

Fibrillazione atriale e ictus

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XIV CONGRESSO NAZIONALE SITE



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Disclosures of Matteo Bertini e Valeria Di Stefano

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

Perché parliamo di fibrillazione atriale nella talassemia?

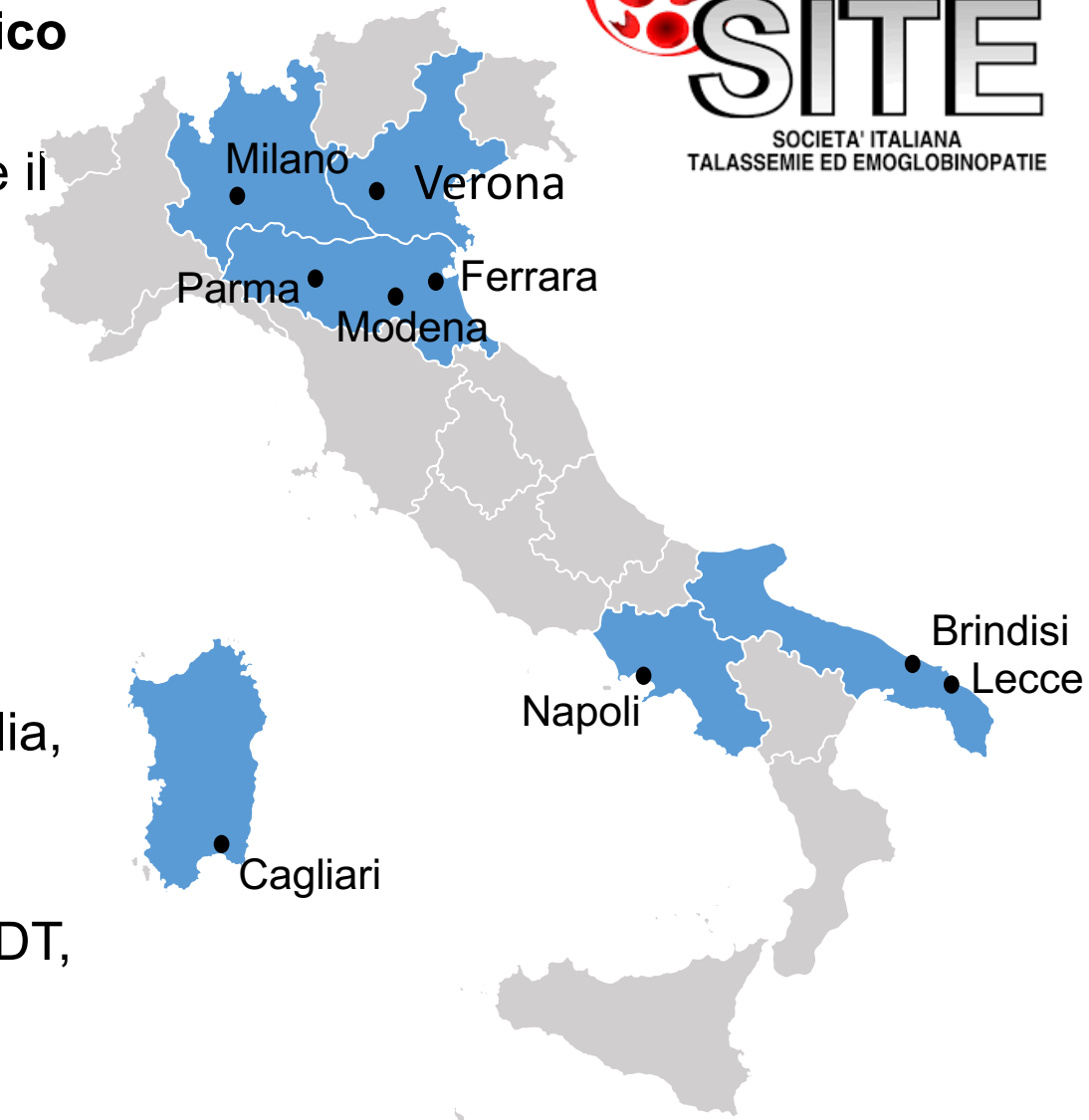
FATHAL: studio osservazionale retrospettivo multicentrico

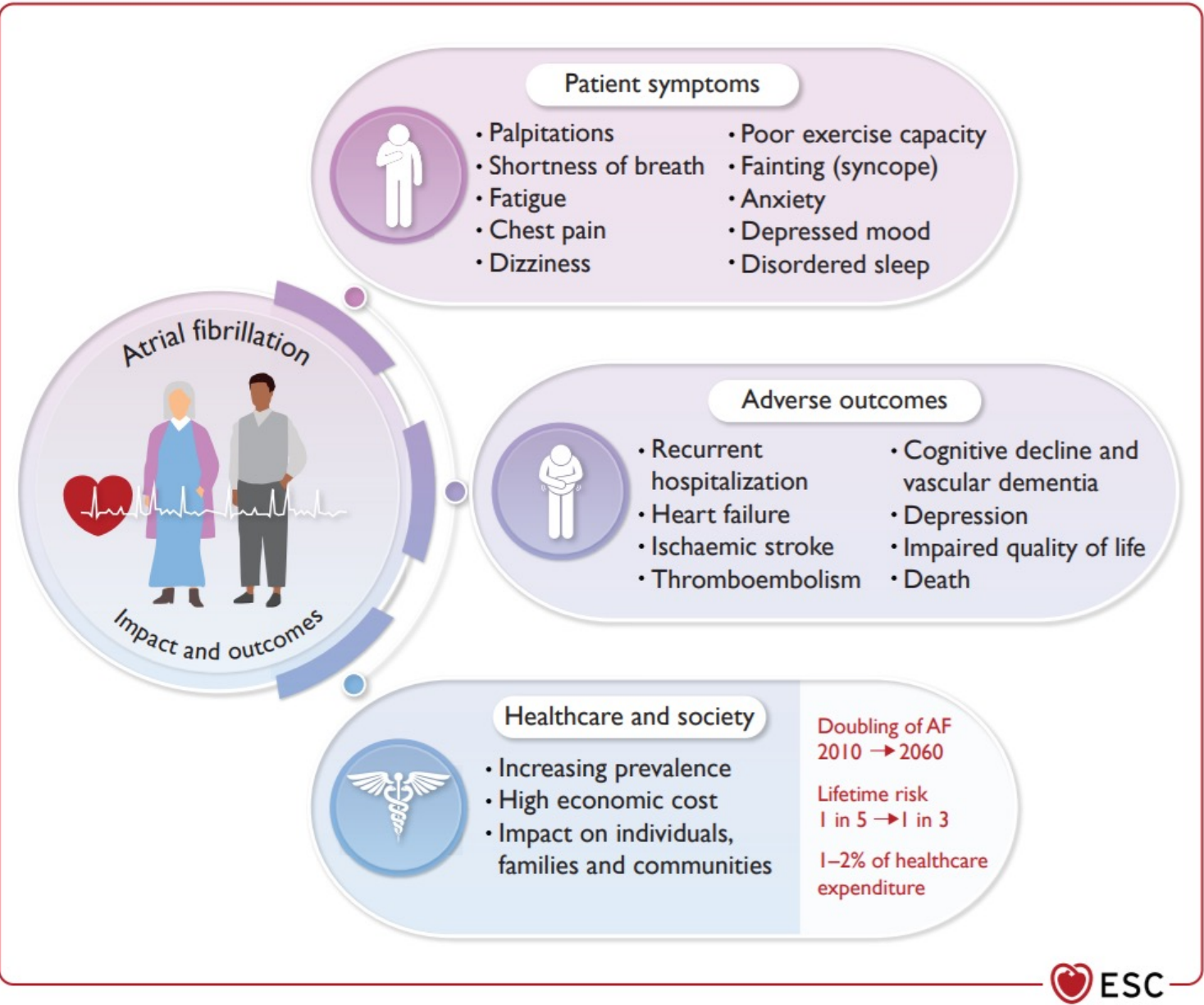
Criteri di inclusione: pazienti seguiti tra il 1° gennaio 2003 e il 31 dicembre 2023 con diagnosi di β -TDT con almeno un episodio di FA

Endpoint primario: prevalenza della FA nei pazienti adulti affetti da β -TDT

Endpoint secondari:

- Gestione clinica della FA nei pazienti affetti da β -TDT in Italia, con particolare attenzione all'**ablazione transcatetere**
- **Valutazione del rischio tromboembolico e degli eventi tromboembolici** correlati alla FA nei pazienti affetti da β -TDT, misurando il rischio tromboembolico sulla base di score di rischio





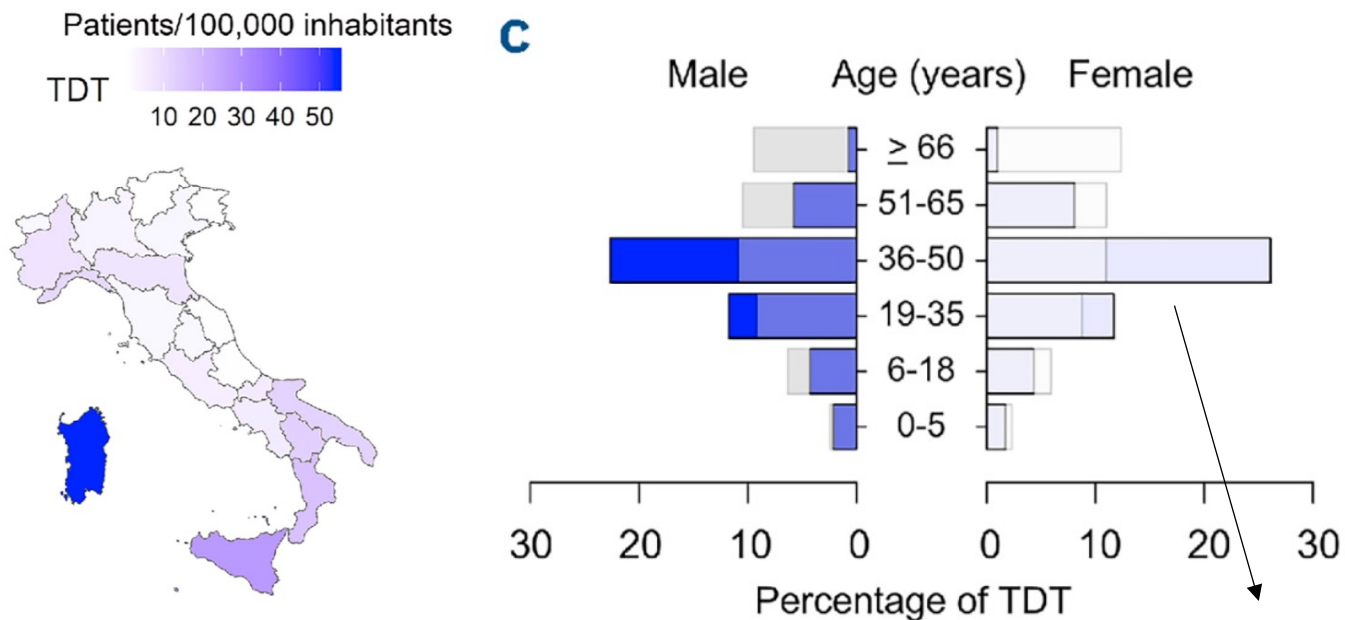
Sovrapposizione dei sintomi con l'anemia

Outcome avversi correlabili alla talassemia

Impatto sul sistema sanitario e pazienti?

Van Gelder IC et al, ESC Guidelines 2024

Dimensioni del problema



5205 TDT

**~50% tra 36 e 50
anni (nel 2019)**

Prevalenza 11.9 % (IC 95% (10.2-13.7))

Studio SITE FATHAL (Di Stefano, under revision)

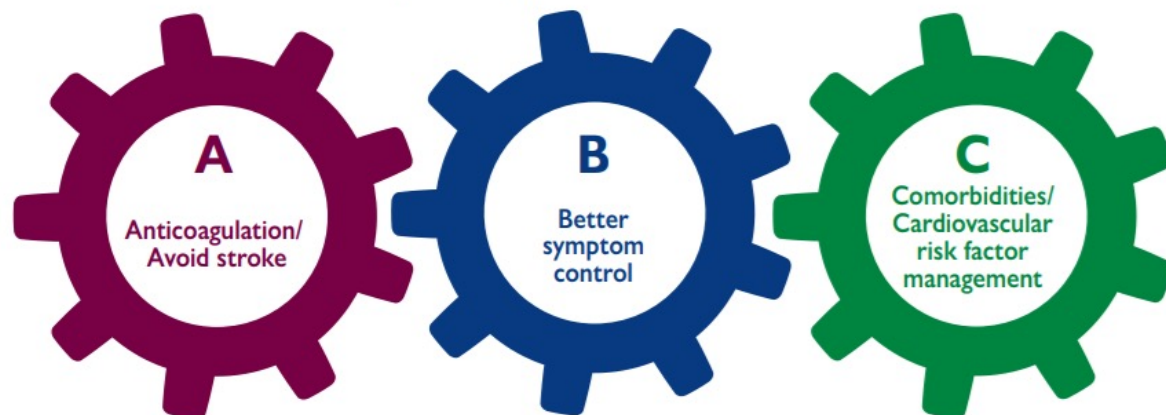
>500 TDT con FA in Italia

di cui

>230 soggetti con meno di 50 anni

~150 tra 51 e 65 anni

Treat AF: The ABC pathway



1. Identify low-risk patients
CHA₂DS₂-VASc 0(m), 1(f)

2. Offer stroke prevention if
CHA₂DS₂-VASc ≥1(m), 2(f)

Assess bleeding risk, address
modifiable bleeding risk factors

3. Choose OAC (NOAC or VKA
with well-managed TTR)

Assess symptoms,
QoL and patient's
preferences

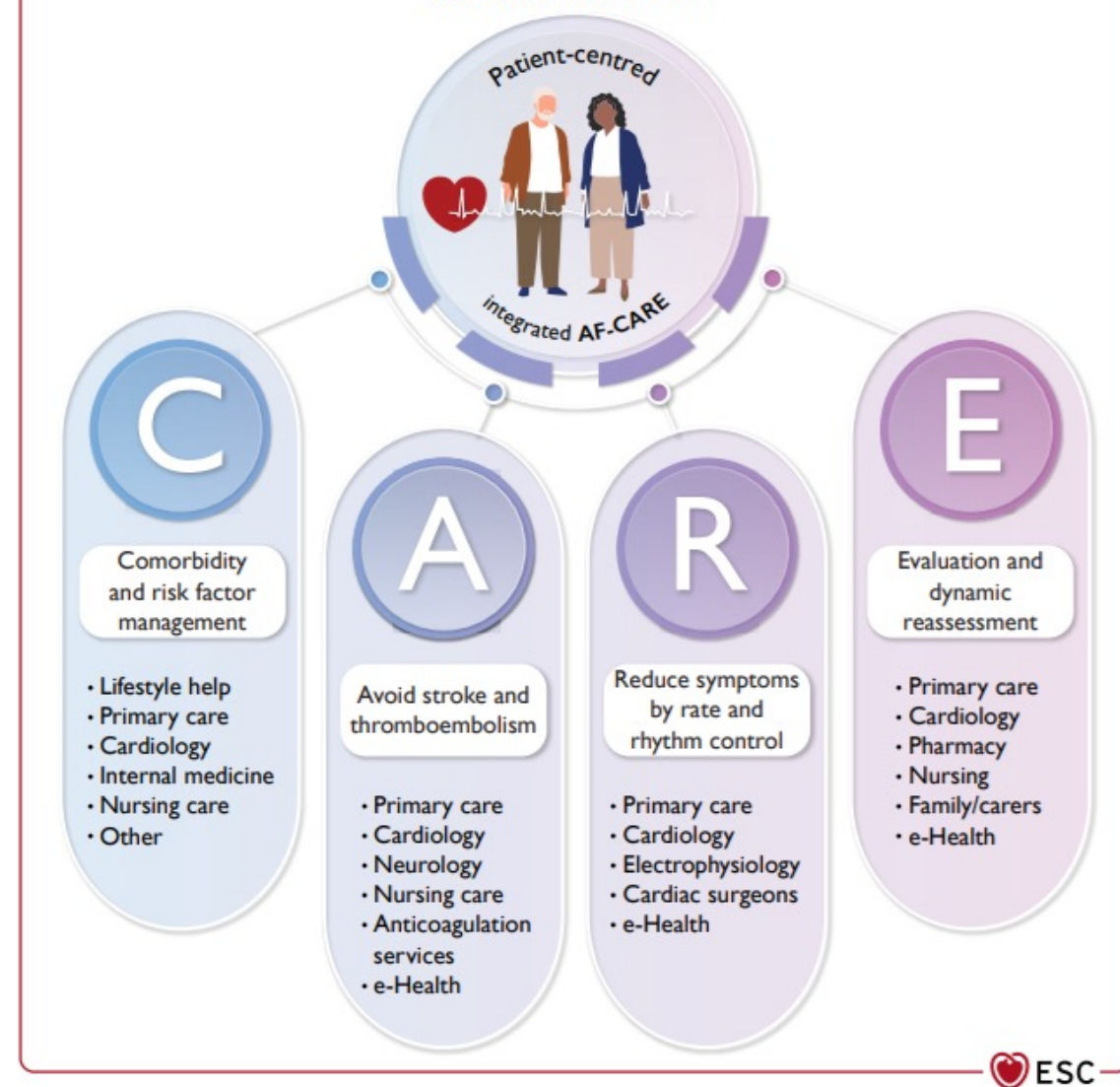
Optimize rate
control

Consider a rhythm
control strategy
(CV, AADs, ablation)

Comorbidities and
cardiovascular risk
factors

Lifestyle changes
(obesity reduction,
regular exercise,
reduction of alcohol use,
etc.)

Atrial fibrillation



Caso clinico - F, 64 anni

Anamnesi patologica remota

- **Talassemia intermedia** β^0/β^+ (cod39/-101) diagnosticata all'età di 13 aa.
Occasional trasfusioni fino a 50 aa (es. per gravidanza) con valori **hb attorno a 8 g/dl**.
Dal 2008 trasfusa ogni 2-3 mesi con hb pre-trasfusionali 8 g/dl;
Dal 2019 intervallo trasfusionale di 5 settimane e hb pre-trasfusionale 8.5 g/dl
- A 13 aa **splenectomia**
- **Masse di eritropoiesi extramidollare** paravertebrali
- All'età di 37 aa ricovero per **pericardite acuta** a verosimile eziologia virale
- **Epatopatia cronica HCV-relata**, HCV eradicato nel 2016
- **Colecistectomia** per calcolosi
- **Ridotta massa ossea, ipercalciuria e ridotta tolleranza glucidica**
- Nel 05/2019 riscontro **di membrane neovascolari** OO per cui eseguite multiple iniezioni intravitreali OD

Caso clinico - F, 64 anni

Terapia domiciliare

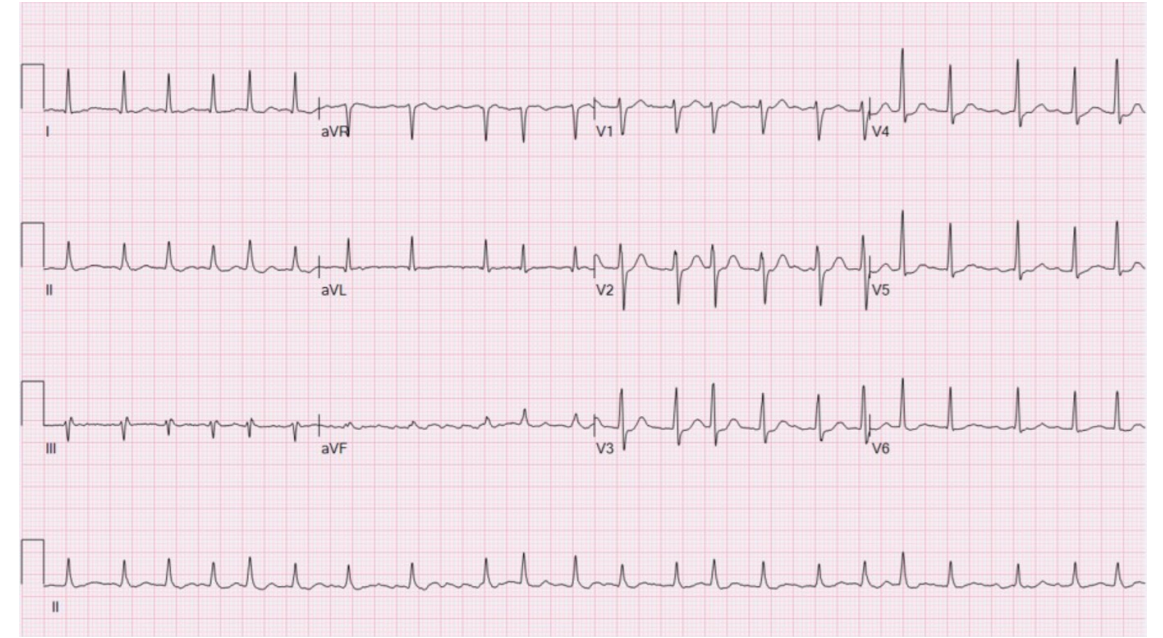
- Acido folico 5 mg 1cp
- Losartan/idroclorotiazide 50/12.5 mg ½ cp die
- Acido ursodesossicolico 450 mg 1 cp die
- Colecalciferolo 50000 UI 1 fl/mese
- Omeprazolo 10 mg 1 cp die
- Acido acetilsalicilico 100 mg 1 cp die
- Calcio carbonato 1 stick die
- Iniezioni intravitreali secondo schema oftalmologico

Caso clinico - F, 64 anni

Anamnesi patologica prossima

Accesso in PS ad aprile 2024 per palpitazioni iniziate da 6 ore

PA 100/60, FC 100-120/min



Fibrillazione atriale

EE: **Hb 8,3 g/dl**, GB 11260/mmc (N 4330/mmc, L 4760/mmc, M 1760/mmc), **PLT 670.000/mmc**. Funzionalità epatica nella norma, creatinina 0,62 mg/dl, non disionie

Sottoposta a CVE con ripristino del RS

Non ulteriori provvedimenti trattandosi di primo episodio

Caso clinico - F, 64 anni

Anamnesi patologica prossima

Dopo 1 mese nuovo accesso in PS per palpitazioni dalla mattina stessa

PA 110/65, FC 110-130/min

Riscontro di FA

Sottoposta a CVE con ripristino del RS

Indicazione a visita aritmologica

Caso clinico - F, 64 anni

Valutazione aritmologica

- Non storia di sovraccarico marziale cardiaco. Ferritina stabilmente intorno a 500 mcg/l
- Anamnesi negativa per problematiche cardiache
- Funzionalità tiroidea (01/2024) nei limiti (TSH Reflex 3,08 mIU/L)
- Ultimo ecocardio prima dell'episodio di FA: Ventricolo sinistro di normali dimensioni e spessori ai limiti superiori della norma, conservata funzione contrattile globale e regionale (FE bp 61%). Disfunzione diastolica di I grado. **Atrio sinistro significativamente dilatato.**



Anticoagulazione sì o no?

Caso clinico - F, 64 anni

Valutazione aritmologica

CHA₂DS₂VASC: 1 (sesso), HAS-BLED: 1 (Cardioaspirin).

Funzione biventricolare nella norma.

Assenza di sovraccarico marziale.

La paziente ha 64 aa e un atrio sinistro marcatamente dilatato

Seguiamo le linee guida ESC?

Initiating oral anticoagulation—Section 6.1		
Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.	I	A
A CHA ₂ DS ₂ -VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation.	I	C
A CHA ₂ DS ₂ -VA score of 1 should be considered an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation.	IIa	C
Oral anticoagulation is recommended in all patients with AF and hypertrophic cardiomyopathy or cardiac amyloidosis, regardless of CHA ₂ DS ₂ -VA score, to prevent ischaemic stroke and thromboembolism.	I	B
Individualized reassessment of thromboembolic risk is recommended at periodic intervals in patients with AF to ensure anticoagulation is started in appropriate patients.	I	B
Direct oral anticoagulant therapy may be considered in patients with asymptomatic device-detected subclinical AF and elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism, excluding patients at high risk of bleeding.	IIb	B

Van Gelder IC et al, ESC Guidelines 2024

Updated definitions for the CHA₂DS₂-VA score

CHA ₂ DS ₂ -VA component		Definition and comments	Points awarded
C	Chronic heart failure	Symptoms and signs of heart failure (irrespective of LVEF, thus including HFpEF, HFmrEF, and HFrEF), or the presence of asymptomatic LVEF ≤40%.	1
H	Hypertension	Resting blood pressure >140/90 mmHg on at least two occasions, or current antihypertensive treatment. The optimal BP target associated with lowest risk of major cardiovascular events is 120–129/70–79 mmHg (or keep as low as reasonably achievable).	1
A	Age 75 years or above	Age is an independent determinant of ischaemic stroke risk. Age-related risk is a continuum, but for reasons of practicality, two points are given for age ≥75 years.	2
D	Diabetes mellitus	Diabetes mellitus (type 1 or type 2), as defined by currently accepted criteria, or treatment with glucose lowering therapy.	1
S	Prior stroke, TIA, or arterial thromboembolism	Previous thromboembolism is associated with highly elevated risk of recurrence and therefore weighted 2 points.	2
V	Vascular disease	Coronary artery disease, including prior myocardial infarction, angina, history of coronary revascularization (surgical or percutaneous), and significant CAD on angiography or cardiac imaging OR Peripheral vascular disease, including: intermittent claudication, previous revascularization for PVD, percutaneous or surgical intervention on the abdominal aorta, and complex aortic plaque on imaging (defined as features of mobility, ulceration, pedunculation, or thickness ≥4 mm).	1
A	Age 65–74 years	1 point is given for age between 65 and 74 years.	1

CHA ₂ DS ₂ -VASc	
Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease	1
Age 65-74	1

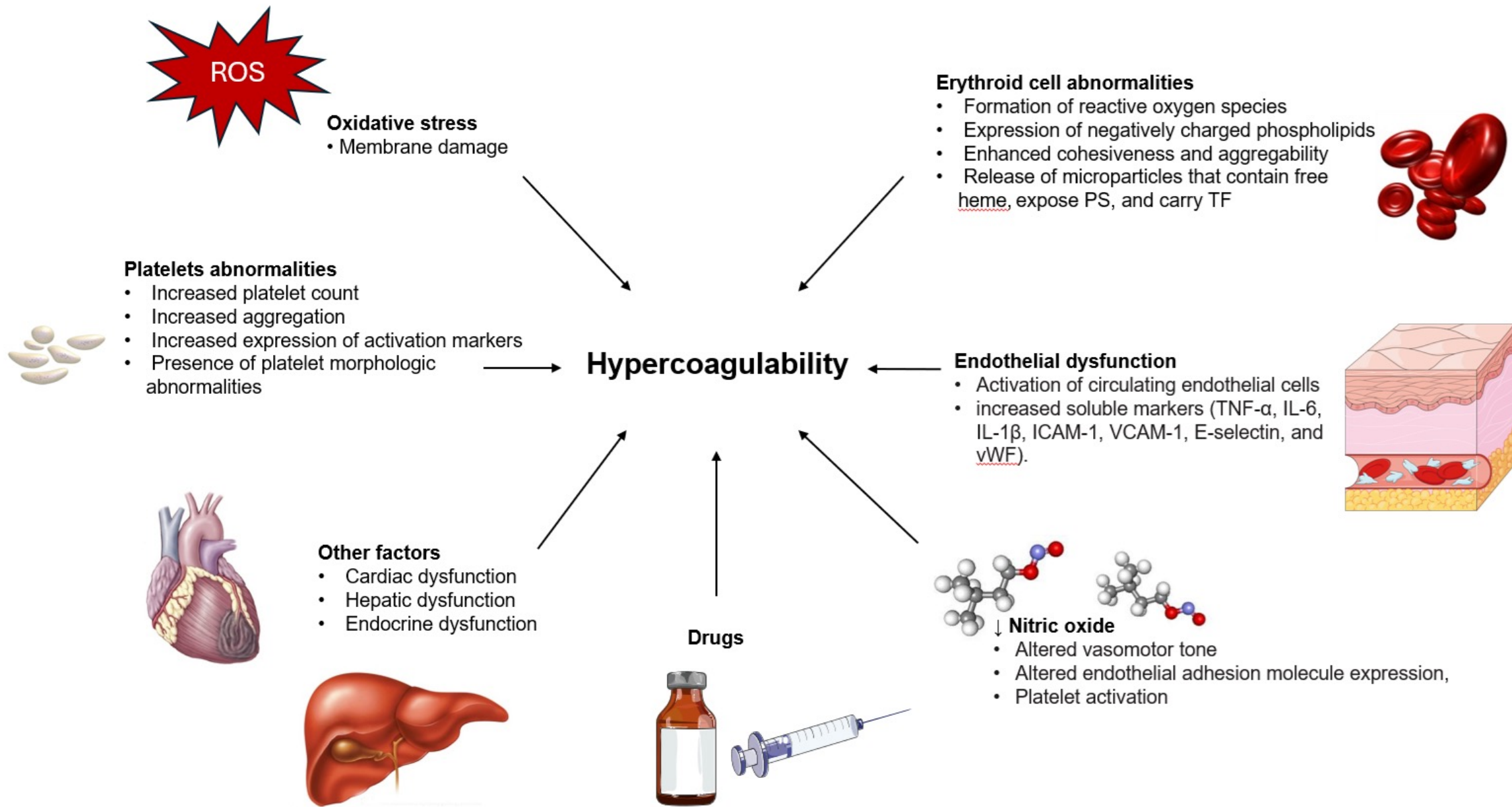
Table 3. C statistic of CHA₂DS₂-VASc for 1-Year Prediction of Ischemic Stroke or TIA Among Patients With Atrial Fibrillation, Optum Clinformatics, 2009–2015

	C Statistic	95% CI
CHA ₂ DS ₂ -VASc score	0.679	0.670–0.686
CHA ₂ DS ₂ -VASc score+race/ethnicity	0.679	0.671–0.688
CHA ₂ DS ₂ -VASc score in models stratified by race/ethnicity		
Whites	0.678	0.669–0.688
Blacks	0.682	0.658–0.706
Hispanics	0.649	0.620–0.679

TIA indicates transient ischemic attack.

Questi parametri sono appropriati per predire il rischio di stroke nei nostri pazienti?

Chen LY et al, Stroke, 2019



Cappellini, MD, Taher A, Motta I, in press

TABLE 1 Thalassemia-related thrombosis risk scoring system (TRT-RSS)

Risk factor at time of assessment	Score
Age >35	2.5
Hemoglobin level ^{a,b} <9 g/dL	2.5
Serum ferritin level ^b ≥1000 µg/L	2.0
Not regularly transfused ^c	3.5
Splenectomized	6.5
TRT-RSS Total Score minimum	0.0
TRT-RSS Total Score maximum	17.0
TRT-RSS risk categories	
Low risk	<9.5
Intermediate risk	9.5-13.5
High risk	>13.5

^aPre-transfusion hemoglobin level in transfused patients.

^bAverage over last 3 months.

^cLess than one transfusion/6 weeks during the last 6 months.

> [Am J Hematol](#). 2019 Aug;94(8):E207-E209. doi: 10.1002/ajh.25502. Epub 2019 May 13.

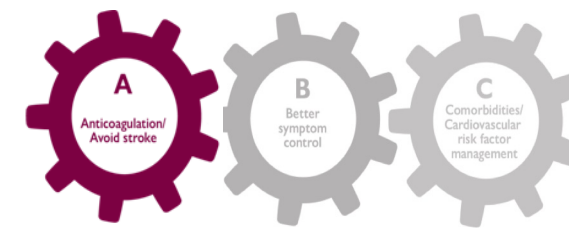
Development of a thalassemia-related thrombosis risk scoring system

Ali T Taher ¹, Maria Domenica Cappellini ², Khaled M Musallam ³

Affiliations + expand

PMID: 31056770 DOI: [10.1002/ajh.25502](#)

Anticoagulation – Avoid stroke



Pt ID	Event	Type	Time from first AF episode (years)	Symptoms at the first AF episode	CHA ₂ DS ₂ -VASc score at the first AF episode (risk)	Ongoing anticoagulant (type)	Ongoing antiplatelet
#1	1	Stroke	-25.5	N	Intermediate	N	N
#2	2	TIA	- 21.9	N	High	NA	NA
#3*	3	Stroke	-13.6	Y	High	N	N
#4*	4a	Stroke	-9.0	Y	High	N	N
	4b	Stroke	-4.0	Y		N	N
	4c	TIA	NA	Y		NA	NA
#5*◇	5a	TIA	- 7.4	N	High	N	N

#12	12	Stroke	9.5	Y	High	N	N
#13	13	TIA	9.8	Y	Low	N	N
#14	14a	Stroke	13.1	Y	Intermediate	NA	NA
	14b	Stroke	16.4	Y		Apixaban	Y
#15	15a	TIA	15	Y	Intermediate	N	Y
	15b	TIA	21	Y		Acenocumarol	Y
	15c	TIA	22	Y		Acenocumarol	Y

Il CHA₂DS₂-VASc non predice il rischio di stroke nei pz β-TDT

Studio SITE FATHAL (Di Stefano, under revision)

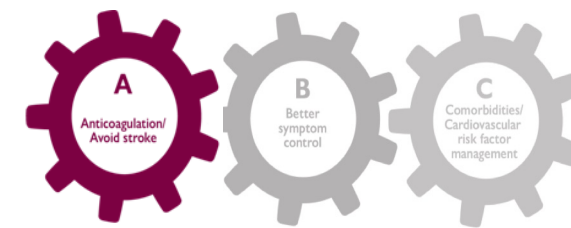
#9	9	Stroke	6.5	Y	Low	N	N
#10	10	Stroke	7.0	N	Intermediate	Warfarin	N
#11	11a	Stroke	9.0	Y	Low	N	Y
	11b	Stroke	14.6	Y		Apixaban	N

#16	16	Stroke	21.7	Y	High	Rivaroxaban	N
#17	17	TIA	NA	Y	High	N	N

Arterial thromboembolic events. * dead; ◇ not splenectomized.

Di Stefano V, under revision

Anticoagulation – Avoid stroke



Pt ID	Event	Type	Time from first AF episode (years)	Symptoms at the first AF episode	CHA ₂ DS ₂ -VASc score at the first AF episode (risk)	Ongoing anticoagulant (type)	Ongoing antiplatelet
#1	1	Stroke	-25.5	N	Intermediate	N	N
#2	2	TIA	- 21.9	N	High	NA	NA
#3*	3	Stroke	-13.6	Y	High	N	N
#4*	4a	Stroke	-9.0	Y	High	N	N
	4b	Stroke	-4.0	Y		N	N

#12	12	Stroke	9.5	Y	High	N	N
#13	13	TIA	9.8	Y	Low	N	N
#14	14a	Stroke	13.1	Y	Intermediate	NA	NA
	14b	Stroke	16.4	Y		Apixaban	Y
#15	15a	TIA	15	Y	Intermediate	N	Y

9/27 (33%) eventi in 5/17 (30%) pz sono avvenuti in corso di terapia anticoagulante

Studio SITE FATHAL (Di Stefano, under revision)

#6	6	Stroke	-0.45	NA	High	N	N
#7	7	Stroke	2.0	NA	High	N	N
#8◇	8	TIA	4.1	Y	High	N	N
#9	9	Stroke	6.5	Y	Low	N	N
#10	10	Stroke	7.0	N	Intermediate	Warfarin	N
#11	11a	Stroke	9.0	Y	Low	N	Y
	11b	Stroke	14.6	Y		Apixaban	N

	15e	Stroke	24.6	Y		Acenocumarol	Y
	15f	Stroke	25.1	Y		Acenocumarol	Y
#16	16	Stroke	21.7	Y	High	Rivaroxaban	N
#17	17	TIA	NA	Y	High	N	N

Arterial thromboembolic events. * dead; ◇ not splenectomized.

Di Stefano V, under revision



**E' meglio stare in ritmo sinusale o
controllare la FC in FA/flutter?**

Antiaritmico o ablazione transcatetere?

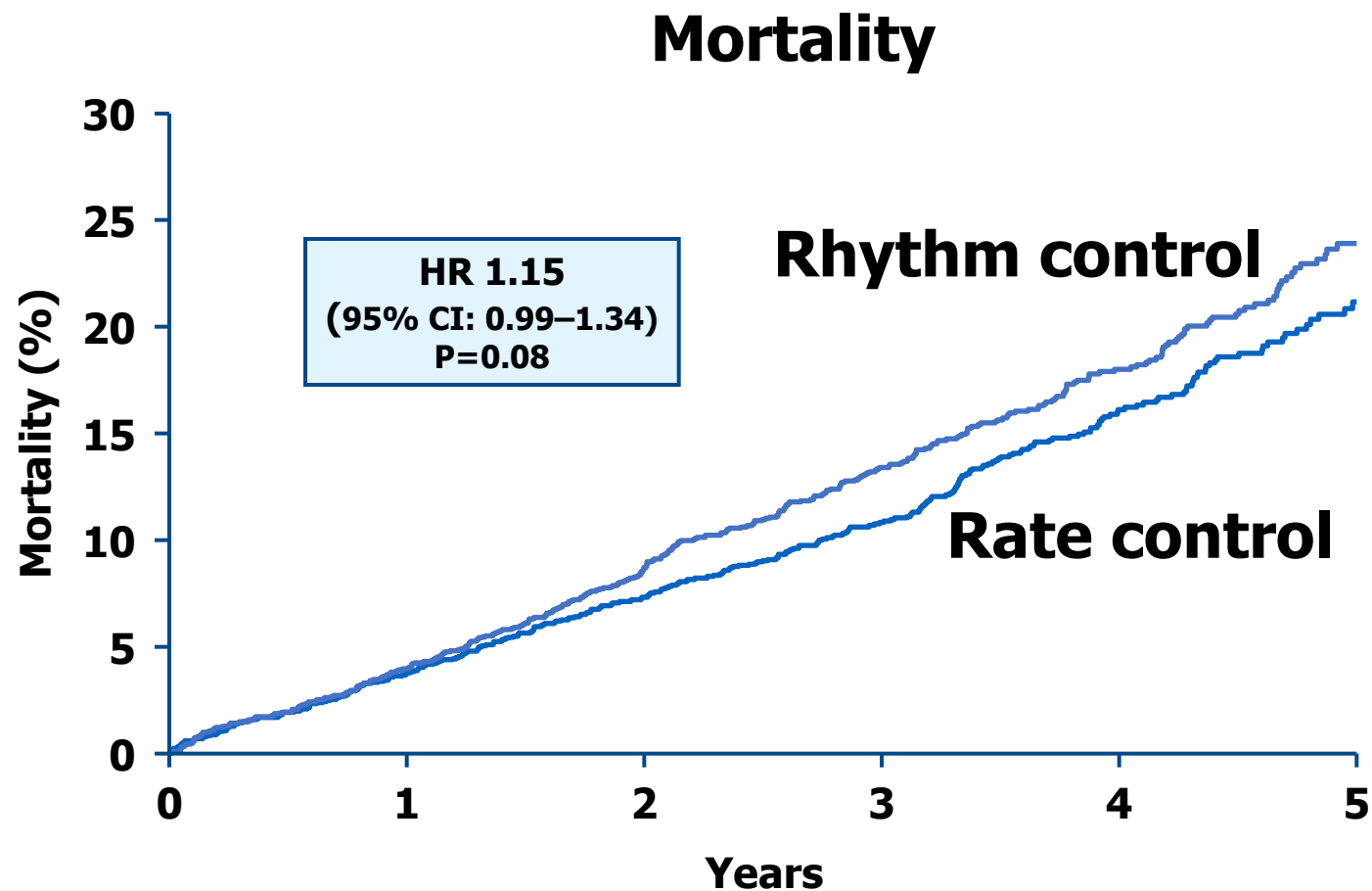


Controllo del ritmo: utilizzare strategie di controllo del ritmo (farmaci, ablazione) oltre a farmaci per controllare la frequenza cardiaca (es. beta bloccanti)

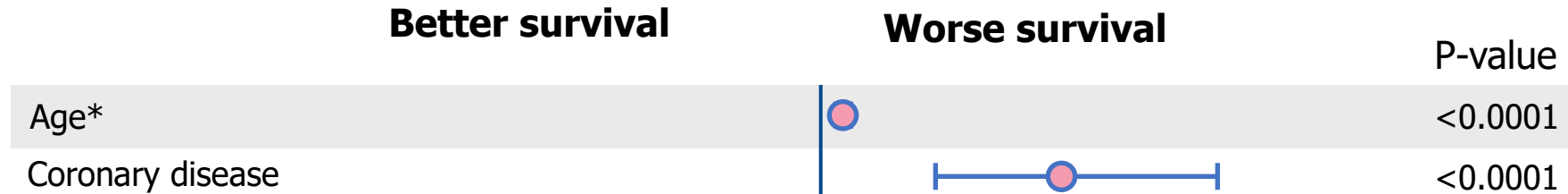
Controllo della frequenza: solo farmaci per controllare la frequenza cardiaca (es. beta bloccanti)

Rate vs Rhythm control: what is the best option?

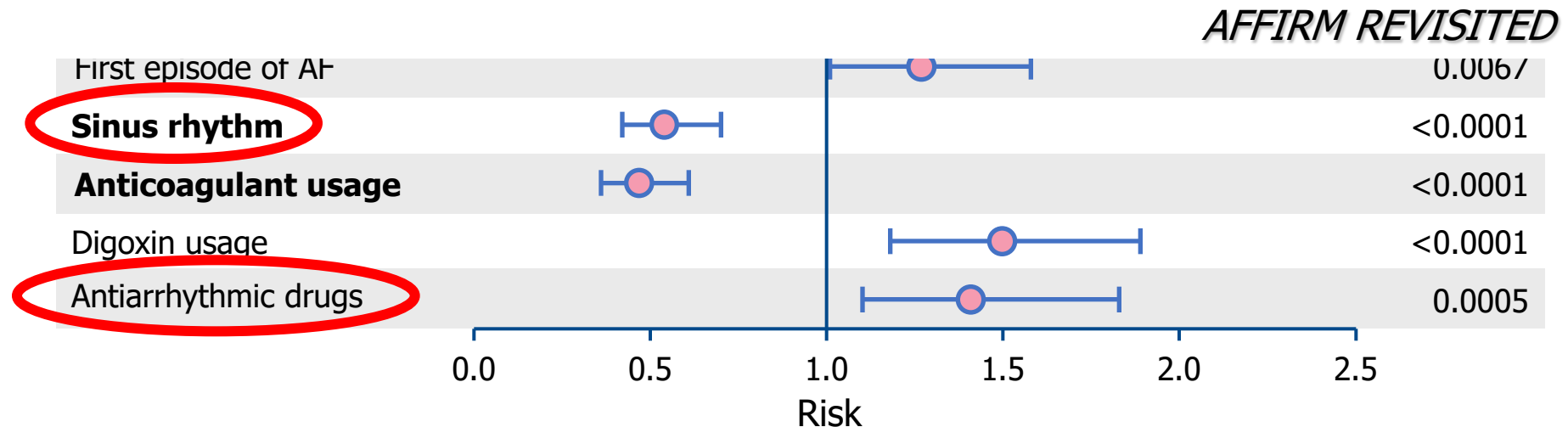
AFFIRM confirms results from RACE



AFFIRM: survival in AF pts



Subgroups analysis of AFFIRM suggest that being in sinus rhythm is better for survival

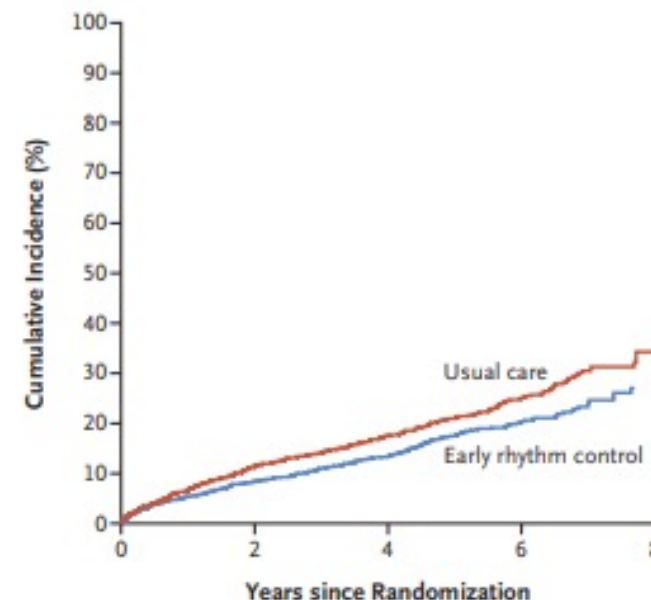
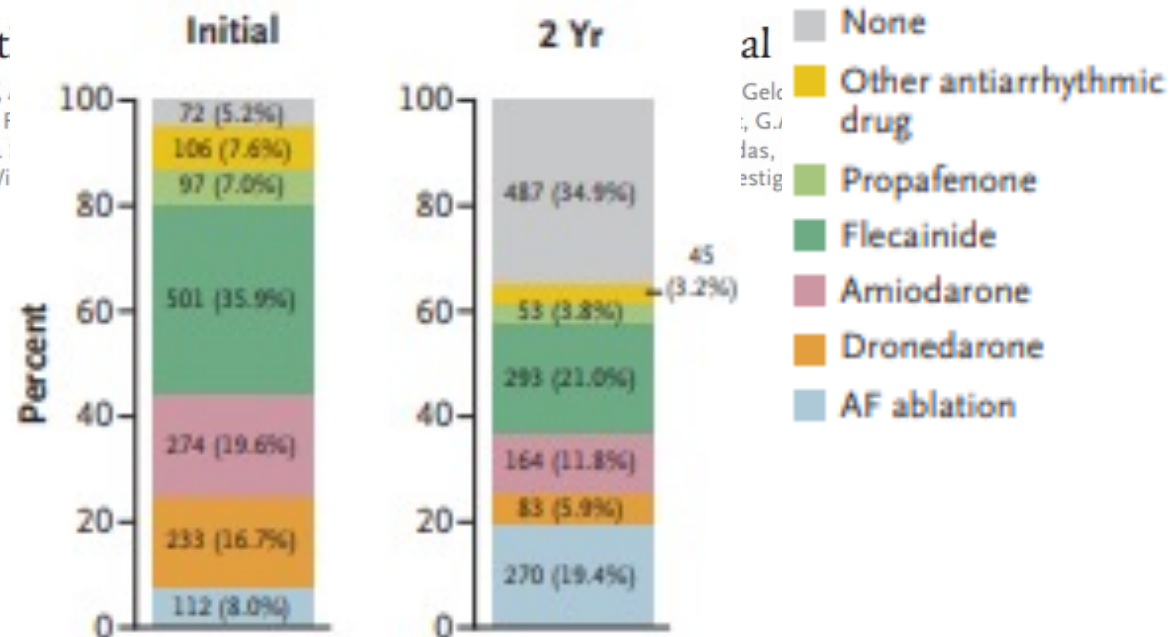


Controllo del ritmo



Early Rhythm Control

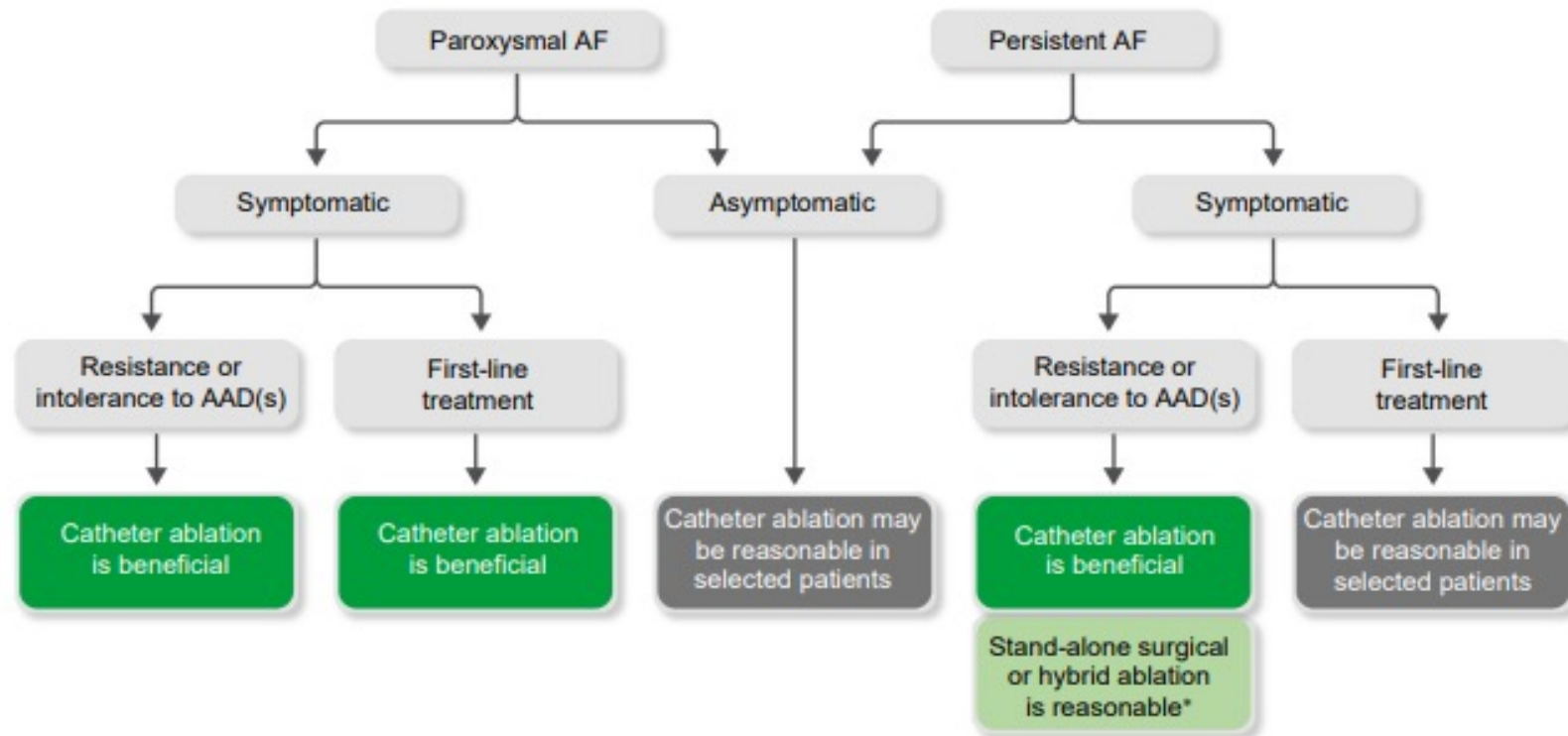
P. Kirchhof,
L.M. Haegeli,
N. Schoen, U.
S. Wi



No. at Risk					
Usual care	1394	1169	888	405	34
Early rhythm control	1395	1193	913	404	26

Controllo del ritmo

**2024 European Heart Rhythm Association/
Heart Rhythm Society/Asia Pacific Heart
Rhythm Society/Latin American Heart Rhythm
Society expert consensus statement on
catheter and surgical ablation of atrial
fibrillation**



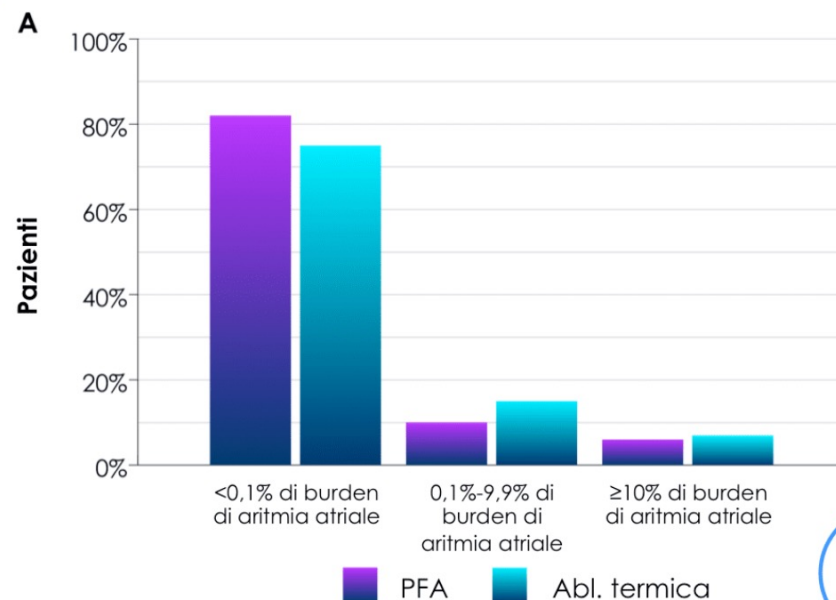


Cos'è il burden di FA?

Il tempo che il paziente passa in FA



I pazienti con burden di aritmia atriale $<0,1\%$ sono statisticamente più numerosi nel braccio PFA¹⁰



Pazienti PFA con burden di aritmia atriale $<0,1\%$

82%

Pazienti abl. termica con burden di aritmia atriale $<0,1\%$

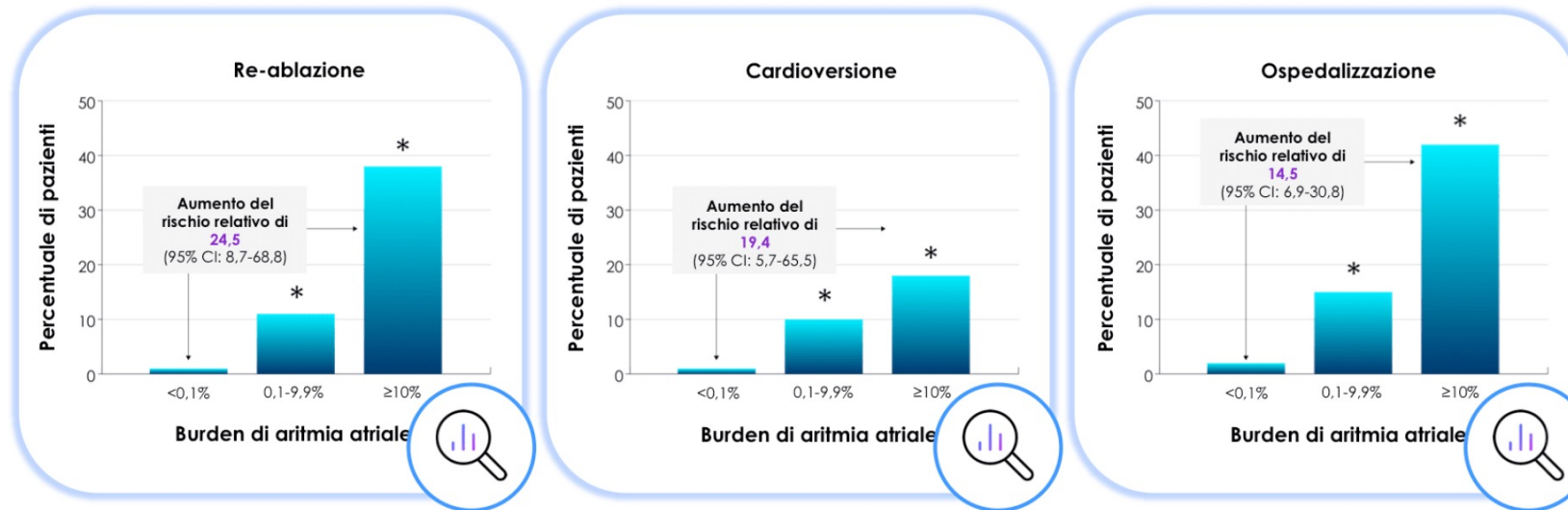
75%

I pazienti con burden di aritmia atriale $<0,1\%$ sono statisticamente più numerosi nel braccio PFA rispetto al braccio di abl. Termica

EP-1962501-AA

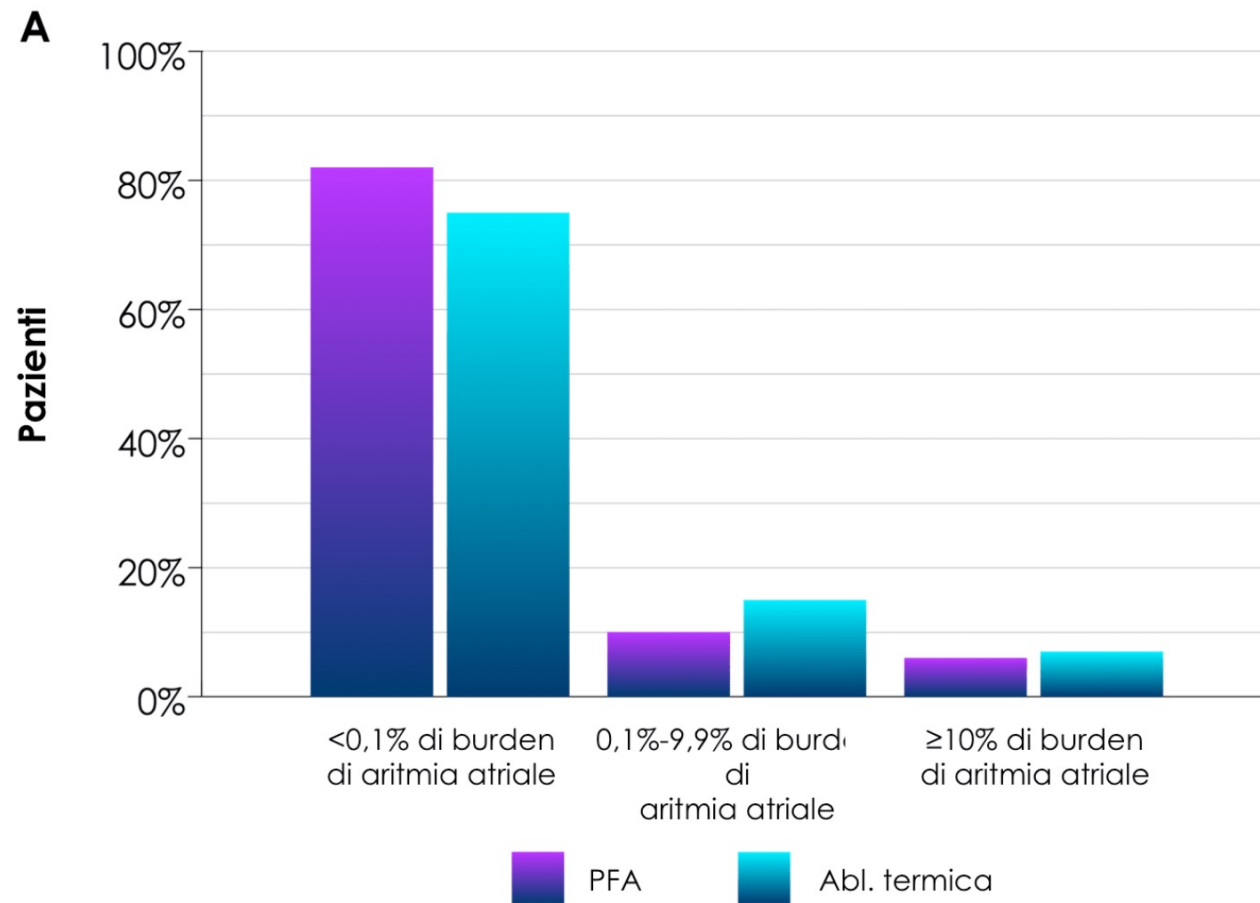


Il burden di aritmia atriale è un parametro clinicamente rilevante: sottostudio ADVENT¹⁰



I pazienti con burden di aritmia atriale <0,1% presentano meno eventi clinici

EP-1962501-AA



EP-1962501-AA



Quale è lo scopo della ablazione?

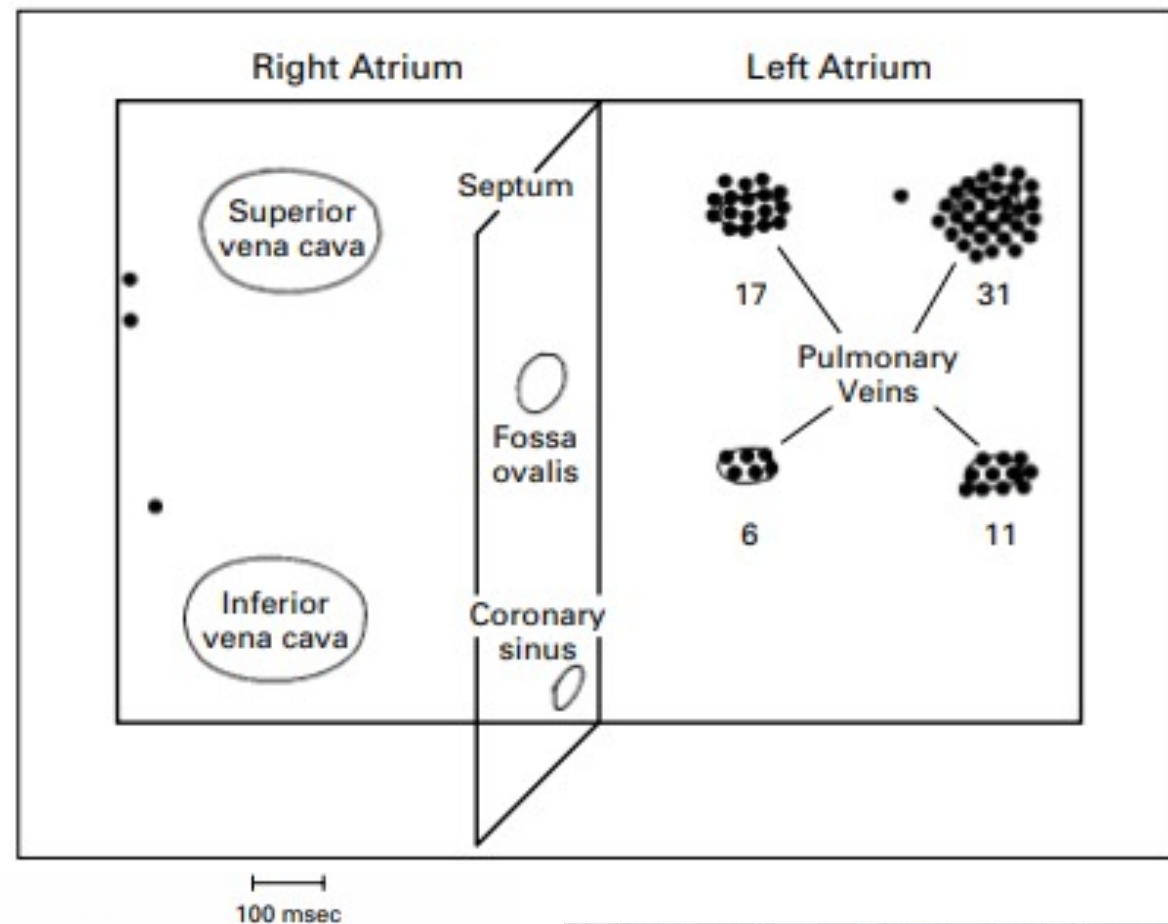
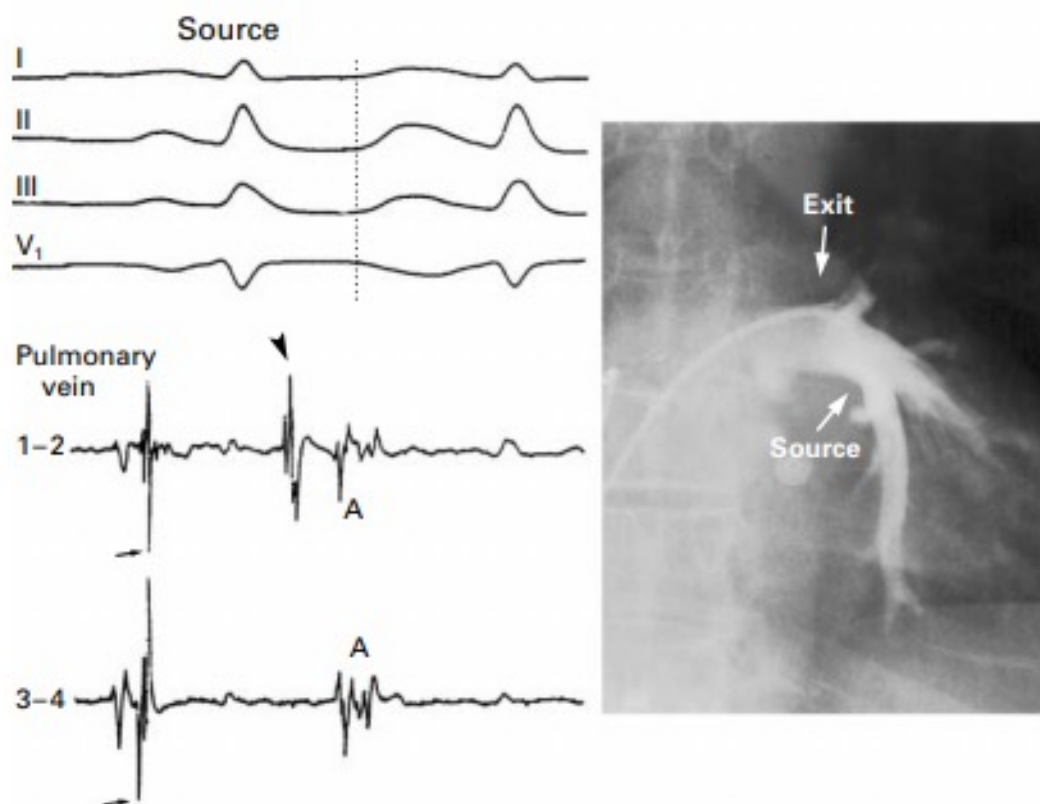
- **Antiaritmico più potente che abbiamo**
- **Riduce il burden di FA (non contano le singole recidive)**
- **Migliora i sintomi**

Ablazione

SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS

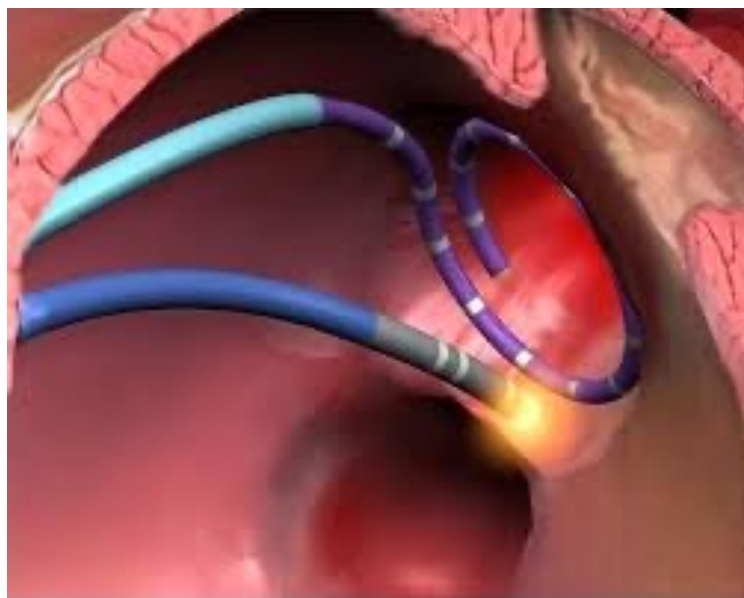
MICHEL HAÏSSAGUERRE, M.D., PIERRE JAÏS, M.D., DIPEN C. SHAH, M.D., ATSUSHI TAKAHASHI, M.D., MÊLÈZE HOCINI, M.D.,
GILLES QUINIOU, M.D., STÉPHANE GARRIGUE, M.D., ALAIN LE MOURoux, M.D., PHILIPPE LE MÉTAYER, M.D.,
AND JACQUES CLÉMENTY, M.D.

The New England Journal of Medicine

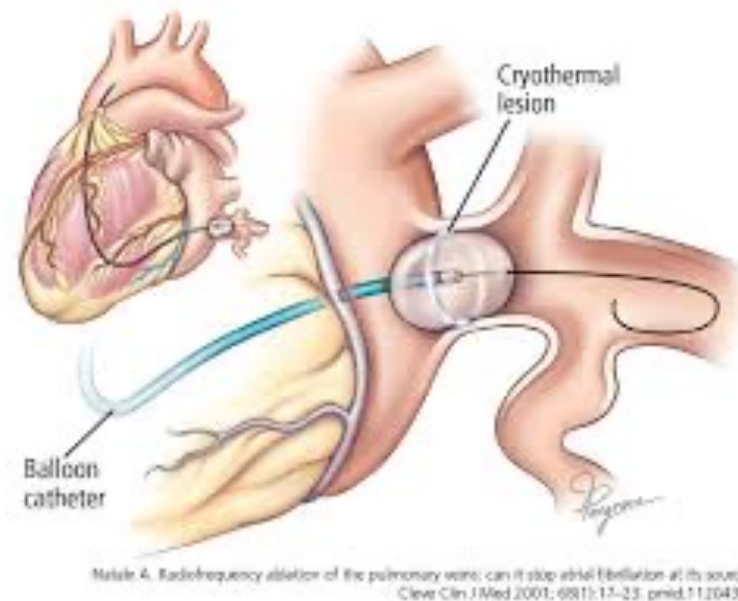


Ablazione

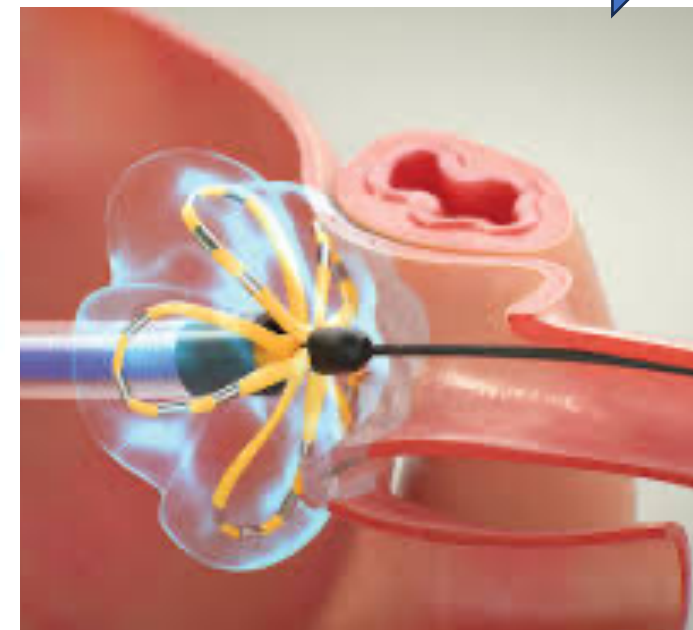
Che tipi di energia si possono utilizzare per isolare le vene polmonari?



Radiofrequenza
(necrosi coagulativa)



Crioablazione
(necrosi coagulativa)



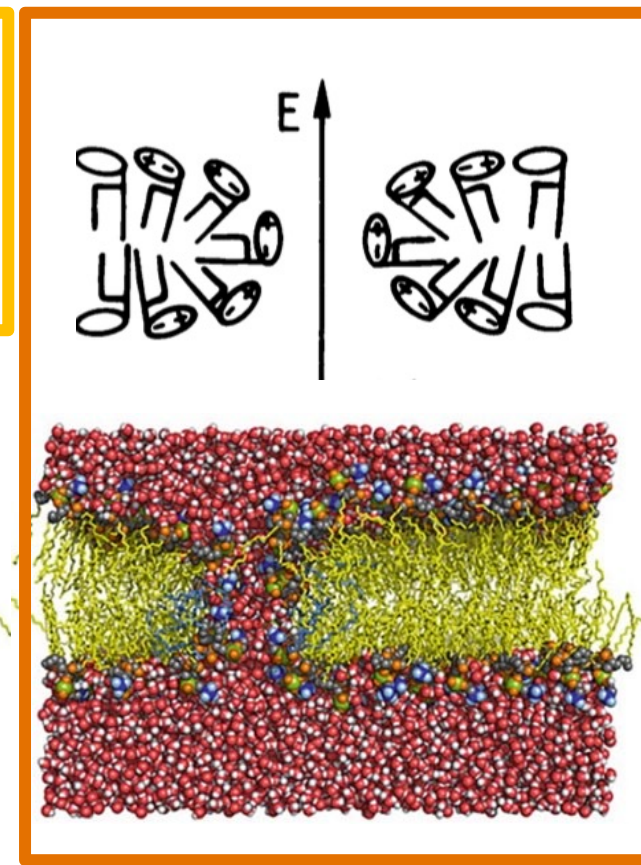
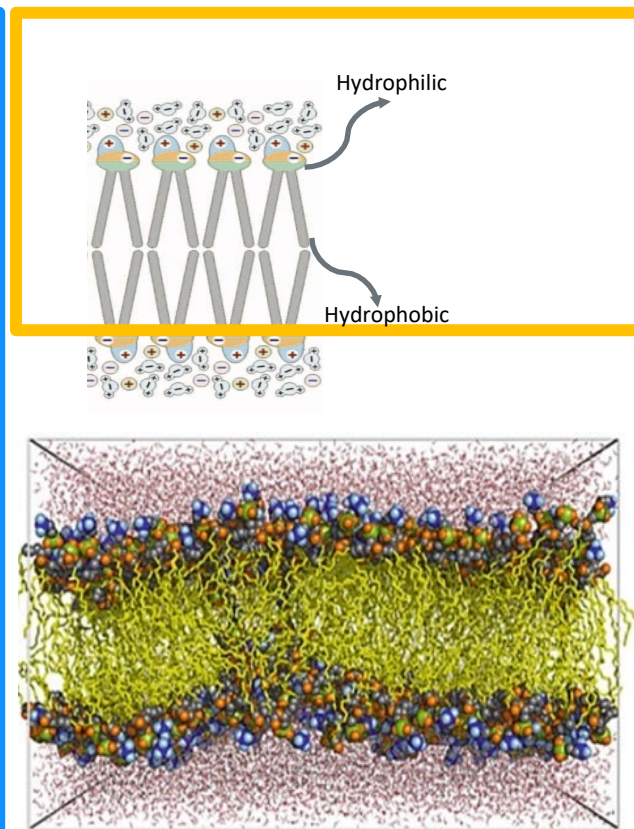
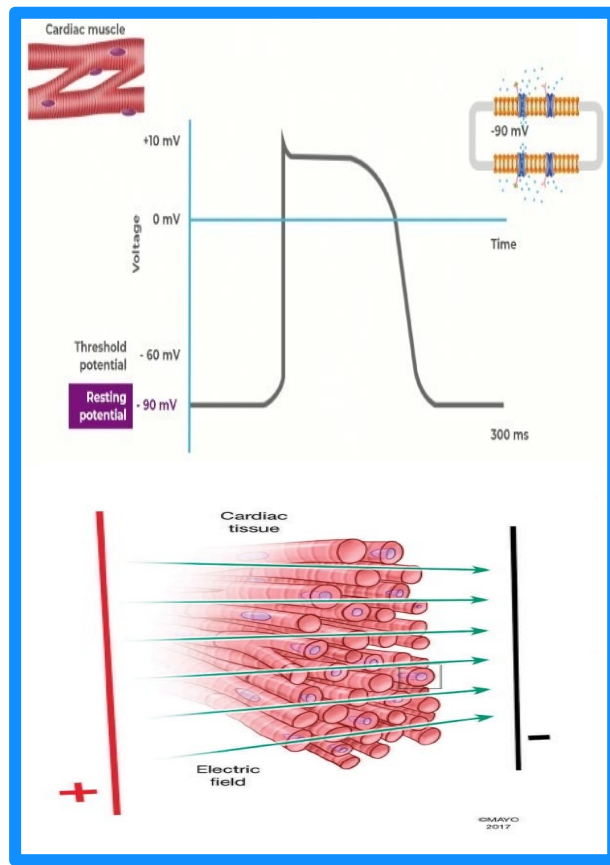
Elettroporazione
(apoptosi)



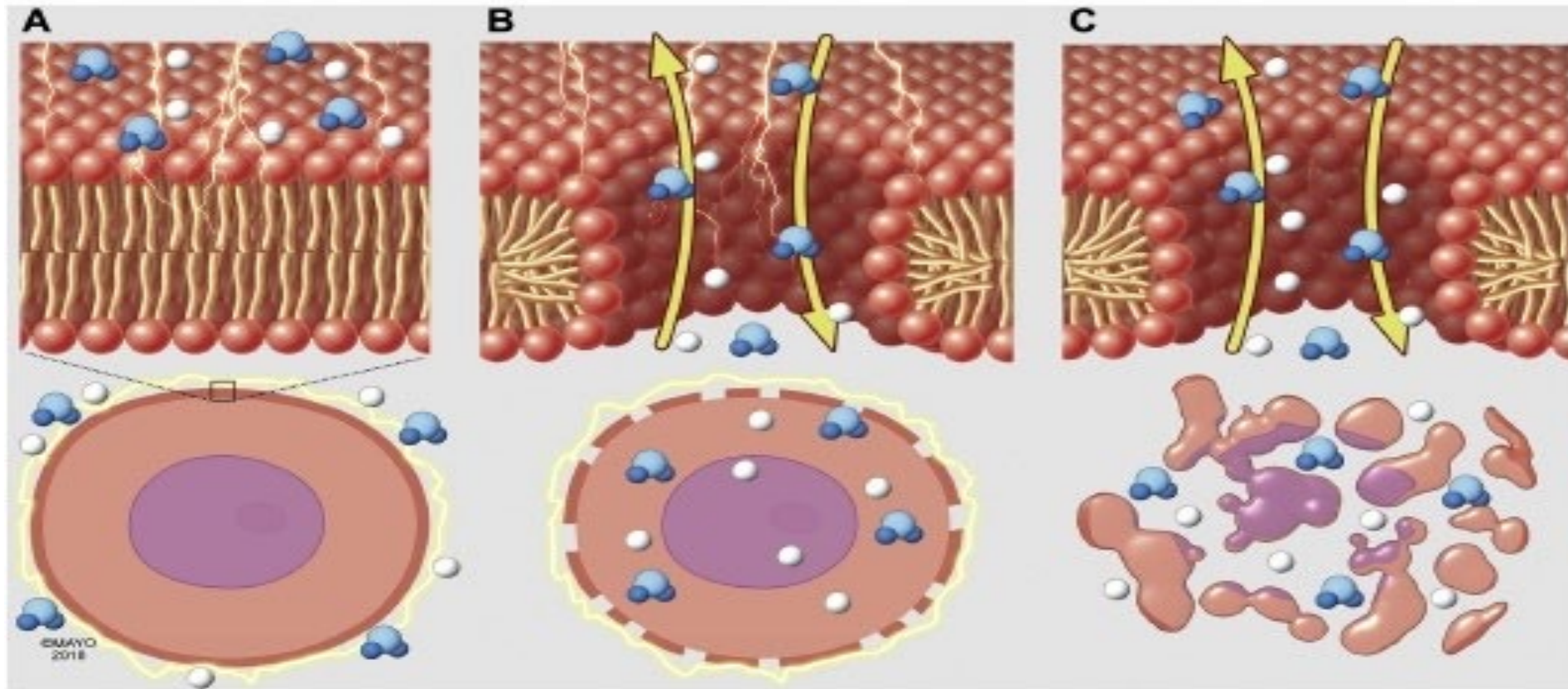
50 pazienti (74 procedure)
Nessuna complicanza

Studio SITE FATHAL (Di Stefano, under revision)

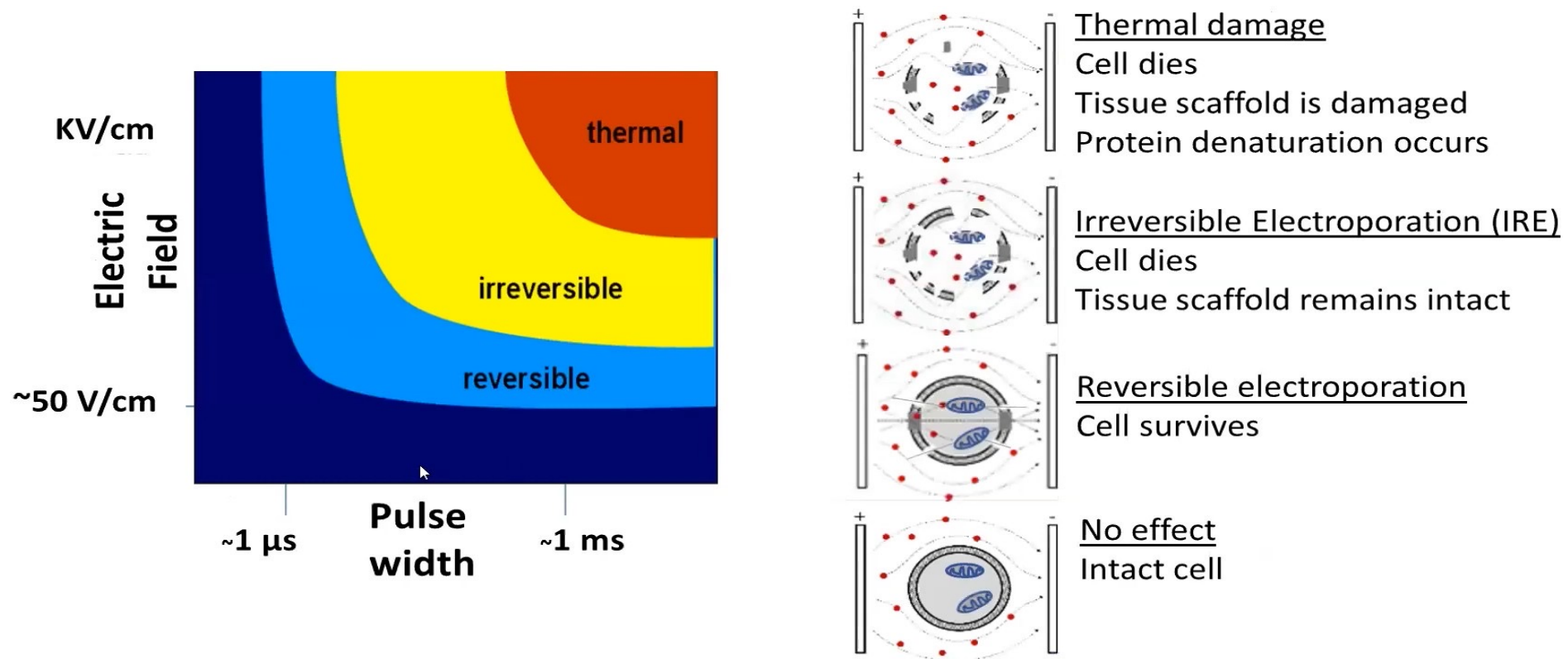
Il fenomeno dell'elettroporazione



Il fenomeno dell'elettroporazione



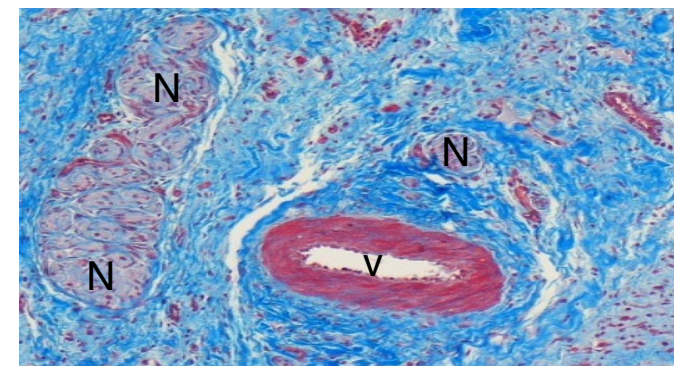
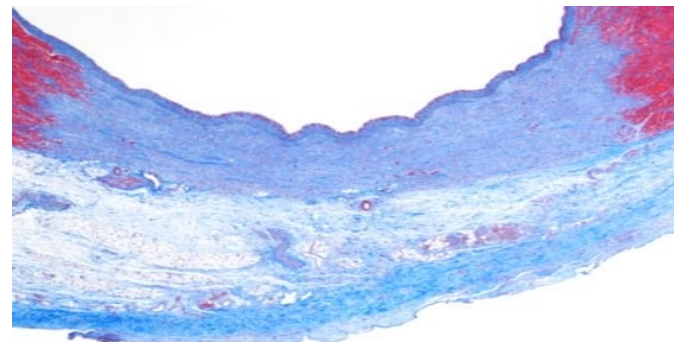
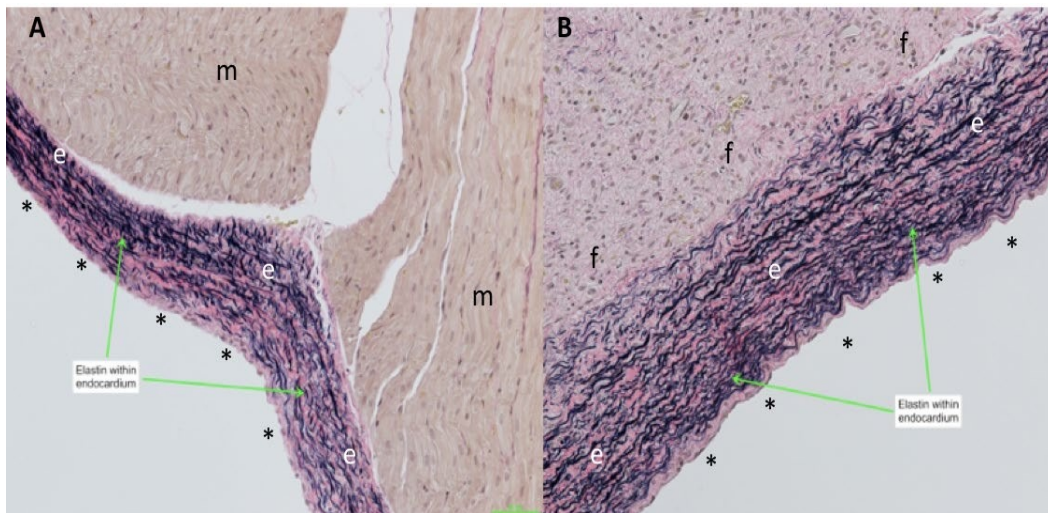
Il fenomeno dell'elettroporazione



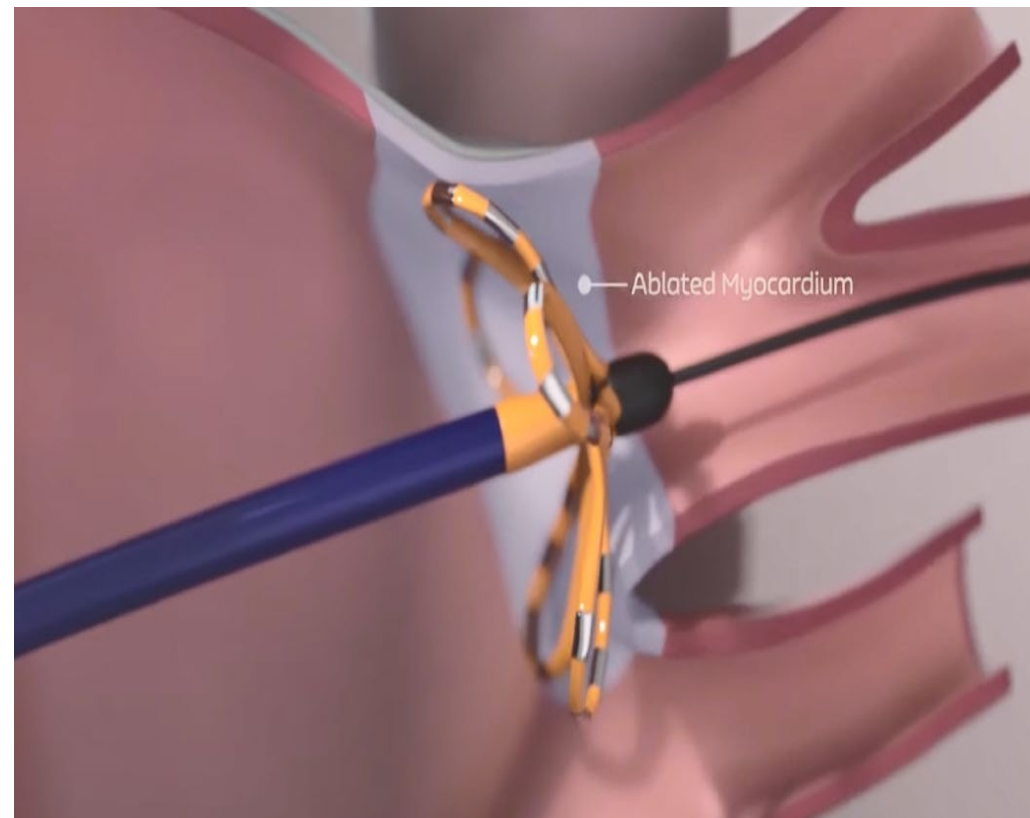
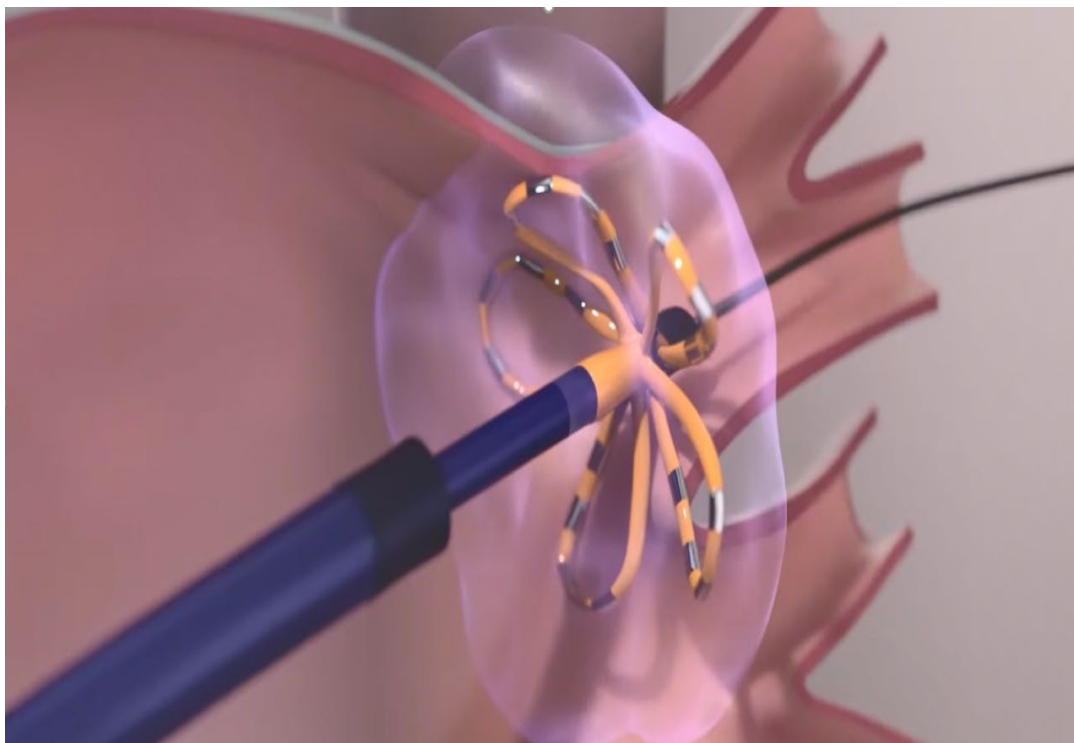
Il fenomeno dell'elettroporazione

MORTE CELLULARE SENZA DISTRUZIONE DELLA STRUTTURA TISSUTALE

Architecture and Elastin Fibers Structurally Unaltered
in Myocardial Ablation Zone



Preserved nerves (N) and vasculature (v) within PFA-treated myocardium (blue)



Take home messages

- Con l'aumento della sopravvivenza la fibrillazione atriale è una complicanza sempre più frequente nei pazienti beta-TDT
- Fino ad ora la gestione si è basata sulle linee guida per la popolazione generale anche se si osservano gestioni differenti da centro a centro (es. utilizzo dell'ablazione)
- Studio SITE FATHAL retrospettivo e prospettico ha lo scopo di valutare la prevalenza e la gestione della fibrillazione atriale nella beta-TDT e di sviluppare delle indicazioni per la sua gestione e trattamento che si basino sulle evidenze ottenute
- Il contributo di più centri possibile è fondamentale per ottenere dati robusti

FATHAL Prospettico

Centro	Stima pazienti
Brindisi	80
Modena	20
Parma	7
Cagliari	250
Verona	6
Lecce	60
Ferrara	100
Milano	100
Napoli	50
Catania	50
	723