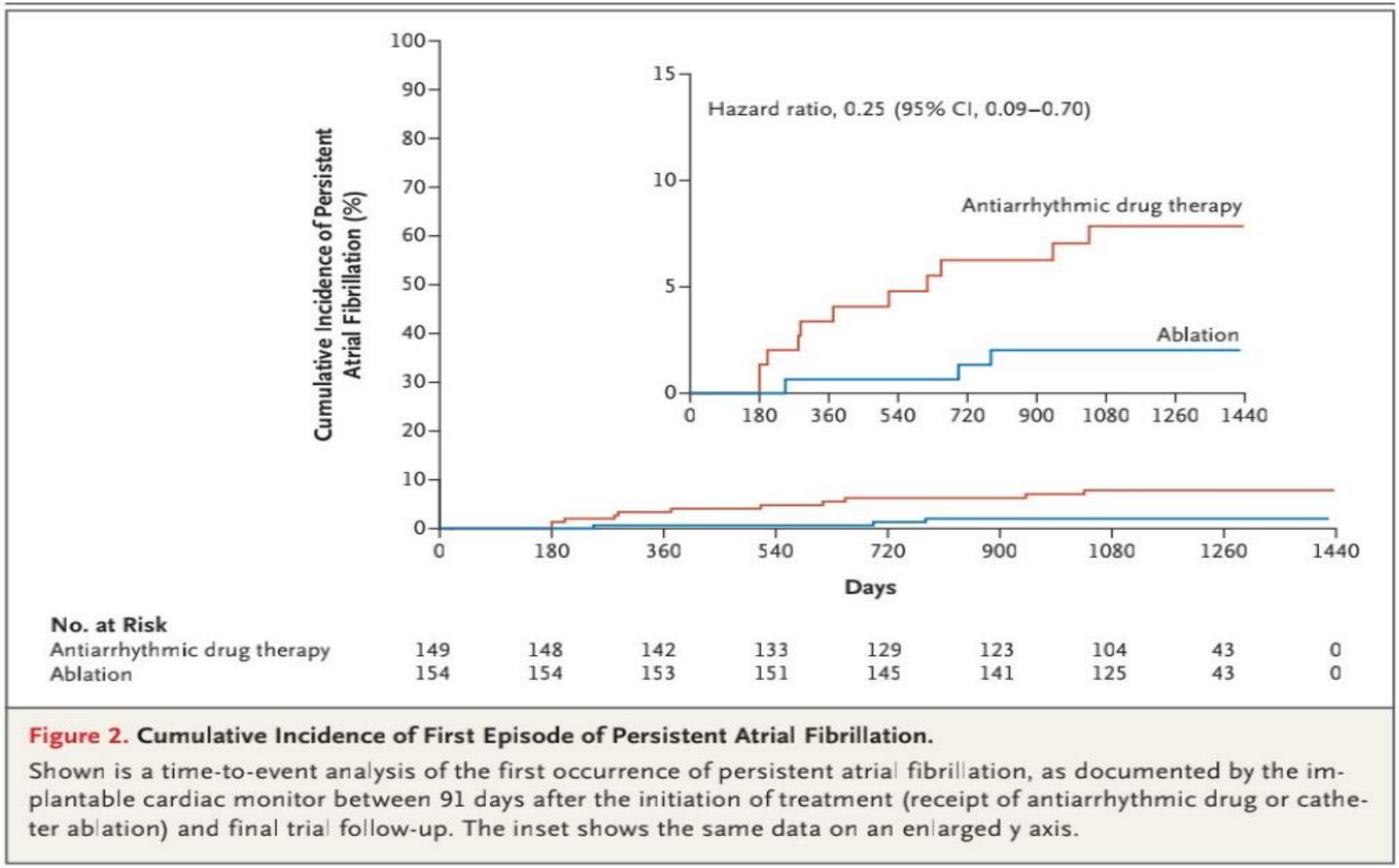
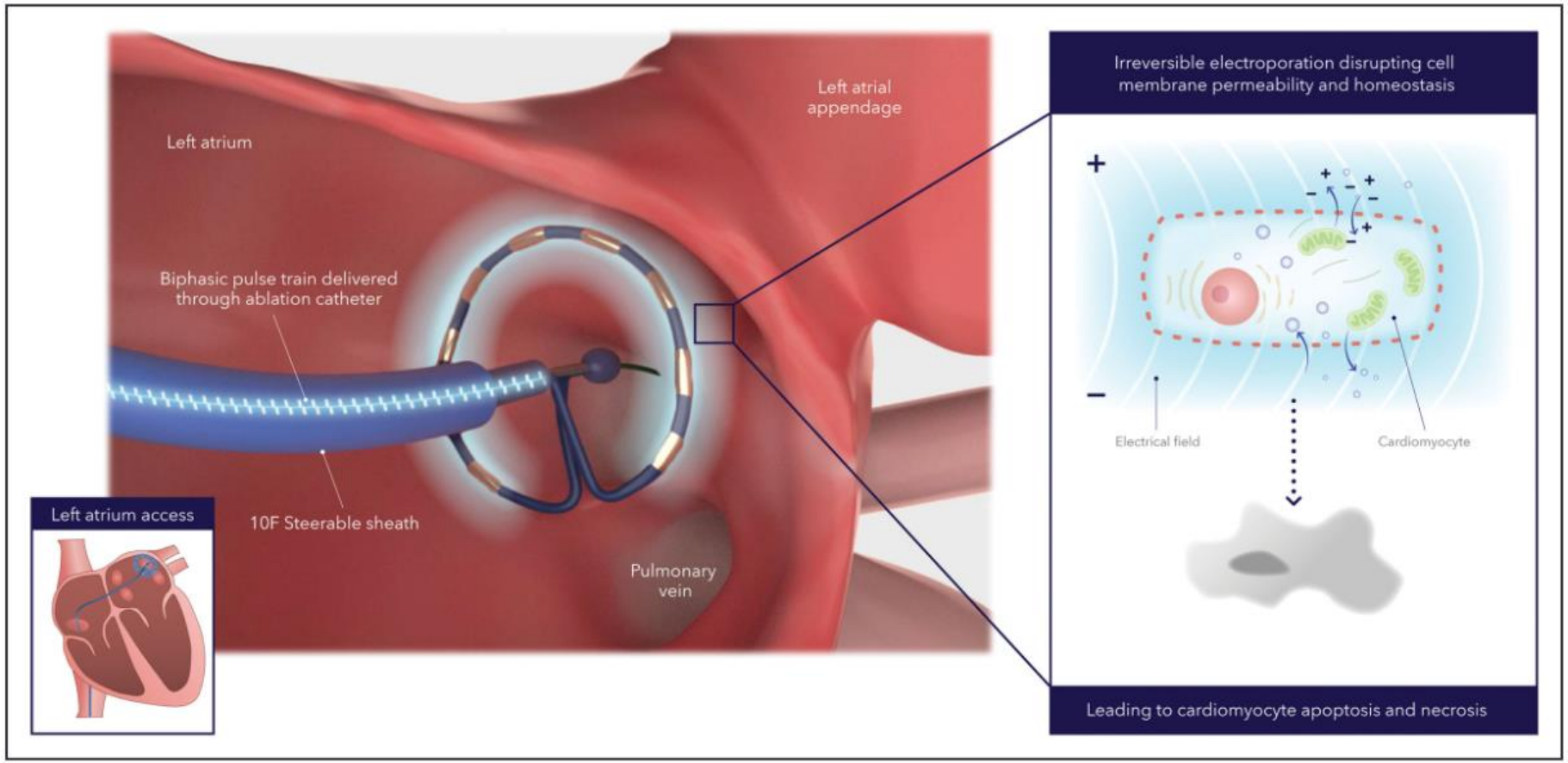


Figure 2. Cumulative Incidence of First Episode of Persistent Atrial Fibrillation.

Shown is a time-to-event analysis of the first occurrence of persistent atrial fibrillation, as documented by the implantable cardiac monitor between 91 days after the initiation of treatment (receipt of antiarrhythmic drug or catheter ablation) and final trial follow-up. The inset shows the same data on an enlarged y axis.

Pulsed Field Ablation (PFA)

- A promising new ablation modality
- Employs a train of microsecond duration high amplitude electrical pulses that ablate myocardium by electroporation of the sarcolemmal membrane without measurable tissue heating
- Myocardium is very susceptible to irreversible injury whereas esophagus, phrenic nerve, pulmonary veins & coronary arteries are relatively resistant to injury.
- Very effective, less procedure time, safe & less procedure related complications



Catheter ablation method with pulsed field ablation system. Alternating positive and negative electrodes sustains a bipolar electrical field around the catheter that extends into the tissue. The electrical field increases cell membrane permeabilization, which then leads to cell function disruption and eventually to cell death (ie, apoptosis and necrosis).

Circulation
Volume 147, Issue 19, 9 May 2023; Pages 1422-1432
https://doi.org/10.1161/CIRCULATIONAHA.123.063988

American Heart Association.

ORIGINAL RESEARCH ARTICLE

Pulsed Field Ablation for the Treatment of Atrial Fibrillation: PULSED AF Pivotal Trial

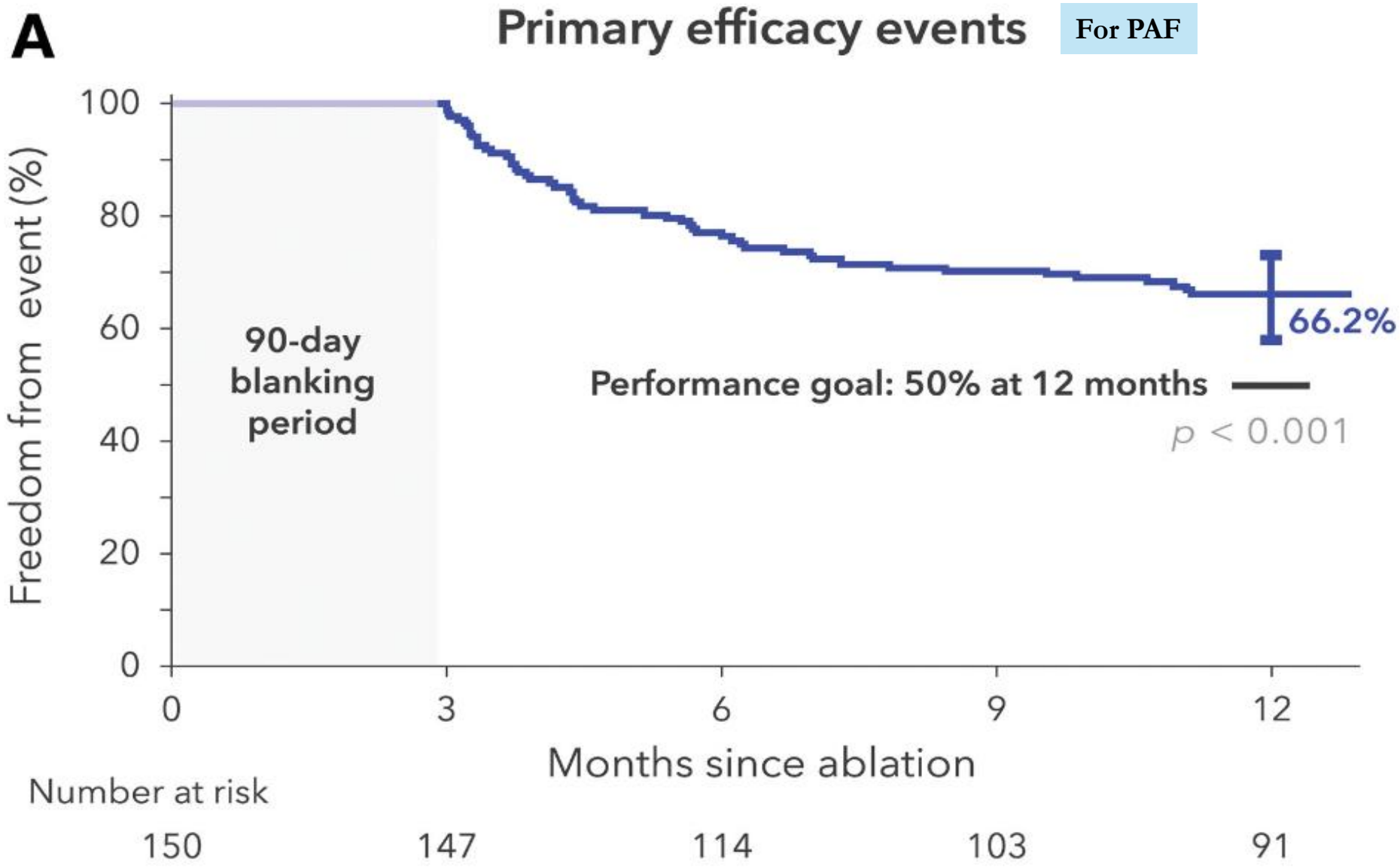
Editorial, see p 1433

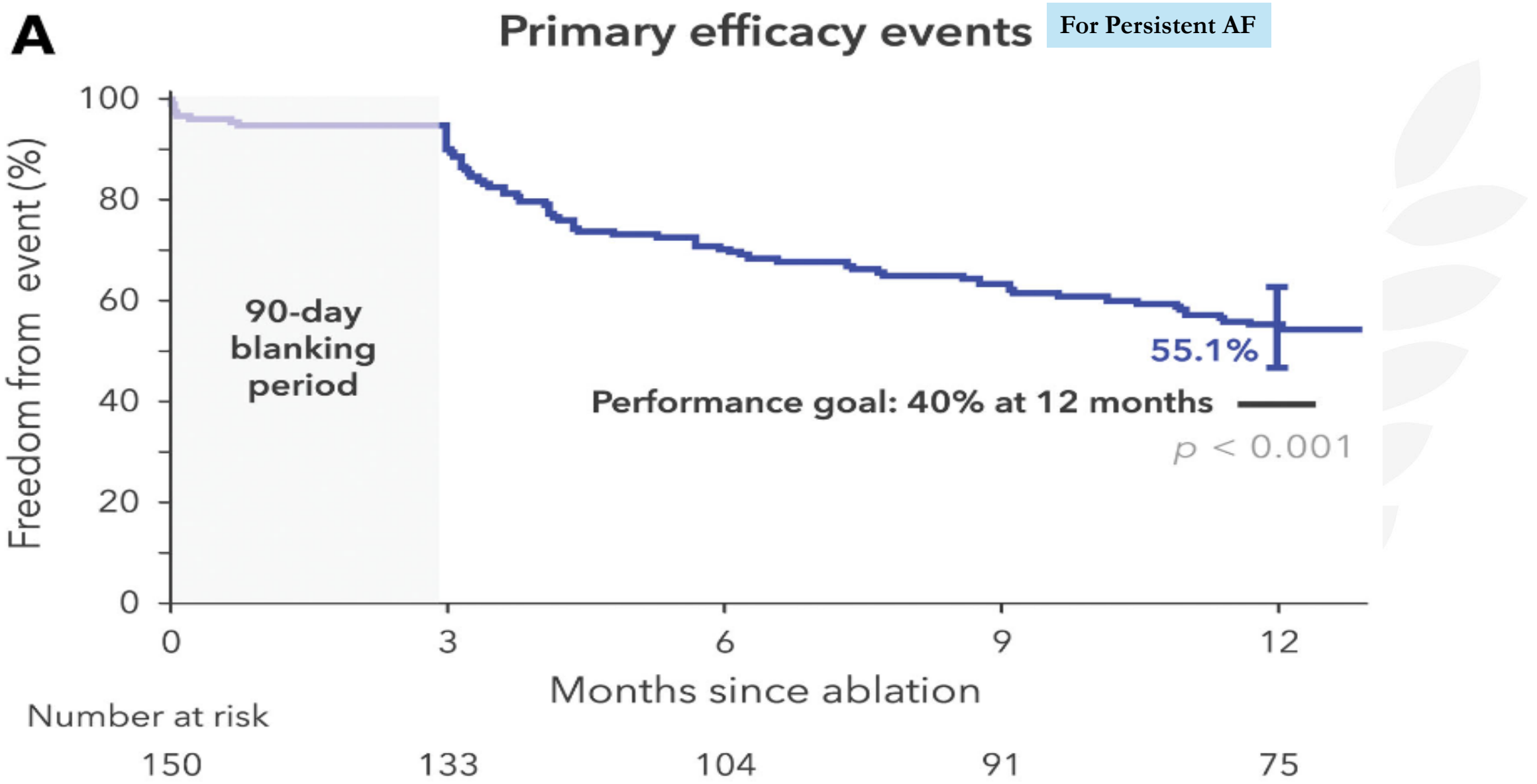
Atul Verma, MD, David E. Haines, MD, Lucas V. Boersma, MD, Nitesh Sood, MD, Andrea Natale, MD, Francis E. Marchlinski, MD, Hugh Calkins, MD, Prashanthan Sanders, MBBS, Douglas L. Packer, MD, Karl-Heinz Kuck, MD, Gerhard Hindricks, MD, Birce Onal, PhD, Jeffrey Cerkvenik, MS, Hiroshi Tada, MD, David B. DeLurgio, MD, and on behalf of the PULSED AF Investigators

https://images.app.goo.gl/FC54VLQ2zziJdWCf6

Pulsed Field Ablation for the Treatment of AF: PULSED AF Pivotal Trial

- Prospective, multicenter, nonrandomized
- Symptomatic PAF/ Persistent AF (150), 1 yr follow-up
- Primary effectiveness end point was freedom from a composite of acute procedural failure, arrhythmia recurrence or antiarrhythmic escalation
- Primary safety end point was freedom from a composite of serious procedure & device related adverse events


A
Primary efficacy events
For PAF
100
80
60
40
20
0
Freedom from event (%)
90-day blanking period
66.2%
Performance goal: 50% at 12 months
p < 0.001
0
3
6
9
12
Months since ablation
Number at risk
150
147
114
103
91


A
Primary efficacy events
For Persistent AF
Freedom from event (%)
100
80
60
40
20
0
90-day blanking period
55.1%
Performance goal: 40% at 12 months
p < 0.001
0
3
6
9
12
Months since ablation
Number at risk
150
133
104
91
75

- The primary safety end point occurred in 1 patient in both paroxysmal & persistent AF

- Conclusions: PULSED AF demonstrated a low rate of primary safety adverse events and provided effectiveness consistent with established ablation technologies using a novel irreversible electroporation energy

9.4.4 - Catheter Ablation of Arrhythmias

Pulsed-field- vs. cryo- vs. radiofrequency ablation: one-year recurrence rates after pulmonary vein isolation in patients with persistent atrial fibrillation

Mr Kueffer T; Doctor Madaffari A; Ms Muehl A; Doctor Maurhofer J; Ms Stefenova A; Doctor Seiler J; Doctor Thalmann G; Doctor Kozhuharov NA; Doctor Servatius H; Professor Tanner H; Associate Professor Haeberlin A; Doctor Baldinger SH; Doctor Noti F; Professor Roten L; Professor Reichlin T.

Department of Cardiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

Aim- To compare procedural & one-yr recurrence data of patients with persistent AF undergoing first PVI using PFA, Cryo, or RFA (N 177)

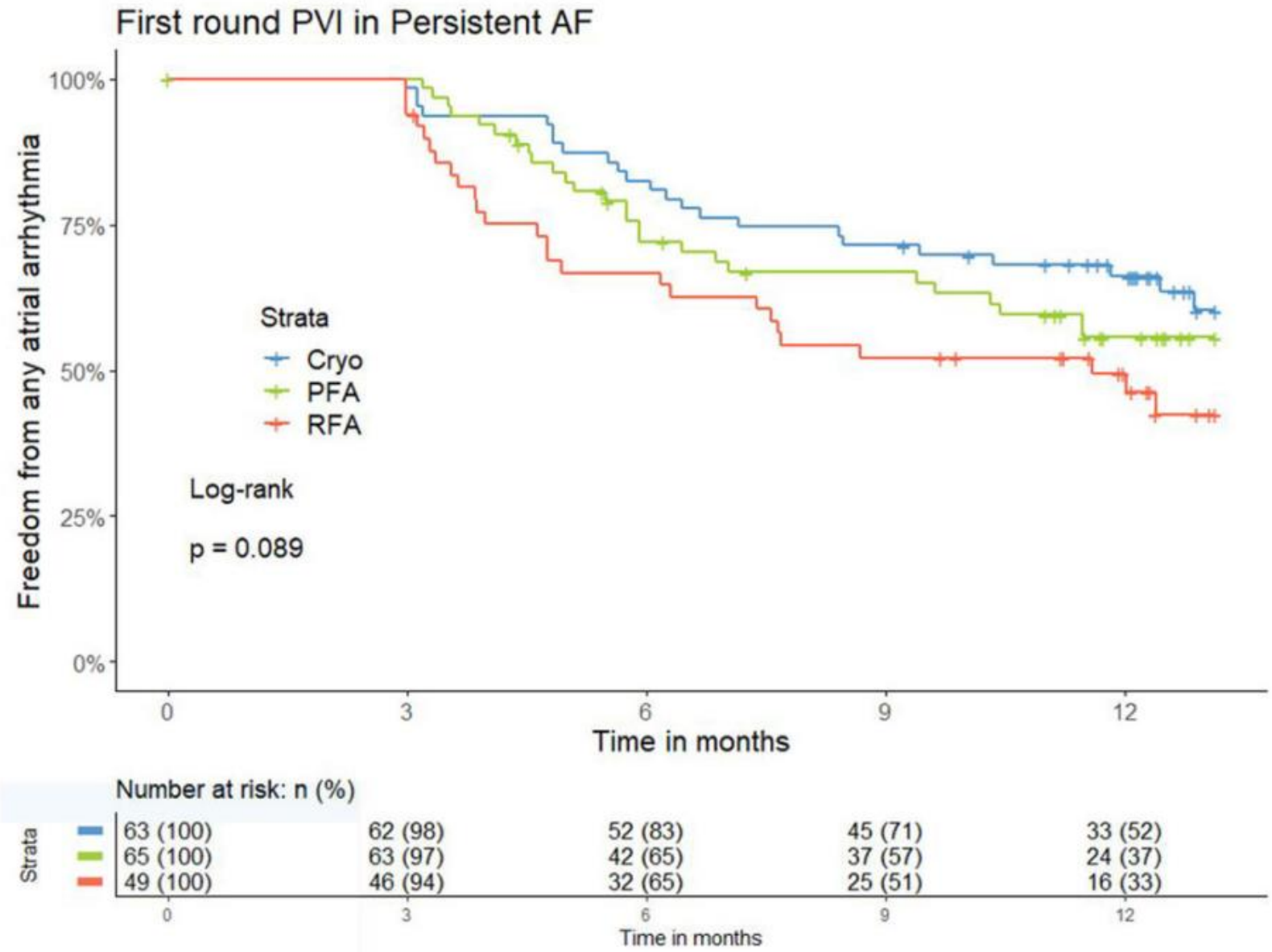


Figure: Freedom from any atrial arrhythmia after first pulmonary vein isolation using different technologies in persistent atrial fibrillation patients

Recurrence of atrial arrhythmias in the KM- analysis after 12 months was not different all 3

Pearls and Pitfalls of PFA

Irreversible electroporation

- tissue-sensitive, preserved tissue compliance

Efficacy and safety

- deep, transmural, durable lesions
- sparing adjunctive tissue
  - no PV stenosis
  - no esophageal lesions
  - no tissue coagulation
  - minimal effects on phrenic nerve
  - low safety risk of overtreatment

Workflow

- standardized and time-efficient, short learning curve using single shot device
- single-tip similar to RF-ablation

Current literature

-excellent limited data mainly from observational studies for PVI

Irreversible electroporation

- cellular mechanisms, necrosis Vs apoptotic pathway

  not entirely understood

Efficacy and safety

- dose dependent, optimal dose unclear
- distinct IRE programming crucial to avoid collateral damage
- vasospasm during PFA adjacent to coronaries
- PFA ≠ PFA
  - validation for each system and indication
  - results not transferable

Workflow

- only 2 ablation systems approved with limited experience

Current literature

- no long-term data available
- no randomized controlled trials available

Future perspectives of PFA

- Expected superior safety profile compared to standard of care technologies
- Novel PFA systems promise unique opportunities to treat atrial and ventricular arrhythmias
- Tailoring PFA for different target lesion depths

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Catheter Ablation in End-Stage Heart Failure with Atrial Fibrillation

Christian Sohns, M.D., Henrik Fox, M.D., Nassir F. Marrouche, M.D., Harry J.G.M. Crijns, M.D., Ph.D., Angelika Costard-Jaeckle, M.D., Leonard Bergau, M.D., Gerhard Hindricks, M.D., Nikolaos Dagres, M.D., Samuel Sossalla, M.D., Rene Schramm, M.D., Ph.D., Thomas Fink, M.D., Mustapha El Hamriti, M.D., Maximilian Moersdorf, M.D., Vanessa Sciacca, M.D., Frank Konietschke, Ph.D., Volker Rudolph, M.D., Jan Gummert, M.D., Jan G.P. Tijssen, Ph.D., and Philipp Sommer, M.D., for the CASTLE HTx Investigators

- **Single center, open label, 97 patients with symptomatic AF & end-stage HF referred for heart transplantation evaluation**

- **Assigned to receive catheter ablation & GDMT or medical therapy**

CASTLE-HTx trial

#ESCCongress

Catheter ablation versus medical therapy to treat atrial fibrillation in end-stage heart failure

Conclusion

Atrial fibrillation (AF) ablation is associated with lower rates of death, urgent heart transplantation or left ventricular assist device (LVAD) implantation compared with medical therapy in patients with end-stage heart failure (HF).

Impact on clinical practice

Patients with end-stage HF eligible for heart transplantation have been excluded from major trials, leaving them with no recommendations or evidence for the optimal treatment of AF and advanced HF. The trial showed that AF ablation improves outcomes in this group.

Study objectives

The CASTLE-HTx trial tested whether AF ablation is superior to medical therapy concerning mortality and need for urgent transplantation or LVAD implantation.

Study population

Patients

- with symptomatic AF
- with end-stage HF eligible for heart transplantation
- in New York Heart Association functional class II, III, or IV
- had left ventricular ejection fraction (LVEF) ≤35%
- were fitted with a cardiac device for continuous monitoring

Where?

Heart and Diabetes Center North Rhine-Westphalia, Bad Oeynhausen, Germany

Primary endpoint

Composite of all-cause mortality, worsening HF requiring urgent heart transplantation, or implantation of LVAD.

Rate%

8.2%

29.9%

hazard ratio 0.24
95% CI 0.11 to 0.52 p<0.001

Who and what?

194 patients

randomised 1:1

First-time catheter ablation of AF

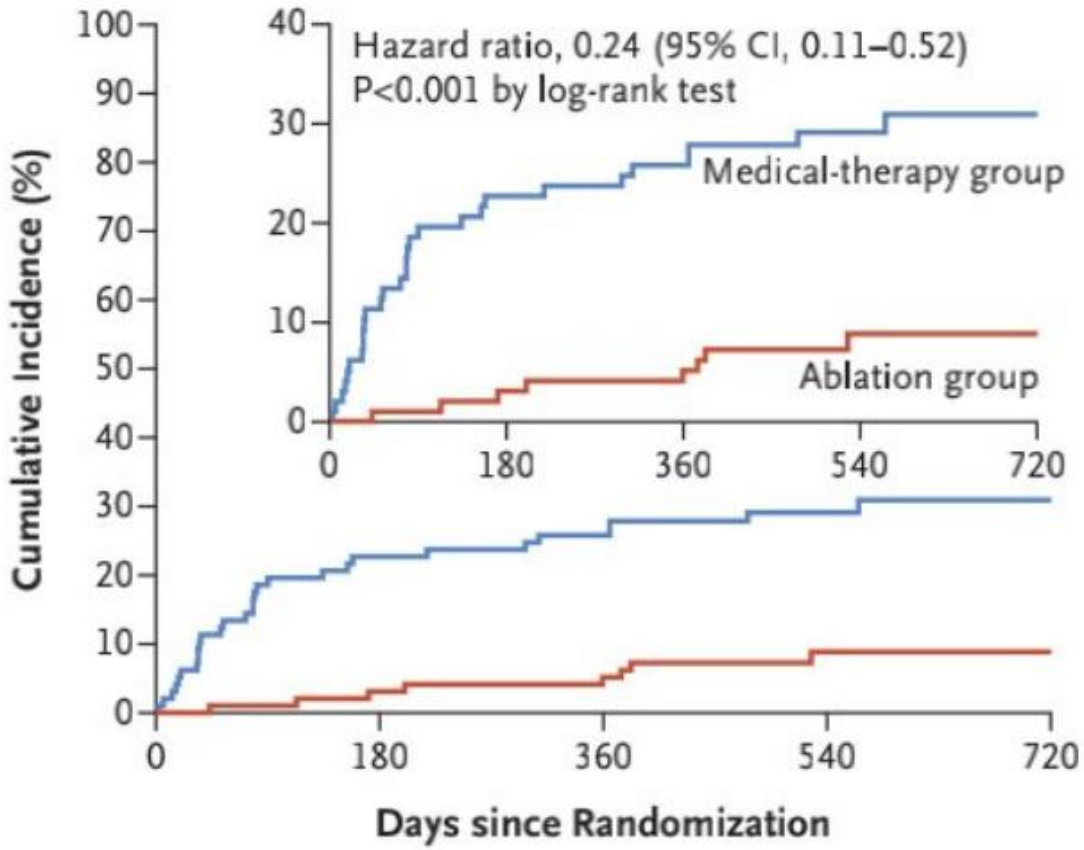
Medical therapy for AF

Both groups received guideline-directed HF therapy.

The study was stopped for efficacy by the Data Safety Monitoring Board 1 year after randomisation was completed.

ESC

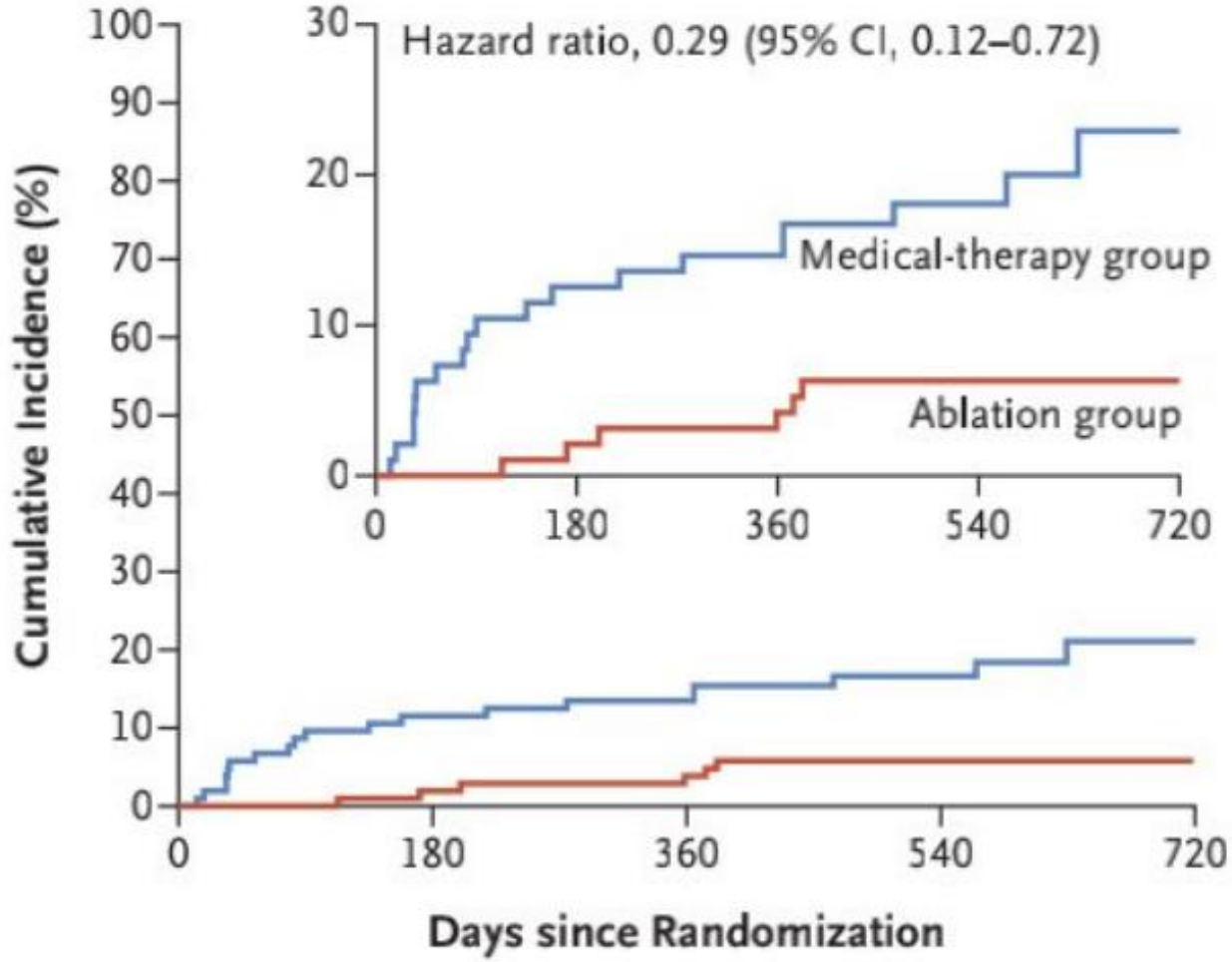
A Primary End Point



No. at Risk

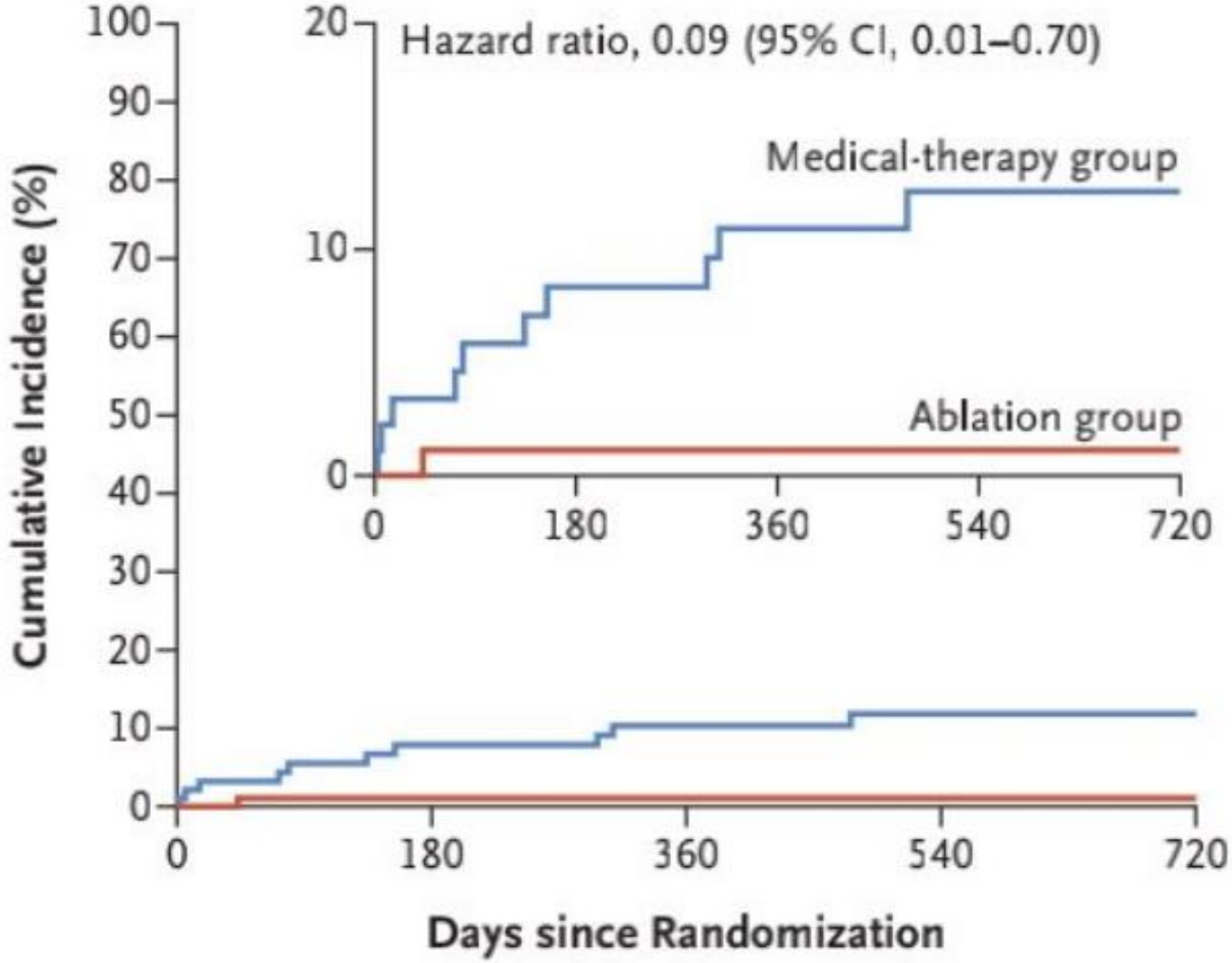
Medical-therapy group	97	75	72	41	12
Ablation group	97	94	88	50	20

B Death from Any Cause



No. at Risk					
Medical-therapy group	97	85	83	45	13
Ablation group	97	95	93	51	20

C Implantation of a Left Ventricular Assist Device



No. at Risk					
Medical-therapy group	97	79	76	42	12
Ablation group	97	94	92	51	20

- **Conclusions : Among patients with AF & end-stage HF, the combination of catheter ablation & GDMT was associated with a lower likelihood of a composite of death from any cause, implantation of a LVAD or urgent heart transplantation than medical therapy alone.**

Reviews in Cardiovascular Medicine

Rev. Cardiovasc. Med. **2022**; 24(2): 44
https://doi.org/10.31083/j.rcm2402044

Systematic Review

Long-Term Efficacy and Safety of Left Atrial Appendage Occlusion (LAAO) vs Direct Oral Anticoagulation (DOAC) in Patients with Atrial Fibrillation: A Systematic Review and Meta-Analysis

Aminah Abdul Razzack[1], Hassan Mehmood Lak[2], Greeshma Erasani[1], Sajedur Rahman[3], Nabeel Hussain[4], Bilal Farhat Ali[5], Srilatha Eapi[6], Farah Yasmin[7], Hala Najeeb[7], Ahmad Mustafa[8], Sanchit Chawla[2], Muhammad Bilal Munir[9], Amr F Barakat[10], Walid Saliba[11], Oussama Wazni[11], Ayman A. Hussein[11,*]

A total 3 studies with 3039 participants, average 2 yr follow-up,
primary end point was CV mortality,
secondary outcomes: incidence of ischemic stroke/TIA & systemic embolism

Study or Subgroup	LAAO Events	LAAO Total	DOAC Events	DOAC Total	Weight	Risk Ratio M-H, Random, 95% CI
Godino 2020	15	193	6	189	27.7%	2.45 [0.97, 6.18]
Nielsen-Kudsk 2021	54	1071	111	1184	40.7%	0.54 [0.39, 0.74]
PRAGUE-17 2020	11	201	15	201	31.6%	0.73 [0.35, 1.56]
Total (95% CI)		**1465**		**1574**	**100.0%**	**0.90 [0.40, 2.03]**
Total events	80		132			

Heterogeneity: $Tau^2 = 0.40$; $Chi^2 = 9.39$, $df = 2$ ($P = 0.009$); $I^2 = 79\%$

Test for overall effect: $Z = 0.25$ ($P = 0.81$)

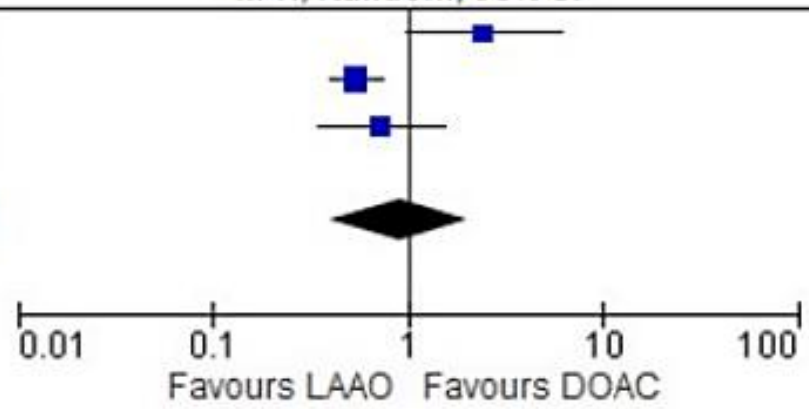


Fig. 1. Forrest plot comparing LAAO to DOAC for the primary efficacy endpoint of cardiovascular mortality.

Study or Subgroup	LAAO Events	LAAO Total	DOAC Events	DOAC Total	Weight	Risk Ratio M-H, Random, 95% CI
Godino 2020	10	193	8	189	16.2%	1.22 [0.49, 3.03]
Nielsen-Kudsk 2021	39	1071	37	1184	68.4%	1.17 [0.75, 1.81]
PRAGUE-17 2020	9	201	8	201	15.4%	1.13 [0.44, 2.86]
Total (95% CI)		**1465**		**1574**	**100.0%**	**1.17 [0.81, 1.68]**
Total events	58		53			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.02$, $df = 2$ ($P = 0.99$); $I^2 = 0\%$

Test for overall effect: $Z = 0.83$ ($P = 0.40$)

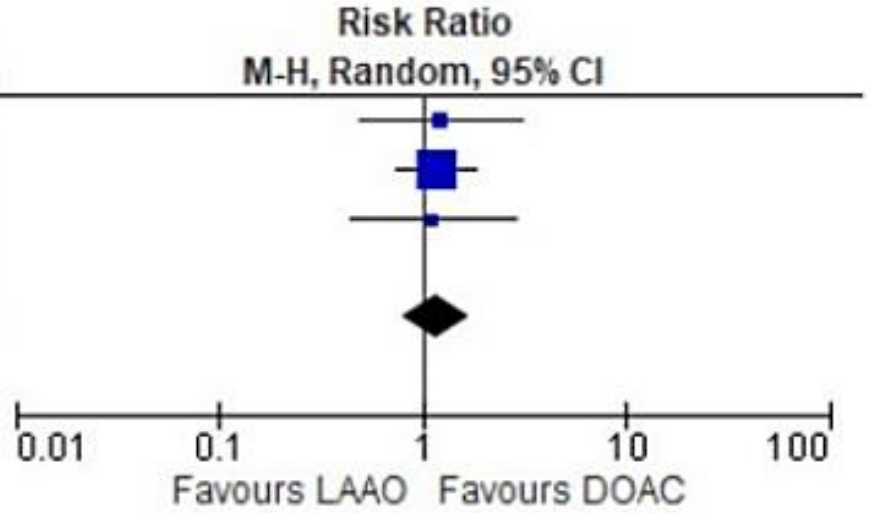


Fig. 2. Forrest plot comparing LAAO to DOAC for the incidence of Ischemicstrokes/TIA.

Study or Subgroup	LAAO Events	LAAO Total	DOAC Events	DOAC Total	Weight	Risk Ratio M-H, Random, 95% CI
Godino 2020	0	193	2	189	52.6%	0.20 [0.01, 4.05]
PRAGUE-17 2020	0	201	1	201	47.4%	0.33 [0.01, 8.13]
Total (95% CI)		**394**		**390**	**100.0%**	**0.25 [0.03, 2.27]**
Total events	0		3			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.06$, $df = 1$ ($P = 0.81$); $I^2 = 0\%$

Test for overall effect: $Z = 1.23$ ($P = 0.22$)

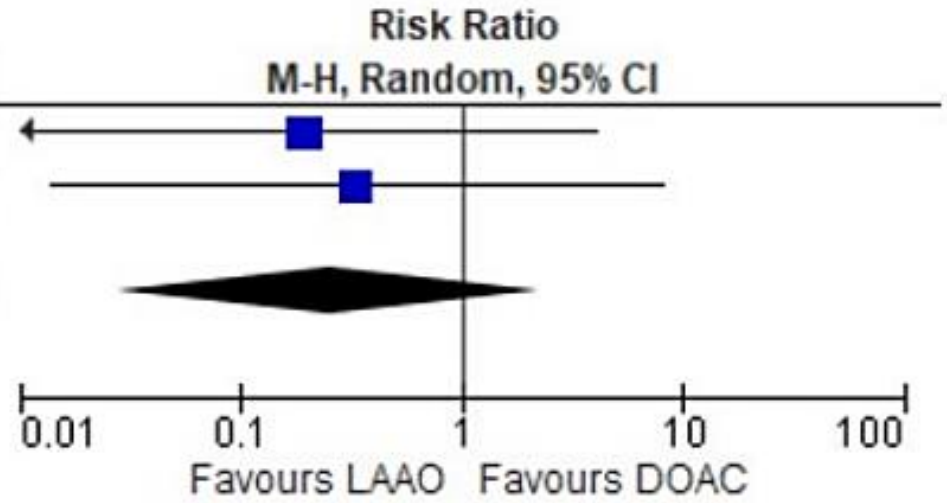


Fig. 3. Forrest plot comparing LAAO to DOAC for the incidence of systemic embolism.

Study or Subgroup	LAAO Events	LAAO Total	DOAC Events	DOAC Total	Weight	Risk Ratio M-H, Random, 95% CI
Godino 2020	23	193	39	189	30.4%	0.58 [0.36, 0.93]
Nielsen-Kudsk 2021	108	1071	183	1184	43.0%	0.65 [0.52, 0.82]
PRAGUE-17 2020	26	201	19	201	26.6%	1.37 [0.78, 2.39]
Total (95% CI)		**1465**		**1574**	**100.0%**	**0.77 [0.50, 1.17]**
Total events	157		241			

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 6.55$, $df = 2$ ($P = 0.04$); $I^2 = 69\%$

Test for overall effect: $Z = 1.22$ ($P = 0.22$)

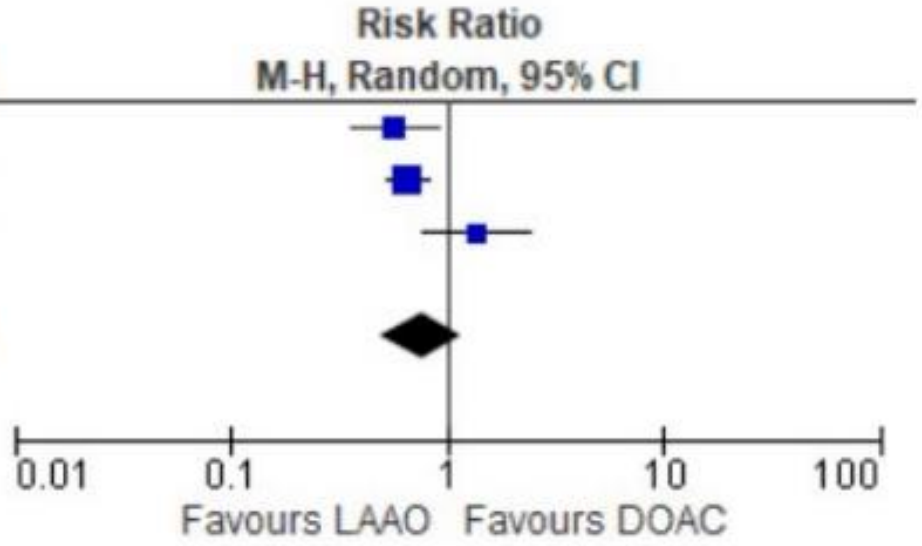


Fig. 4. Forrest plot comparing LAAO to DOAC for the safety endpoint.

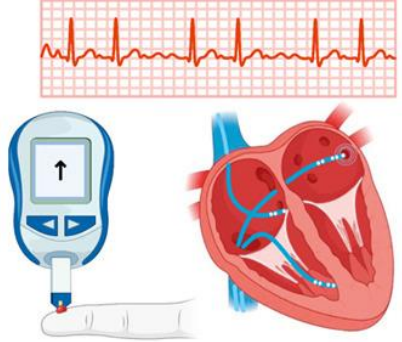
Conclusions: Among patients with AF, LAAO was comparable to DOAC with similar efficacy & safety profiles

JACC: Clinical Electrophysiology
Available online 9 August 2023
In Press, Corrected Proof What's this?

Original Research Paper

Impact of SGLT2 Inhibitors on Atrial Fibrillation Recurrence After Catheter Ablation in Patients With Type-2-Diabetes

Moh'd Rasheed Abu-Qaoud MD [a], Ashish Kumar MD [b], Tushar Tarun MD [c], Sonu Abraham MD [a], Javaria Ahmad MD [a], Sumanth Khadke MD [a], Raya Husami MD [a], Guy Kulbak MD [a], Sibasis Sahoo MD [g], James L. Januzzi Jr. MD [d], Tomas G. Neilan MD, MPH [d], Suzanne J. Baron MD, MSc [a], David Martin MD [e], Anju Nohria MD, MSc [e], Matthew R. Reynolds MD, MSc [a], Mikhail Kosiborod MD [f], Sourbha S. Dani MD, MSc [a], Sarju Ganatra MD [a]



Patients with a history of type-2 DM who had undergone AF ablation

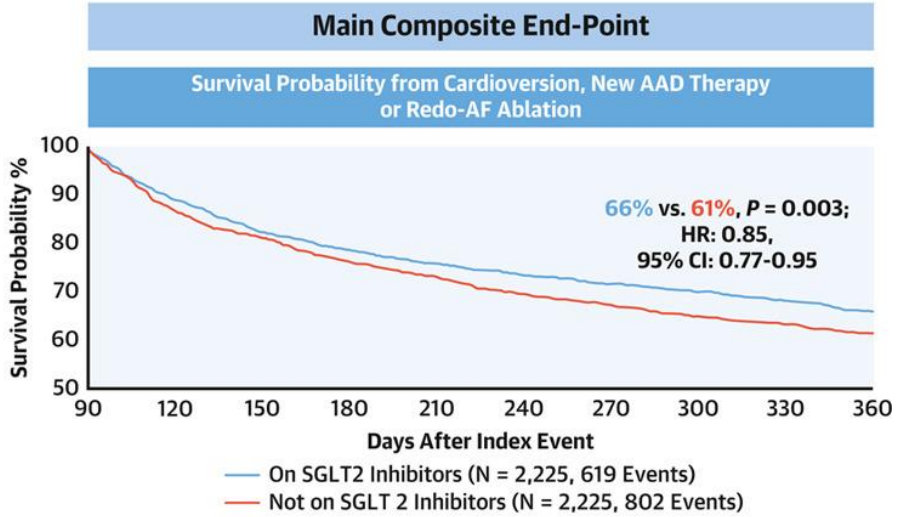
- Baseline use of SGLT2i
- No SGLT2i use

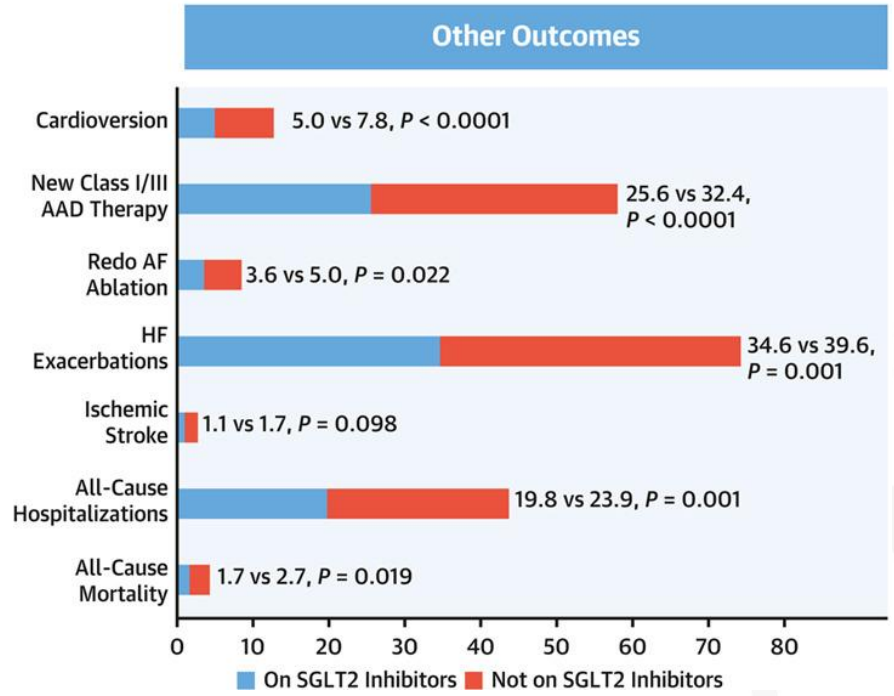
Propensity score matching

3-month blanking period after AF ablation

n = 2,225 | n = 2,225

Main composite end-point:
- The need for cardioversion or,
- New class I or III AAD therapy or,
- Redo AF ablation





Conclusion: Use of SGLT2 inhibitors in patients with type 2 DM is associated with a lower risk of arrhythmia recurrence after AF ablation; reduced need for cardioversion, AAD therapy or re-do AF ablation.

What should be changed in 2023?

- Although RF based AF ablation is still Gold Standard, a new ablation technique: pulsed field ablation is effective & safe, much less procedure time
- Balloon based Cryo-ablation is an alternative energy sources for PVI has also been successful in initial treatment of PAF associated with a lower incidence of persistent AF.
- Catheter ablation of AF in patients with end-stage heart failure combined with GDMT may be associated with mortality benefit (reduction of AF burden)
- LAAO is non-inferior, comparable to DOAC with similar efficacy & safety profiles
- SGLT2 inhibitors seemed to have anti-arrhythmic properties, associated with a lower incidence and recurrence of AF.

Conclusion

- AF is a chronic & progressive disorder, and it is associated with increased risks of thromboembolism and heart failure.
- Catheter ablation as initial therapy may modify the pathogenic mechanism of AF and alter progression to persistent AF.
- PFA & Cryo-ablation are emerging treatment options and have become the alternative solutions to conventional thermal ablation
- LAAO as an alternative to anticoagulation if anticoagulation is contraindicated or not tolerated

THANK YOU