

Sistema Socio Sanitario



Regione
Lombardia

ASST Cremona



UNIVERSITÀ
DEGLI STUDI
DI BRESCIA

FIBRILLAZIONE ATRIALE: Controllo della frequenza e del ritmo

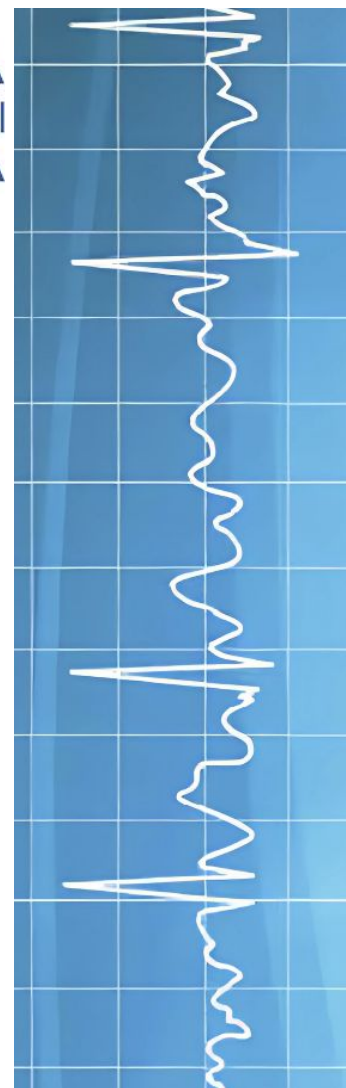
Dr. Manuel Cerini

**CARDIO-GERIATRIA NEI SETTING
RESIDENZIALI**

9 MAGGIO 2025

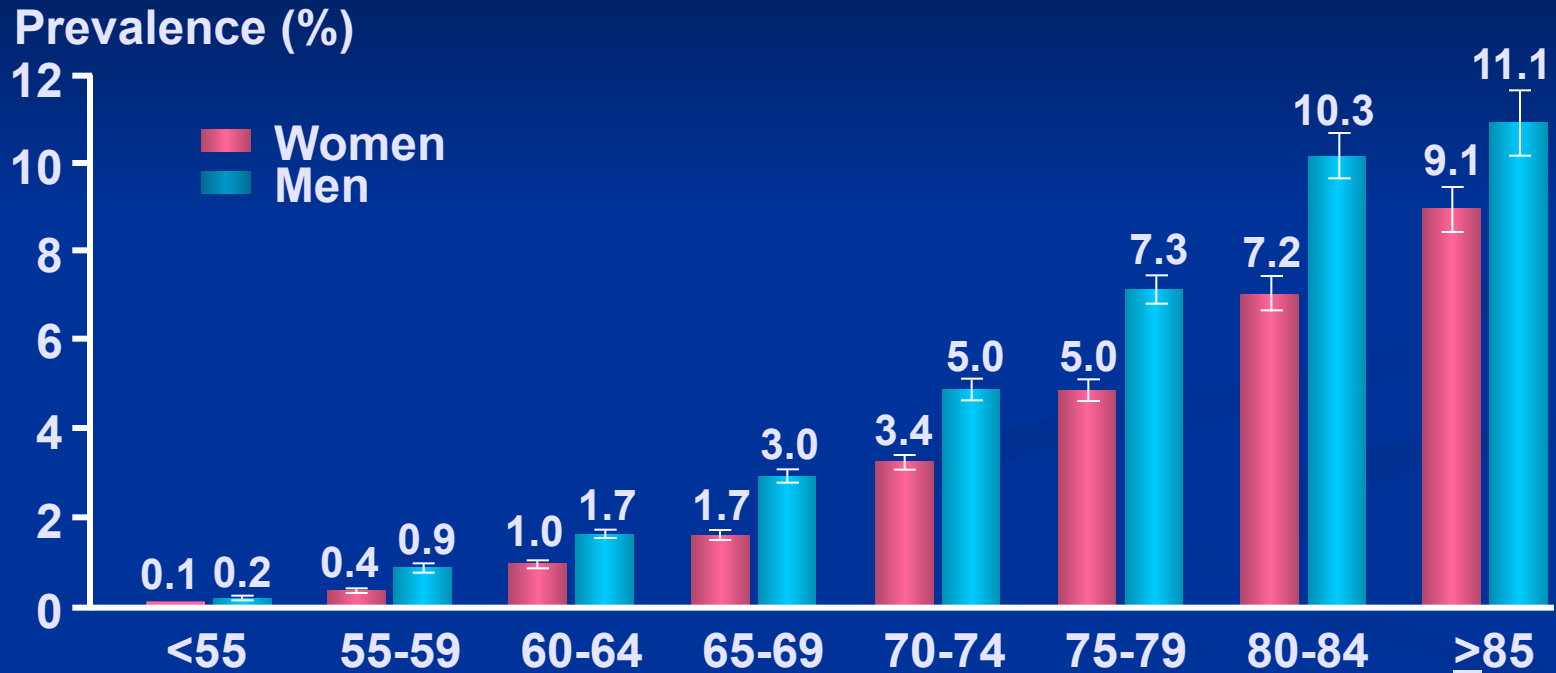
ore 15.00 | Sala BENACO ASC Cremona Solidale

Focus sulla gestione dello scompenso cardiaco e
della fibrillazione atriale



ATRIA study

Prevalence of diagnosed AF stratified by age and sex

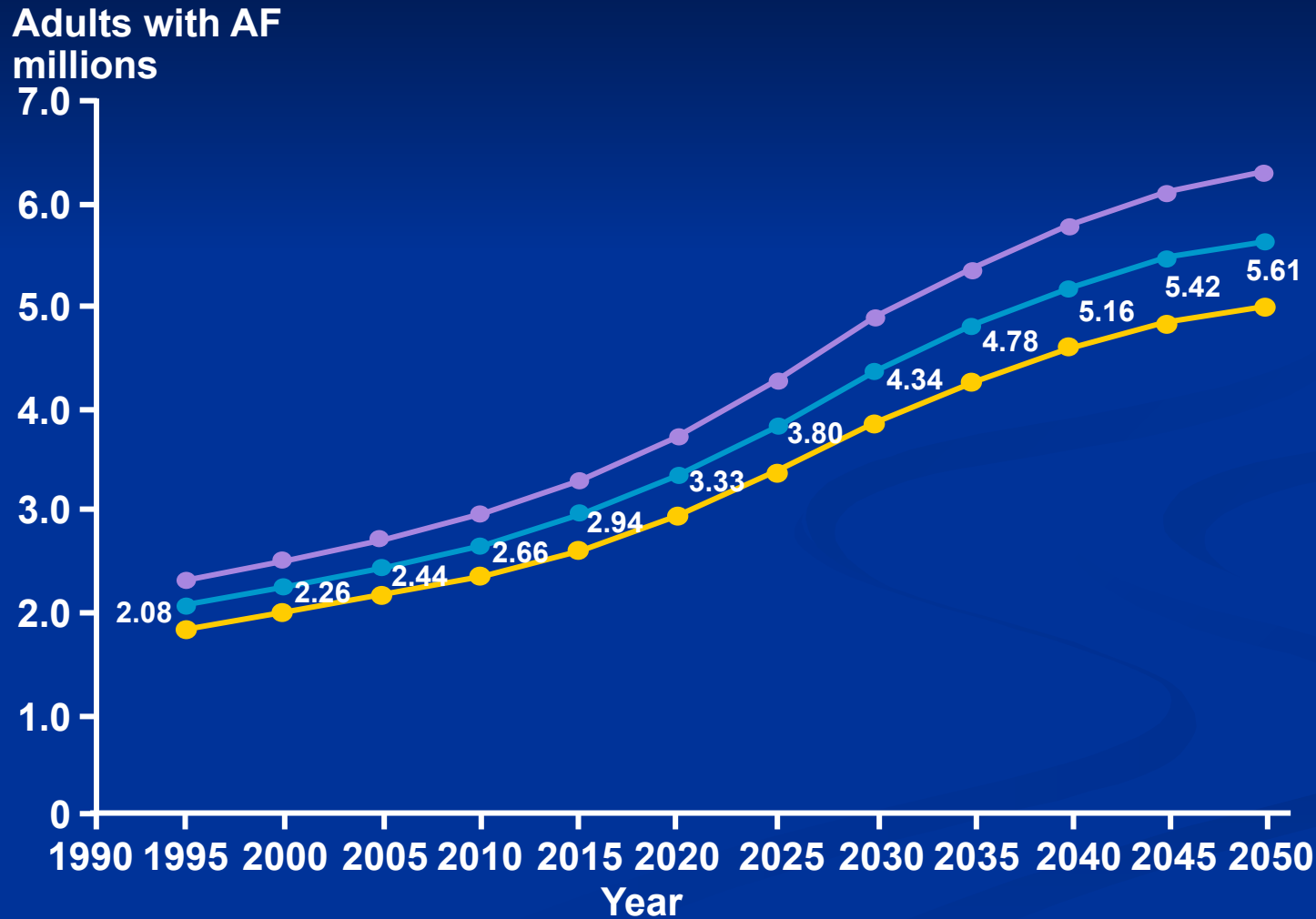


No

Women	530	310	566	896	1498	1572	1291	1132	
Men	1259	634	934	1426	1907	1886	1374	759	

ATRIA study

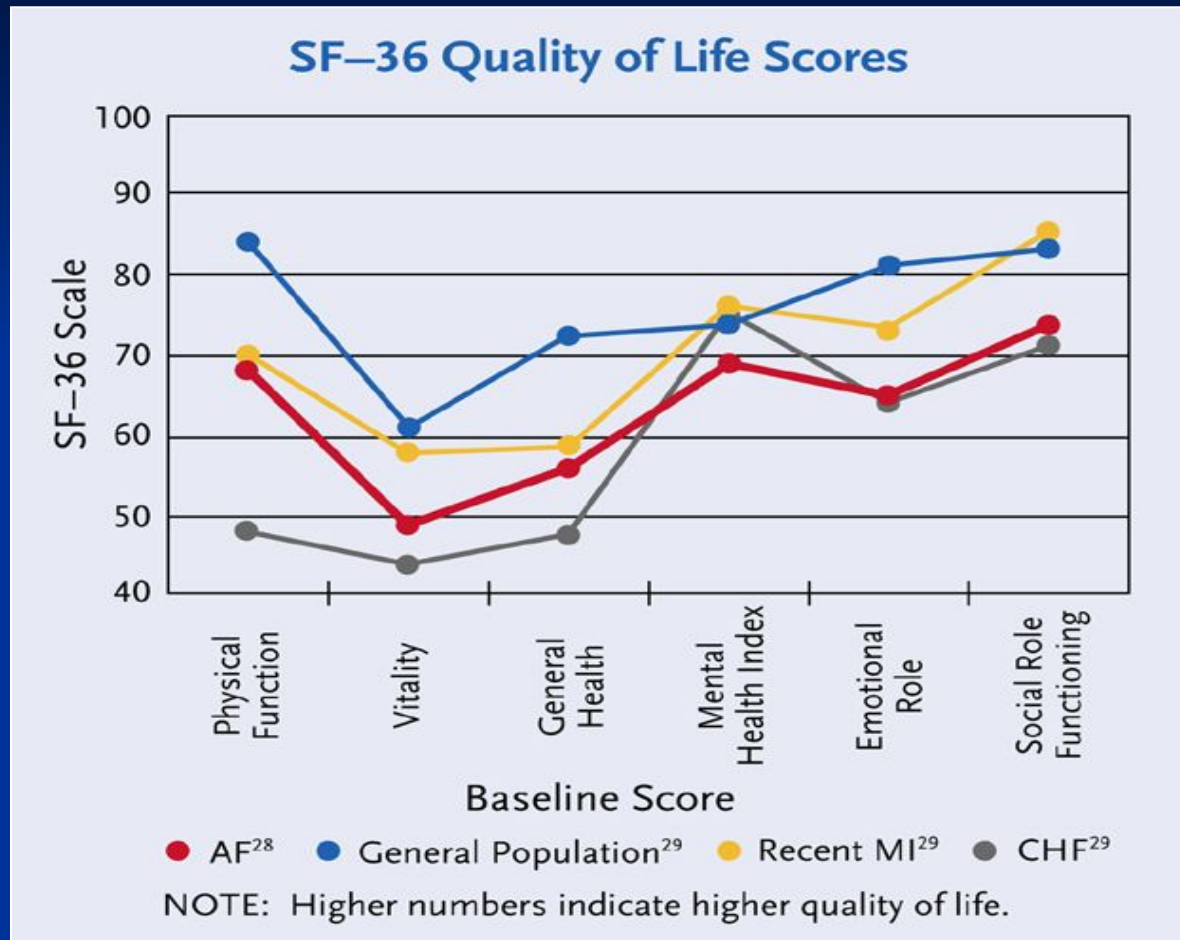
Projected number of adults with AF in the US between 1995 and 2050



Impatto della Fibrillazione Atriale

Event	Association with AF
Death	L'FA incrementa di 2 volte il rischio di mortalità nelle donne e di 1.5 negli uomini
Stroke	20–30% of all strokes are due to AF. A growing number of patients with stroke are diagnosed with 'silent', paroxysmal AF.
Hospitalizations	10–40% of AF patients are hospitalized every year.
Quality of life	Quality of life is impaired in AF patients independent of other cardiovascular conditions.
Left ventricular dysfunction and heart failure	Left ventricular dysfunction is found in 20–30% of all AF patients. AF causes or aggravates LV dysfunction in many AF patients, while others have completely preserved LV function despite long-standing AF.
Cognitive decline and vascular dementia	Cognitive decline and vascular dementia can develop even in anticoagulated AF patients. Brain white matter lesions are more common in AF patients than in patients without AF.

L'FA riduce il QoL



²⁸ Jung W, Herwig S, Newman D et al. JACC. 1999;33(2):104A

²⁹ Ware JE, Snow KK, Kosinski M, Gandek B. New England Medical Center Health Survey, 1993.

Sintomi più frequenti

□ Frequenza cardiaca

□ Perdita del contributo
atriale

□ Tromboembolismo

✓ Palpitazioni (54%)

✓ Dispnea (44%)

✓ Astenia e facile affaticabilità (14%)

✓ Dolore toracico (10%)

✓ Vertigini e sincope (10%)

Classificazione Sintomi EHRA (European Heart Rhythm Association)

Modified EHRA score	Symptoms	Description
1	None	AF does not cause any symptoms.
2a	Mild	Normal daily activity not affected by symptoms related to AF.
2b	Moderate	Normal daily activity not affected by symptoms related to AF, but patient troubled by symptoms.
3	Severe	Normal daily activity affected by symptoms related to AF.
4	Disabling	Normal daily activity discontinued.

La prevalenza dell'FA aumenta con lo scompenso cardiaco

<i>NYHA class</i>	<i>Prevalence of AF (%)</i>
I (least severe)	4
II–III	10–26
III–IV	20–29
IV (most severe)	50

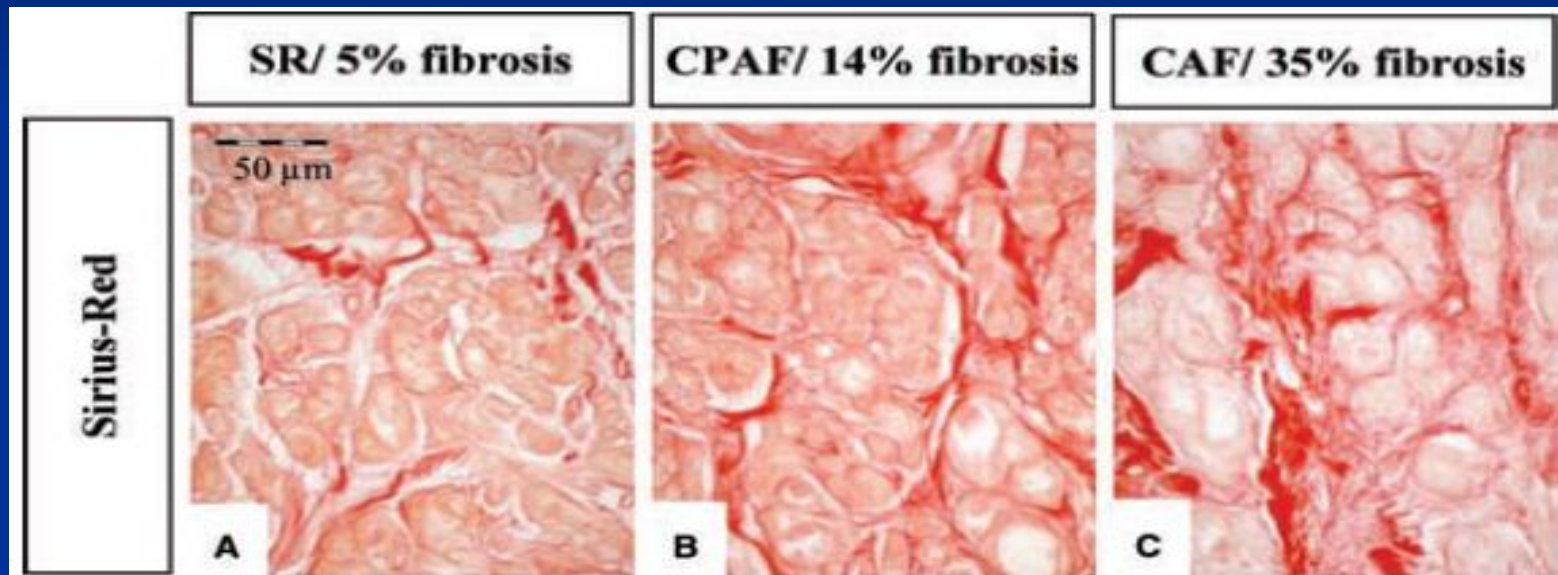
L' FA è una patologia progressiva



“Natural time course of AF”

AF Treatment Must be Provided Before the Fibrosis Process Makes Intervention More Difficult

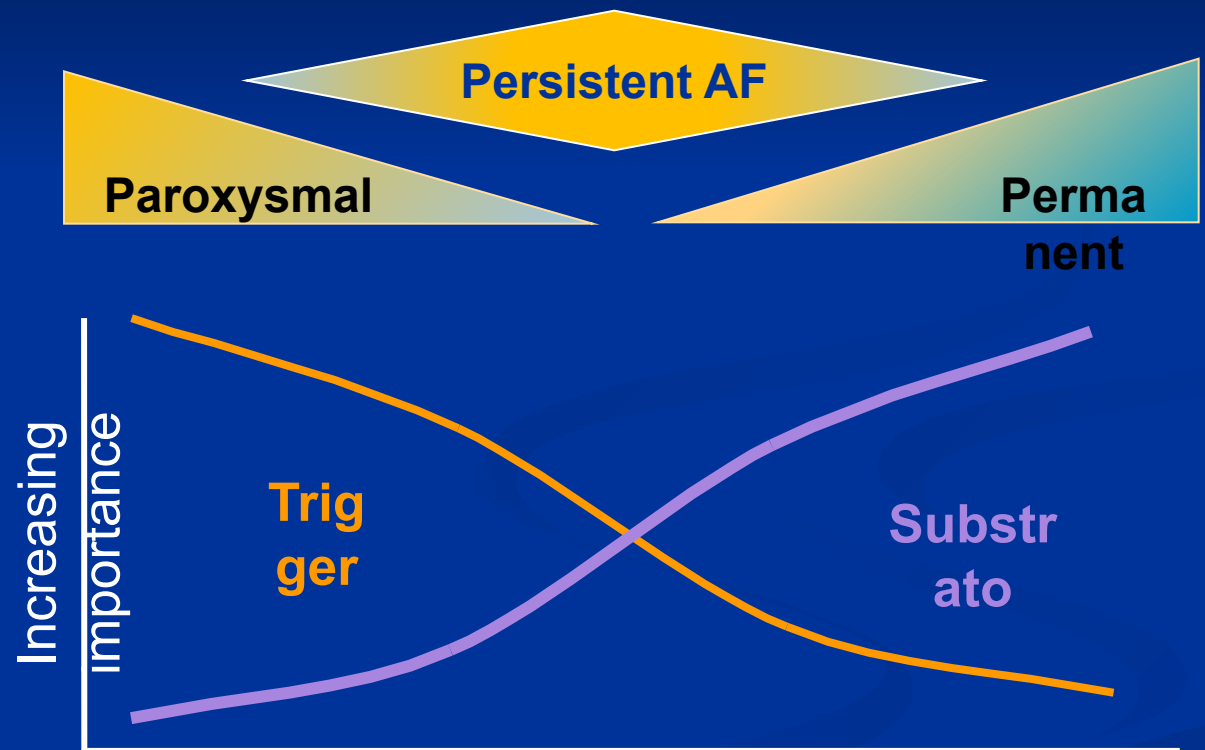
Human Atrial Fibrogenesis is Enhanced with Increasing Duration of AF



A. Patients in sinus rhythm (SR) with no history of AF, **B.** Patients with paroxysmal (self-terminating) and early persistent (not spontaneously self-terminating) AF were defined as one or more episodes of documented AF, the longest episode being less than 6 months in duration, **C.** Persistent AF with failed or un-attempted cardioversion was defined as AF of >6 months duration.

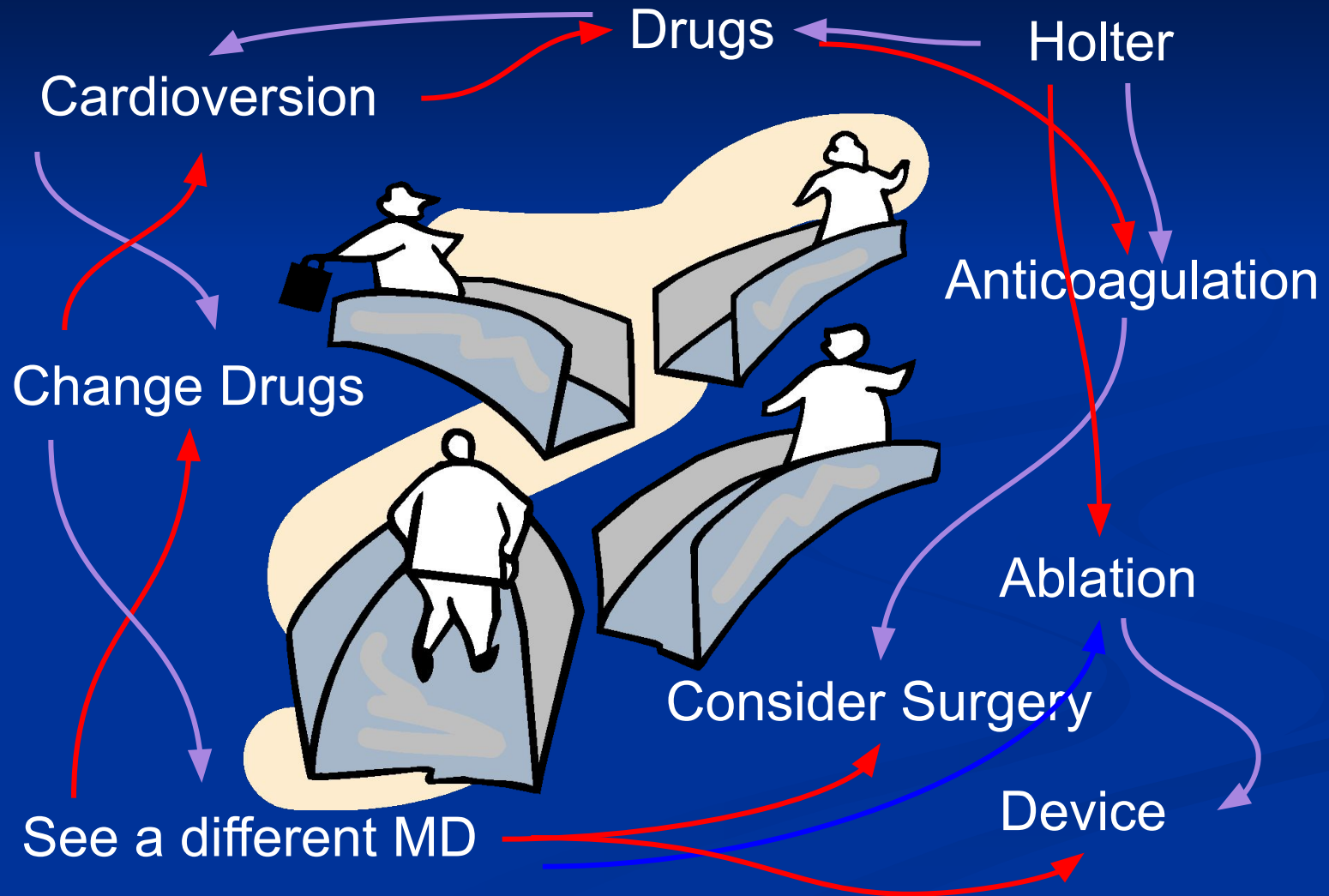
La Fibrillazione Atriale è un patologia eterogenea

- ✓ Diabetes
- ✓ Heart failure
- ✓ Obesity
- ✓ Coronary artery disease
- ✓ Hypertension
- ✓ Ageing
- ✓ Genetic predisposition



“Atrial fibrillation begets atrial fibrillation”

Gestione della Fibrillazione Atriale



Obiettivi del Trattamento

- ✓ Intervention, rhythm-control (*Maintenance of normal sinus rhythm*)
- ✓ Termination of the tachyarrhythmia (*Restoration of normal heart rate*)
- ✓ Symptom-reduction, rate-control (*Control of the heart rate*)
- ✓ Stroke reduction (*Reduction in thrombo-embolic complications*)
- ✓ Quality of Life (Control of symptoms)

Strategie terapeutiche

- Controllo del ritmo (inclusa la cardioversione)

O

- Controllo della frequenza

Più

- Terapia anticoagulante

Ritmo versus Frequenza

REVIEW

Annals of Internal Medicine

Tabella 3. Studi randomizzati

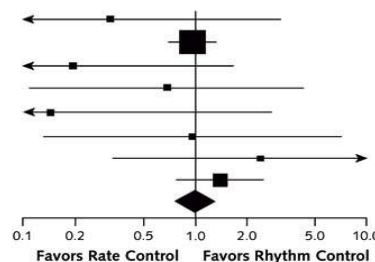
Rate- and Rhythm-Control Therapies in Patients With Atrial Fibrillation A Systematic Review

Sana M. Al-Khatib, MD, MHS; Nancy M. Allen LaPointe, PharmD; Raneen Chatterjee, MD, MPH; Matthew J. Crowley, MD; Matthew E. Dupre, PhD; David F. Kong, MD; Renato D. Lopes, MD, PhD; Thomas J. Povsic, MD, PhD; Shveta S. Raju, MD; Bimal Shah, MD; Andrzej S. Kosinski, PhD; Amanda J. McBroom, PhD; and Gillian D. Sanders, PhD

I vantaggi del mantenimento del RS non vengono messi in discussione, tuttavia la caparbia ricerca del ritmo sinusale nei pazienti asintomatici non risulta vantaggiosa.

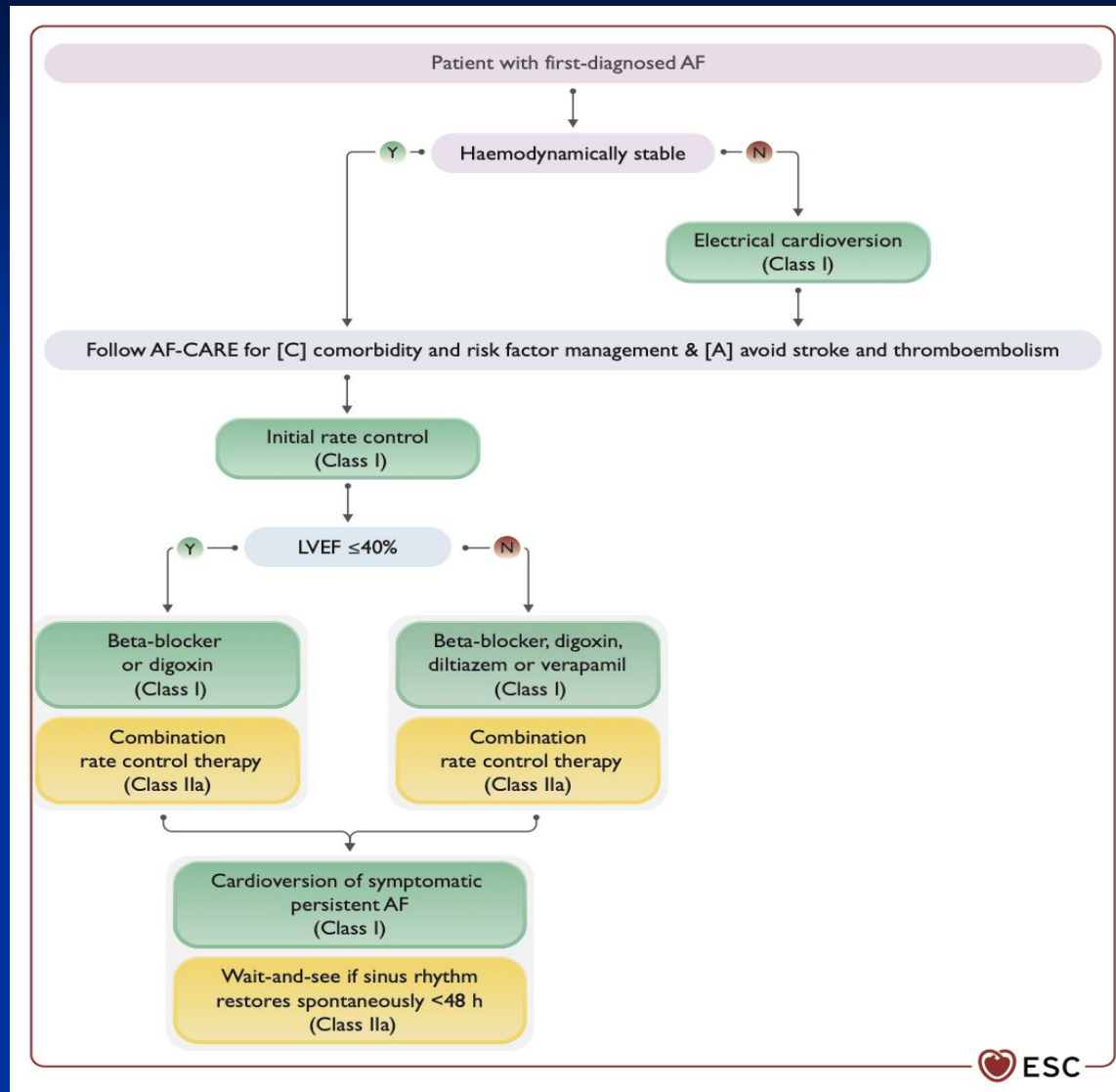


		C.	Stroke/Total, n/N			
			Rate Control	Rhythm Control		
AF-CHF	2008	1376	Brignole et al, 2002 (17)	0.319 (0.032–3.142)	1/69	3/68
		694	Wyse et al, 2002 (27)	0.964 (0.701–1.326)	77/2027	80/2033
			Carlsson et al, 2003 (18)	0.192 (0.022–1.673)	1/100	5/100
			Okçün et al, 2004 (20)	0.685 (0.110–4.276)	3/84	2/39
			Opolski et al, 2004 (21)	0.143 (0.007–2.801)	0/101	3/104
			Petrac et al, 2005 (22)	0.960 (0.130–7.091)	2/52	2/50
			Yildiz et al, 2008 (28)	2.391 (0.330–17.342)	2/66	2/155
Ritmo		682	Talajic et al, 2010 (24)	1.392 (0.776–2.495)	28/694	20/682
			Overall	0.994 (0.759–1.302)		



CV, cardiovascolare; FA, fibrillazione

FA di nuovo riscontro



Antiarrhythmic drugs for sinus rhythm restoration

Drug	Administration route	Initial dosing	Subsequent dosing [long-term approach]	Acute success rate and time to sinus rhythm	Contraindications and precautions
Flecainide	Oral	200–300 mg	[long-term 50–150 mg twice daily]	50%–60% at 3 h and 75%–85% at 6–8 h (3–8 h)	• Should not be used in patients with severe structural or coronary artery disease, Brugada syndrome, or severe renal failure (CrCl <35 mL/min/1.73 m²). • Prior documentation of safety and efficacy in an inpatient setting is recommended prior to pill-in-the-pocket use. • An AVN-blocking agent should be administered to avoid 1:1 conduction if transformation to AFL. • Drug infusion should be discontinued in case of QRS widening >25% or bundle branch block occurrence. • Caution is needed in patients with sinus node disease and AVN dysfunction. • Do NOT use for conversion of atrial flutter.
	Intravenous	1–2 mg/kg over 10 min		52%–95% (Up to 6 h)	
Propafenone	Oral	450–600 mg	[long-term 150–300 mg three times daily]	45%–55% at 3 h, 69%–78% at 8 h (3–8 h)	
	Intravenous	1.5–2 mg/kg over 10 min		43%–89% (Up to 6 h)	
Amiodarone	Intravenous (/oral)	300 mg intravenous over 30–60 min	900–1200 mg intravenous over 24 hours (or 200 mg oral three times daily for 4 weeks). [long-term 200 mg oral daily]	44% (8–12 h to several days)	• May cause phlebitis (use a large peripheral vein, avoid i.v. administration >24 h and use preferably volumetric pump). • May cause hypotension, bradycardia/atrioventricular block, QT prolongation. • Only if no other option in patients with hyperthyroidism (risk of thyrotoxicosis). • Consider the broad range of drug interactions.

Cardioversione farmacologica

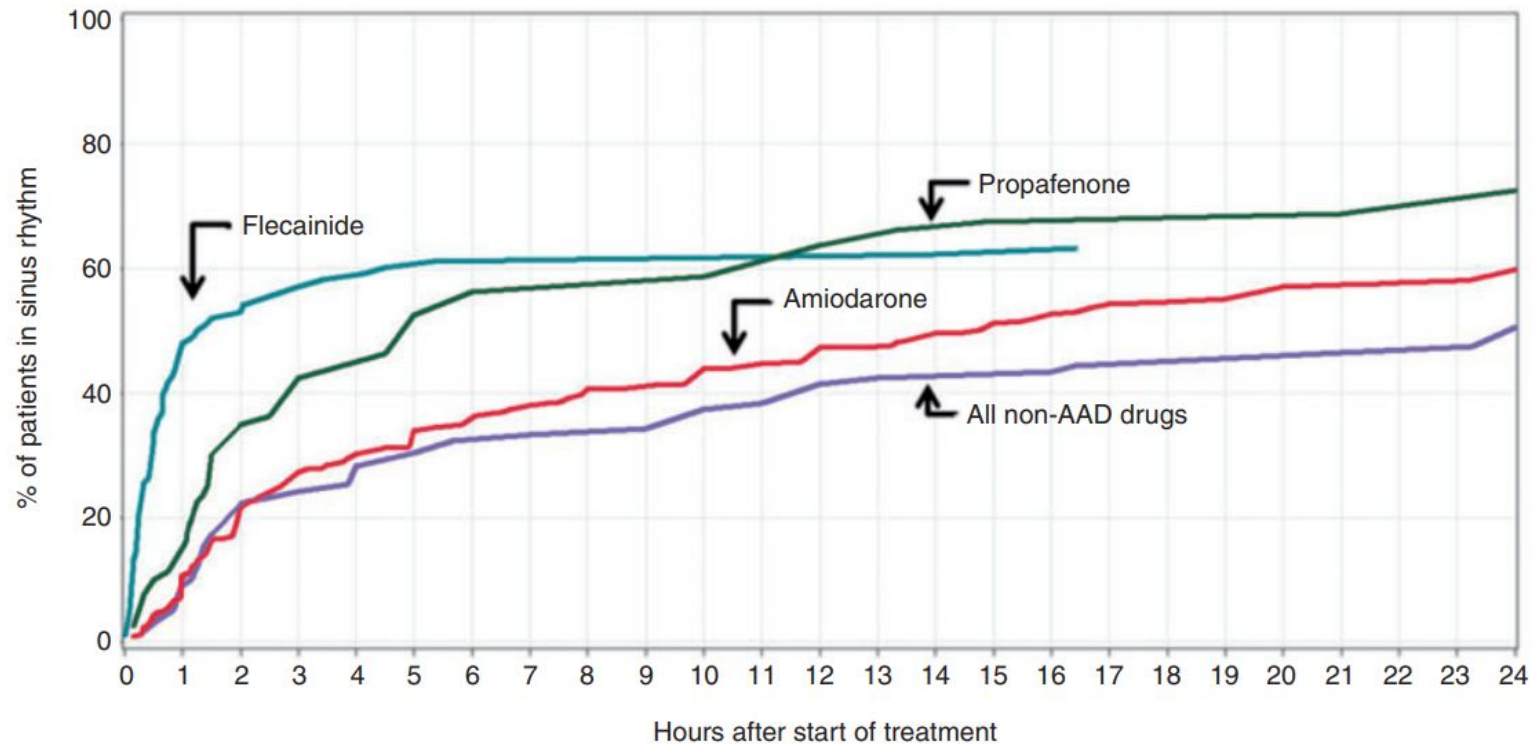


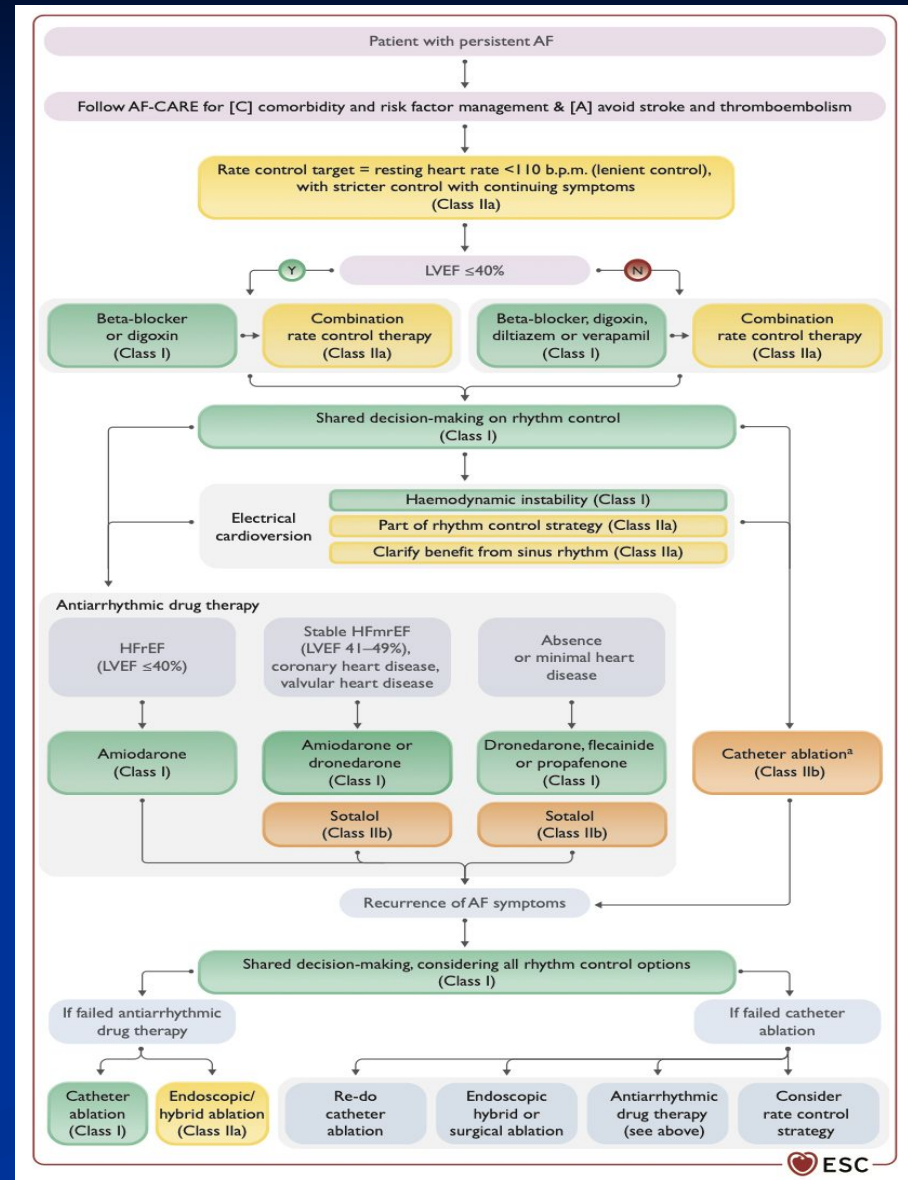
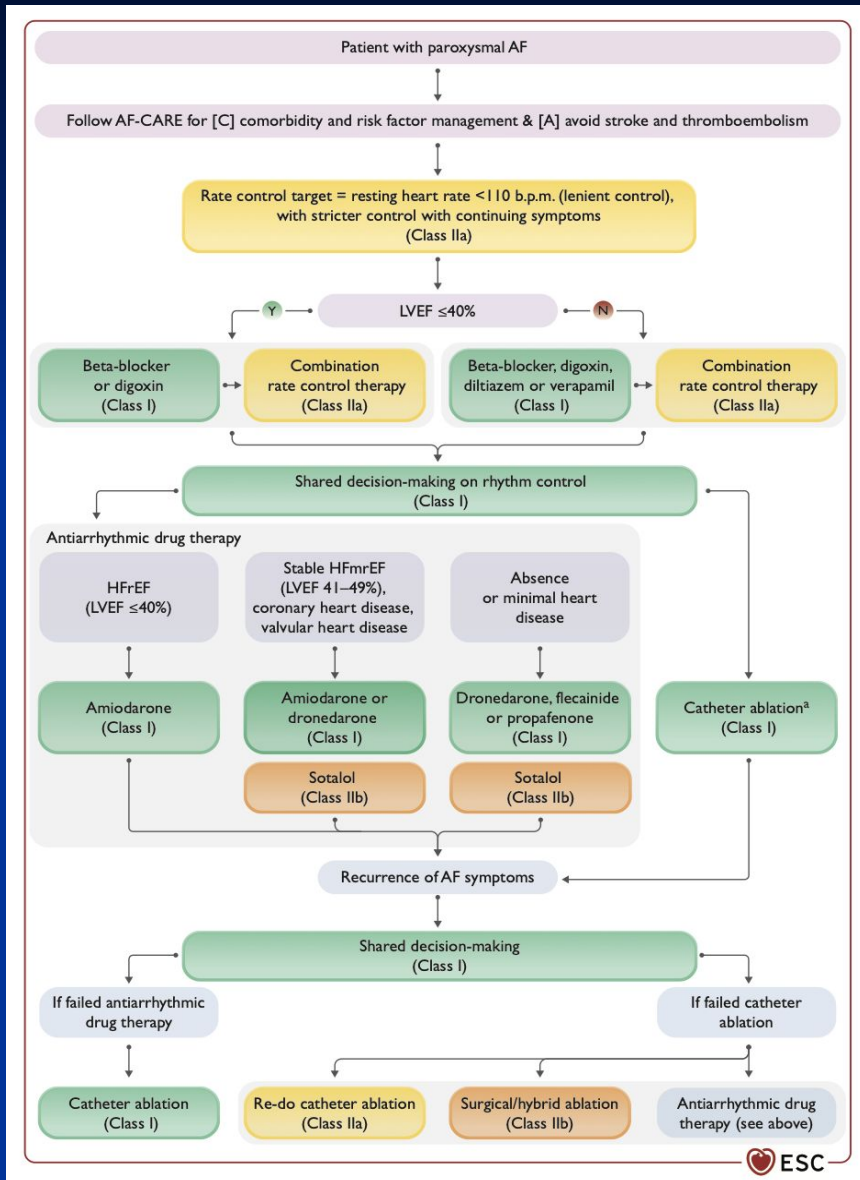
Figure 3 Conversion to sinus rhythm over time after start of drug therapy for recent-onset AF. Class Ic AADs foreshorten time to sinus rhythm significantly. Amiodarone and non-AAD (rate control drugs) are associated with spontaneous conversion, with minimal conversion action of amiodarone discernable from 6 h on. At the end of the day around 60–70% of patients reached sinus rhythm. Modified after Crijns et al.,¹⁰ with permission. AAD, antiarrhythmic drug; AF, atrial fibrillation.

Trattamento “Pill-in-the-Pocket”

Flecainide – Propafenone
(200-300mg) (450-600mg)

- La terapia deve essere preventivamente testata in ambiente ospedaliero
- Età < 75 aa
- Senza o con lieve cardiopatia
- Sintomatico per FA
- Accessi ben tollerati emodinamicamente
- Accessi non molto frequenti (< 1/mese)
- Rimanere a riposo almeno 3-4H

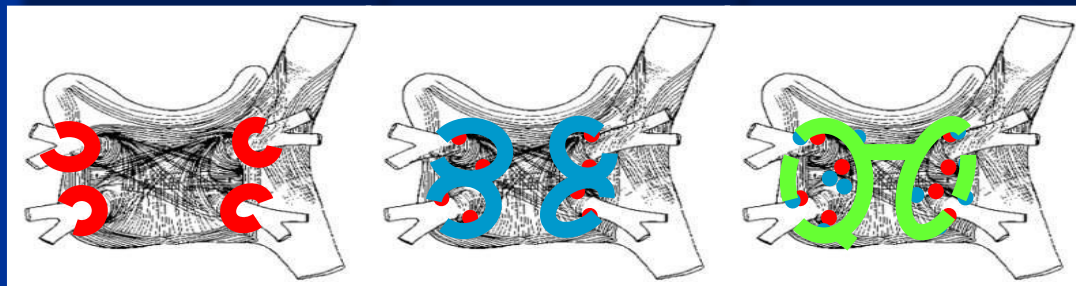
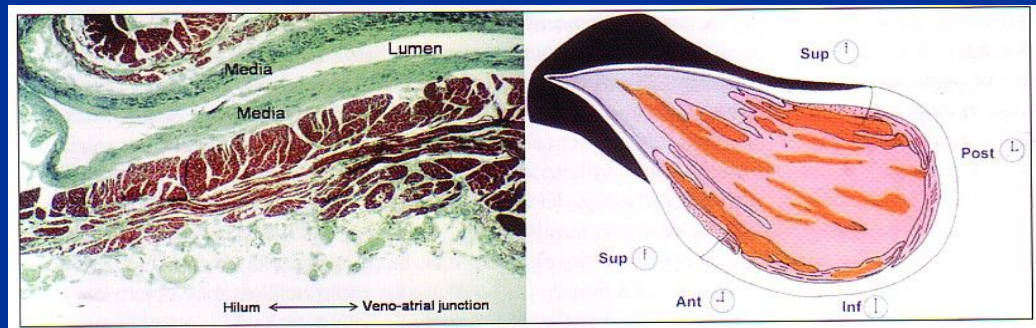
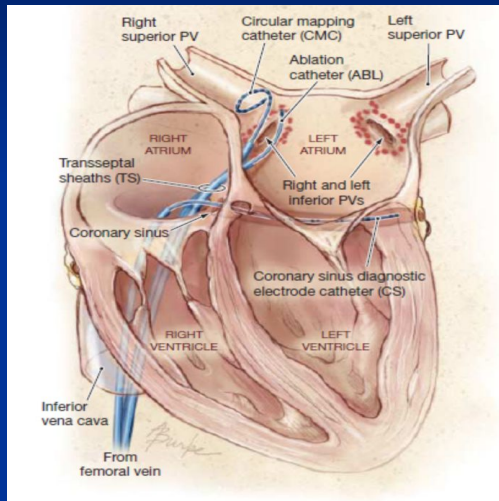
Controllo del Ritmo



Isolamento delle Vene Polmonari

2012 HRS Consensus Statement

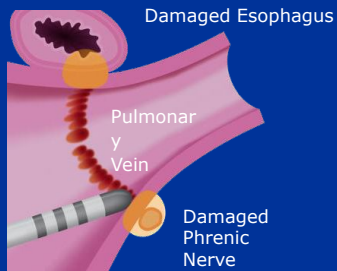
“Ablation strategies which target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures.”



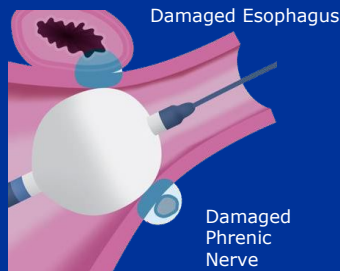
PVI: Differenti approcci

Le lesioni termiche possono estendersi anche ai tessuti circostanti

RADIOFREQUENCY
ABLATION



CRYO
ABLATION

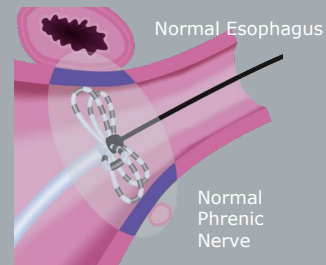


Possibili complicanze:

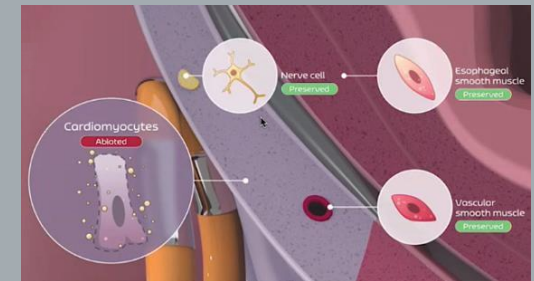
- Stenosi VP • Fistula AE
- Paralisi nervo frenico

PFA agisce sul miocardio riducendo i rischi collaterali ¹

PULSED
FIELD
ABLATION



I cardiomiociti hanno una soglia più bassa per l'elettroporazione

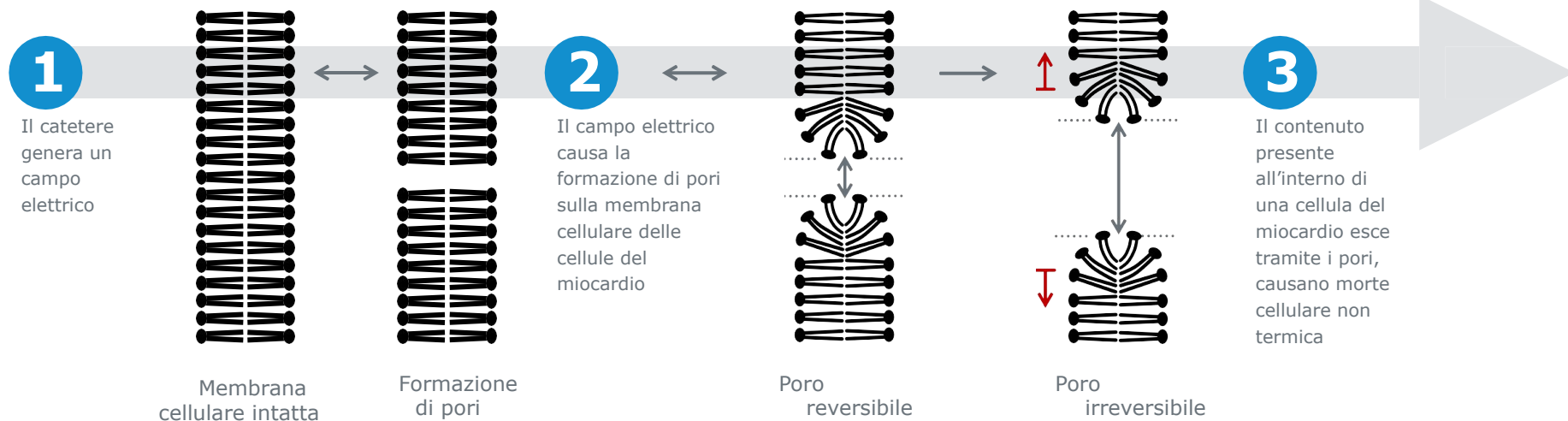


Altri tessuti/cellule sono più resistenti all'elettroporazione, rimanendo illesi seppur esposti al campo elettrico

Biofisica dell'Elettroporazione

Elettroporazione irreversibile:

formazione di pori sulla membrana cellulare e morte cellulare tramite campo elettrico

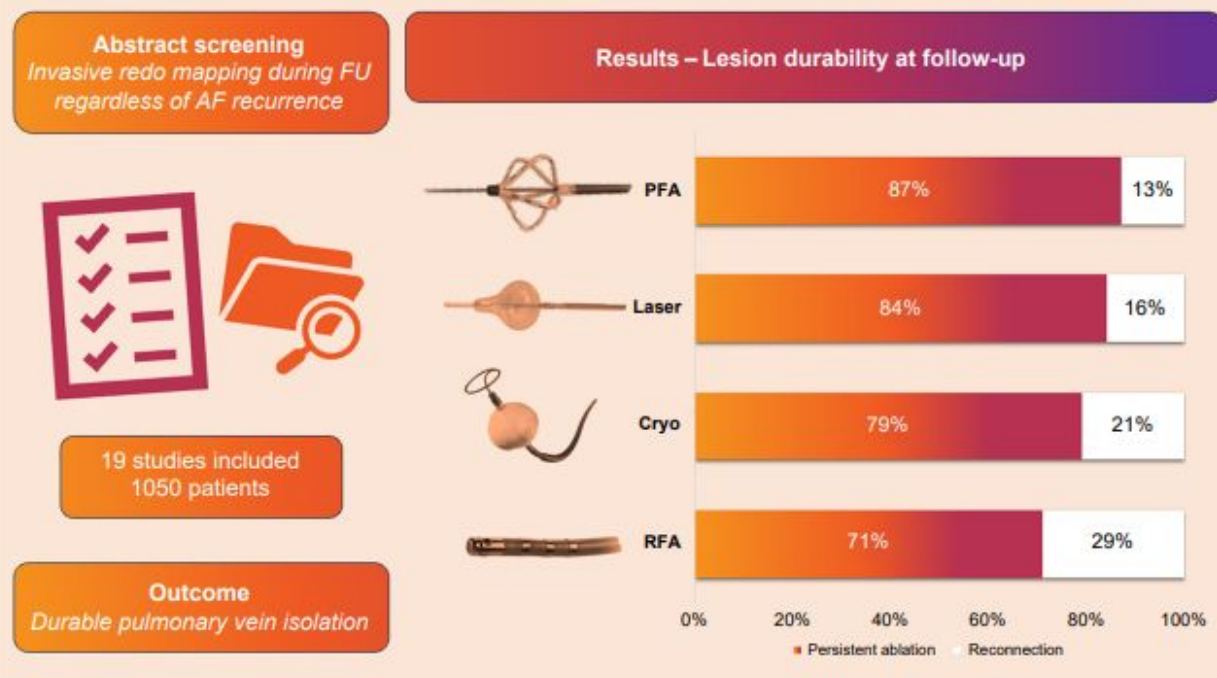




Durability of pulmonary vein isolation for atrial fibrillation: a meta-analysis and systematic review

Teodor Serban ^{1,2}, Diego Mannhart ^{1,2}, Qurrat-ul-ain Abid ³, Andres Höchli⁴, Sorin Lazar ⁵, Philipp Krisai ^{1,2}, Arianna Sofia Bettelini^{1,2}, Sven Knecht ^{1,2}, Michael Kühne ^{1,2}, Christian Sticherling ^{1,2}, Jeanne du Fay de Lavallaz ^{1,2†}, and Patrick Badertscher ^{1,2*†}

Graphical Abstract



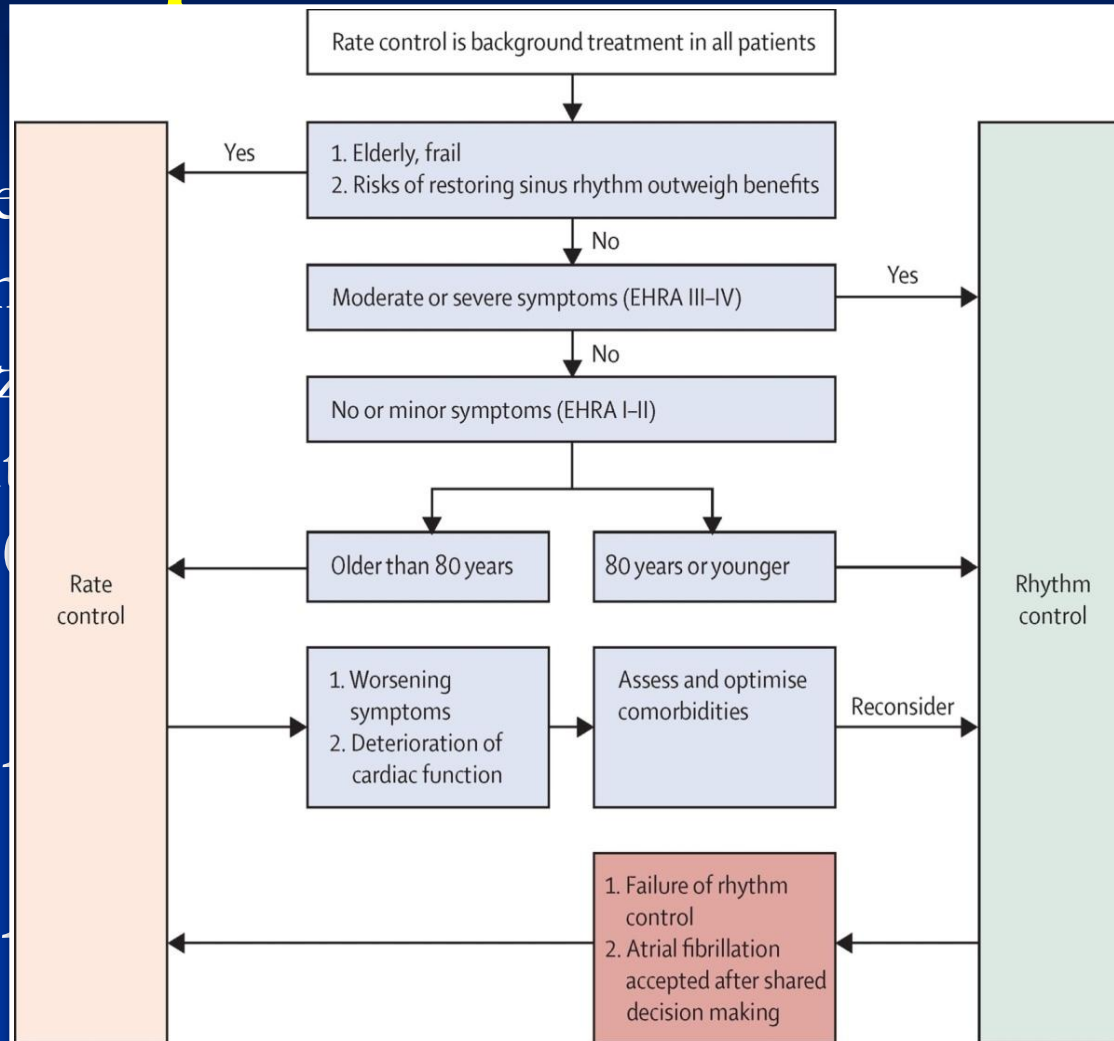
Keywords

Atrial Fibrillation • Pulmonary Vein Isolation • Radiofrequency Ablation • Cryoballoon Ablation • Laser Balloon • Pulsed-Field Ablation

Controllo della Frequenza Ventricolare

Ridurre la frequenza ventricolare nei pazienti con fibrillazione atriale sintomatica... mantenere la frequenza ventricolare di 60-90 bpm

Controllare la frequenza ventricolare nei pazienti con fibrillazione atriale sintomatica... mantenere la frequenza ventricolare di 60-90 bpm

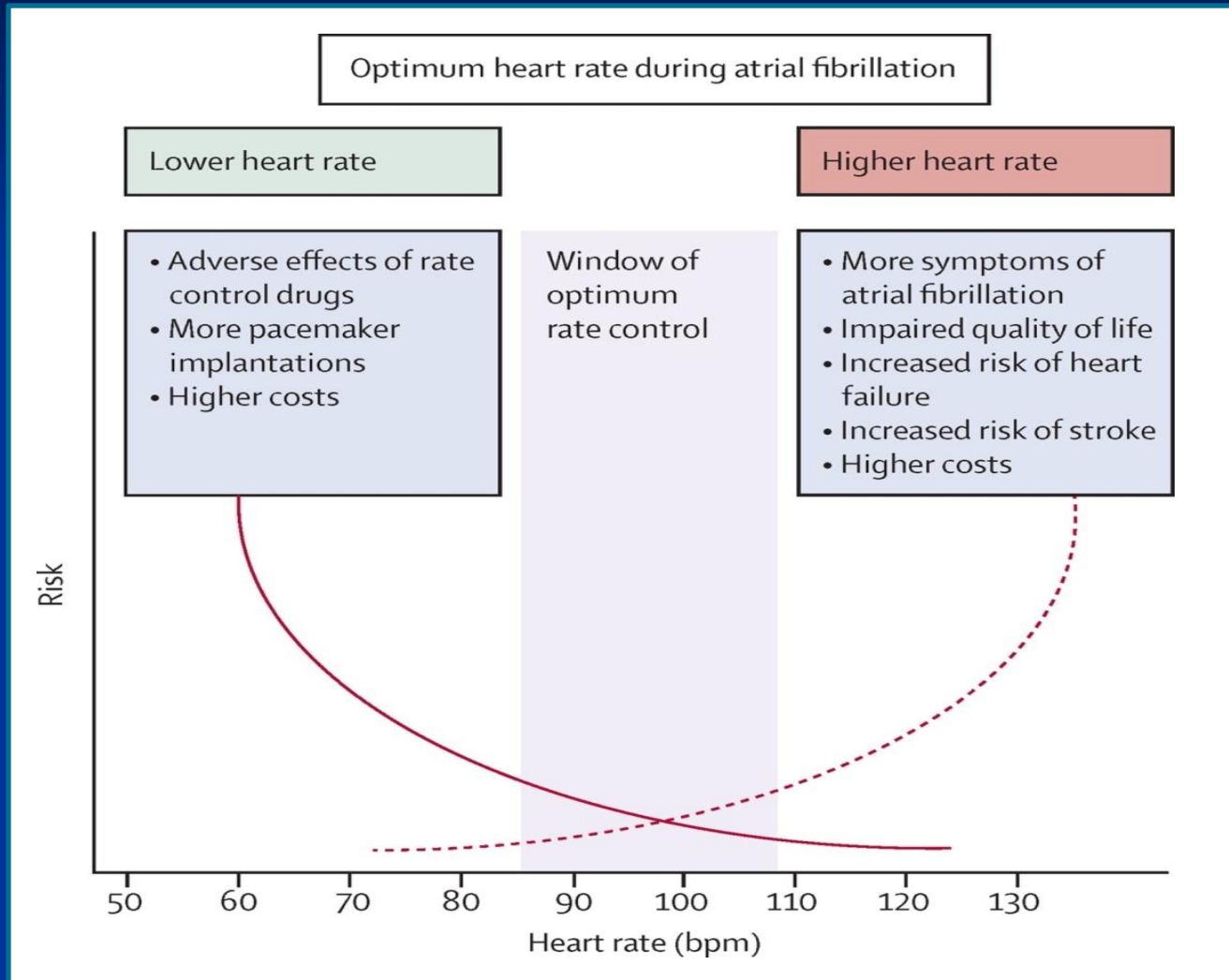


Controllo della frequenza cardiaca

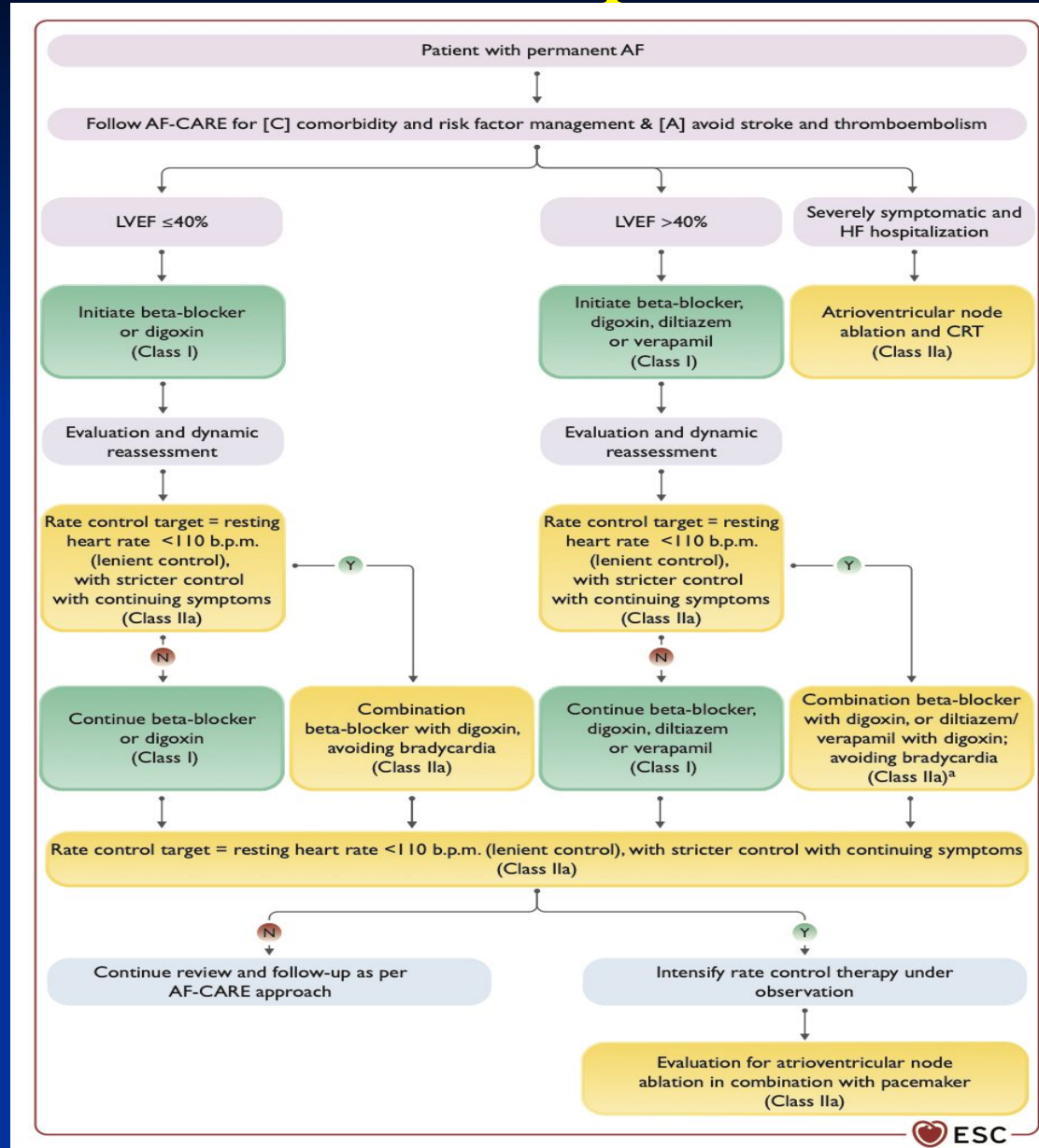
Agent ^a	Intravenous administration	Usual range for oral maintenance dose	Contraindicated
Beta-blockers^b			
Metoprolol tartrate	2.5–5 mg bolus over 2 mins; up to 15 mg maximal cumulative dose	25–100 mg twice daily	In case of asthma, non-selective beta-blockers should be avoided. Contraindicated in acute HF and history of severe bronchospasm.
Metoprolol XL (succinate)	N/A	50–200 mg once daily	
Bisoprolol	N/A	1.25–20 mg once daily	
Atenolol ^c	N/A	25–100 mg once daily	
Esmolol	500 µg/kg i.v. bolus over 1 min; followed by 50–300 µg/kg/min	N/A	
Landiolol	100 µg/kg i.v. bolus over 1 min; followed by 10–40 µg/kg/min	N/A	
Nebivolol	N/A	2.5–10 mg once daily	
Carvedilol	N/A	3.125–50 mg twice daily	
Non-dihydropyridine calcium channel antagonists			
Verapamil	2.5–10 mg i.v. bolus over 5 min	40 mg twice daily to 480 mg (extended release) once daily	Contraindicated if LVEF ≤40%. Adapt doses in hepatic and renal impairment.
Diltiazem	0.25 mg/kg i.v. bolus over 5 min, then 5–15 mg/h	60 mg three times daily to 360 mg (extended release) once daily	
Digitalis glycosides			
Digoxin	0.5 mg i.v. bolus (0.75–1.5 mg over 24 h in divided doses)	0.0625–0.25 mg once daily	High plasma levels associated with adverse events.
Digitoxin	0.4–0.6 mg	0.05–0.1 mg once daily	Check renal function before starting digoxin and adapt dose in CKD patients.
Other			
Amiodarone ^d	300 mg i.v. diluted in 250 mL 5% dextrose over 30–60 min (preferably via central venous cannula), followed by 900–1200 mg i.v. over 24 h diluted in 500–1000 mL via a central venous cannula	200 mg once daily after loading Loading: 200 mg three times daily for 4 weeks, then 200 mg daily or less as appropriate (reduce other rate control drugs according to heart rate)	Contraindicated in iodine sensitivity. Serious potential adverse effects (including pulmonary, ophthalmic, hepatic, and thyroid). Consider numerous drug interactions.

Rate control in atrial fibrillation

Isabelle C Van Gelder, Michiel Rienstra, Harry J G M Crijns, Brian Olshansky



Controllo della frequenza cardiaca



Rate Control: Drugs or Ablate&Pace?



ESC

European Society
of Cardiology

European Heart Journal (2021) **42**, 4731–4739
doi:10.1093/eurheartj/ehab569

FASTTRACK CLINICAL RESEARCH

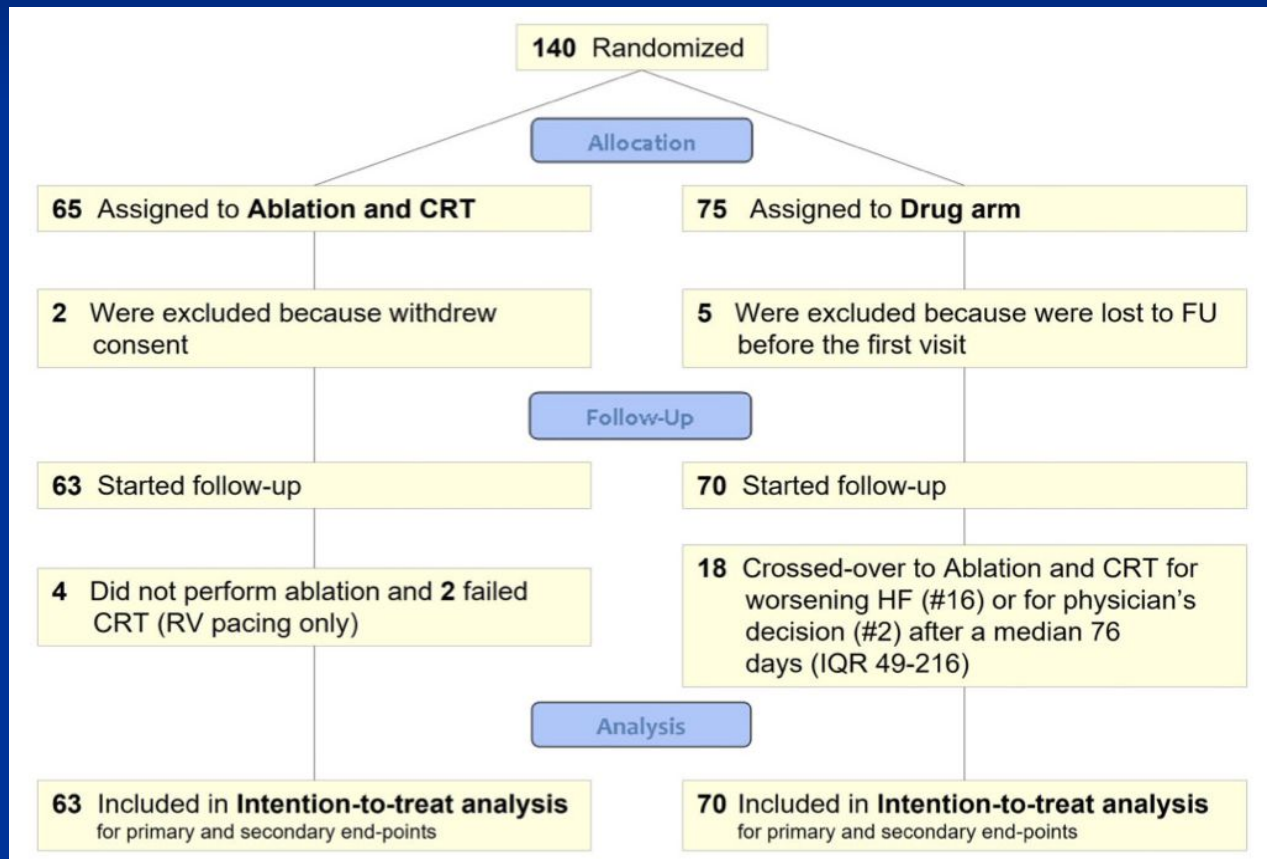
Arrhythmias

AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial

Michele Brignole ^{1,2*}, **Francesco Pentimalli** ³, **Pietro Palmisano** ⁴, **Maurizio Landolina**⁵, **Fabio Quartieri**⁶, **Eraldo Occhetta**⁷, **Leonardo Calò** ⁸, **Giuseppe Mascia** ⁹, **Lluís Mont**¹⁰, **Kevin Vernooy** ¹¹, **Vincent van Dijk**¹², **Cor Allaart**¹³, **Laurent Fauchier** ¹⁴, **Maurizio Gasparini** ¹⁵, **Gianfranco Parati** ^{2,16}, **Davide Soranna**¹⁷, **Michiel Rienstra** ¹⁸, and **Isabelle C. Van Gelder**¹⁸; for the **APAF-CRT Trial Investigators**[†]

AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial

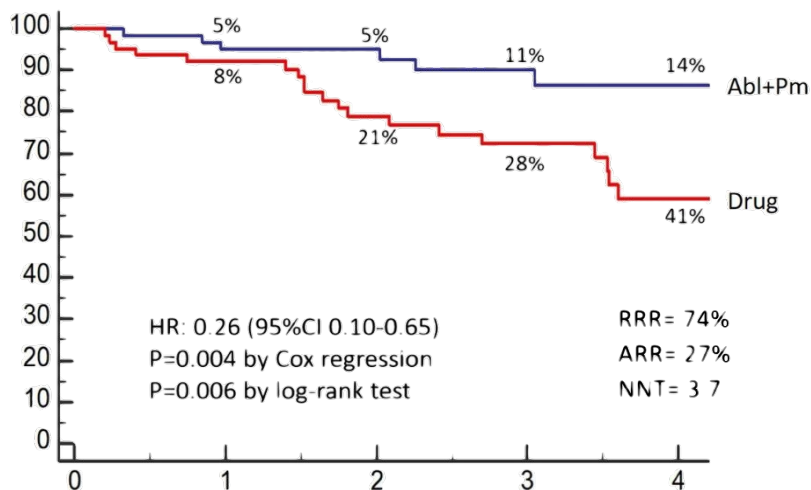
Permanent AF, Narrow QRS & at least 1 HF hospitalization last year



AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial

Permanent AF, Narrow QRS & at least 1 HF hospitalization last year

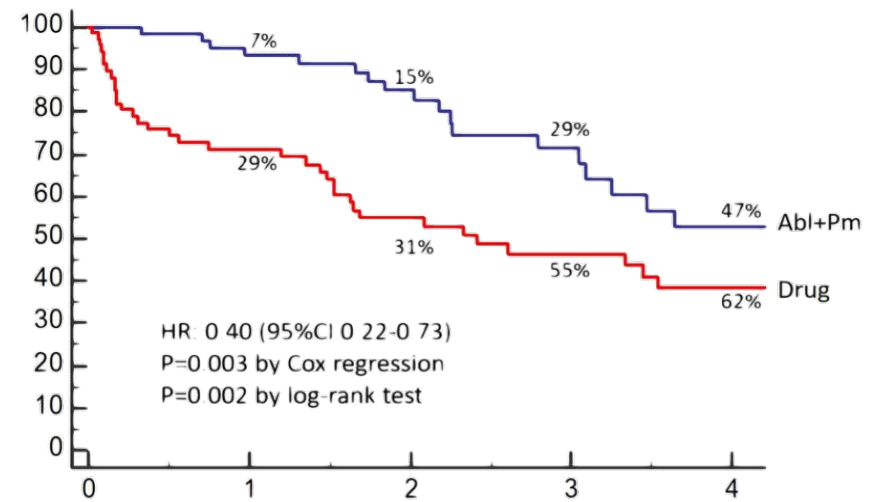
Primary endpoint: death from any cause



Number at risk

Abl+Pm	63	52	41	27	12
Drug	70	56	38	29	9

Secondary endpoint: death from any cause or hospitalization for HF



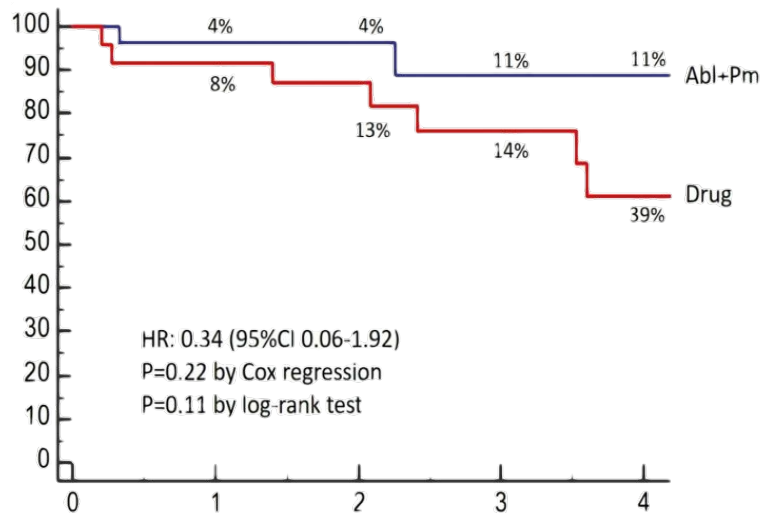
Number at risk

Abl+Pm	63	51	36	21	9
Drug	70	44	27	21	7

AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial

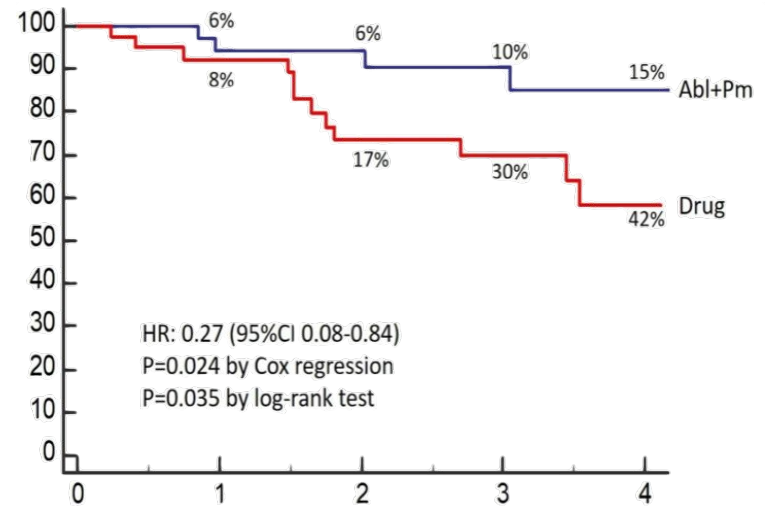
Permanent AF, Narrow QRS & at least 1 HF hospitalization last year

Death from any cause in patients with EF < 35%



Abl+Pm	63	51	36	21	9
Drug	70	44	27	21	7

Death from any cause in patients with EF > 35%



AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: the APAF-CRT mortality trial

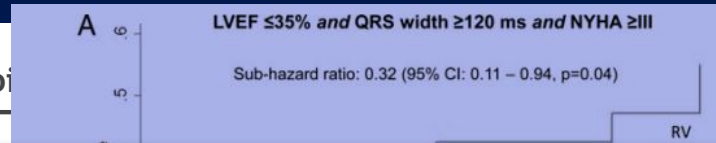
Permanent AF, Narrow QRS & at least 1 HF hospitalization last year

CONCLUSIONS

- ✓ Rate-control by Ablation+CRT was superior to rate-control by pharmacological therapy in reducing mortality in patients with permanent AF and narrow QRS;
- ✓ The benefit was observed in patients with preserved EF with no interaction between patients with EF >35% and those ≤35%;
- ✓ The benefit was due to the combination of the *strict rate control* and *rate regularization achieved* by AV junction ablation together with biventricular pacing, which counteracted the adverse effects of right ventricular pacing;
- ✓ APAF-CRT trial results support Ablation+CRT as a *first line therapy* in patients with permanent AF and narrow QRS who were hospitalized for HF.

CRT vs. RV Pacing

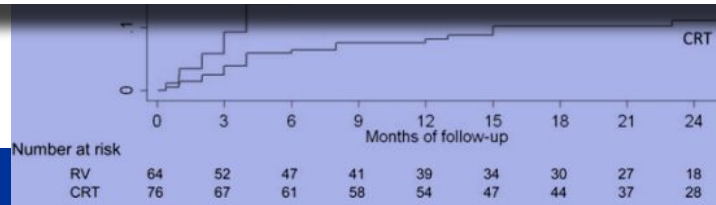
Primary endpoint
worsening HF



CONCLUSIONS

- ✓ CRT pacing is superior to RV pacing after AVJ ablation.
- ✓ Concerning therapy, AF patients are not similar to SR patients;
- ✓ Concerning CRT indication AF patients are not similar to SR patients

CRT

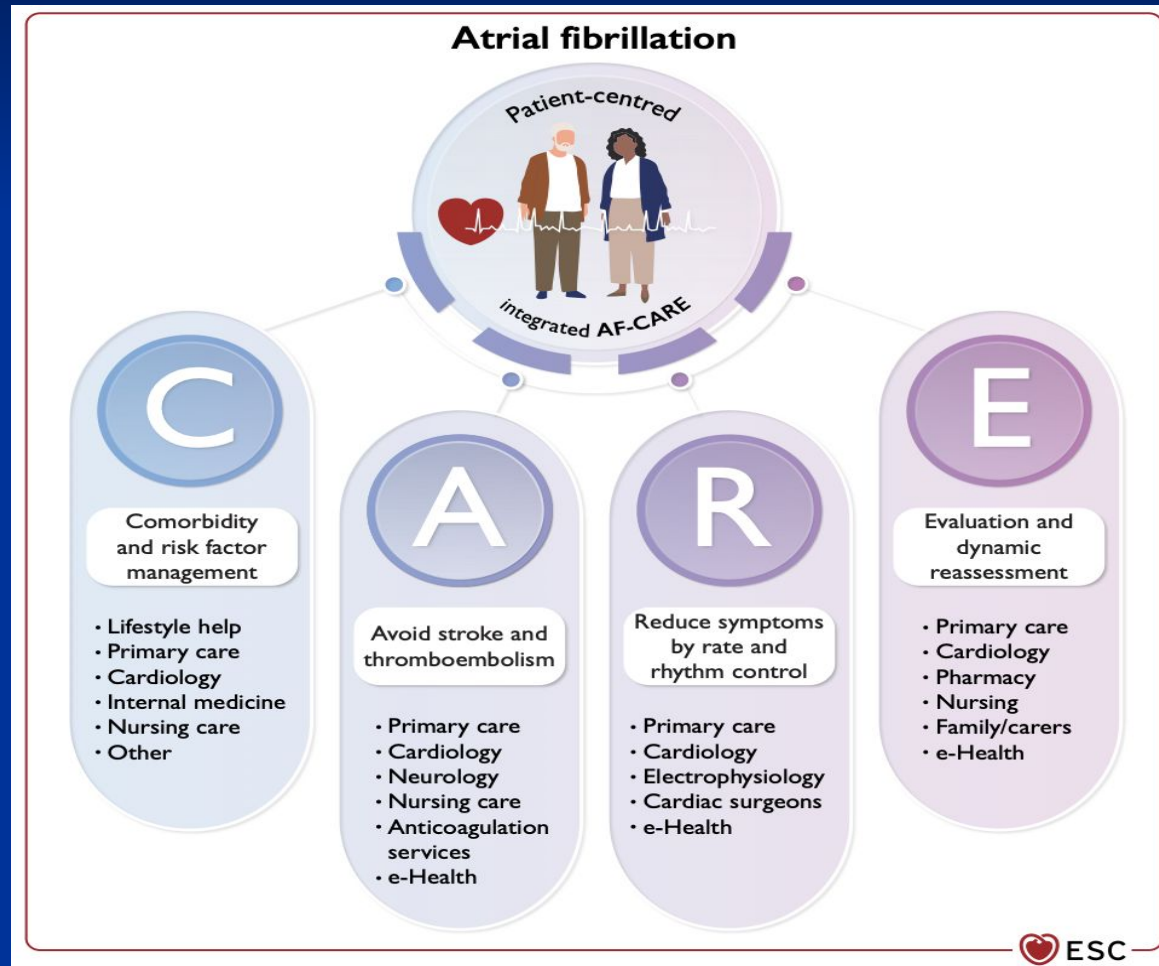


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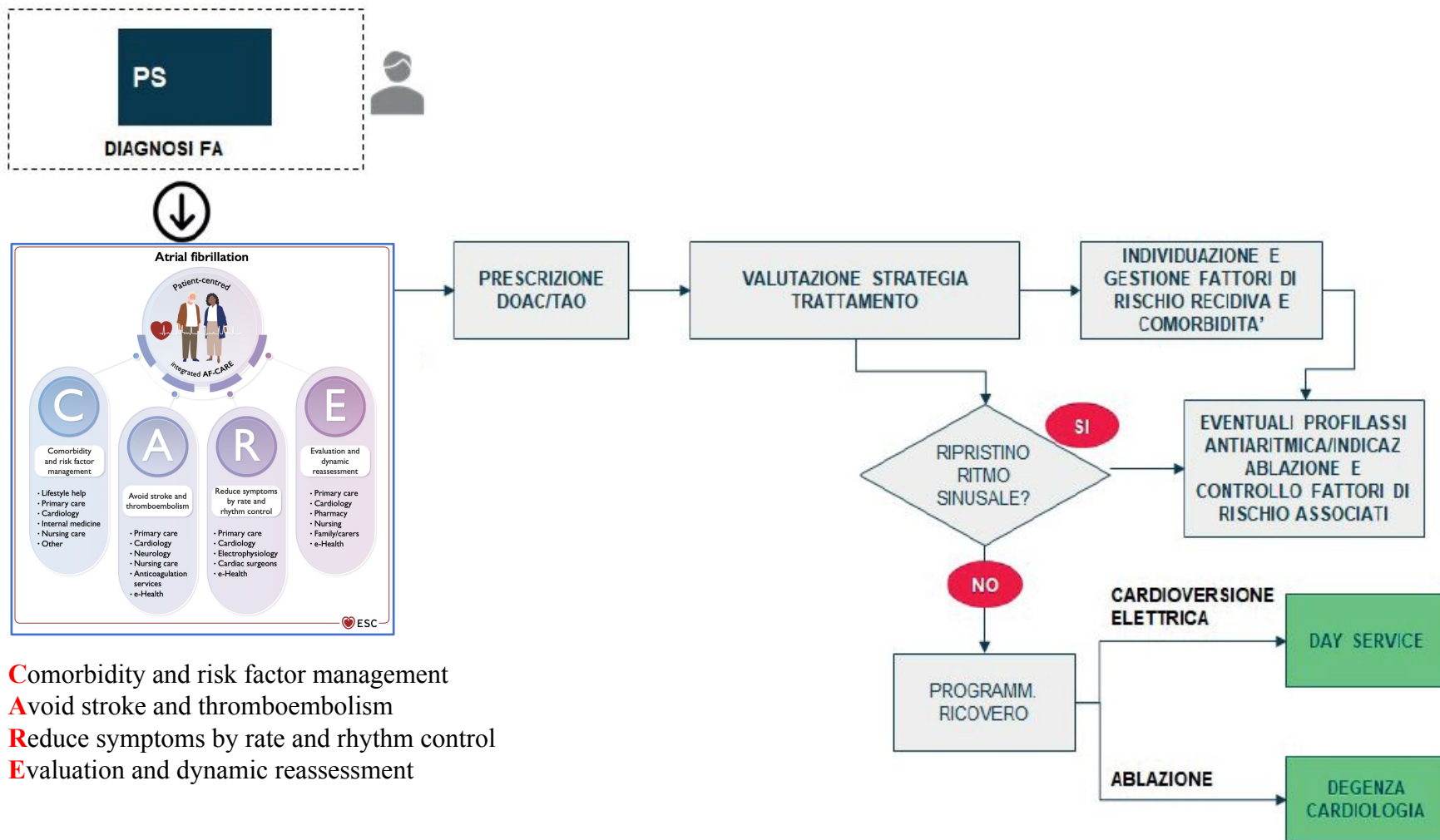
Conclusioni

- La Fibrillazione atriale ha un importante impatto sulla qualità e sull'aspettativa di vita dei pazienti che ne sono affetti
- Il trattamento della FA deve tener conto della complessità del paziente (età, comorbidità e relative terapia...), pertanto deve essere “personalizzata”
- Pensare all'ablazione della Fibrillazione atriale prima possibile

Approccio multidisciplinare alla Fibrillazione Atriale



COMPLETAMENTO DIAGNOSTICO – OUTPATIENT – AMBULATORIO FA/ARITMOLOGICO



C Comorbidity and risk factor management
A Avoid stroke and thromboembolism
R Reduce symptoms by rate and rhythm control
E Evaluation and dynamic reassessment

Figura 5. Sintesi del percorso del paziente con fibrillazione atriale post-dimissione.

DOAC, anticoagulanti orali diretti; FA, fibrillazione atriale; PS, Pronto Soccorso; TAO, terapia anticoagulante orale.