

CARDIO-GERIATRIA NEI SETTING RESIDENZIALI

9 MAGGIO 2025

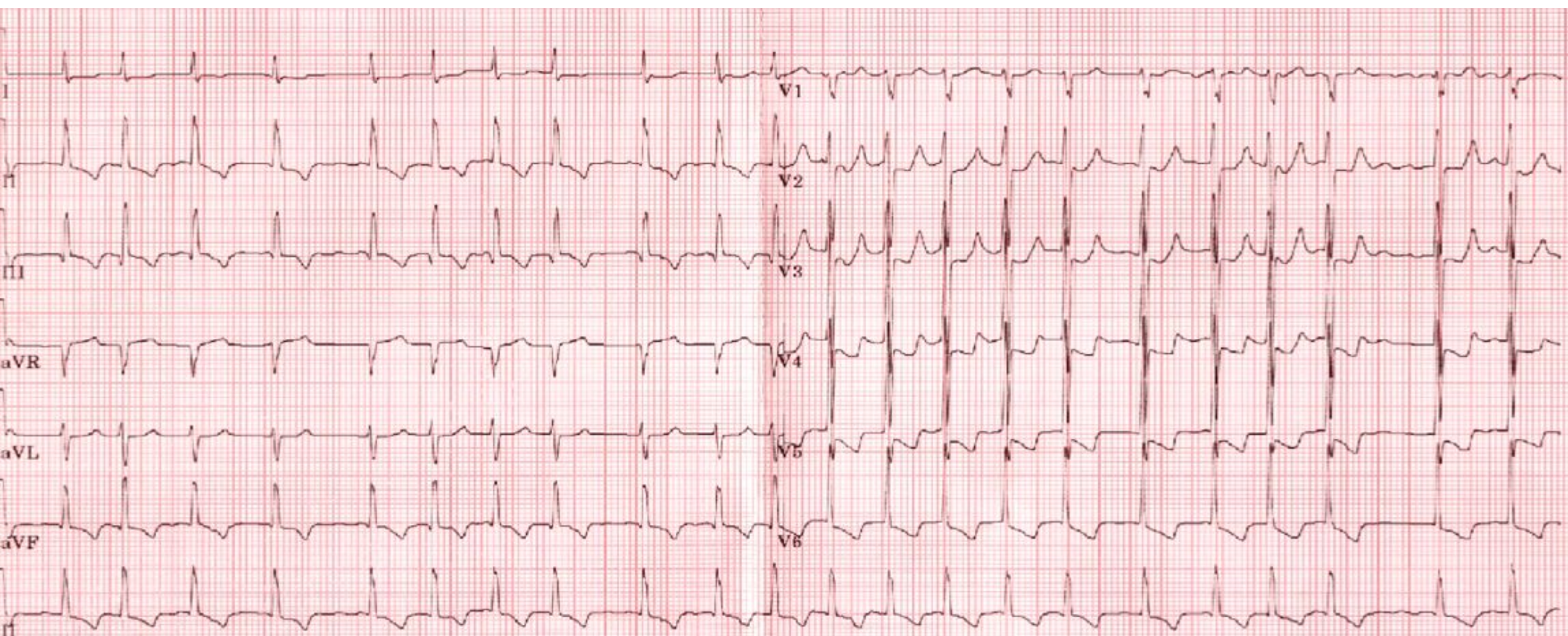
ore 15.00 | Sala BENACO ASC Cremona Solidale

Focus sulla gestione dello scompenso cardiaco e
della fibrillazione atriale



Scompenso cardiaco e fibrillazione atriale: quali specificità nell'anziano in RSA

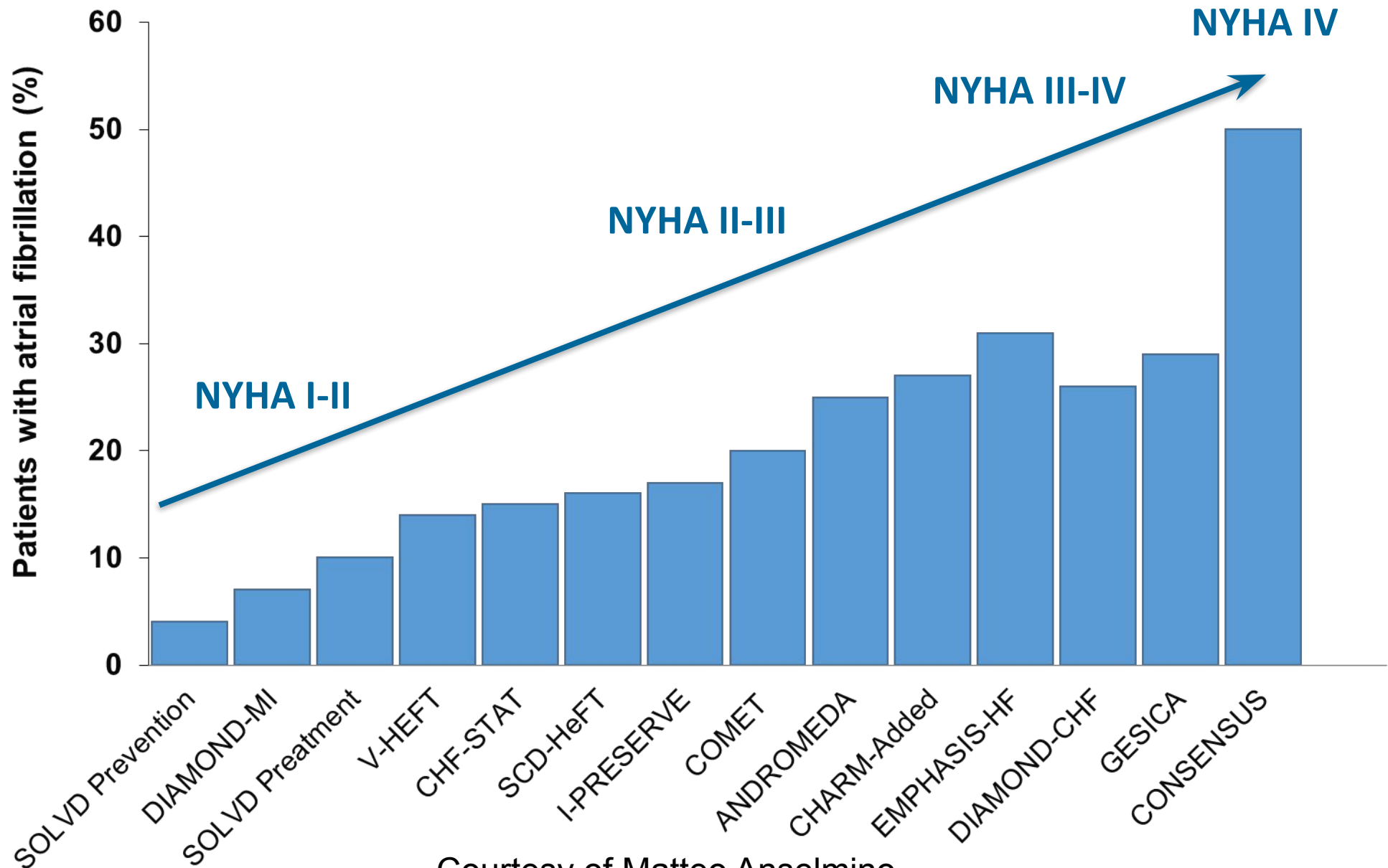
Prof Carlo Mario Lombardi



Epidemiology of AIC: the case of AF

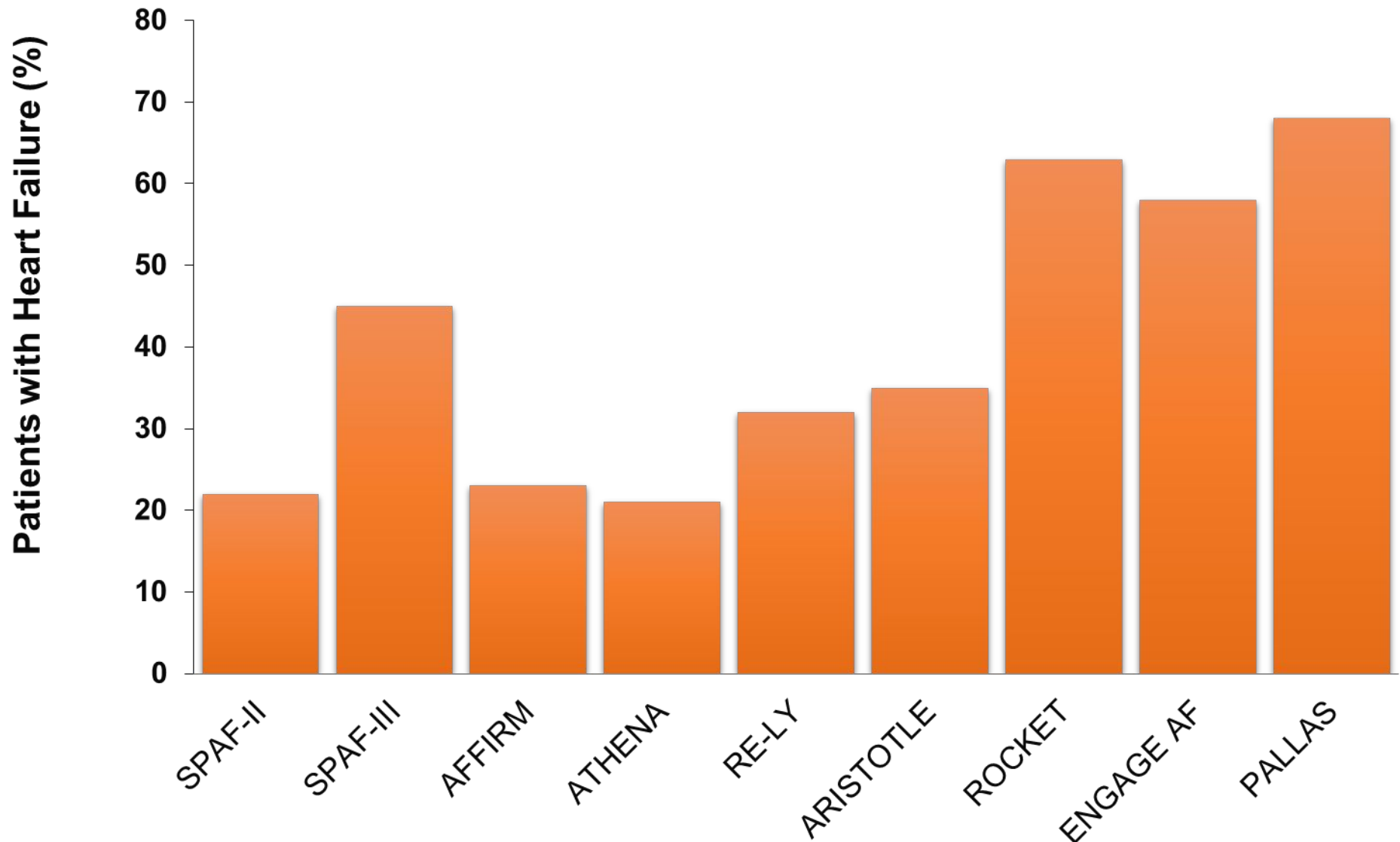
- L'aritmia più comune
- Circa il 50% dei pazienti con FA ha una disfunzione sistolica del ventricolo sinistro
- 10%-50% dei pazienti con scompenso cardiac riconoscono della FA la causa principale del deterioramento clinic
- Negli studi clinici spesso sono esclusi ipazienti con FA

Prevalence of AF in HF trials



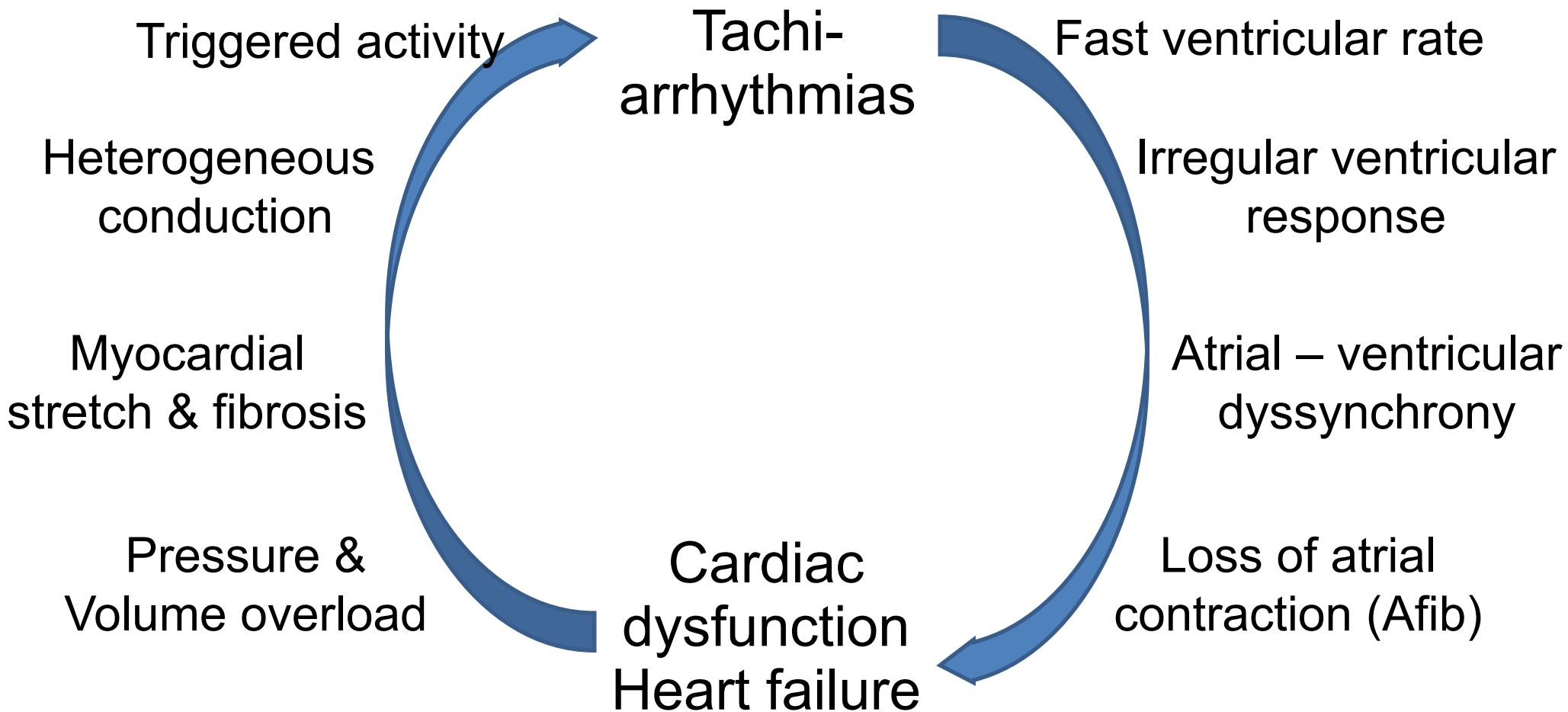
Courtesy of Matteo Anselmino

Prevalence of HF in AF trials

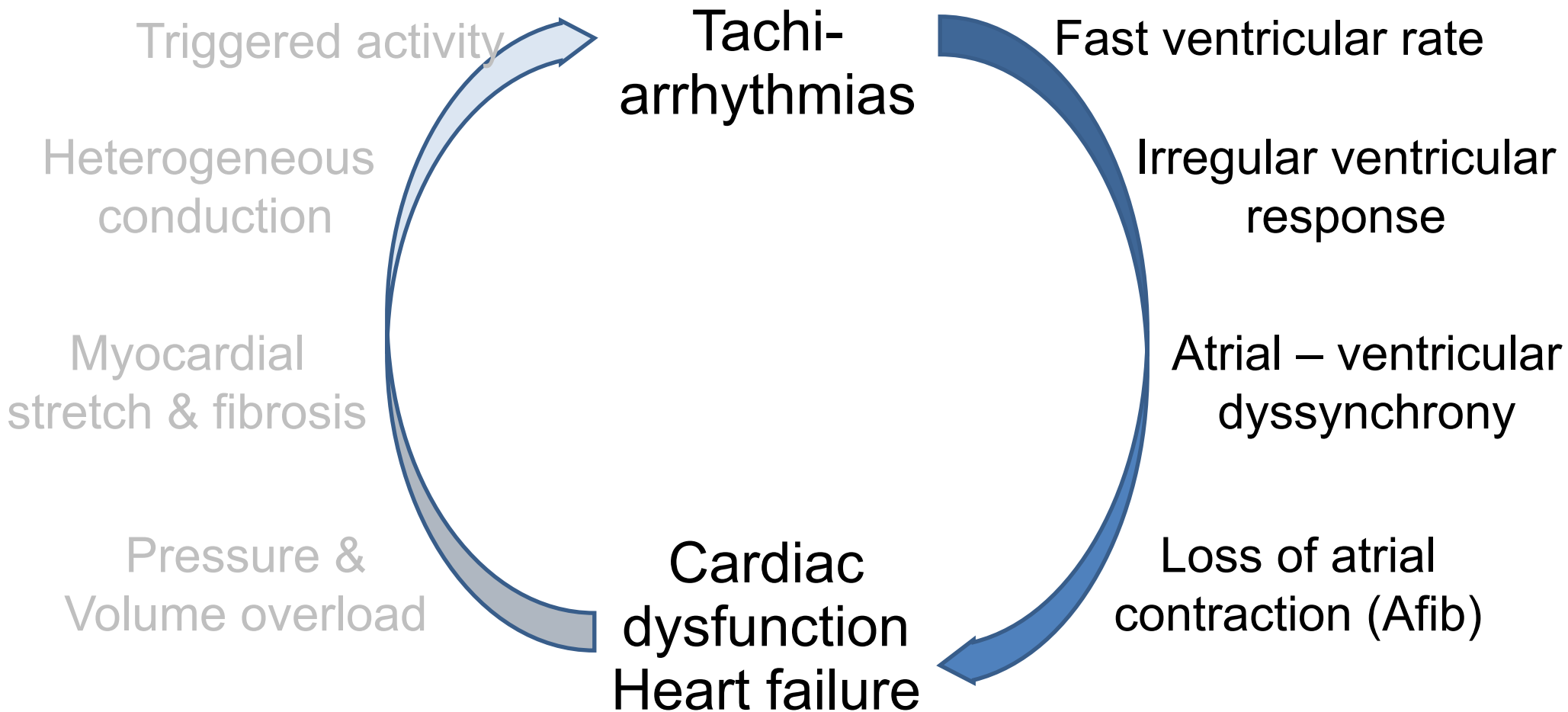


Courtesy of Matteo Anselmino

Tachyarrhythmias and Heart Failure: Which comes first?



Tachyarrhythmias and Heart Failure: Which comes first?



Arrhythmia Induced Cardiomyopathy (AIC) or Tachycardiomyopathy

- An impairment of LV function caused by atrial or ventricular tachyarrhythmias, partially or completely reversible after normalization of the heart rate.
- **Pure or arrhythmia induced**
 - The only cause of the myocardial dysfunction
- **Impure or arrhythmia mediated**
 - The arrhythmia exacerbates ventricular dysfunction and HF in a patient with concomitant heart disease

Atrial Fibrillation Begets Heart Failure and Vice Versa

Temporal Associations and Differences in Preserved Versus Reduced Ejection Fraction

Rajalakshmi Santhanakrishnan, MBBS; Na Wang, MA; Martin G. Larson, SD;
Jared W. Magnani, MD, MSc; David D. McManus, MD; Steven A. Lubitz, MD, MPH;
Patrick T. Ellinor, MD, PhD; Susan Cheng, MD; Ramachandran S. Vasan, MD;
Douglas S. Lee, MD, PhD; Thomas J. Wang, MD; Daniel Levy, MD;
Emelia J. Benjamin, MD, ScM; Jennifer E. Ho, MD

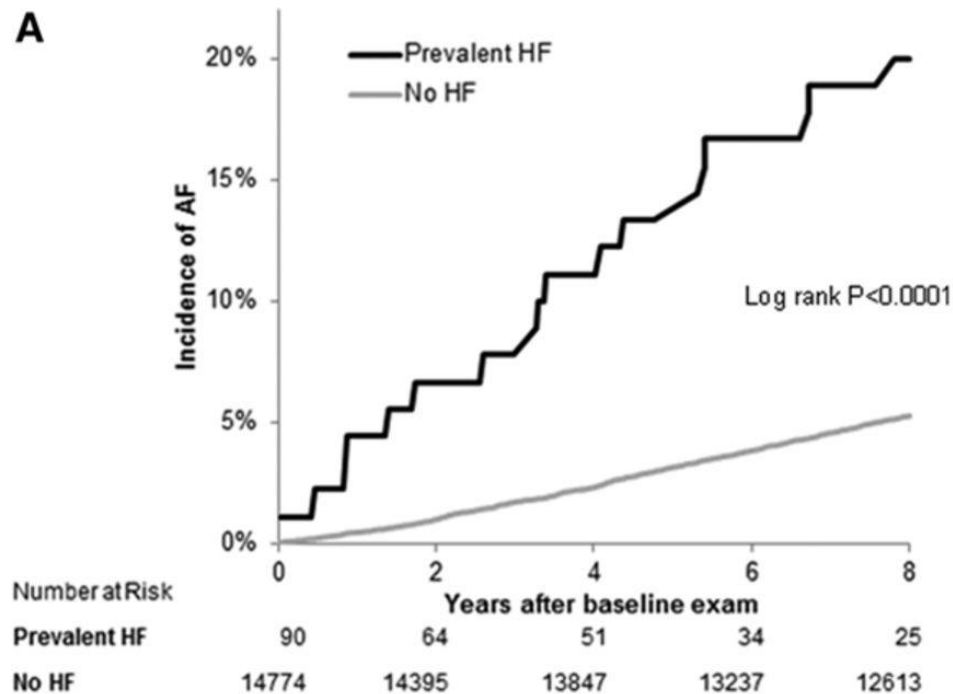
Background—Atrial fibrillation (AF) and heart failure (HF) frequently coexist and together confer an adverse prognosis. The association of AF with HF subtypes has not been well described. We sought to examine differences in the temporal association of AF and HF with preserved versus reduced ejection fraction.

Methods and Results—We studied Framingham Heart Study participants with new-onset AF or HF between 1980 and 2012. Among 1737 individuals with new AF (mean age, 75 ± 12 years; 48% women), more than one third (37%) had HF. Conversely, among 1166 individuals with new HF (mean age, 79 ± 11 years; 53% women), more than half (57%) had AF. Prevalent AF was more strongly associated with incident HF with preserved ejection fraction (multivariable-adjusted hazard ratio [HR], 2.34; 95% confidence interval [CI], 1.48–3.70; no AF as referent) versus HF with reduced ejection fraction (HR, 1.32; 95% CI, 0.83–2.10), with a trend toward difference between HF subtypes (P for difference=0.06). Prevalent HF was associated with incident AF (HR, 2.18; 95% CI, 1.26–3.76; no HF as referent). The presence of both AF and HF portended greater mortality risk compared with neither condition, particularly among individuals with new HF with reduced ejection fraction and prevalent AF (HR, 2.72; 95% CI, 2.12–3.48) compared with new HF with preserved ejection fraction and prevalent AF (HR, 1.83; 95% CI, 1.41–2.37; P for difference=0.02).

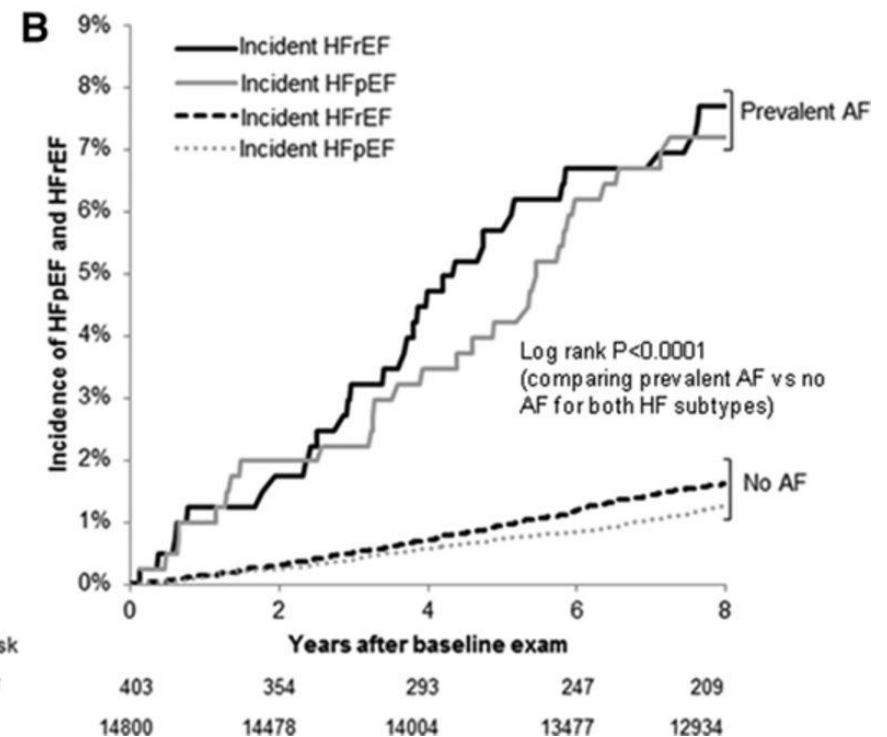
Conclusions—AF occurs in more than half of individuals with HF, and HF occurs in more than one third of individuals with AF. AF precedes and follows HF with both preserved and reduced ejection fraction, with some differences in temporal association and prognosis. Future studies focused on underlying mechanisms of these dual conditions are warranted. (*Circulation*. 2016;133:484-492. DOI: 10.1161/CIRCULATIONAHA.115.018614.)

Cumulative incidence of atrial fibrillation (AF) and heart failure (HF) among those with and without the other condition.

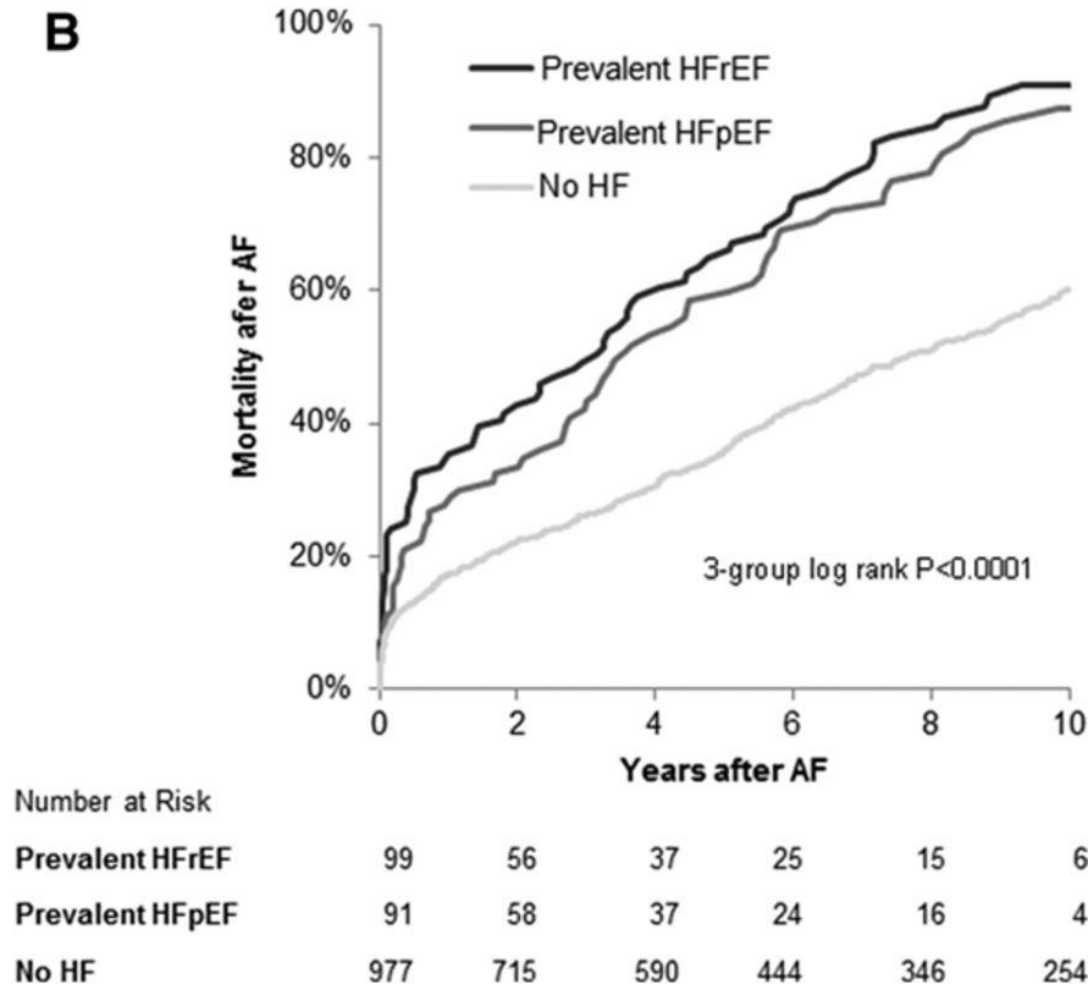
Incidence of AF (n=795)



Incidence of HF (n=487)

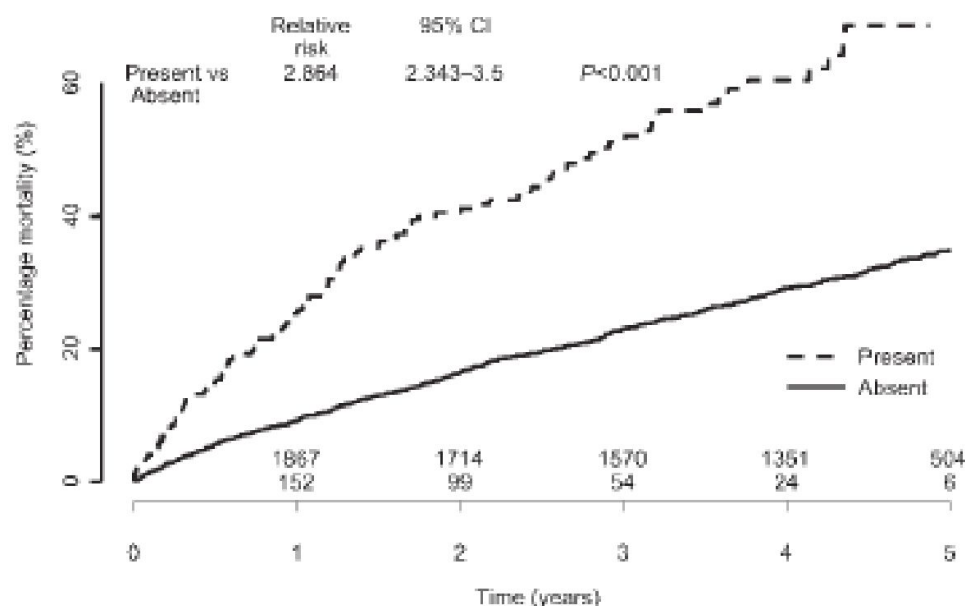


All-cause mortality after new onset atrial fibrillation (AF)



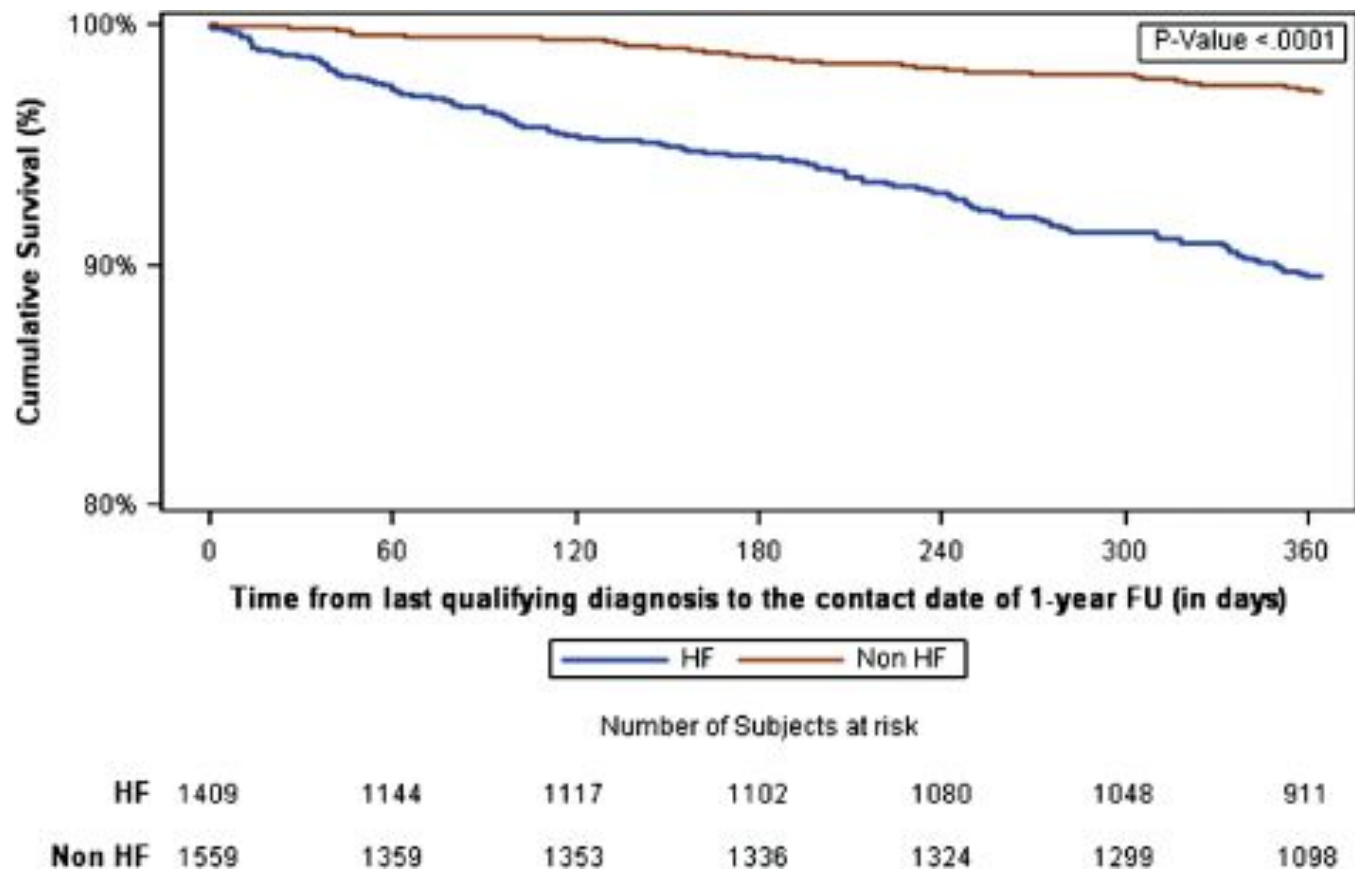
Prognostic relevance of atrial fibrillation in patients with chronic heart failure on long-term treatment with beta-blockers: results from COMET

Karl Swedberg^{1*}, Lars G. Olsson¹, Andrew Charlesworth², John Cleland³, Peter Hanrath⁴, Michel Komajda⁵, Marco Metra⁶, Christian Torp-Pedersen⁷, and Philip Poole-Wilson⁸

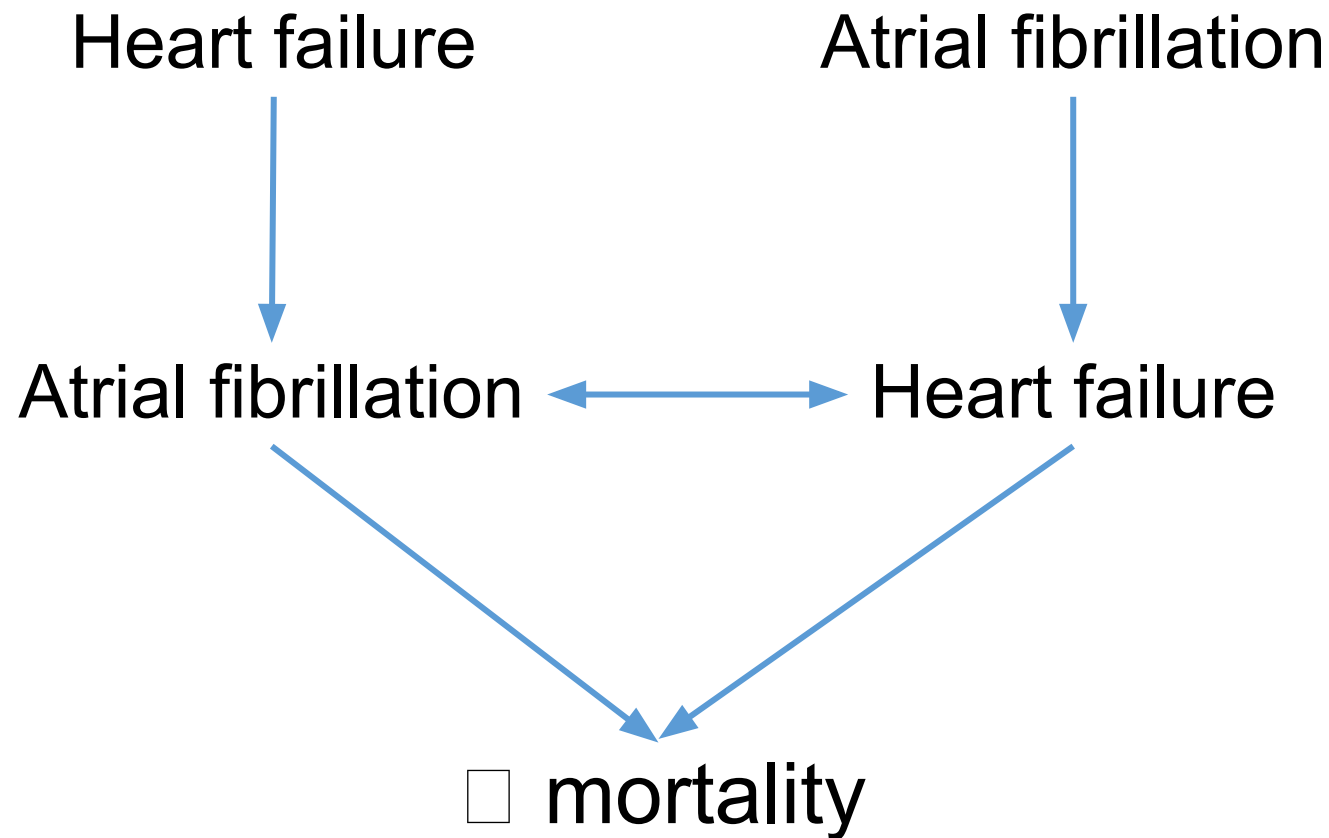


Conclusion In CHF, atrial fibrillation significantly increases the risk for death and heart failure hospitalization, but is not an independent risk factor for mortality after adjusting for other predictors of prognosis. Treatment with carvedilol compared with metoprolol offers additional benefits among patients with atrial fibrillation. Onset of new atrial fibrillation in patients on long-term beta-blocker therapy is associated with significant increased subsequent risk of mortality and morbidity.

Heart failure in patients with atrial fibrillation in Europe: a report from the EURObservational Research Programme Pilot survey on AF



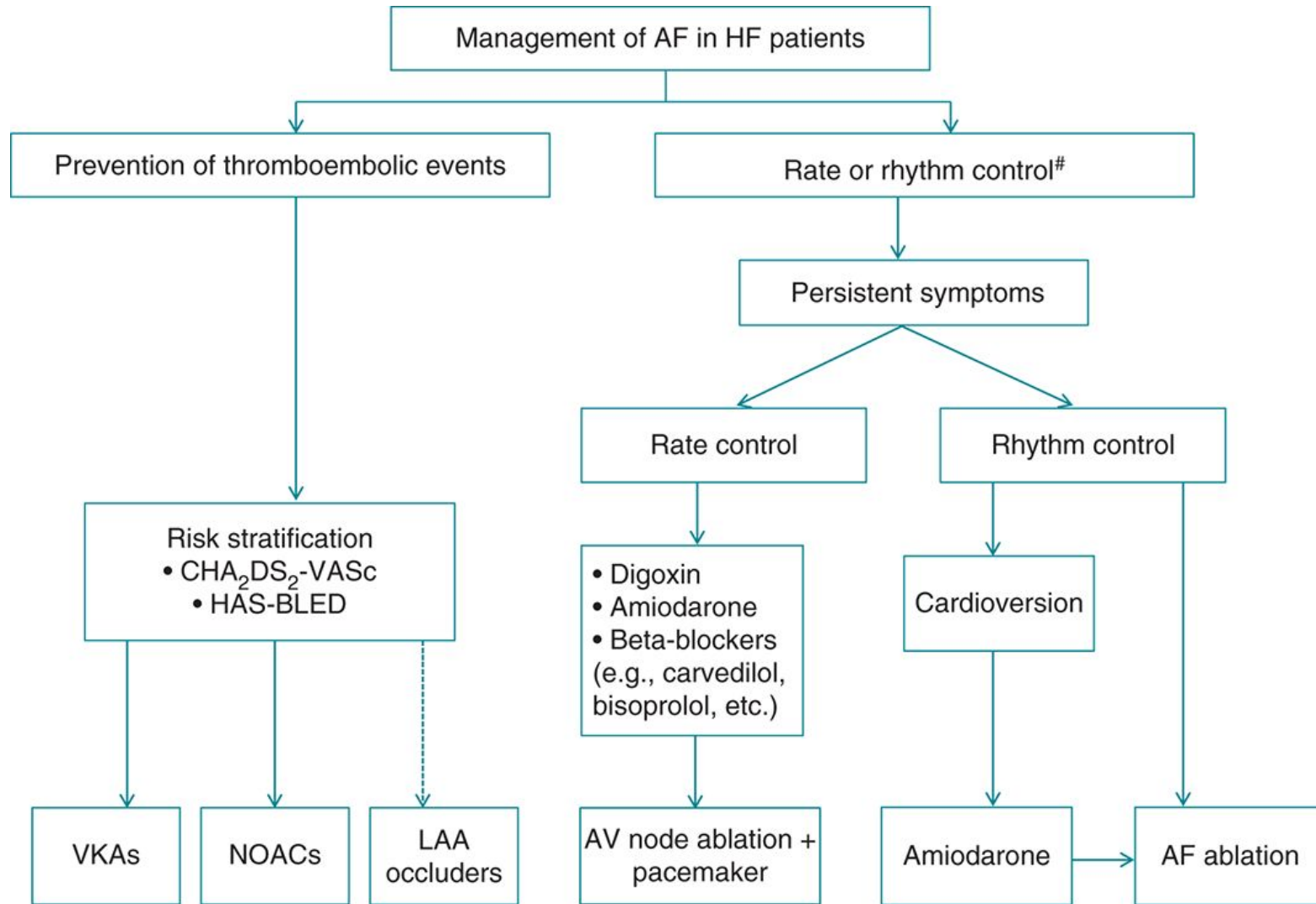
Poor prognosis in patients with heart failure & atrial fibrillation: cause or epiphenomenon?



Punti Chiave della gestione del paziente con fibrillazione atriale e scompenso cardiaco

1. Terapia anticoagulante
2. Controllo del ritmo cardiaco

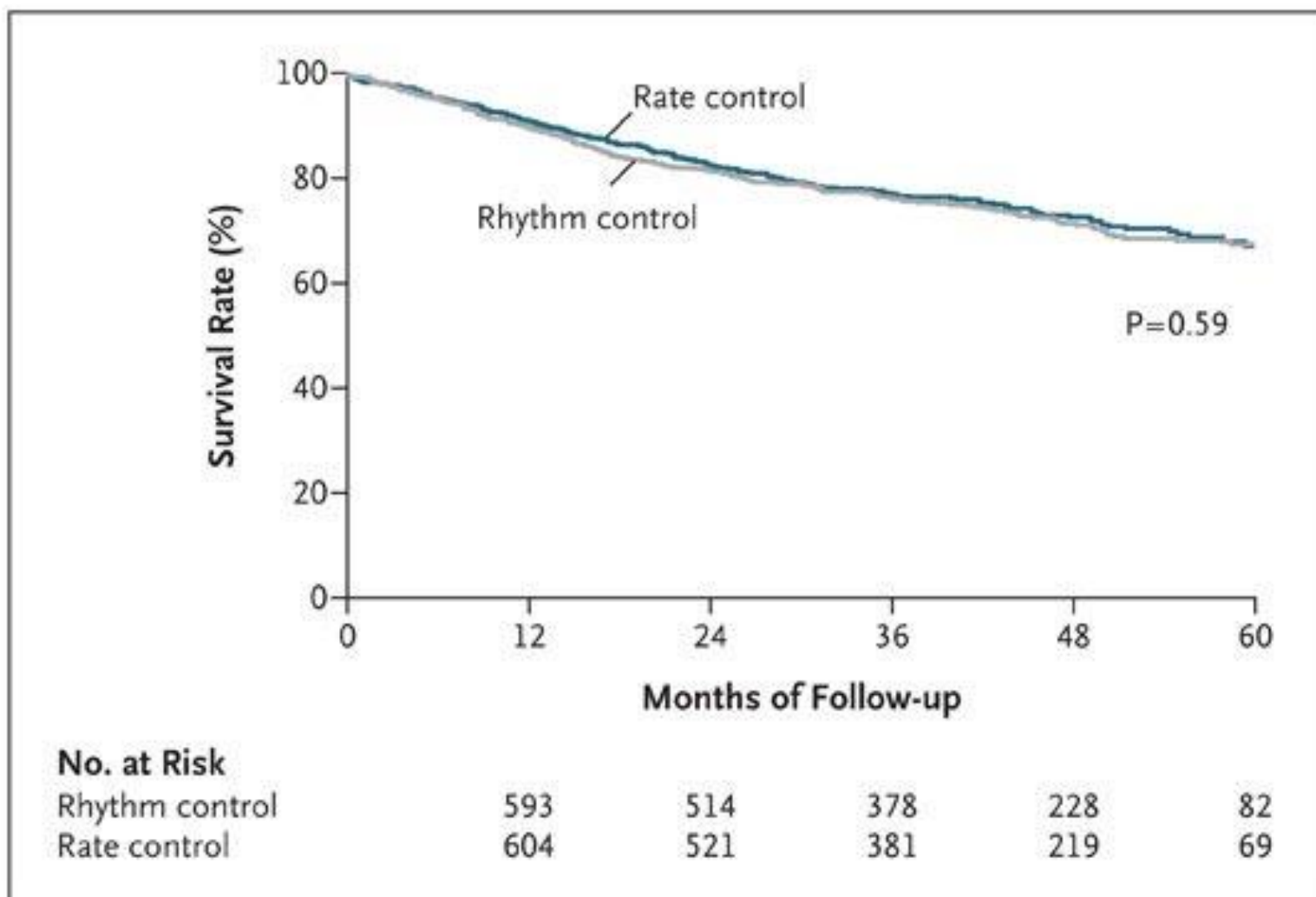
Management of atrial fibrillation in heart failure patients



Rate control vs. Rhythm control trials

Trial	Inclusion criteria	Primary outcome Parameter	Patients reaching primary outcome (n)		
			Rate ctrl	Rhythm ctrl	P
PIAF (2000) 252 Patients	Persistent AF (7-360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM (2002) 4060 Patients	Paroxysmal AF or persistent AF, age ≥ 65 years, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE (2002) 522 Patients	Persistent AF or flutter for <1 year and 1-2 cardioversions over 2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, pacemaker implantation, thrombo-embolic events, severe adverse effects of antiarrhyt. drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF (2003) 200 Patients	Persistent AF (>4 weeks and <2 years), LA size >45 mm, CHF NYHA II-IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	0.99
HOT CAFÈ (2004) 205 Patients	First clinically overt persistent AF (≥ 7 days and <2 years), age 50-75 years	Composite: death, thrombo-embolic events; intracranial/major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF (2008) 1376 Patients	LVEF $\leq 35\%$, symptoms of CHF, history of AF (≥ 6 h or DCC <last 6 months)	Cardiovascular death	175/1376 (25%)	182/1376 (27%)	0.59
J-RHYTHM (2009) 823 Patients	Paroxysmal AF	Composite of total mortality, symptomatic cerebral infarction, systemic embolism, major bleeding, hospitalization for heart failure, or physical/psychological disability	89/405 (22.0%)	64/418 (15.3%)	0.012

Kaplan-Meier Estimates of Death from Cardiovascular Causes (Primary Outcome)



Rhythm control versus Rate control in patients with AF and HF

- No evidence from RCTs favoring either strategy
- Large observational studies have suggested a benefit of the rhythm control strategy on long-term mortality and stroke rates.
- In RCTs up to 40% of the patients were in sinus rhythm in the rate control group.
- The untoward effects of antiarrhythmic drugs may have worsened outcomes in the rhythm control group



ESC
European Society
of Cardiology

European Heart Journal (2021) 42, 3599–3726
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Theresa A. McDonagh* (Chairperson) (United Kingdom), Marco Metra* (Chairperson) (Italy), Marianna Adamo (Task Force Coordinator) (Italy), Roy S. Gardner (Task Force Coordinator) (United Kingdom), Andreas Baumbach (United Kingdom), Michael Böhm (Germany), Haran Burri (Switzerland), Javed Butler (United States of America), Jelena Celutkienė (Lithuania), Ovidiu Chioncel (Romania), John G.F. Cleland (United Kingdom), Andrew J.S. Coats (United Kingdom), Maria G. Crespo-Leiro (Spain), Dimitrios Farmakis (Greece), Martine Gilard (France), Stephane Heymans

Management of HFrEF

To reduce mortality - for all patients

ACE-I/ARNI

BB

MRA

SGLT2i

To reduce HF hospitalization/mortality - for selected patients

Volume overload

Diuretics

SR with LBBB ≥ 150 ms

CRT-P/D

SR with LBBB 130–149 ms or non LBBB ≥ 150 ms

CRT-P/D

Ischaemic aetiology

ICD

Non-ischaemic aetiology

ICD

Atrial fibrillation

Anticoagulation

Atrial fibrillation

Digoxin

PVI

Coronary artery disease

CABG

Iron deficiency

Ferric carboxymaltose

Aortic stenosis

SAVR/TAVI

Mitral regurgitation

TEE MV Repair

Heart rate SR > 70 bpm

Ivabradine

Black Race

Hydralazine/ISDN

ACE-I/ARNI intolerance

ARB

For selected advanced HF patients

Heart transplantation

MCS as BTT/BTC

Long-term MCS as DT

To reduce HF hospitalization and improve QOL - for all patients

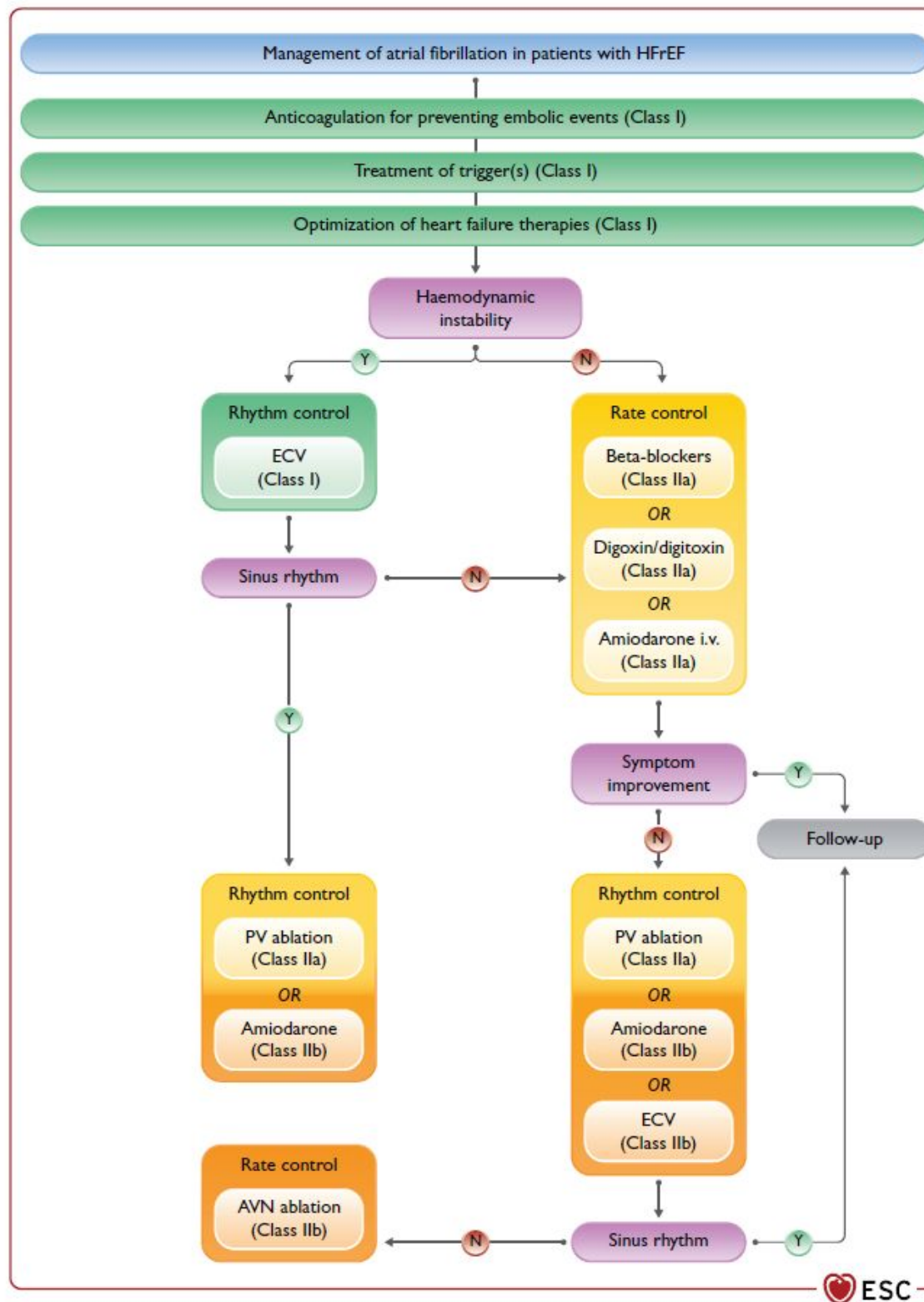
Exercise rehabilitation

Multi-professional disease management



2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)



2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Rate control

Beta-blockers should be considered for short- and long-term rate control in patients with HF and AF.⁵³⁵

IIa

B

Digoxin should be considered when the ventricular rate remains high, despite beta-blockers, or when beta-blockers are contraindicated or not tolerated.⁵³⁶

IIa

C

Cardioversion

Urgent ECV is recommended in the setting of acute worsening of HF in patients presenting with rapid ventricular rates and haemodynamic instability.

I

C

Cardioversion may be considered in patients in whom there is an association between AF and worsening of HF symptoms despite optimal medical treatment.^{7,541}

IIb

B

AF catheter ablation

In cases of a clear association between paroxysmal or persistent AF and worsening of HF symptoms, which persist despite MT, catheter ablation should be considered for the prevention or treatment of AF.^{552–554,557}

IIa

B

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Recommendations	Class ^a	Level ^b
Anticoagulation		
Long-term treatment with an oral anticoagulant is recommended in all patients with AF, HF, and CHA ₂ DS ₂ -VASc score ≥ 2 in men or ≥ 3 in women. ⁷	I	A
DOACs are recommended in preference to VKAs in patients with HF, except in those with moderate or severe mitral stenosis or mechanical prosthetic heart valves. ^{528,558}	I	A
Long-term treatment with an oral anticoagulant should be considered for stroke prevention in AF patients with a CHA ₂ DS ₂ -VASc score of 1 in men or 2 in women. ^{7,559}	IIa	B

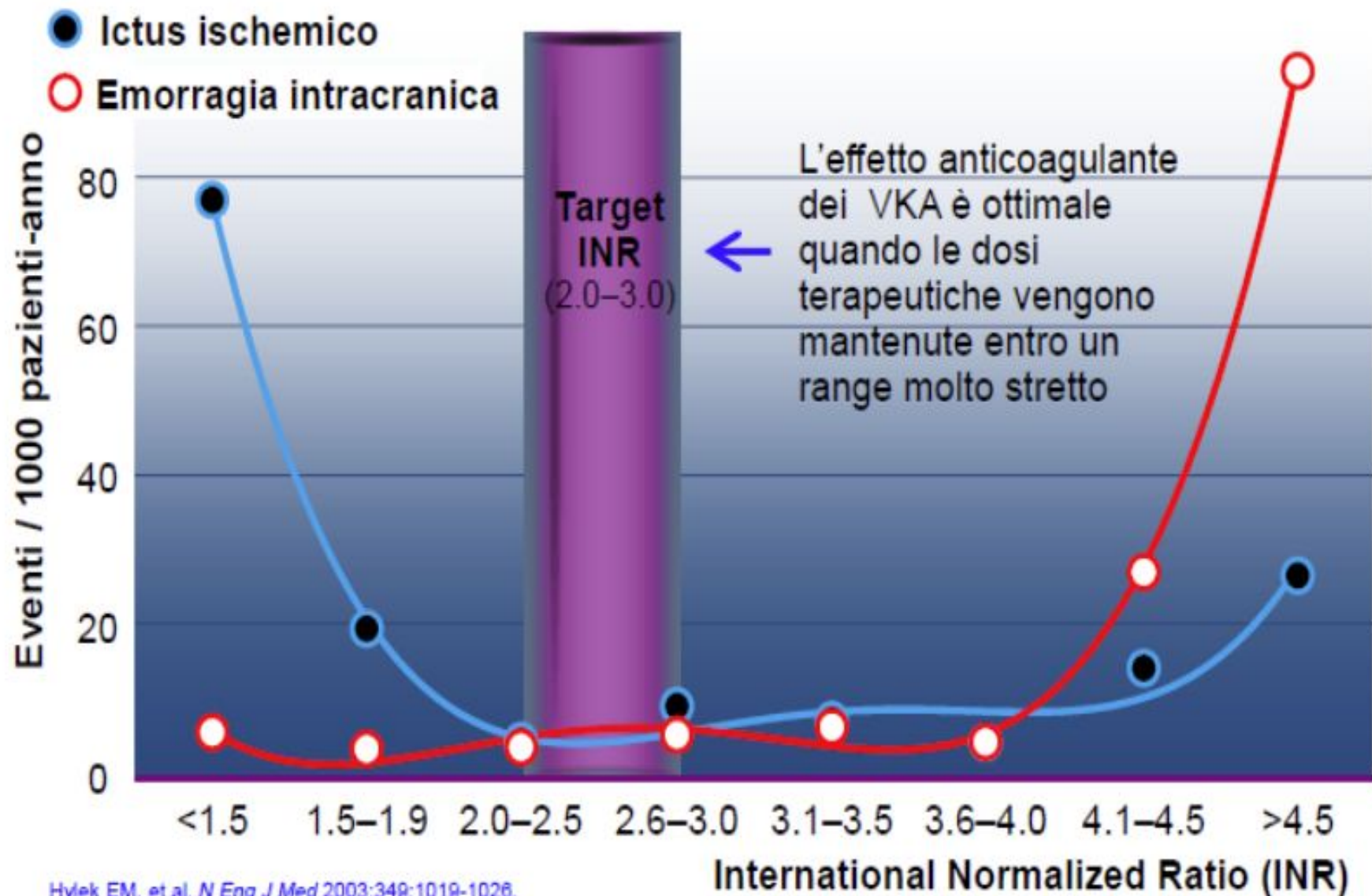
Terapia anticoagulante: una questione di equilibrio ...

Rischi (sicurezza)

Benefici (efficacia)



Terapia anticoagulante: una questione di equilibrio ...



European Heart Journal Advance Access published August 27, 2016



European Heart Journal
doi:10.1093/eurheartj/ehw210

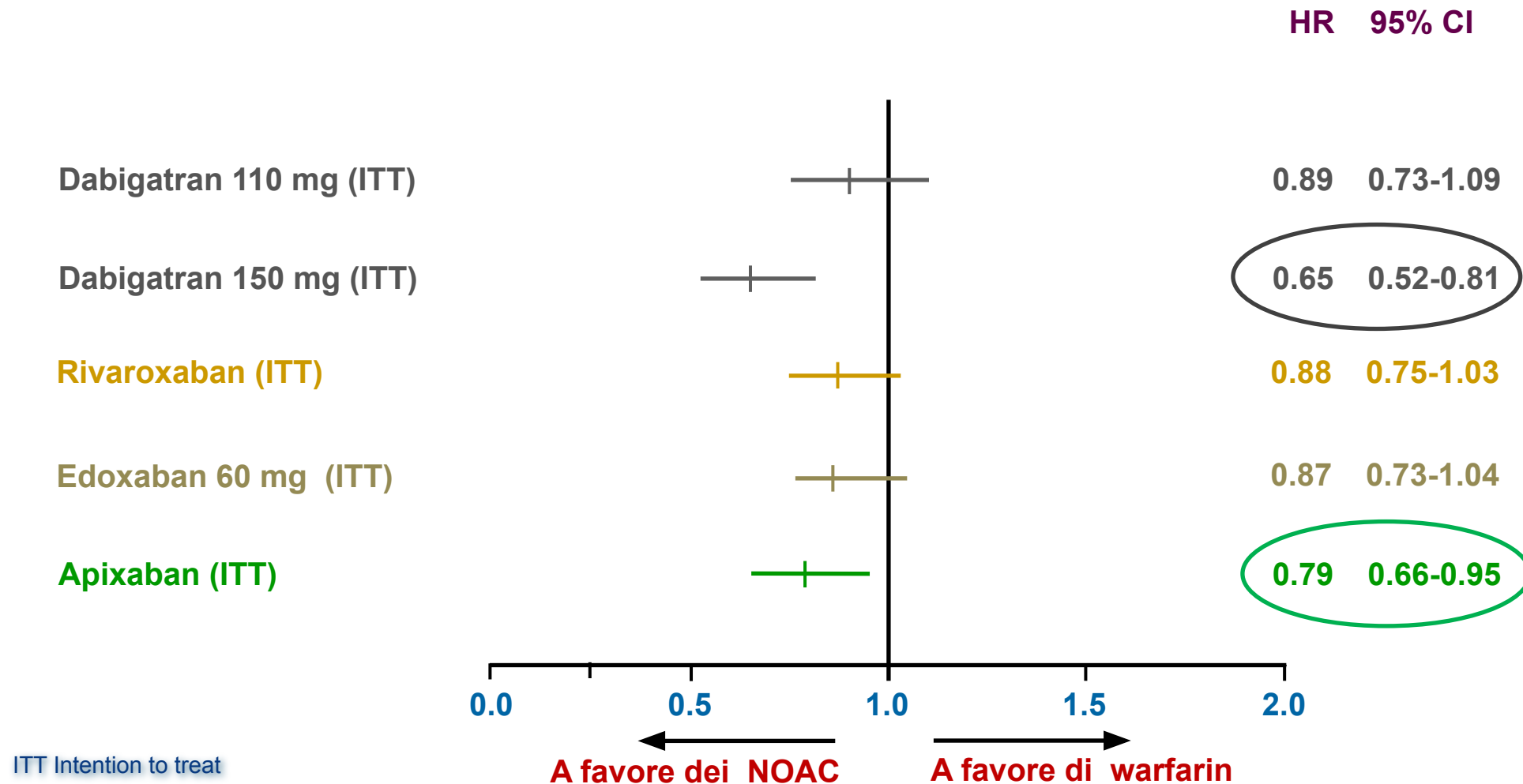
ESC GUIDELINES

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

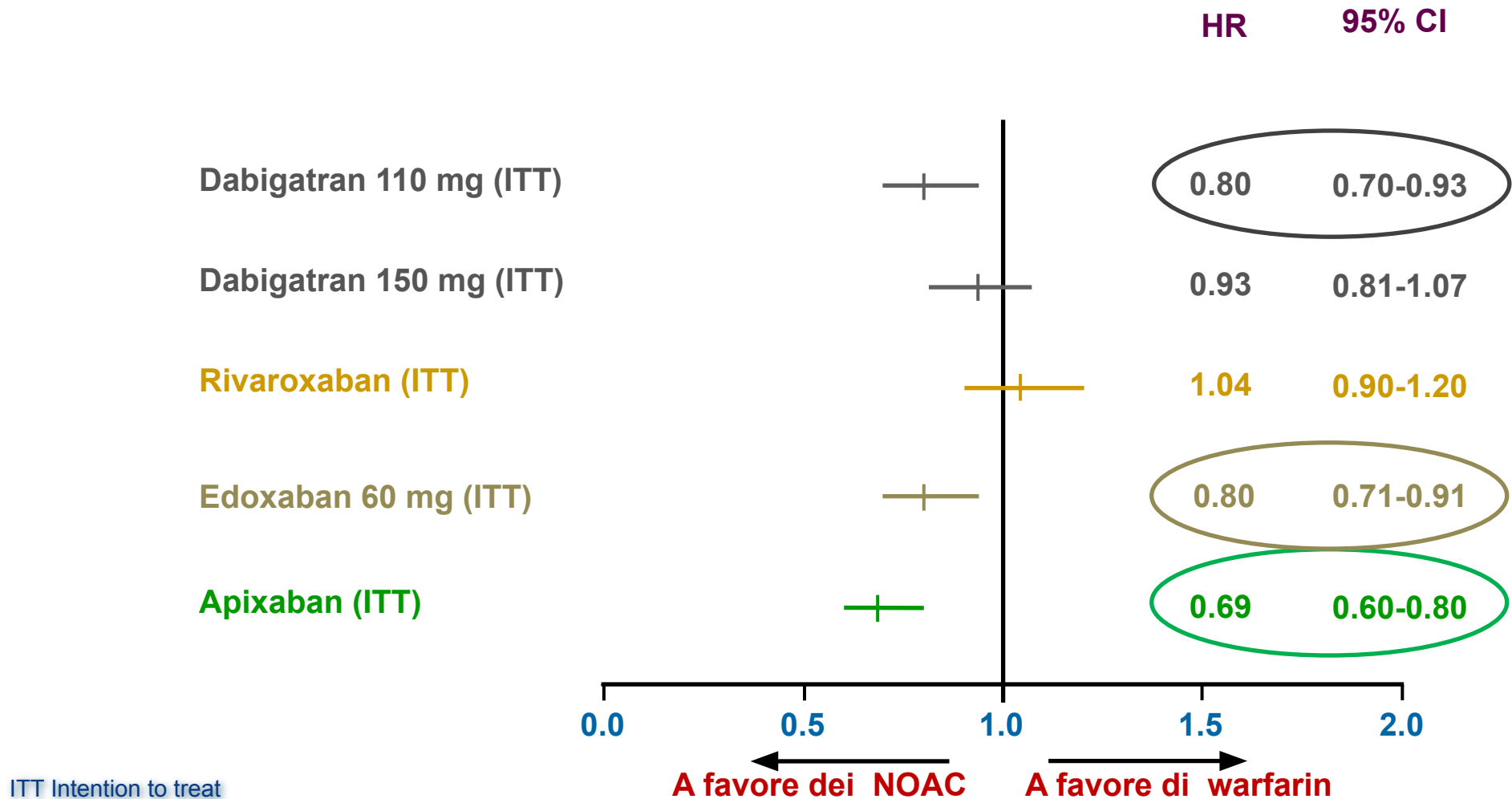
Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

NOAC vs. warfarin: Ictus e ES



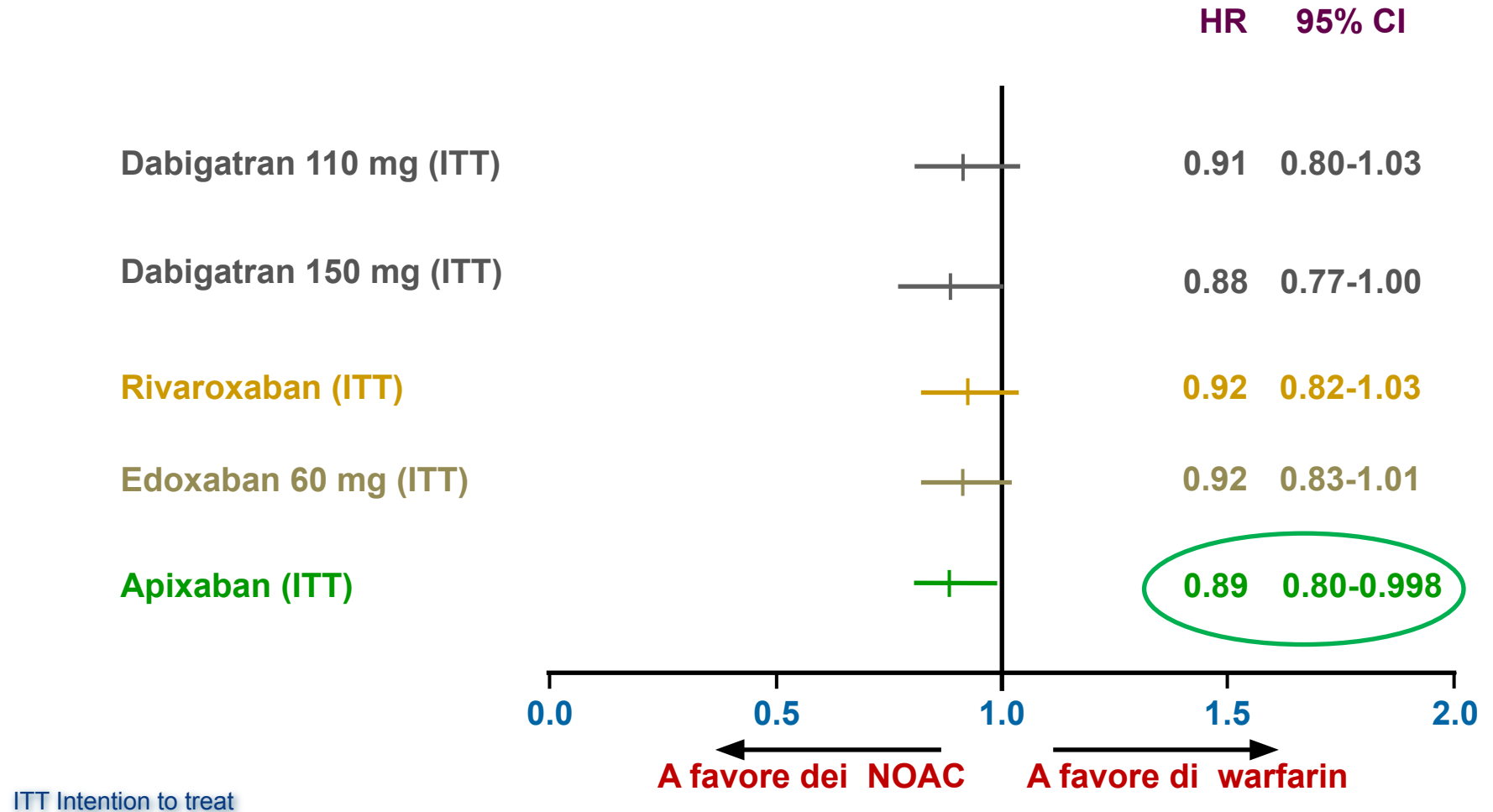
1. Connolly et al. NEJM 2010;363:1875-6, suppl app.
2. Patel et al. NEJM 2011;365:883-91, suppl app.
3. Granger et al. NEJM 2011;365:981-92.

NOAC vs. warfarin: sanguinamenti maggiori



1. Connolly et al. NEJM 2010;363:1875-6, suppl app.
2. Patel et al. NEJM 2011;365:883-91, suppl app.
3. Granger et al. NEJM 2011;365:981-92.

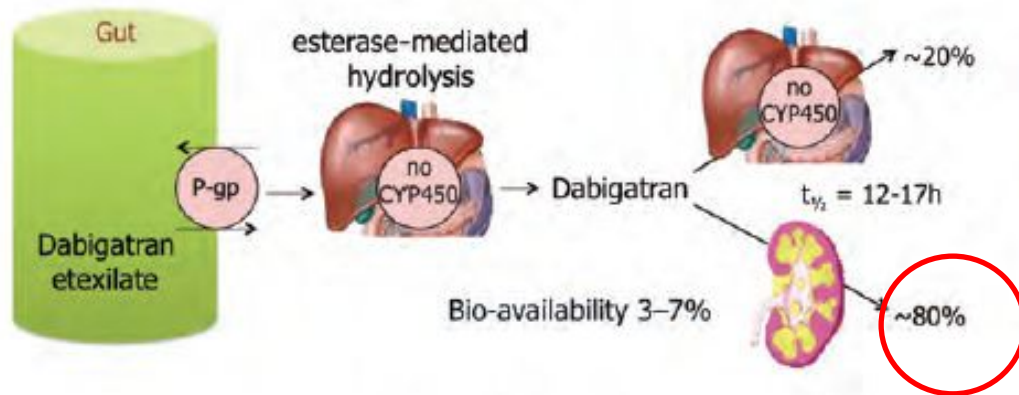
NOAC vs. warfarin: mortalità da tutte le cause



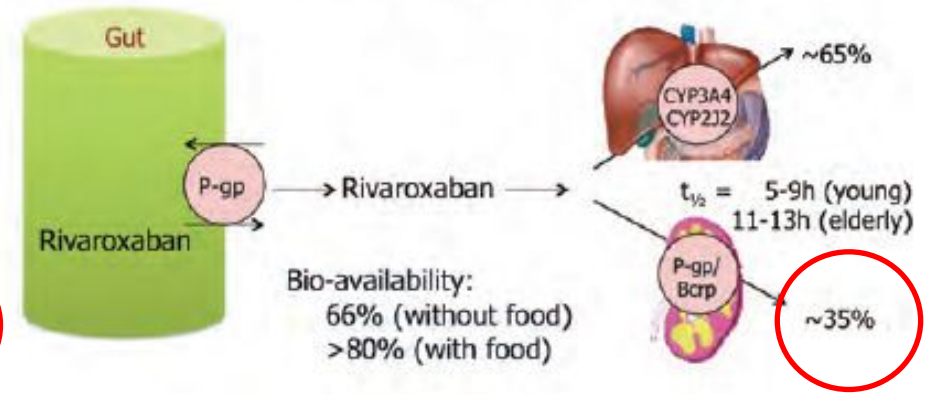
1. Connolly et al. NEJM 2010;363:1875-6, suppl app.
2. Patel et al. NEJM 2011;365:883-91, suppl app.
3. Granger et al. NEJM 2011;365:981-92.

Clinical pharmacology of dabigatran, edoxaban, rivaroxaban and apixaban

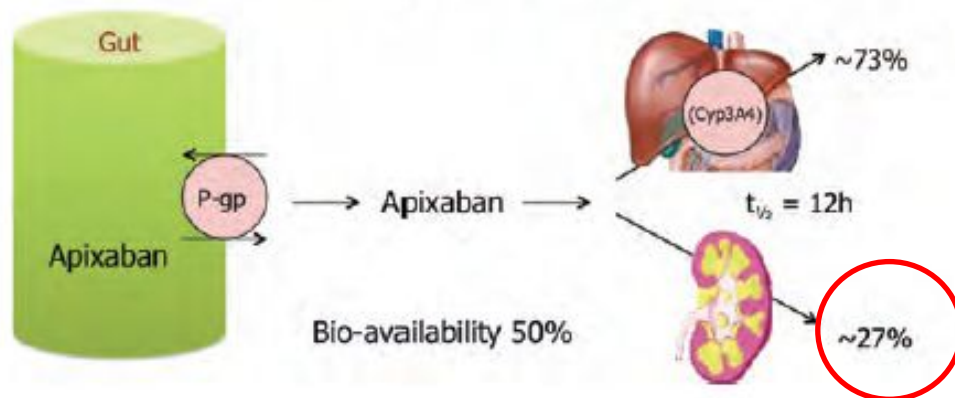
Dabigatran



Rivaroxaban



Apixaban



Edoxaban

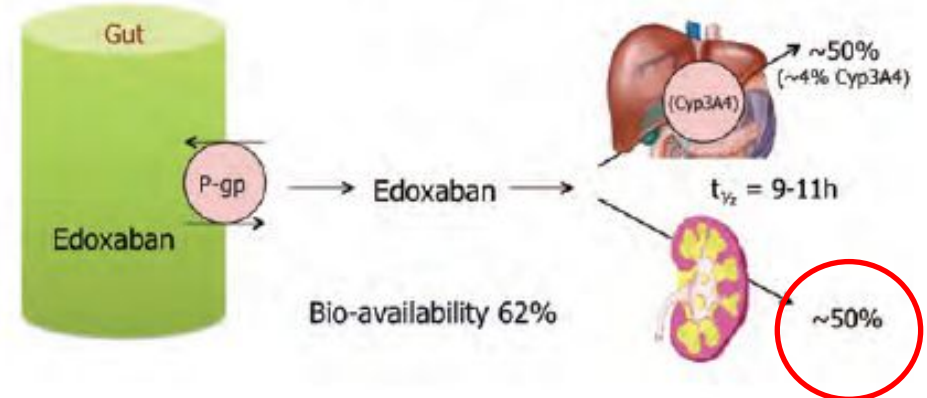


Table 3: Major efficacy (analyzed as intention to treat) and safety outcomes in the atrial fibrillation studies (10–12). Hazard ratios or relative risks are in relation to warfarin and are in bold type when showing a statistically significant reduction.

Efficacy (reduction of stroke or sys- temic embolism)		Safety (major bleeding)	
Best			
1	Dabigatran 150 mg BID RR 0.66 (95% CI, 0.53–0.82)	Edoxaban 30 mg daily HR 0.47 (97.5% CI, 0.41–0.55)	1
2	Apixaban 5 mg BID HR 0.79 (95% CI, 0.66–0.95)	Apixaban 5 mg BID HR 0.69 (95% CI, 0.60–0.80)	2
3		Dabigatran 110 mg BID RR 0.80 (95% CI, 0.69–0.93)	3
4		Edoxaban 60 mg daily HR 0.80 (97.5% CI, 0.71–0.91)	4
5			5
6			6
Worst*			
RR, relative risk; HR, hazard ratio; CI, confidence interval; BID, twice daily. *Note that “worst” risk estimate is still non-inferior to warfarin.			

NEI PAZIENTI ANZIANI



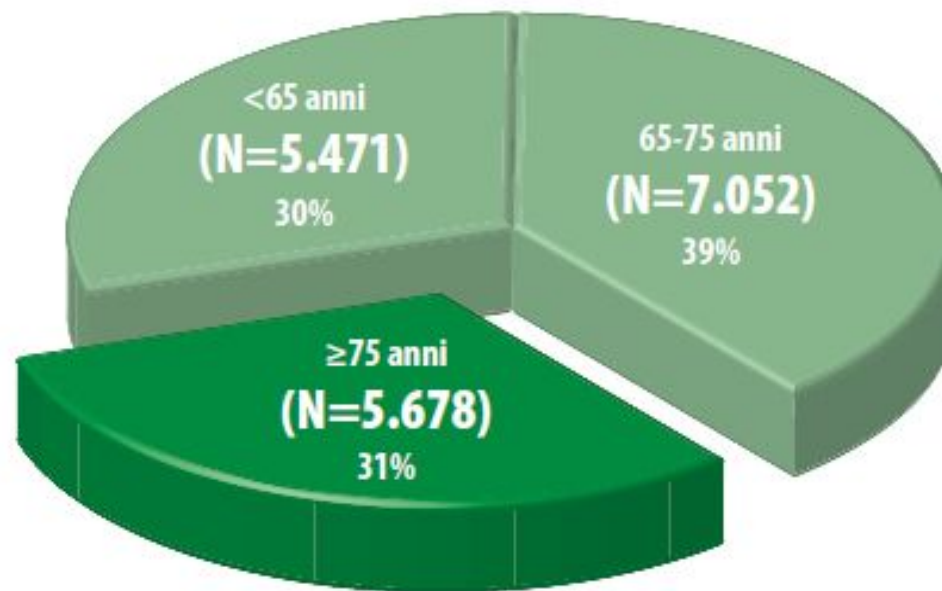
Efficacia e sicurezza nel paziente anziano



Efficacy and safety of apixaban compared with warfarin according to age for stroke prevention in atrial fibrillation: observations from the ARISTOTLE trial

Patients	N. (%)	
patients enrolled	18.201	
< 65 year	5.471	
65 to <75 year	7.052	
≥ 75 year	5.678	≥ 80 year 2.352 ≥ 90 year 84

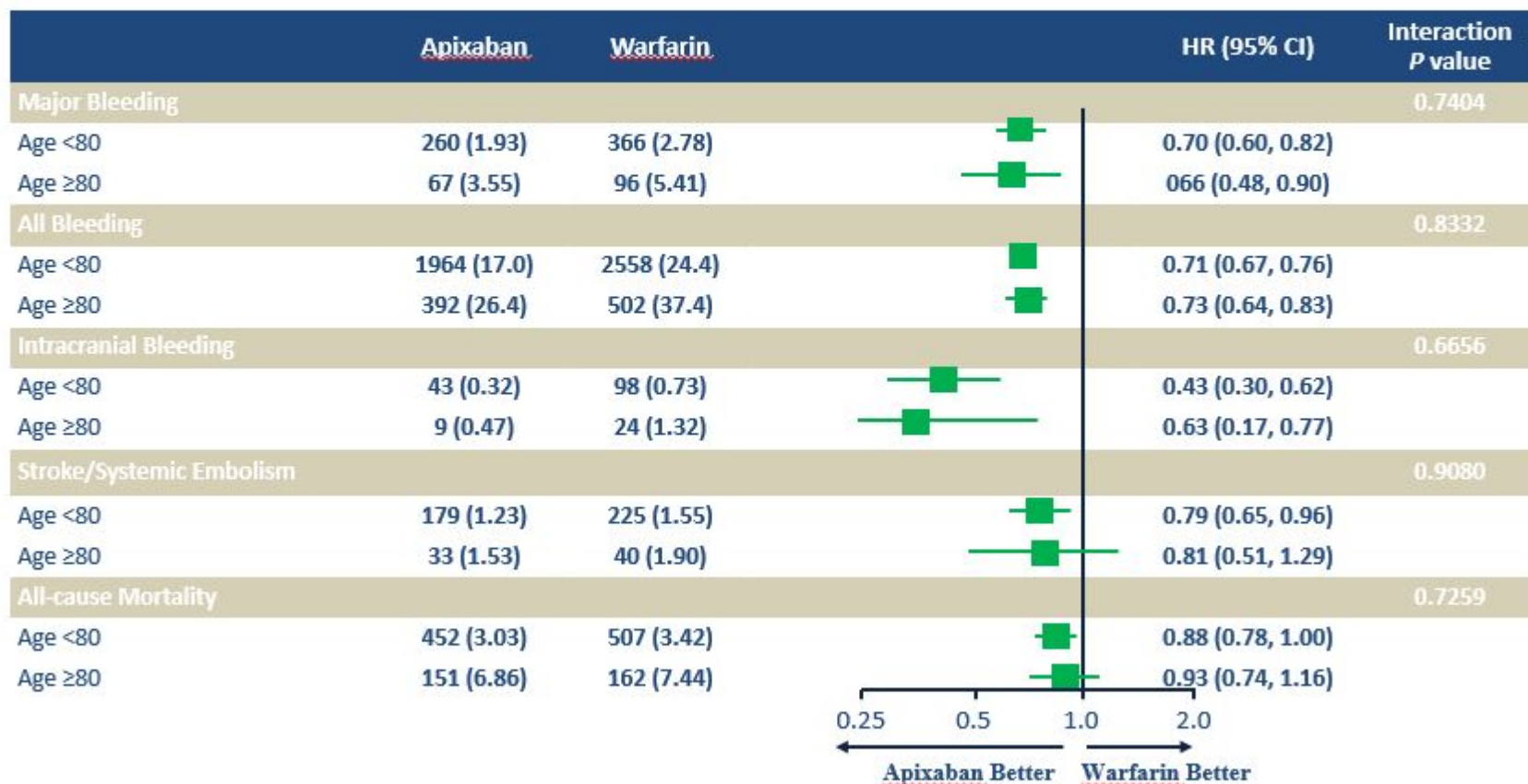
**Efficacia e sicurezza di apixaban vs warfarin in rapporto all'età
nella prevenzione dell'ictus in pazienti con fibrillazione atriale:
osservazioni basate sullo studio clinico ARISTOTLE⁴**



Nello studio ARISTOTLE, 2436 pazienti avevano un'età ≥80 anni (13% della popolazione)⁴

ARISTOTLE: Efficacy and safety benefits of apixaban vs. warfarin were consistent in patients ≥ 80 years

2352 patients (13%) were ≥ 80 years of age in ARISTOTLE



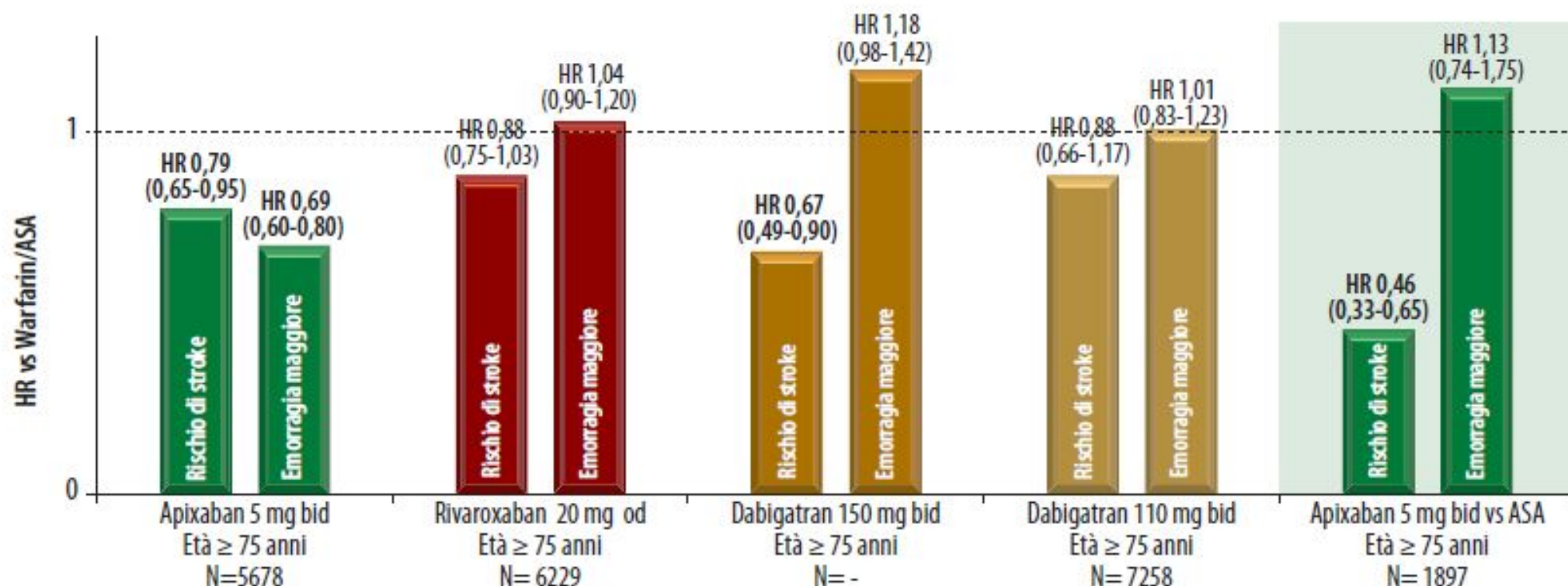
HR, hazard ratio; CI, confidence interval

Adapted from Halvorsen S et al. ACC Congress; March 9-11, 2013; San Francisco, CA.

L'anticoagulazione in pazienti di età ≥ 75 anni con fibrillazione atriale: il ruolo dei nuovi anticoagulanti orali⁵

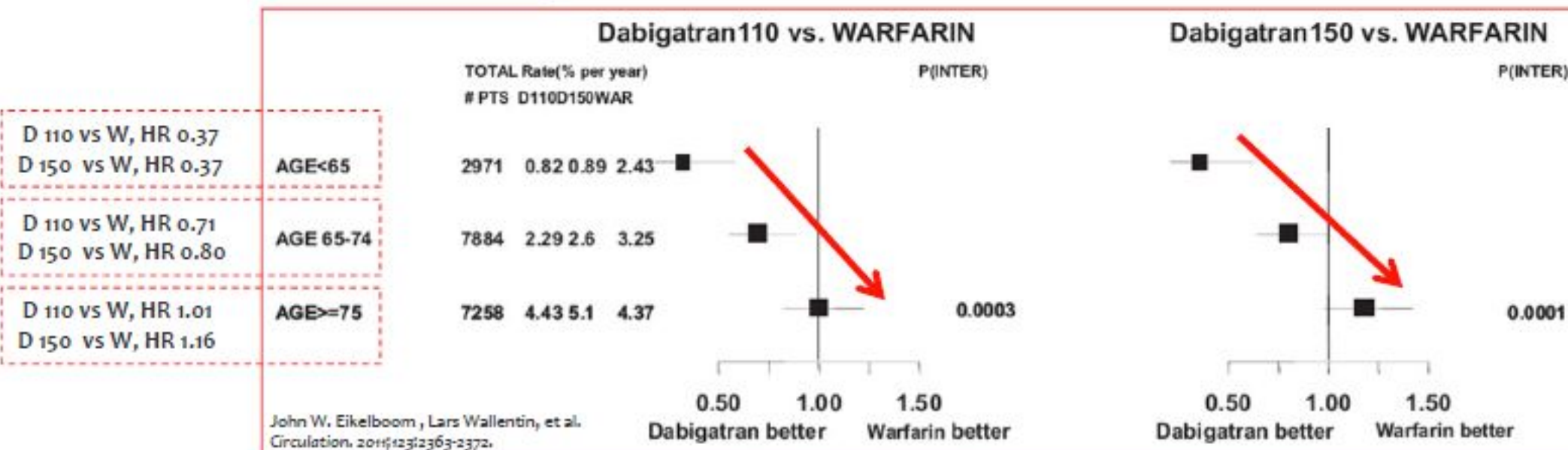
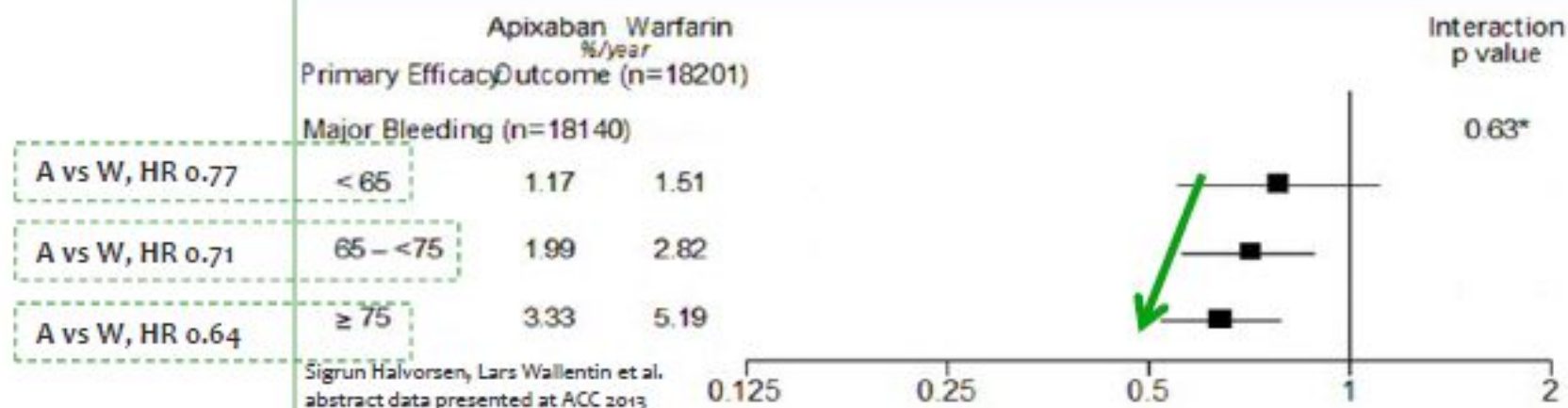
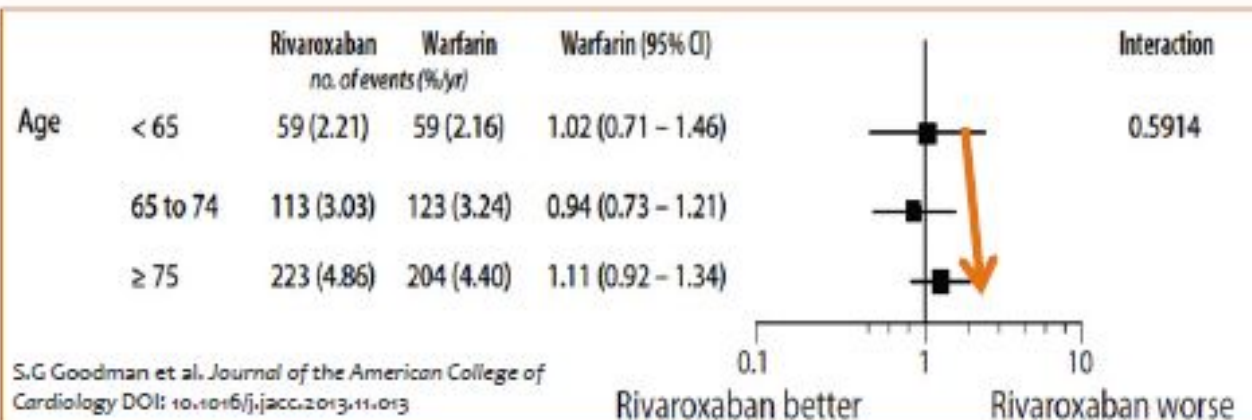
- L'età avanzata incrementa il rischio di emorragia maggiore con antagonisti della vitamina K⁶

CONFRONTO TRA I NUOVI ANTICOAGULANTI IN PAZIENTI ≥ 75 ANNI NEI RISPETTIVI TRIALS VS WARFARIN⁵



- Quando confrontato con warfarin, apixaban è risultato più efficace nel ridurre gli ictus e la mortalità per tutte le cause e aveva un minor rischio di sanguinamento maggiore senza significative interazioni con l'età⁵

RELAZIONE SANGUINAMENTO MAGGIORE - ETA'



Prevention

Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: part 2

Hans-Christoph Diener^{1*}, James Aisenberg², Jack Ansell³, Dan Atar⁴, Günter Breithardt⁵, John Eikelboom⁶, Michael D. Ezekowitz^{7,8,9}, Christopher B. Granger¹⁰, Jonathan L. Halperin¹¹, Stefan H. Hohnloser¹², Elaine M. Hylek¹³, Paulus Kirchhof^{14,15}, Deirdre A. Lane¹⁶, Freek W.A. Verheugt¹⁷, Roland Veltkamp¹⁸, and Gregory Y.H. Lip^{19,20}

Table 2 Major haemorrhage by age subgroups

	No. of events (%/year)	No. of events (%/year)	Hazard ratio (95% CI)	P-value
ARISTOTLE	Apixaban 5 mg twice daily	Warfarin		
<65	56 (1.2)	72 (1.5)	0.78 (0.55–1.11)	0.63
65 to <75	120 (2.0)	166 (2.8)	0.71 (0.56–0.89)	
≥75	151 (3.3)	224 (5.2)	0.64 (0.52–0.79)	
RE-LY	Dabigatran 110 mg twice daily	Warfarin		
<75	138 (1.89)	215 (3.04)	0.62 (0.50–0.77)	0.0003
≥75	204 (4.43)	206 (4.37)	1.01 (0.83–1.23)	
	Dabigatran 150 mg	Warfarin		
<75	153 (2.12)	215 (3.04)	0.70 (0.57–0.86)	0.0001
≥75	246 (5.10)	206 (4.37)	1.18 (0.98–1.42)	
ROCKET AF	Rivaroxaban 20 mg once daily	Warfarin		
<65	59 (2.21)	59 (2.16)	1.02 (0.71–1.46)	0.59
65 to <75	113 (3.03)	123 (3.24)	0.94 (0.73–1.21)	
≥75	223 (4.86)	204 (4.40)	1.11 (0.92–1.34)	
ENGAGE AF-TIMI	Edoxaban 60 mg once daily	Warfarin		
<75	(2.02)	(2.62)		0.57
≥75	(4.01)	(4.83)		

The trials were different in the baseline risk for bleeding complications.

A nationwide registry study to compare bleeding rates in patients with atrial fibrillation being prescribed oral anticoagulants

Sigrun Halvorsen^{1,2*}, Waleed Ghanima^{2,3}, Ingunn Fride Tvette⁴, Cecilie Hoxmark⁵, Pål Falck⁶, Oddvar Solli⁶, and Christian Jonasson⁷

¹Department of Cardiology, Oslo University Hospital Ullevål, Oslo, Norway; ²Institute of Clinical Medicine, University of Oslo, Oslo, Norway; ³Department of Hematology, Østfold Hospital, Kalnes, Norway; ⁴Norwegian Computing Center, Oslo, Norway; ⁵Bristol-Myers Squibb Norway AS, Oslo, Norway; ⁶Pfizer AS, Oslo, Norway; and ⁷HUNT Research Center, Faculty of Medicine, NTNU—Norwegian University of Science and Technology, Trondheim, Norway

Received and revised on 21 September 2016; accepted 21 September 2016; online publish-ahead-of-print 27 September 2016

OAC	IR	HR (95% CI)	P
Major or CRNM			
Warfarin	14.64	1 (ref.)	
Dabigatran	10.00	0.84 (0.72,0.99)	0.036
Rivaroxaban	14.68	1.14 (0.99,1.30)	0.067
Apixaban	10.82	0.72 (0.61,0.86)	<0.001

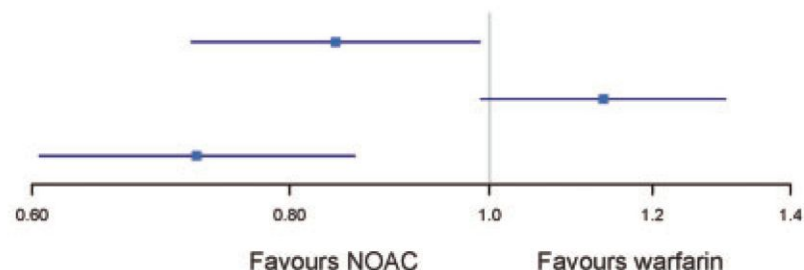
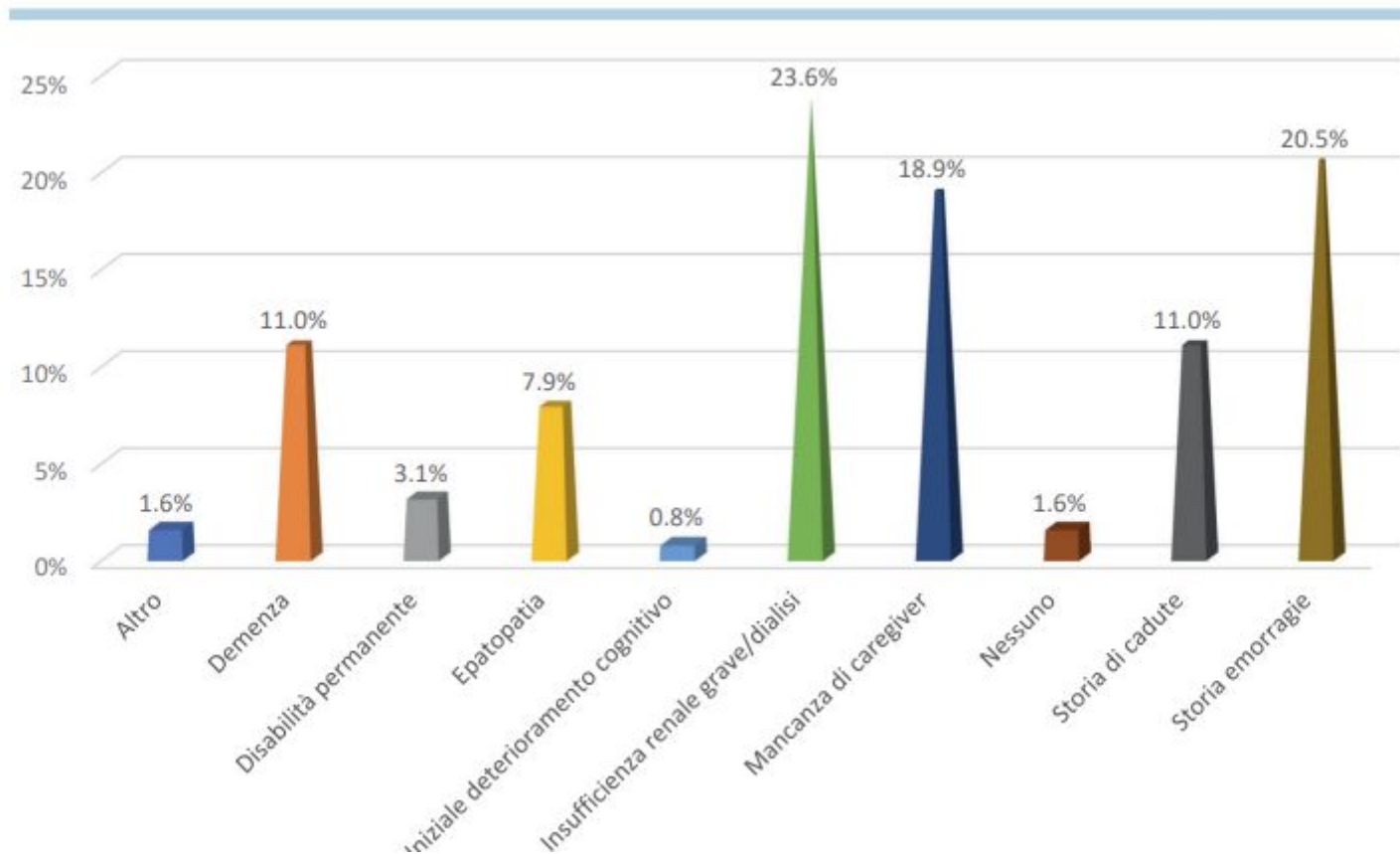


Figure 5 Risk of major or CRNM bleeding for dabigatran, rivaroxaban, and apixaban compared with warfarin in the subgroup of patients ≥ 75 years. Crude IR for first bleeding episode are given as events per 100 person-years. CI, confidence interval; CRNM, clinically relevant non-major bleeding; HR, adjusted hazard ratio; IR, incidence rate; OAC, oral anticoagulant.

Percorso clinico decisionale nel paziente anziano fragile con fibrillazione atriale: la proposta di un gruppo di lavoro multidisciplinare

Niccolò Marchionni¹, Stefano Fumagalli², Mario Bo³, Alessandro Boccanelli⁴, Giuseppe Boriani⁵,
Andrea Rubboli⁶, Francesco Violi⁷, Giuseppe Di Pasquale⁸

potenziale controindicazione all'uso degli anticoagulanti



Criteri proposti per la prescrizione degli anticoagulanti orali diretti in pazienti anziani con fibrillazione atriale sulla base di una sommaria valutazione multidimensionale

Fit, completa autonomia

RACCOMANDATA
Indipendentemente dall'età

Fenotipo fragile o pre-fragile, CFS <5
Autonomia preservata (B-ADL <2)
Impairment cognitivo (MMSE >18/30)

DA CONSIDERARE

Severo deterioramento cognitivo (MMSE <18) e/o
perdita di autonomia (B-ADL >2)
e/o ridotta aspettanza di vita (CFS >6)
Nessuna evidenza di beneficio clinico

SCORAGGIATA

Raccomandazioni

- Un rapido screening cognitivo (SPMSQ) è consigliabile in tutti gli anziani con FA, per valutarne la potenziale aderenza alla terapia ed eventualmente identificare un “responsabile” della cura e del follow-up.
- Una formale valutazione delle comorbidità non è indispensabile, ma occorre identificare specifiche patologie associate a cattiva prognosi a breve termine.
- Uno screening del livello di autonomia nelle funzioni di base (BADL) è importante sia per la valutazione prognostica che per la definizione del beneficio atteso dalla TAO.
- Strumenti di facile uso per l'identificazione dei pazienti anziani con ridotta aspettanza di vita (es. CFS), soprattutto se associata a perdita di autonomia o severo deterioramento cognitivo, permettono di identificare quei pazienti per i quali non vi è evidenza di beneficio clinico netto con la TAO.

HAS-BLED

CHA ₂ DS ₂ -VASc risk factor	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left ventricular ejection fraction	+1
Hypertension Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment	+1
Age 75 years or older	+2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin	+1
Previous stroke, transient ischaemic attack, or thromboembolism	+2
Vascular disease Previous myocardial infarction, peripheral artery disease, or aortic plaque	+1
Age 65–74 years	+1
Sex category (female)	+1

Letter	Clinical Characteristic	Points
H	Hypertension	1
A	Abnormal Liver or Renal Function	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INR	1
E	Elderly (age > 65)	1
D	Drugs or Alcohol	1 or 2
Maximum Score		9

Take-home messages

- La tachicardiomiopatia è una condizione frequente con la FA come principale causa
- Va considerata soprattutto in pazienti con FA e IC di recente insorgenza senza altra causa nota
- L'IC è, per definizione, almeno parzialmente reversibile dopo trattamento dell'aritmia
- In caso di FA, non sono stati dimostrati benefici con terapia medica con una strategia di controllo del ritmo rispetto al controllo della frequenza cardiaca
- La terapia elettrica può dare risultati migliori soprattutto se eseguita precocemente
- E' auspicabile un controllo della frequenza cardiaca su valori $\leq 90/\text{min}$

Take-home messages

- se il paziente anziano “merita” la terapia anticoagulante con i DOAC, questa dovrebbe essere prescritta alla dose appropriata secondo le raccomandazioni delle società scientifiche
- non vi è infatti alcun segnale di maggior sicurezza ma, al contrario, di ridotta efficacia nella prevenzione dell'ictus con l'uso inappropriato di basse dosi nell'anziano, come nel resto della popolazione generale