La fibrillazione atriale non-valvolare: Clinica, diagnosi differenziale, trattamento

Giuseppe Ambrosio - Perugia

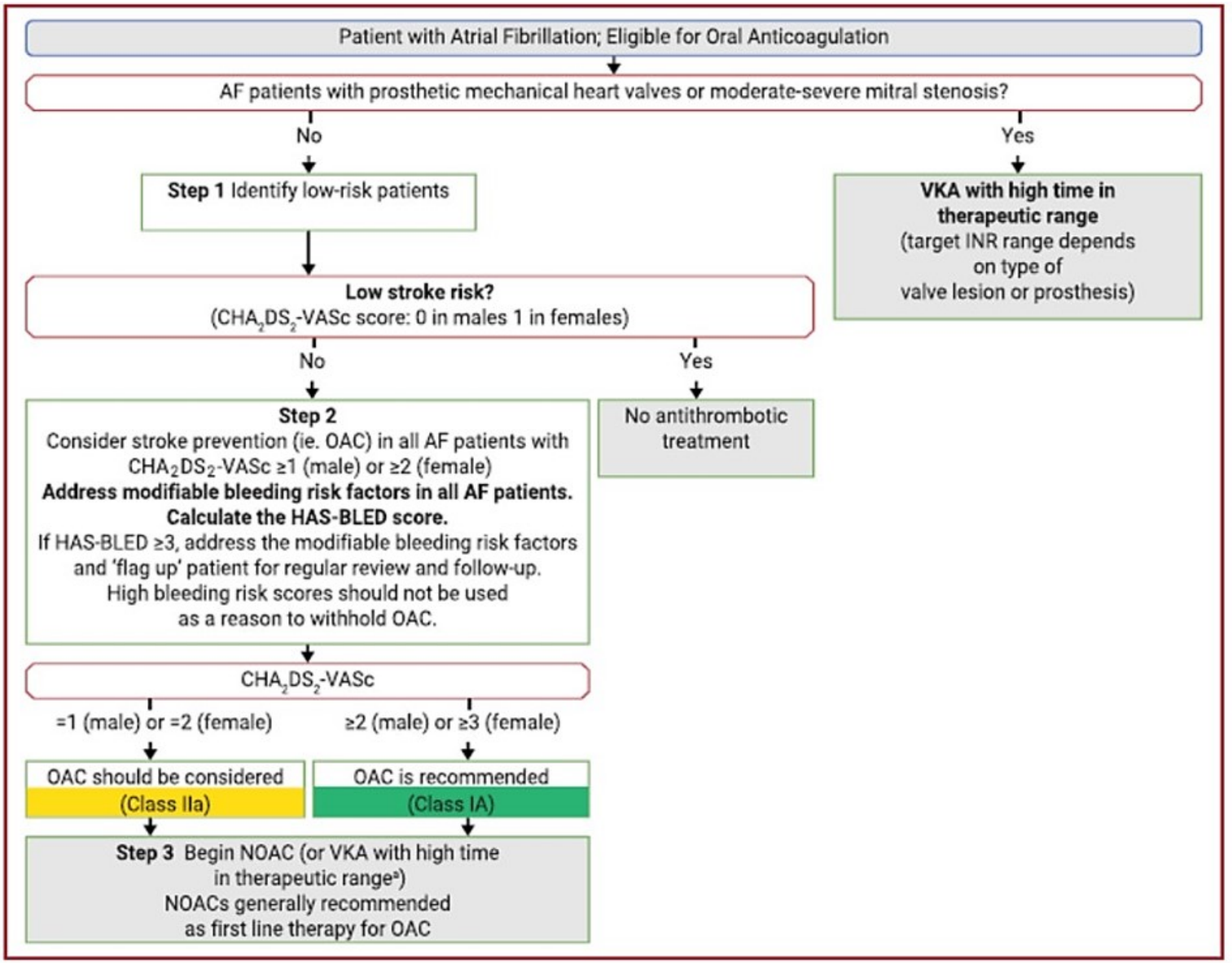
Nota AIFA 97

La diagnosi di fibrillazione atriale valvolare comprende i portatori di valvulopatia su base reumatica, sostanzialmente (sic…) la stenosi mitralica moderata o grave.

Non sembra esserci correlazione fra la scelta dell'anticoagulante e il rischio trombo embolico nella insufficienza mitralica e nella valvulopatia aortica.

Ma anche…
… protesi valvolari meccaniche ….!

ESC European Society of Cardiology
European Heart Journal (2020) 00, 1–125
doi:10.1093/eurheartj/ehaa612



Fibrillazione Atriale – NOAC

Il bilancio tra rischio trombo-embolico e rischio di sanguinamento

CHA_2DS_2-VASc Score

- 1 point for Congestive Heart Failure/ LV Dysfunction
- 1 point for Hypertension
- 1 point for Age 65-74 years
- 2 points for Age ≥ 75 years
- 1 point for Diabetes Mellitus
- 2 points for Prior Stroke or TIA[1] or TE[2]
- 1 point for Vascular Disease[3]
- 1 point for Sex category (female gender)

CHA_2DS_2-VASc Score*	One year event rate (95% CI) of hospital admission and death due to thromboembolism† per 100 person years
0	0.78 (0.78 – 1.04)
1	2.01 (1.70 – 2.36)
2	3.71 (3.36 – 4.09)
3	5.92 (5.53 – 6.34)
4	9.27 (8.71 – 9.86)
5	15.26 (14.35 – 16.24)
6	19.74 (18.21 – 21.41)
7	21.5 (18.75 – 24.64)
8	22.38 (16.29 – 30.76)
9	23.64 (10.62 – 52.61)

*Score 0: Patients can be administered aspirin
*Score 1: Patients can be administered aspirin or anticoagulant therapy
*Score ≥2: Patients should be administered anticoagulant therapy
†Includes peripheral artery embolism, ischemic stroke, and pulmonary embolism

[1]TIA = Transient ischemic attack; [2]TE = Thromboembolism
[3]Prior myocardial infarction, peripheral artery disease, aortic plaque

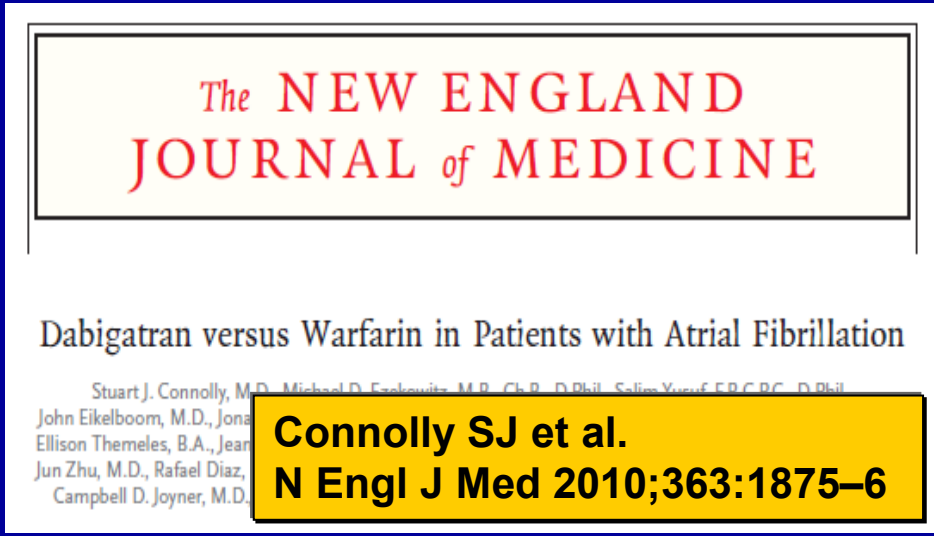
1. Lip GY et al. Chest 2010;137:263-272
2. Olesen JB, et al. BMJ 2011;342:d124
3. Task Force or the Management of Atrial Fibrillation of the ESC. Eur Heart J 2010;31:236902429

Redefining Risk: HAS-BLED

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

ESC Guidelines: *Eur Heart J*. 2010;31:2369-2429

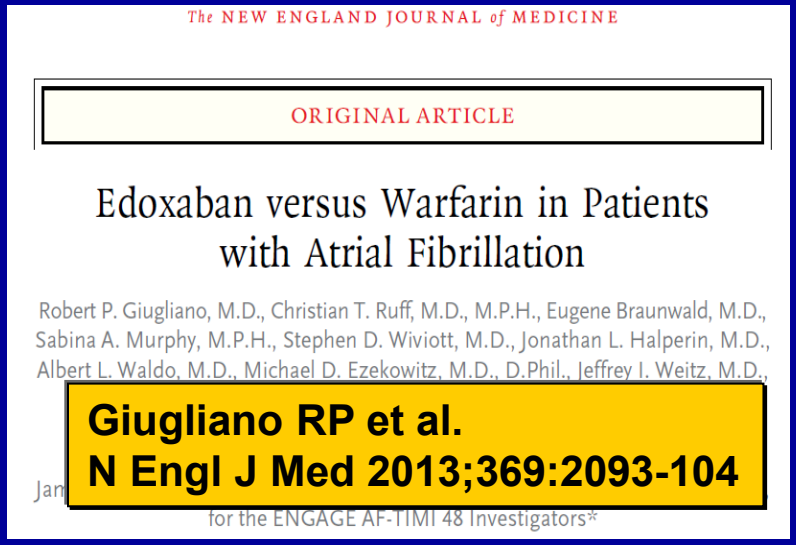
Pisters R, et al. Chest 2010; 138(5): 1093-1100


The NEW ENGLAND JOURNAL of MEDICINE

Dabigatran versus Warfarin in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., Michael D. Ezekowitz, M.B., Ch.B., D.Phil., Salim Yusuf, F.R.C.P.C., D.Phil., John Eikelboom, M.D., Jona... Ellison Themeles, B.A., Jean... Jun Zhu, M.D., Rafael Diaz, ... Campbell D. Joyner, M.D.

Connolly SJ et al.
N Engl J Med 2010;363:1875–6


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

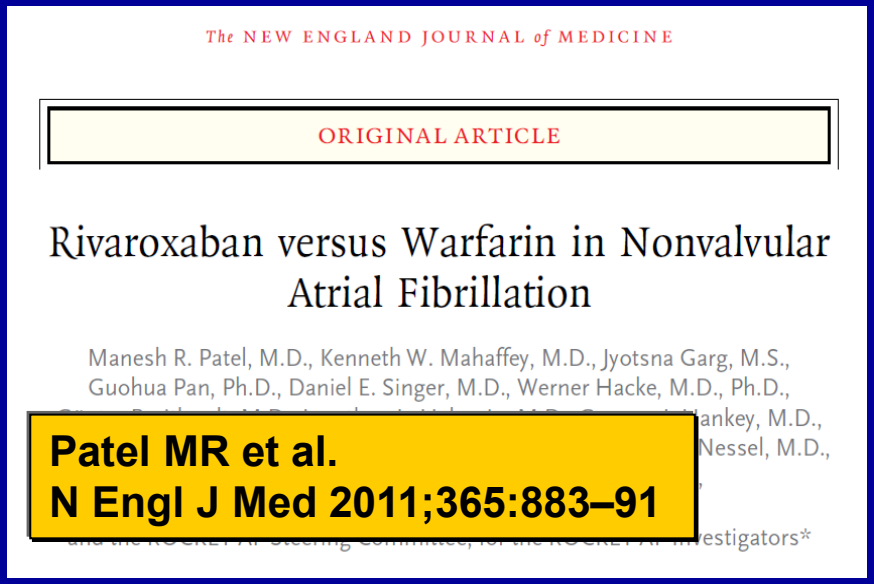
Edoxaban versus Warfarin in Patients with Atrial Fibrillation

Robert P. Giugliano, M.D., Christian T. Ruff, M.D., M.P.H., Eugene Braunwald, M.D., Sabina A. Murphy, M.P.H., Stephen D. Wiviott, M.D., Jonathan L. Halperin, M.D., Albert L. Waldo, M.D., Michael D. Ezekowitz, M.D., D.Phil., Jeffrey I. Weitz, M.D., Jan...

for the ENGAGE AF-TIMI 48 Investigators*

Giugliano RP et al.
N Engl J Med 2013;369:2093-104

I 4 Grandi Trials…


The NEW ENGLAND JOURNAL of MEDICINE

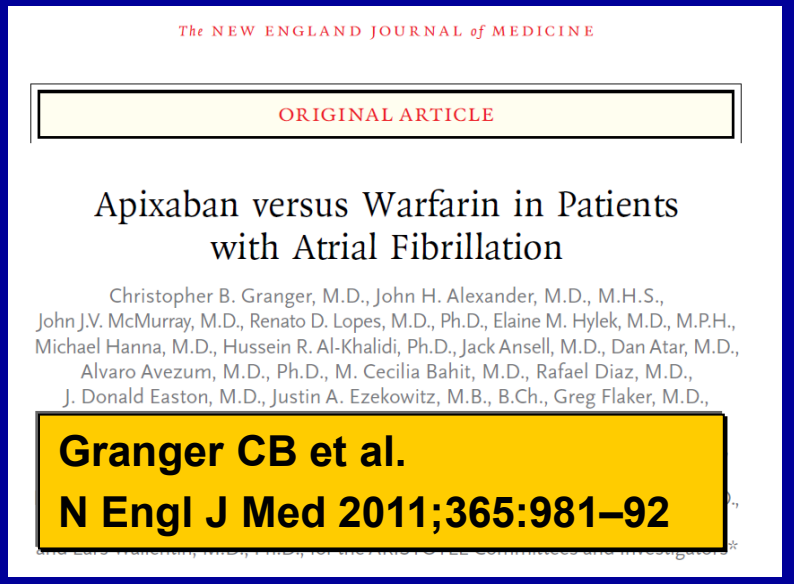
ORIGINAL ARTICLE

Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation

Manesh R. Patel, M.D., Kenneth W. Mahaffey, M.D., Jyotsna Garg, M.S., Guohua Pan, Ph.D., Daniel E. Singer, M.D., Werner Hacke, M.D., Ph.D., ...ankey, M.D., ...Nessel, M.D., ...

...estigators*

Patel MR et al.
N Engl J Med 2011;365:883–91


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Apixaban versus Warfarin in Patients with Atrial Fibrillation

Christopher B. Granger, M.D., John H. Alexander, M.D., M.H.S., John J.V. McMurray, M.D., Renato D. Lopes, M.D., Ph.D., Elaine M. Hylek, M.D., M.P.H., Michael Hanna, M.D., Hussein R. Al-Khalidi, Ph.D., Jack Ansell, M.D., Dan Atar, M.D., Alvaro Avezum, M.D., Ph.D., M. Cecilia Bahit, M.D., Rafael Diaz, M.D., J. Donald Easton, M.D., Justin A. Ezekowitz, M.B., B.Ch., Greg Flaker, M.D., ...

Granger CB et al.
N Engl J Med 2011;365:981–92

Profilo di Rischio Tromboembolico ed Emorragico (Rispetto al Warfarin)

	Dabigatran 150 mg	Dabigatran 110 mg	Rivaroxaban	Apixaban	Edoxaban 60 mg	Edoxaban 30 mg
	RE-LY		ROCKET-AF	ARISTOTLE	ENGAGE-AF TIMI 51	
Stroke/SE: Non inferiorità	Dimostrata *HR 0.66 (0.53-0.82)*	Dimostrata *HR 0.90 (0.74-1.10)*	Dimostrata *HR 0.79 (0.66-0.96)*	Dimostrata *HR 0.79 (0.66-0.95)*	Dimostrata *HR 0.79 (0.63-0.99)*	Dimostrata *HR 1.07 (0.87-1.31)*
Stroke/SE: Superiorità	Dimostrata *HR 0.66 (0.53-0.82)*			Dimostrata *HR 0.79 (0.66-0.95)*		
Riduzione ictus emorragico	Dimostrata *HR 0.26 (0.14-0.49)*	Dimostrata *HR 0.31 (0.17-0.56)*	Dimostrata *HR 0.59 (0.37-0.93)*	Dimostrata *HR 0.51 (0.35-0.75)*	Dimostrata *HR 0.54 (0.38-0.77)*	Dimostrata *HR 0.33 (0.22-0.50)*
Riduzione emorragie cerebrali	Dimostrata *HR 0.41 (0.28-0.60)*	Dimostrata *HR 0.30 (0.19-0.45)*	Dimostrata *HR 0.67 (0.47-0.93)*	Dimostrata *HR 0.42 (0.38-0.58)*	Dimostrata *HR 0.47 (0.34-0.63)*	Dimostrata *HR 0.30 (0.21-0.43)*
Riduzione ictus ischemico	Dimostrata *HR 0.76 (0.59-0.97)*					
Riduzione mortalità totale				Dimostrata *HR 0.89 (0.80-0.998)*		Dimostrata *HR 0.87 (0.79-0.96)*
Riduz. mortalità cardiovascolare	Dimostrata *HR 0.85 (0.72-0.99)*				Dimostrata *HR 0.86 (0.77-0.97)*	Dimostrata *HR 0.85 (0.76-0.96)*
Riduz. emorragie maggiori		Dimostrata *HR 0.80 (0.70-0.93)*		Dimostrata *HR 0.57 (0.46-0.70)*	Dimostrata *HR 0.80 (0.71-0.91)*	Dimostrata *HR 0.47 (0.41-0.55)*
Riduz. emorragie fatali		Dimostrata *HR 0.58 (0.35-0.97)*	Dimostrata *HR 0.50 (0.31-0.79)*	Dimostrata *HR 0.50 (0.33-0.74)*	Dimostrata *HR 0.55 (0.36-0.84)*	Dimostrata *HR 0.35 (0.21-0.57)*
Riduz. emorragie intestinali						Dimostrata *HR 0.67 (0.53-0.83)*

TRI Thrombosis Research Institute

Garfield
global anticoagulant registry in the field

GARFIELD:
Antithrombotic therapy in the context of today's clinical practice of A-Fib

The Global Anticoagulant Registry in the Field:
Research network in 34 countries; n = 60,000

Italy active sites - 48 n >2,000

Professor Ambrosio
Italy Coordinator

Heart Online First, published on September 19, 2016 as 10.1136/heartjnl-2016-309832

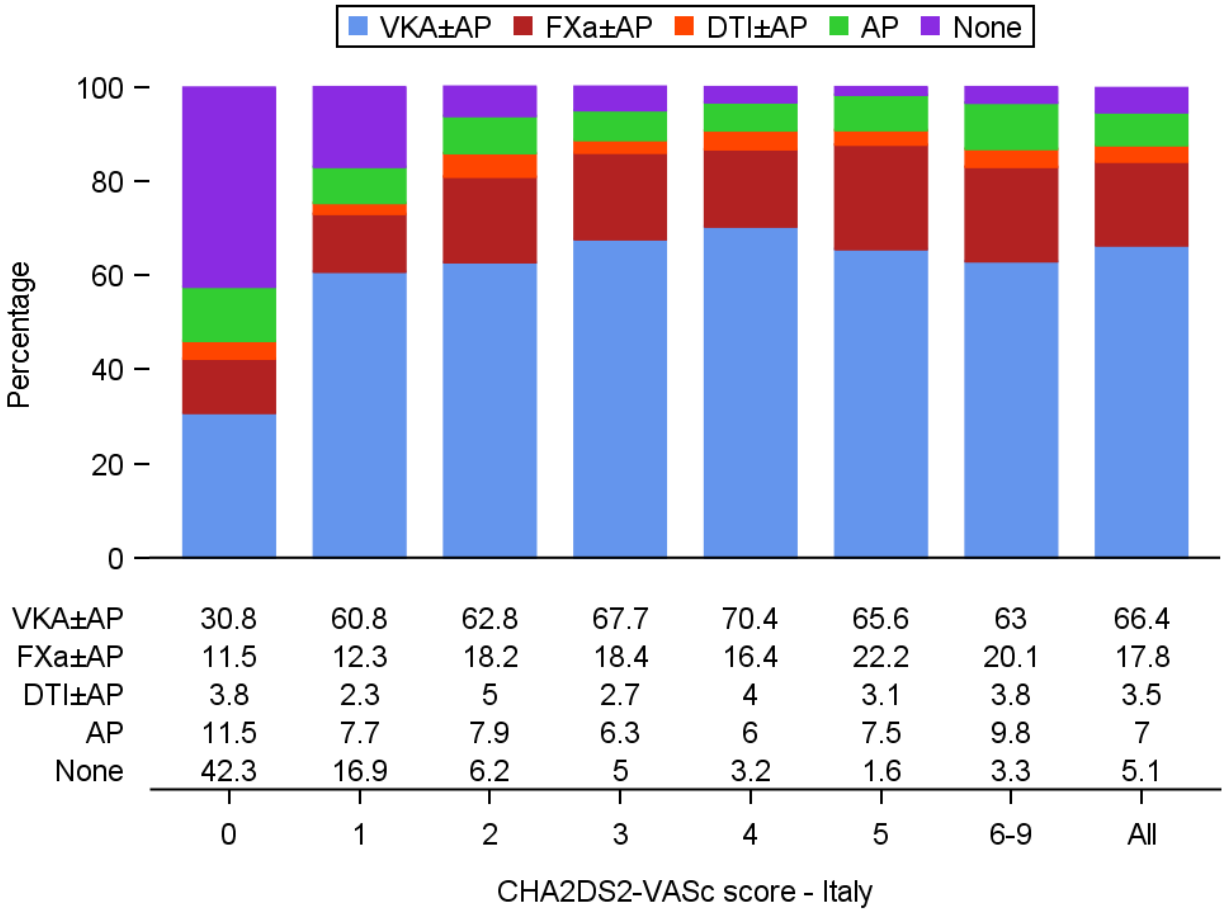
OPEN ACCESS

ORIGINAL ARTICLE

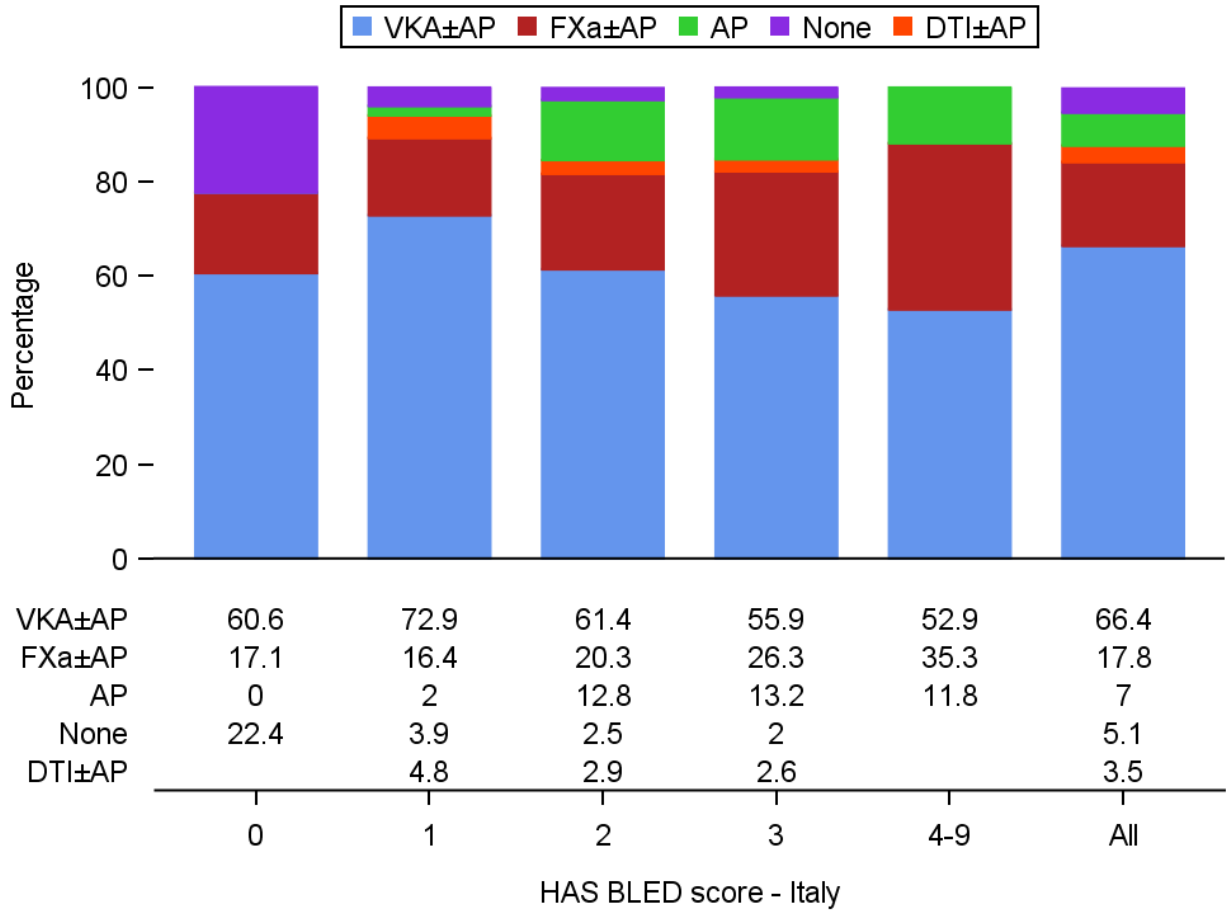
Evolving antithrombotic treatment patterns for patients with newly diagnosed atrial fibrillation

A John Camm,[1] Gabriele Accetta,[2] Giuseppe Ambrosio,[3] Dan Atar,[4,5] Jean-Pierre Bassand,[6] Eivind Berge,[7] Frank Cools,[8] David A Fitzmaurice,[9] Samuel Z Goldhaber,[10] Shinya Goto,[11] Sylvia Haas,[12] Gloria Kayani,[2] Yukihiro Koretsune,[13] Lorenzo G Mantovani,[14] Frank Misselwitz,[15] Seil Oh,[16] Alexander G G Turpie,[17] Freek W A Verheugt,[18] Ajay K Kakkar,[2,19] for the GARFIELD-AF Investigators

Treatment of newly diagnosed AF in Italy by CHA_2DS_2-VASc score



Treatment of newly diagnosed AF in Italy by HAS-BLED score



Prospective Cohorts 1–5. Italy: N=1685/2191

Clinical Outcomes in Asymptomatic and Symptomatic Atrial Fibrillation Presentations in GARFIELD-AF: Implications for AF Screening

Harry Gibbs, MB PhD,[a] Ben Freedman, MB PhD,[b] Marten Rosenqvist, PhD,[c] Saverio Virdone, MSc,[d] Wael Al Mahmeed, MD,[e] Giuseppe Ambrosio, MD, PhD,[f] A. John Camm, MD,[g] Barry Jacobson, MD,[h] Carlos Jerjes-Sanchez, MD,[i] Gloria Kayani,[d] Ali Oto, MD,[j] Elizaveta Panchenko, PhD,[k] Hany Ragy, MD,[l] Ajay K. Kakkar, PhD[d,m], for the GARFIELD-AF Investigators *

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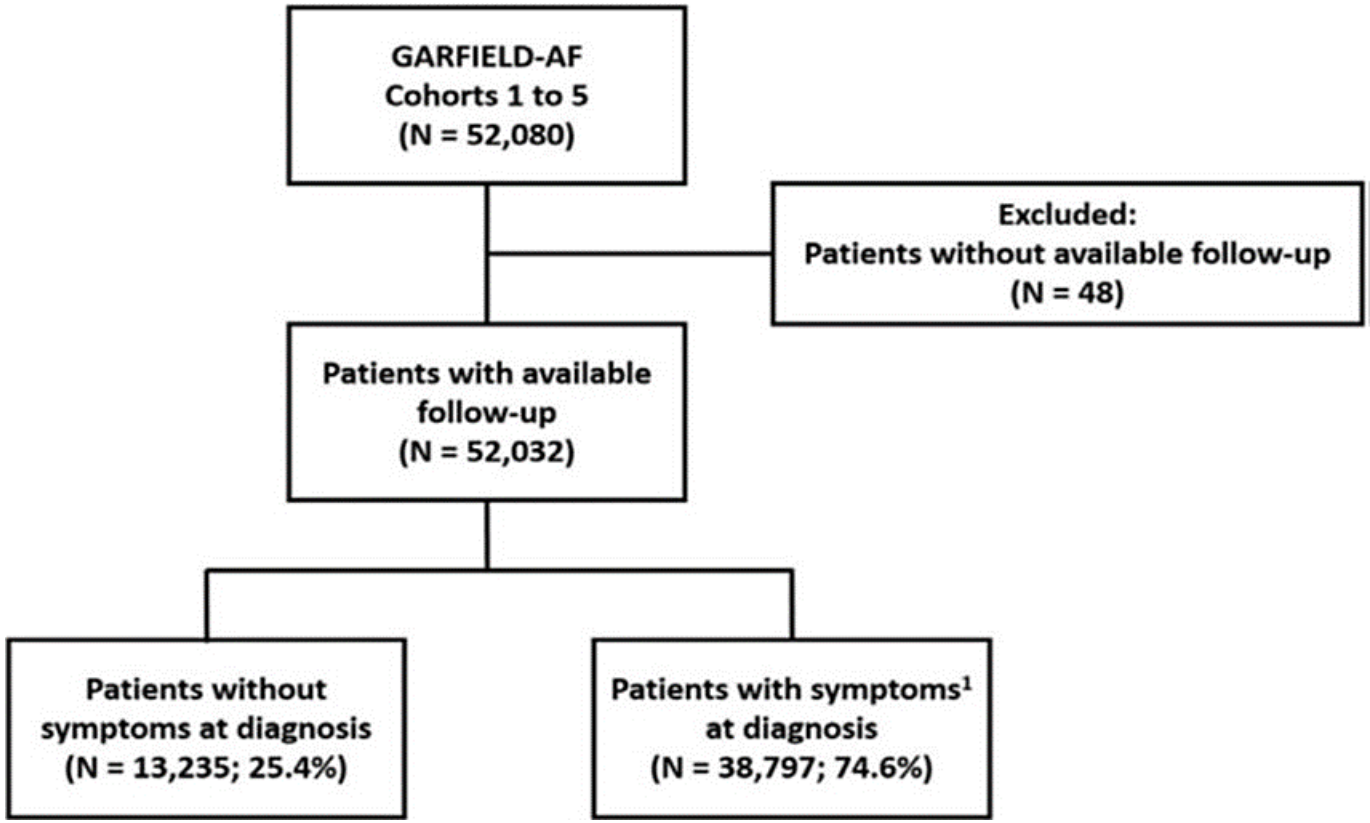
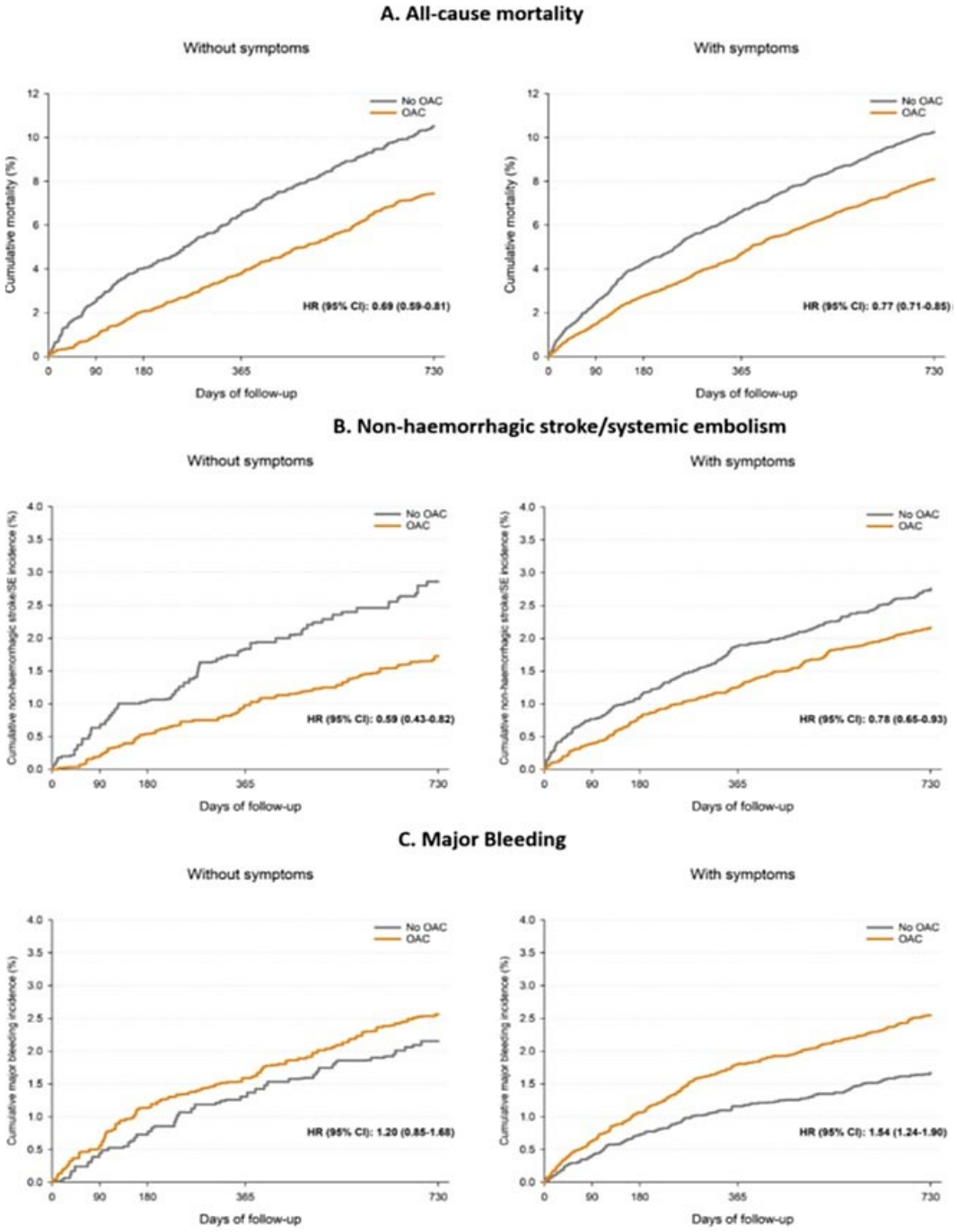
2021





Major outcomes do not differ between asymptomatic and symptomatic atrial fibrillation presentation, and are comparably reduced by anticoagulation.

Opportunistic screening-detected asymptomatic atrial fibrillation likely has the same prognosis as asymptomatic atrial fibrillation at presentation;

It likely responds similarly to anticoagulation thromboprophylaxis.

Outcomes in Newly Diagnosed Atrial Fibrillation and History of Acute Coronary Syndromes: Insights from GARFIELD-AF

Freek W.A. Verheugt, MD, PhD,[a] Giuseppe Ambrosio, MD, PhD,[b] Dan Atar, MD, PhD,[c] Jean-Pierre Bassand, MD,[d,e] A. John Camm, MD,[f] Juan Pablo Costabel, MD,[g] David A. Fitzmaurice, MBChB, MRCGP, MD,[h] Laura Illingworth, MSc,[e] Samuel Z. Goldhaber, MD,[i] Shinya Goto, MD, PhD,[j] Sylvia Haas, MD,[k] Petr Jansky, MD, PhD,[l] Gloria Kayani, BSc,[e] Janina Stepinska, MD, PhD,[m] Alexander G.G. Turpie, MD,[n] Martin van Eickels, MD,[o] Ajay K. Kakkar, MBBS, PhD[e,p], for the GARFIELD-AF Investigators

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2019

Demographics and clinical characteristics of GARFIELD-AF patients with and without history of ACS

	No ACS (N=46,916)	ACS (N=4914)
Female, %	45.5	31.7
Age at AF diagnosis (years), median	71.0	73.0
Heart failure	18.8	30.3
Coronary artery bypass graft	1.3	21.2
Hypercholesterolaemia	38.9	67.0
Vascular disease	5.7	99.0
Stenting	3.1	42.5
Diabetes mellitus	20.9	33.4

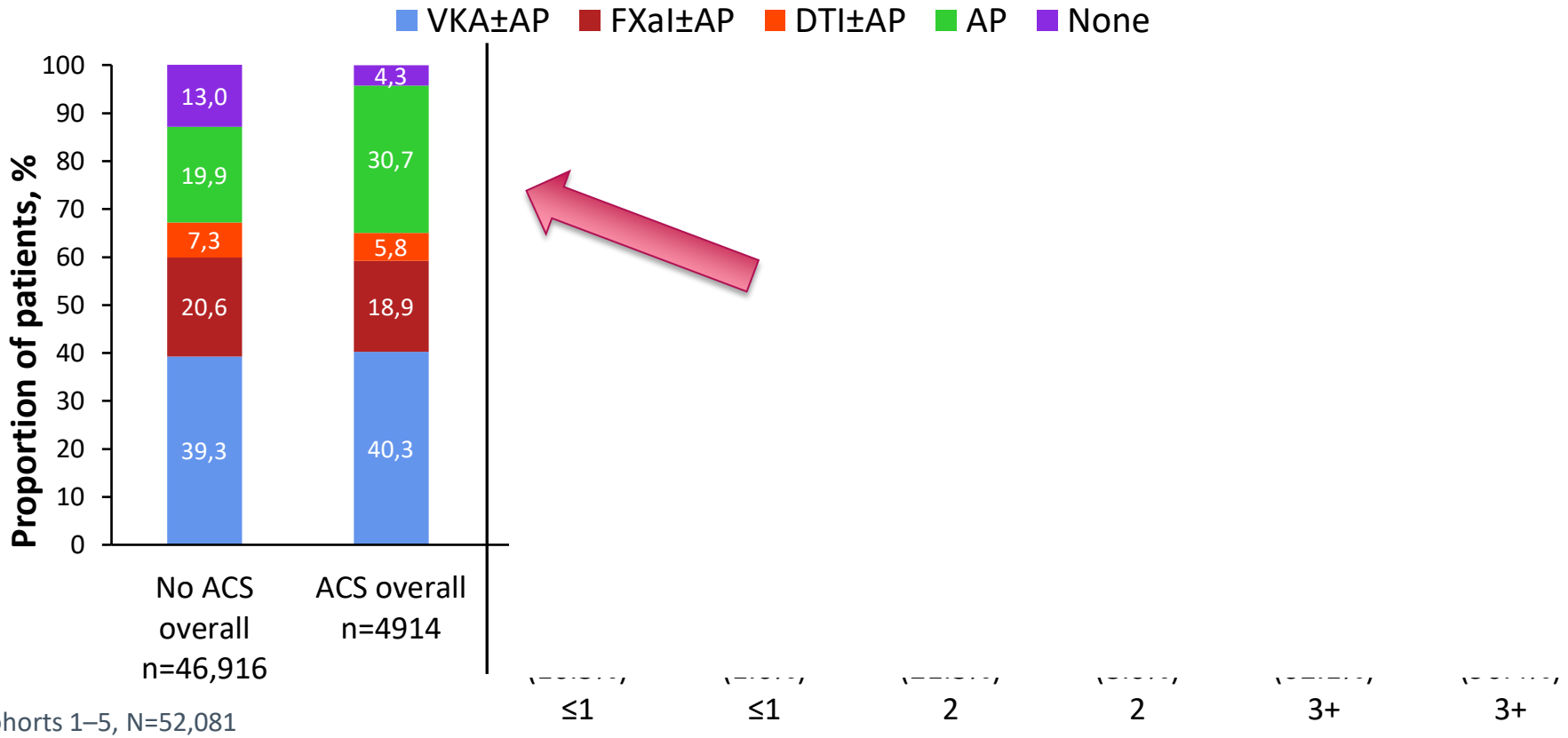
Demographics and clinical characteristics of GARFIELD-AF patients with and without history of ACS cont'd

	No ACS (N=46,916)	ACS (N=4914)
Smoking, %		
Non-smoker	66.7	53.1
Ex-smoker	22.3	36.1
CHA_2DS_2-VASc score, median	3.0	4.0
HAS-BLED score, median	1.0	2.0

Cohorts 1–5, N=52,081

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Antithrombotic therapy at diagnosis in patients with and without history of ACS

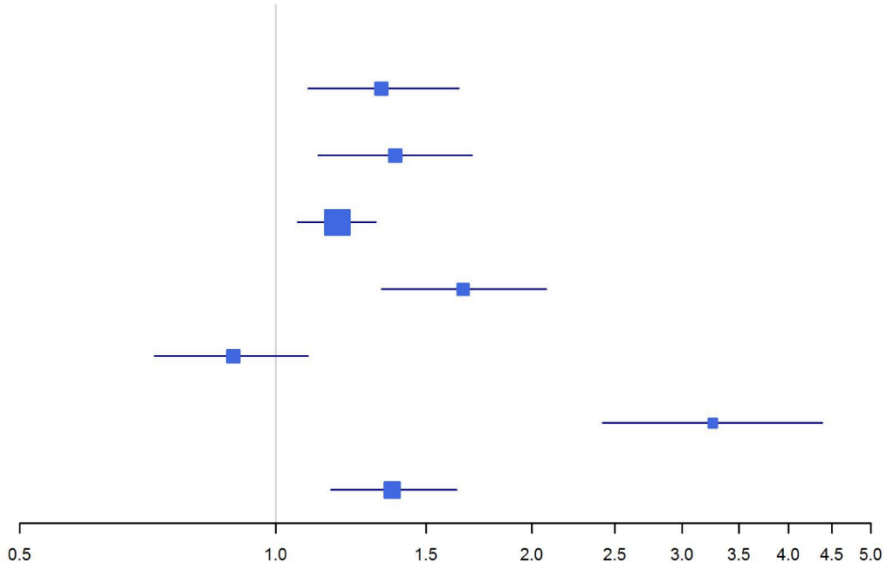


Cohorts 1–5, N=52,081

AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist

Adjusted HRs for 2-year outcomes for patients with *vs.* no history of ACS

Outcomes	n (%)	aHR
Stroke/SE	851 (2.1)	1.33
Major bleeding	503 (1.3)	1.38
All-cause mortality	2744 (6.9)	1.18
Cardiovascular mortality	1012 (2.5)	1.66
Non-cardiovascular mortality	1028 (2.6)	0.89
New ACS	480 (1.2)	3.26
Congestive heart failure	1214 (3.0)	1.37



HRs were adjusted for age group, gender, race, smoking, diabetes, hypertension, previous stroke/TIA/SE, history of bleeding, cardiac failure, peripheral vascular disease, moderate-to-severe renal disease, AC *vs.* no AC treatment, type of AF, and alcohol consumption

Cohorts 1–4, N=39,903

Conclusions

1. GARFIELD-AF registry shows that patients with newly diagnosed atrial fibrillation (AF) and history of acute coronary syndrome (ACS) have worse long-term outcomes
2. They were less likely to receive oral anticoagulation.
3. ACS patients presented with a higher bleeding risk and factors that also increase stroke and mortality risk
4. In patients with AF, with prior ACS, patients are increasingly on combined AP and AC therapy
5. This combined antithrombotic therapy is associated with an increase in bleeding
6. The major contributors to adverse outcomes in patients with AF and prior ACS are cardiovascular death and new ACS
7. These data support the current recommendations to omit any antiplatelet therapy 1 year after the onset of ACS in patients with AF.

Characteristics, treatment, and outcomes of newly diagnosed atrial fibrillation patients with heart failure: GARFIELD-AF

Giuseppe Ambrosio[1]*, A. John Camm[2], Jean-Pierre Bassand[3,4], Ramon Corbalan[5], Gloria Kayani[3], Erberto Carluccio[1], Lorenzo G. Mantovani[6,7], Saverio Virdone[3], Ajay K. Kakkar[3,8] for the GARFIELD-AF Investigators

ESC Heart Failure 2021

Heart failure begets AF and (probably) vice versa

Circulation

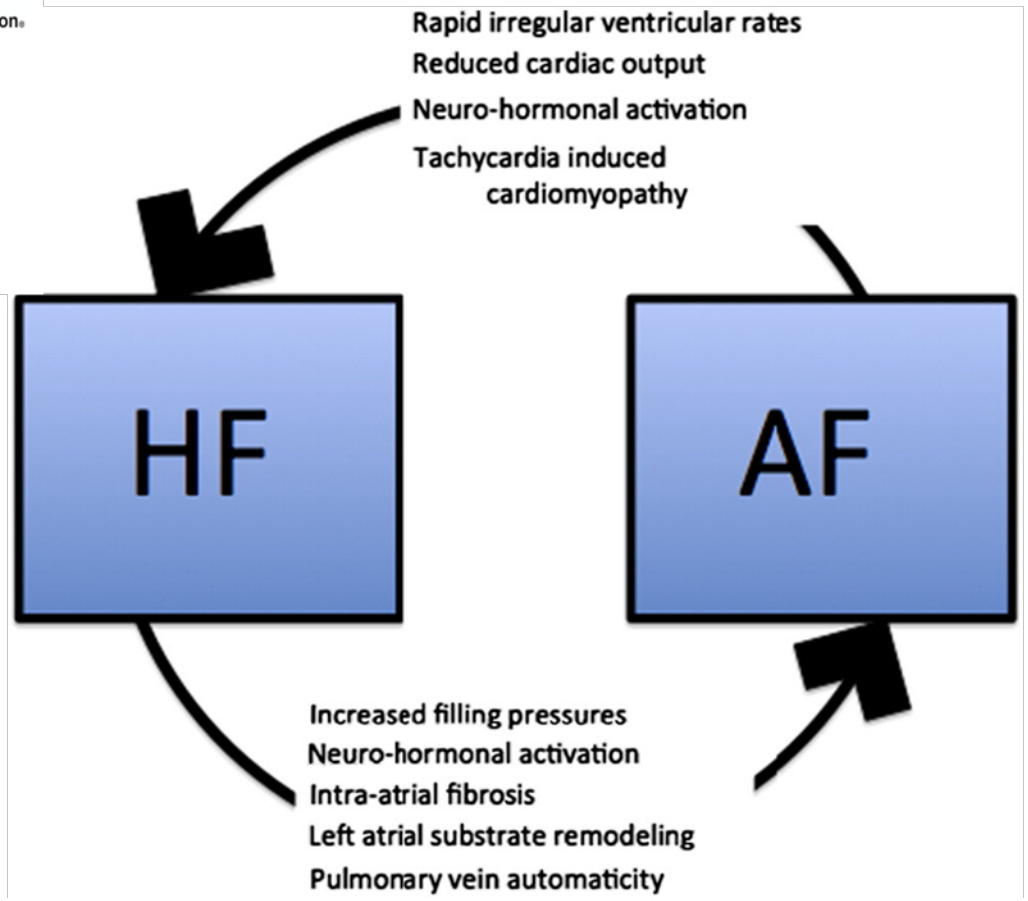
American Heart Association.

Promotion of Atrial Fibrillation by Heart Failure in Dogs: Atrial Remodeling of a Different Sort

Danshi Li, Samir Fareh, Tack Ki Leung and Stanley Nattel

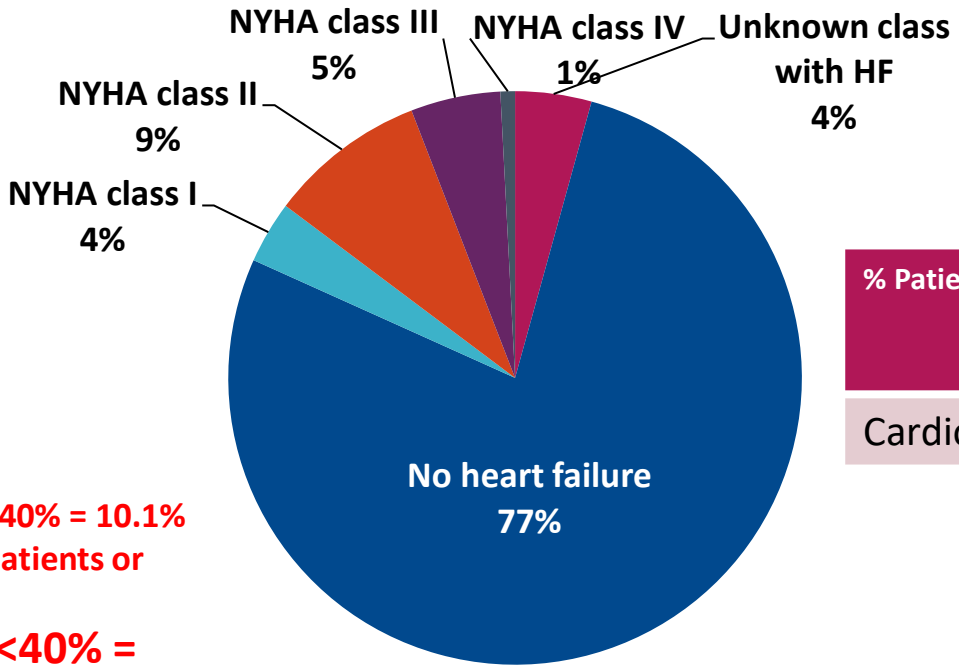
Circulation. 1999;100:87-95
doi: 10.1161/01.CIR.100.1.87
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539



Methods

52,014 patients recruited into GARFIELD-AF
between March 2010 and August 2016
NYHA classification available for 49,773 patients
LVEF available in 58% of patients



% Patients	No HF (n=41,676)	NYHA Class I–II (n=6441)	NYHA Class III–IV (n=3063)
Cardiology %	64.2	70.0	73.7

EF <40% = 10.1% all patients or

EF <40% = 35.6% HF

Cohorts 1–5, N=52,014; NYHA, New York Heart Association

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Clinical characteristics of patients

	No Heart failure N= 40,269	Heart failure N=11,738
Female, %	44.6	42.9
Age at diagnosis median (IQR)	71.0 (63.0 to 78.0)	71.0 (62.0 to 79.0)
Type 2 diabetes, %	21.5	24.4
History of hypertension, %	75.9	77.7
Vascular disease, %	**12.8**	**21.7**
Moderate-to-severe CKD, %	**9.1**	**14.7**
Prior stroke/TIA %	11.6	10.9
History of bleeding %	2.4	3.0
CHA_2DS_2-VASc score, mean (SD)	**2.9 (1.5)**	**4.0 (1.6)**

Cohorts 1–5, N=52,014; NYHA, New York Heart Association

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

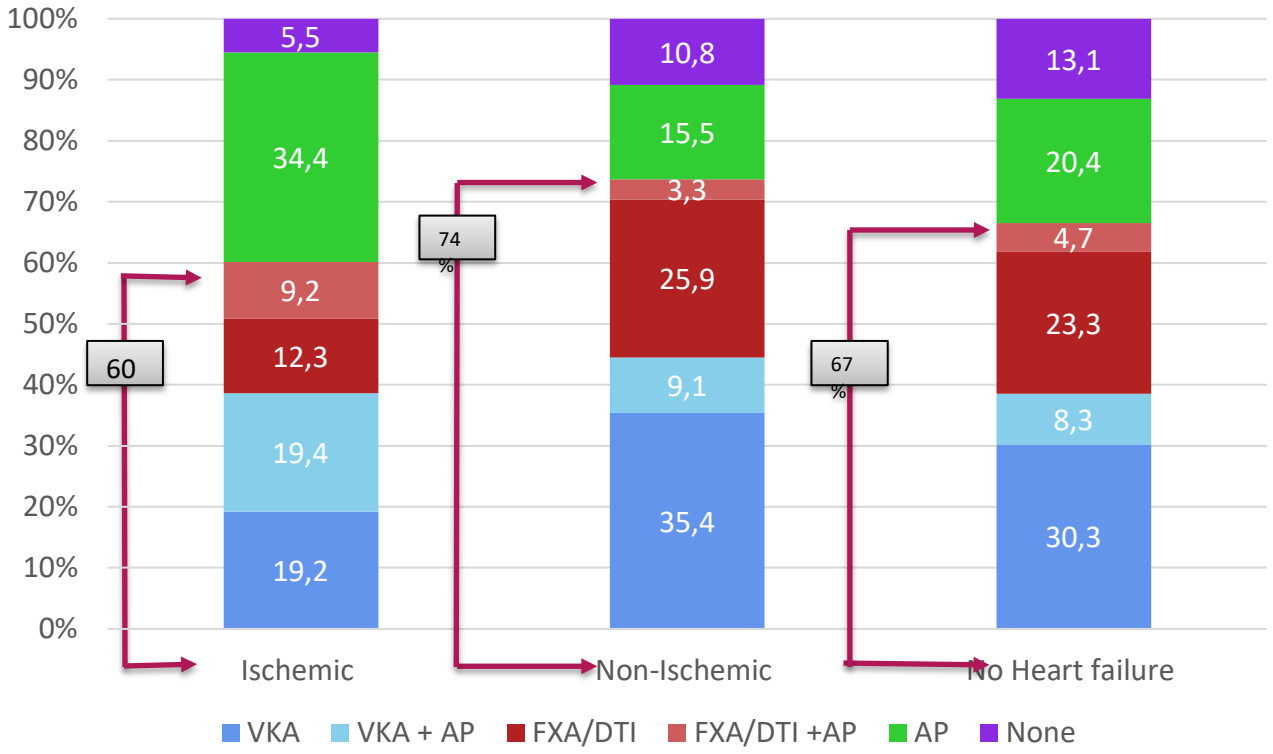
Clinical characteristics of patients

	Ischemic (N= 4,717)	Non-ischemic (N=7,021)	No heart failure (N=40,269)
Female, %	40.3	44.6	44.6
Age at diagnosis median (IQR)	71.0 (63.0 to 78.0)	71.0 (62.0 to 79.0)	71.0 (63.0 to 78.0)
Type 2 diabetes, %	**28.3**	**20.2**	**20.5**
History of hypertension, %	**84.6**	**73.1**	**75.9**
Vascular disease, %	**47.3**	**4.7**	**12.8**
Moderate-to-severe CKD, %	**16.2**	**13.7**	**9.1**
Prior stroke/TIA	**12.6**	**9.7**	**11.6**
History of bleeding	**3.4**	**2.8**	**2.4**
CHA_2DS_2-VASc score, mean (SD)	**4.4 (1.6)**	**3.8 (1.5)**	**2.9 (1.5)**

Cohorts 1–5; CKD, chronic kidney disease; TIA, transient ischaemic attack

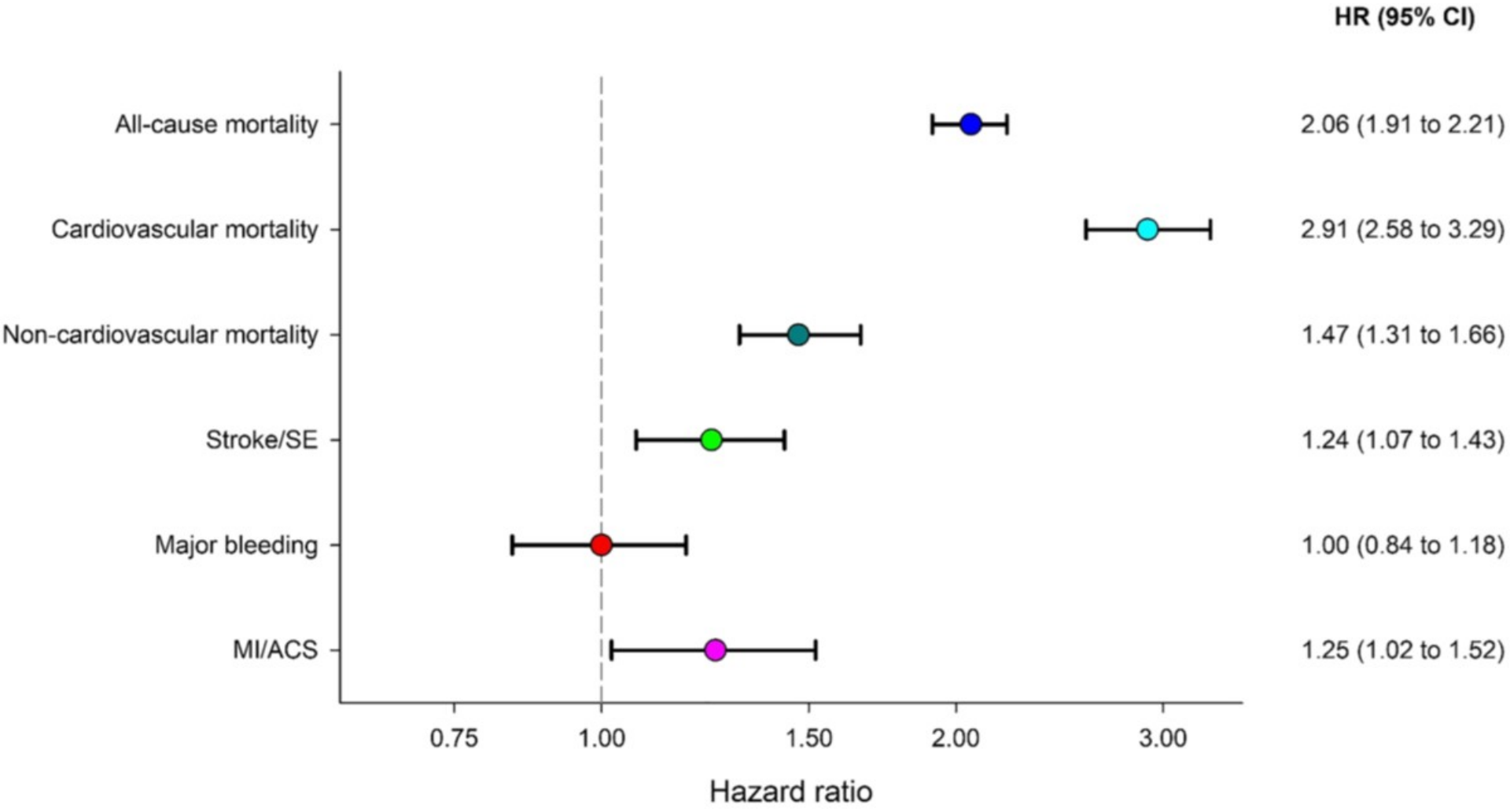
The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Antithrombotic treatment patterns

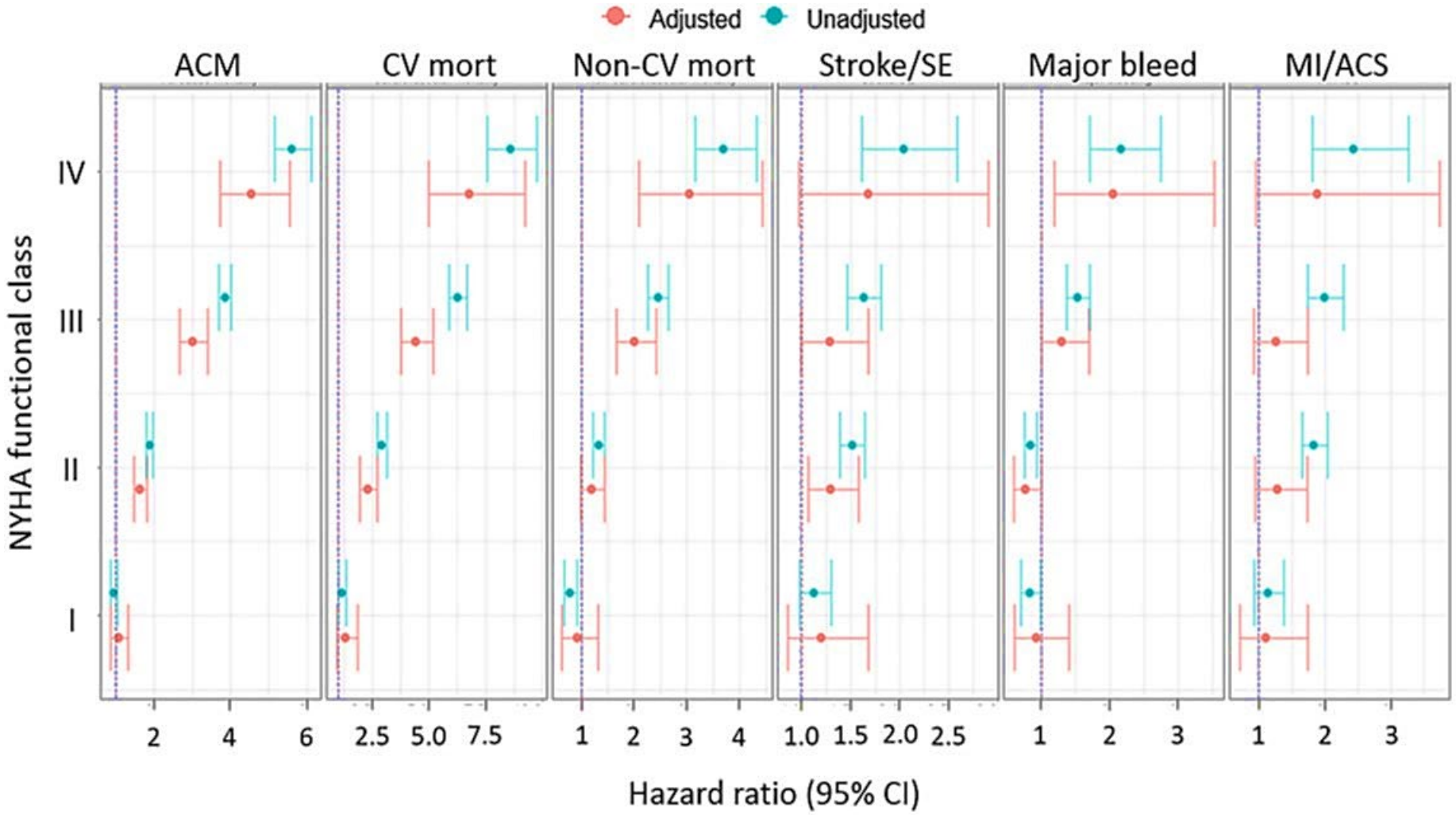


AP, antiplatelet; CHF, congestive heart failure; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonists

Major adverse outcomes in atrial fibrillation patients with heart failure vs. without heart failure (reference): adjusted hazard ratios (HRs)



Unadjusted and adjusted 2 year outcomes [hazard ratios vs. no heart failure (HF)] in patients stratified by severity of HF. Severity of HF is stratified via the New York Heart Association (NYHA) functional classes I–IV.

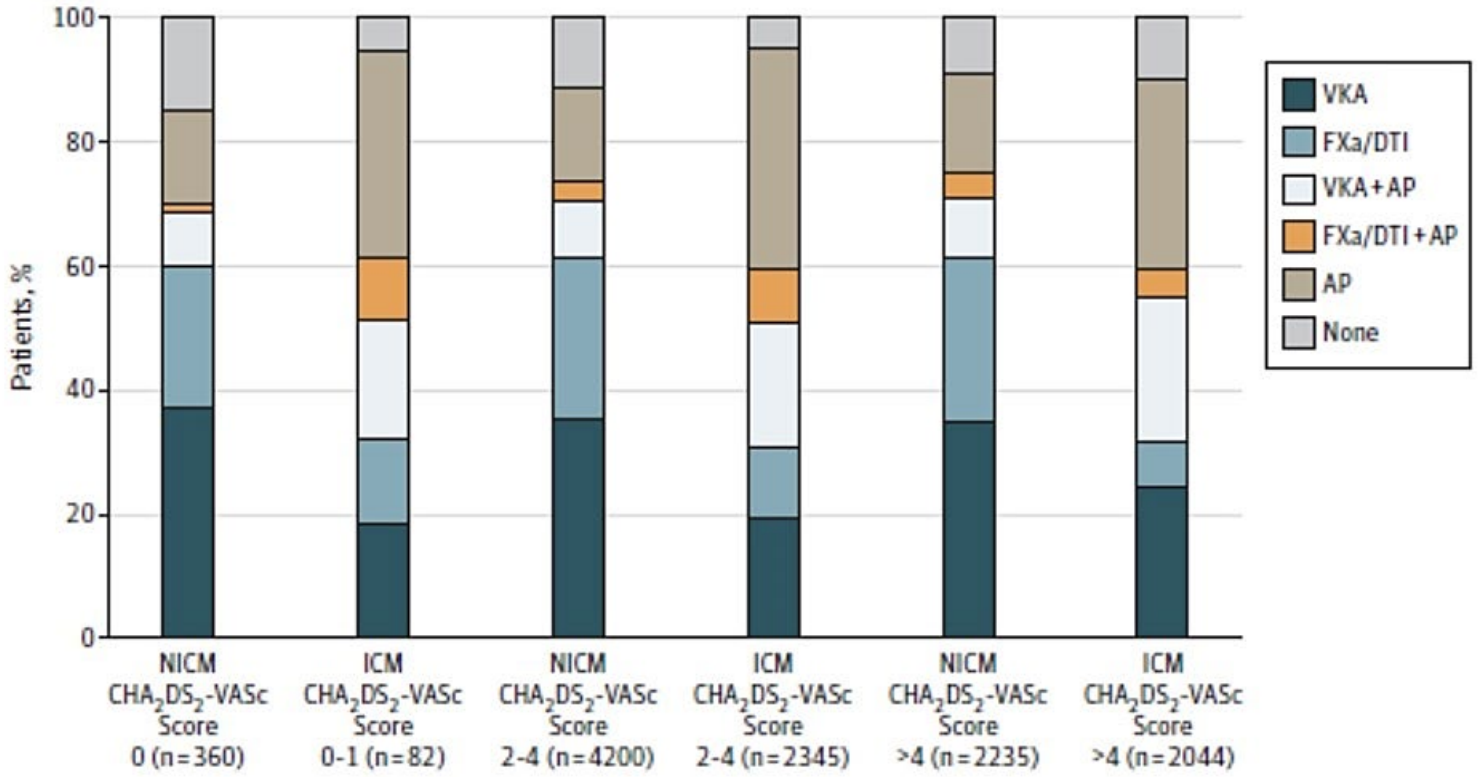


Analysis of Outcomes in Ischemic vs Nonischemic Cardiomyopathy in Patients With Atrial Fibrillation A Report From the GARFIELD-AF Registry

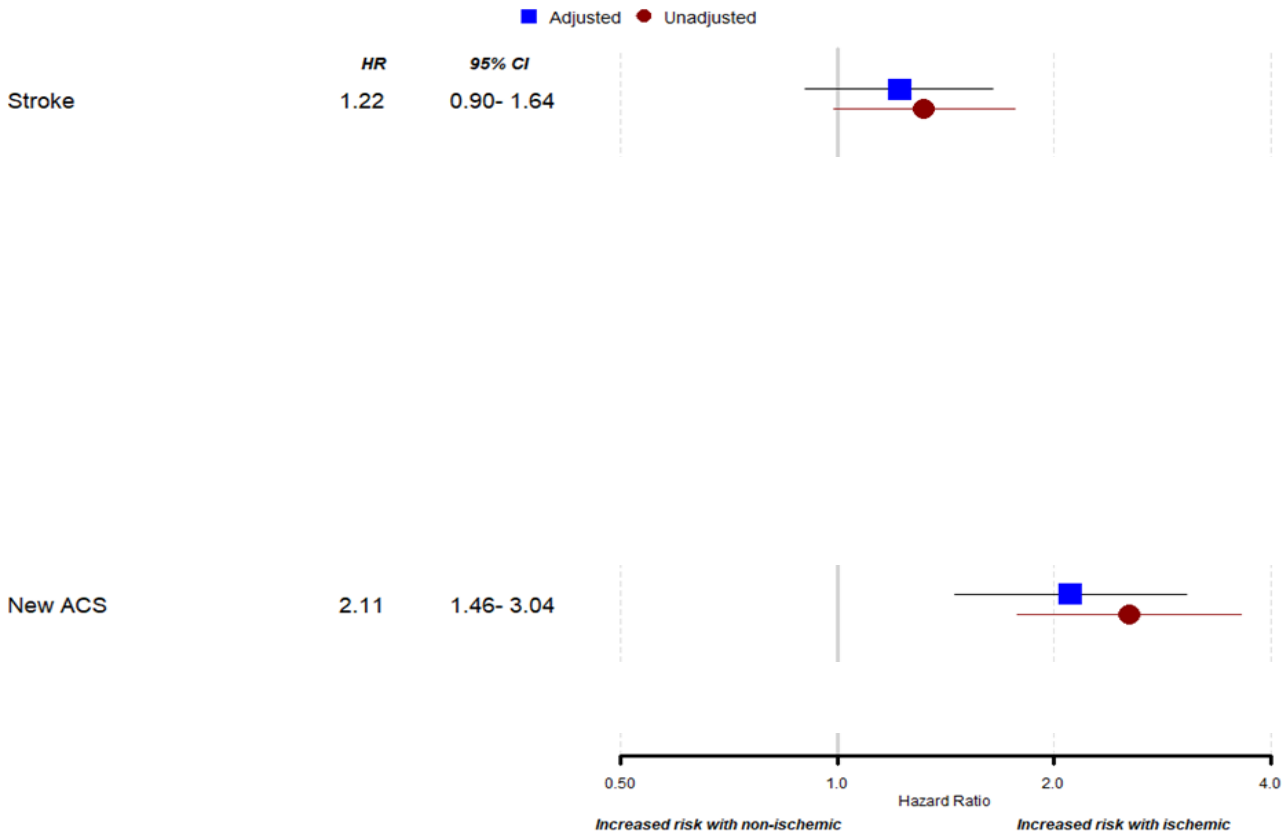
Ramon Corbalan, MD; Jean-Pierre Bassand, MD; Laura Illingworth, MSc; Giuseppe Ambrosio,MD, PhD; A. John Camm, MD; David A. Fitzmaurice, MD; Keith A. A. Fox, MBChB; Samuel Z. Goldhaber,MD, PhD; Shinya Goto,MD, PhD; Sylvia Haas, MD;Gloria Kayani, BSc; Lorenzo G. Mantovani, MSc; Frank Misselwitz, MD, PhD; Karen S. Pieper, MS; Alexander G. G. Turpie, MD; FreekW. A. Verheugt, MD; Ajay K. Kakkar, MBBS, PhD; for the GARFIELD-AF Investigators

JAMA Cardiology 2019

Figure 1. Percentage of Prescription of Anticoagulants and Antiplatelets (AP) and Their Combination in Ischemic Cardiomyopathy (ICM) and Nonischemic Cardiomyopathy (NICM) According to CHA_2DS_2-VASc Score



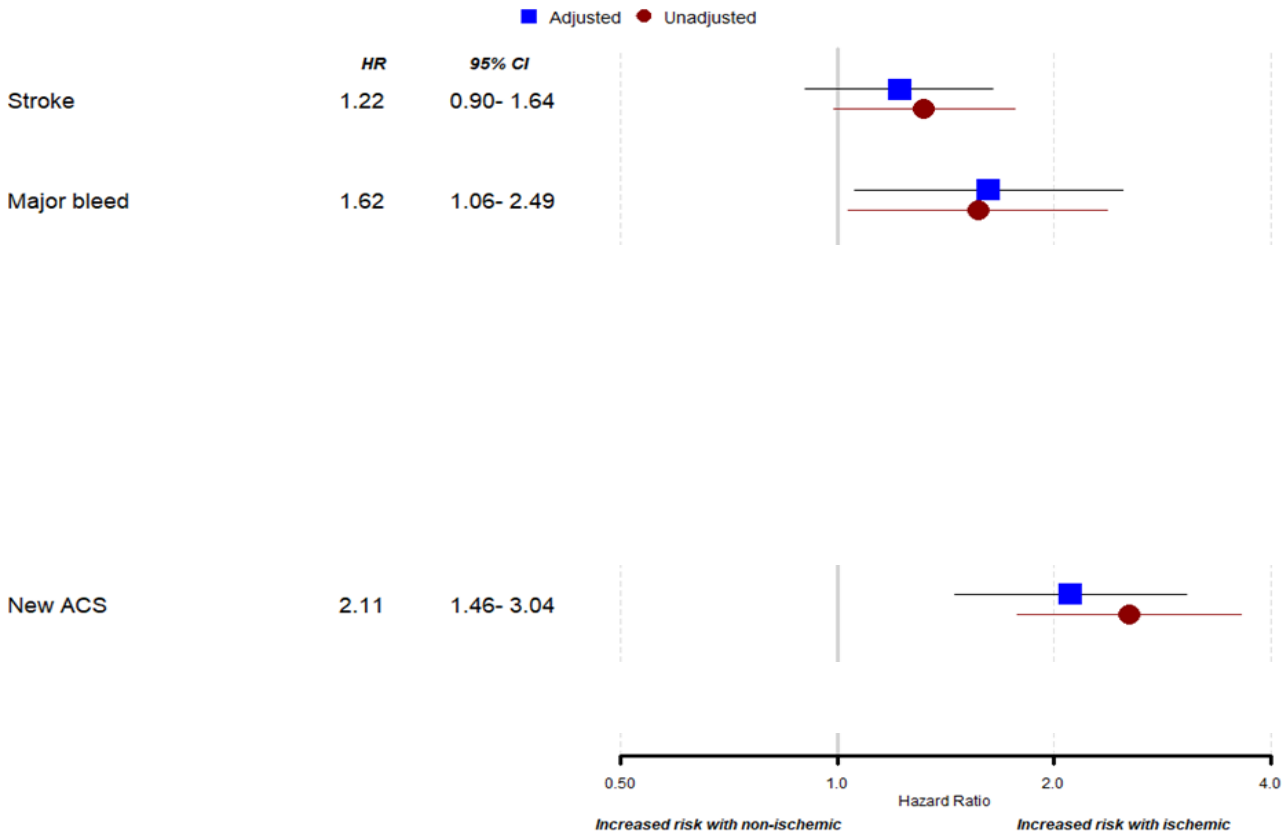
Outcomes for Ischemic versus non-Ischemic HF patients



Rates have been adjusted for age, sex, race smoking diabetes, hypertension, history of bleeding, moderate to severe kidney disease, type of medication, type of AF and heavy alcohol use.

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

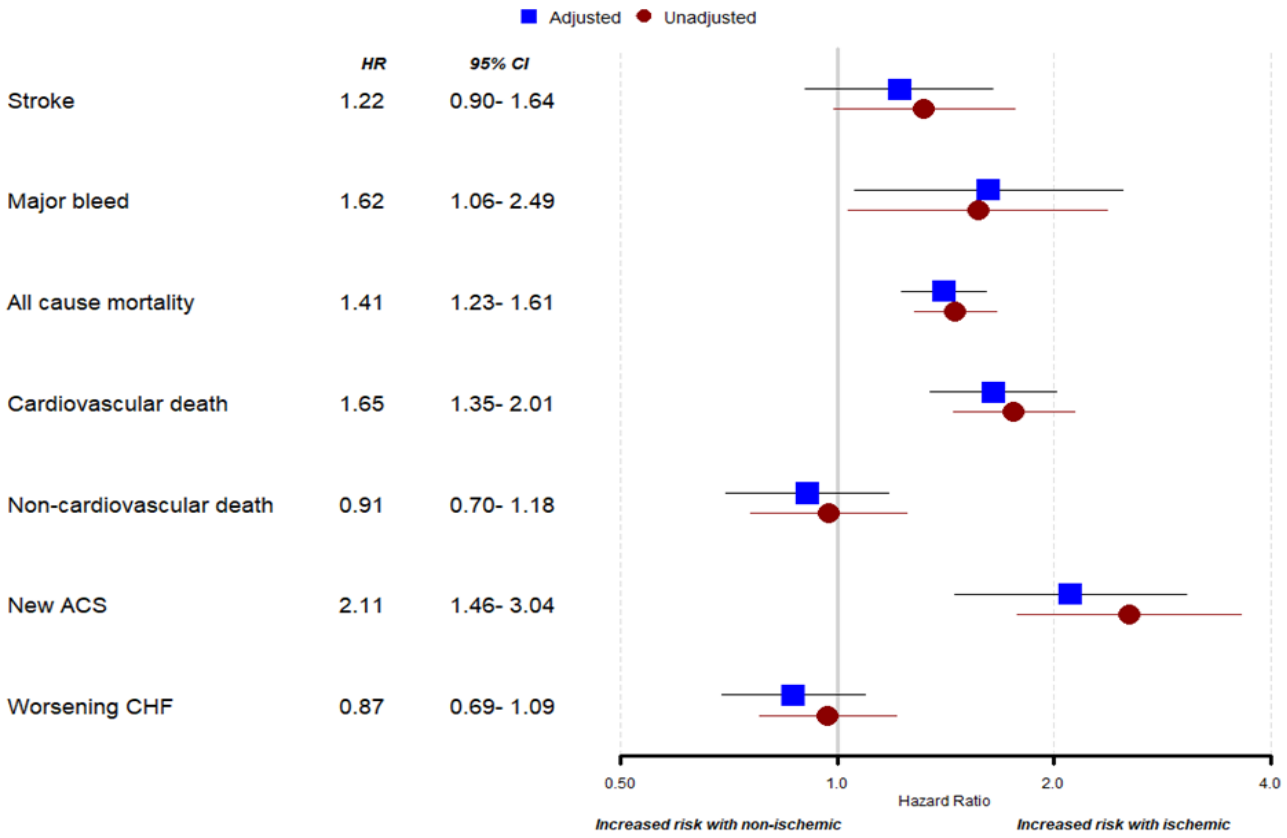
Outcomes for Ischemic versus non-Ischemic HF patients



Rates have been adjusted for age, sex, race smoking diabetes, hypertension, history of bleeding, moderate to severe kidney disease, type of medication, type of AF and heavy alcohol use.

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Outcomes for Ischemic versus non-Ischemic HF patients



Rates have been adjusted for age, sex, race smoking diabetes, hypertension, history of bleeding, moderate to severe kidney disease, type of medication, type of AF and heavy alcohol use.

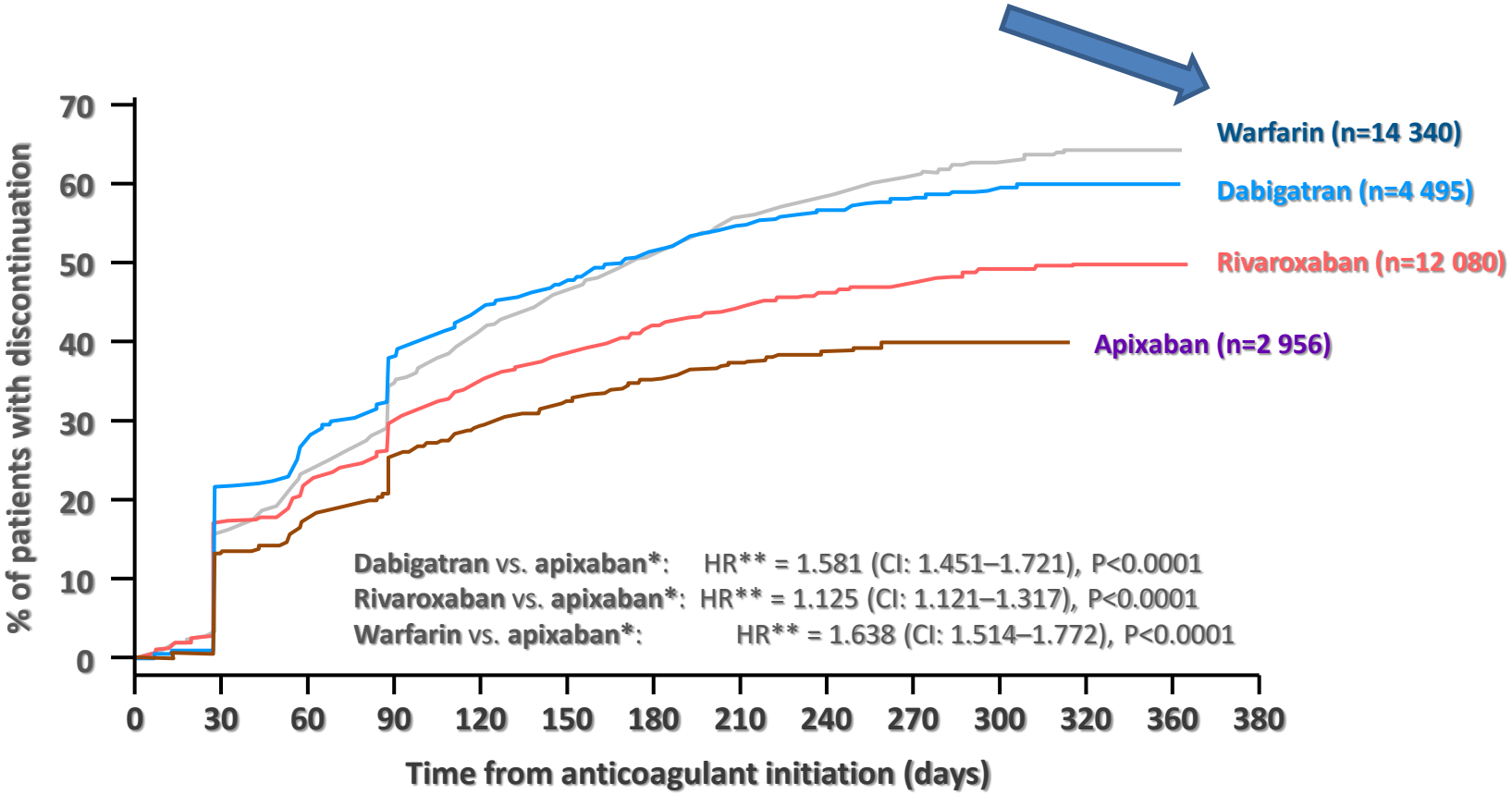
Conclusions

- About ¼ of patients with newly-diagnosed AF present with HF, of whom ≈ 40% had ischemic etiology
- HF patients are older/sicker than those without HF
- Ischemic HF patients have more comorbidities (diabetes, hypertension)
- Ischemic patients were more often sub-optimally anticoagulated, and received AP alone more often
- Ischemic patients had worse outcomes than patient with non-ischemic HF
- They also had more bleedings
- Also in terms of all-cause and cardiovascular death, ischemic HF patients score worse, despite being more likely to receive guideline-directed therapy than non-ischemic HF patients

Cohorts 1–5, N=52,081

The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer AG

Discontinuation rates of NOACs in real world



* Effect size is versus apixaban which acts as a reference category.

** Analysis controlled for other variables including age, gender, onset of embolic or primary ischemic stroke, dyspepsia or stomach discomfort, congestive heart failure, coronary artery disease, diabetes, hypertension, renal disease, myocardial infarction, history of TIA or stroke and history of bleeding.

Pan *et al*. Presented at the ESC Congress 2014. Abstract #5112.

Main reasons why anticoagulants were not given in CHA_2DS_2-VASc ≥2 patients with and without history of ACS

Reason, %	No ACS (n=9010)	ACS (n=1214)
Already taking antiplatelet drugs for other medical condition	4.9	17.5
Patient refusal	9.5	10.5
Previous bleeding event	2.1	2.3
Other/unknown	**53.8**	**41.8**
Physician's choice	**29.2**	**25.9**
Bleeding risk	**27.6**	**46.3**
Concern over patient compliance	14.2	15.6
Guideline recommendation	10.2	7.9
Fall risk	13.9	11.7
Low risk of stroke	34.1	18.4

Cohorts 1–5, N=52,081

Anticoagulation in Patients at Risk For Falls Should we be concerned ?

Choosing Antithrombotic Therapy for Elderly Patients With Atrial Fibrillation Who Are at Risk for Falls

Malcolm Man-Son-Hing, MD, MSc, FRCPC; Graham Nichol, MD, MPH, FRCPC; Anita Lau; Andreas Laupacis, MD, MSc, FRCPC

"…persons taking warfarin must fall about 295 (535/1.81) times in 1 year for anticoagulation **not** to be the optimal therapy…"

term warfarin use) for patients with atrial fibrillation who are 65 years of age and older, are at risk for falling, and have no other contraindications to antithrombotic therapy. Input data were obtained by systematic review of MEDLINE. Outcomes were expressed as quality-adjusted life-years.

Results: For patients with average risks of stroke and

Conclusions: For elderly patients with atrial fibrillation, the choice of optimal therapy to prevent stroke depends on many clinical factors, especially their baseline risk of stroke. However, patients' propensity to fall is not an important factor in this decision.

Arch Intern Med. 1999;159:677-685

ESC European Society of Cardiology
European Journal of Preventive Cardiology
doi:10.1093/eurjpc/zwab096

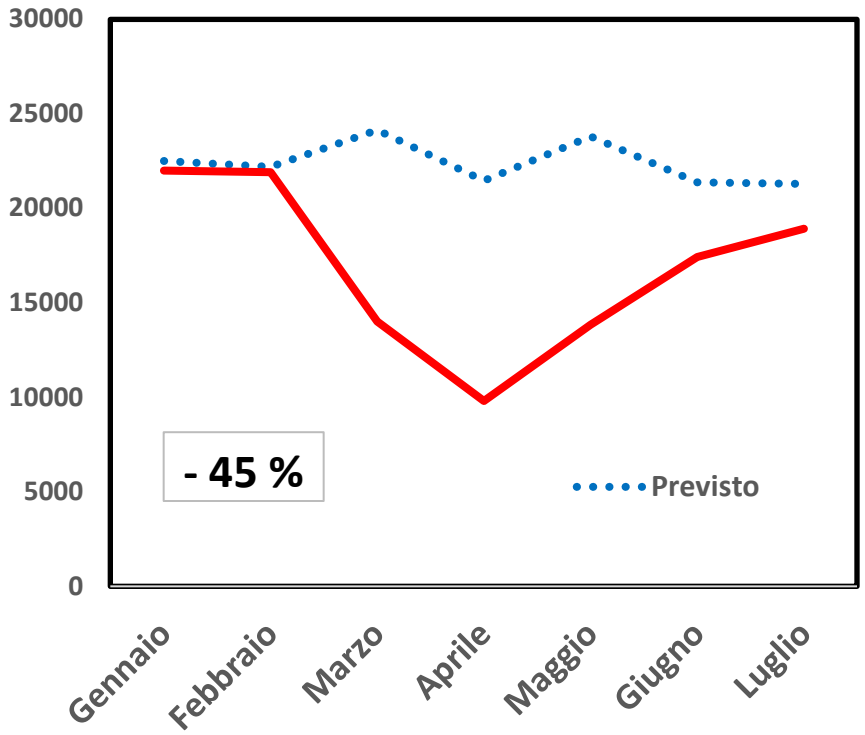
RESEARCH LETTER
Population level factors

Under-prescription of direct oral anticoagulants for treatment of non-valvular atrial fibrillation and venous thromboembolism in the COVID-19 lockdown period

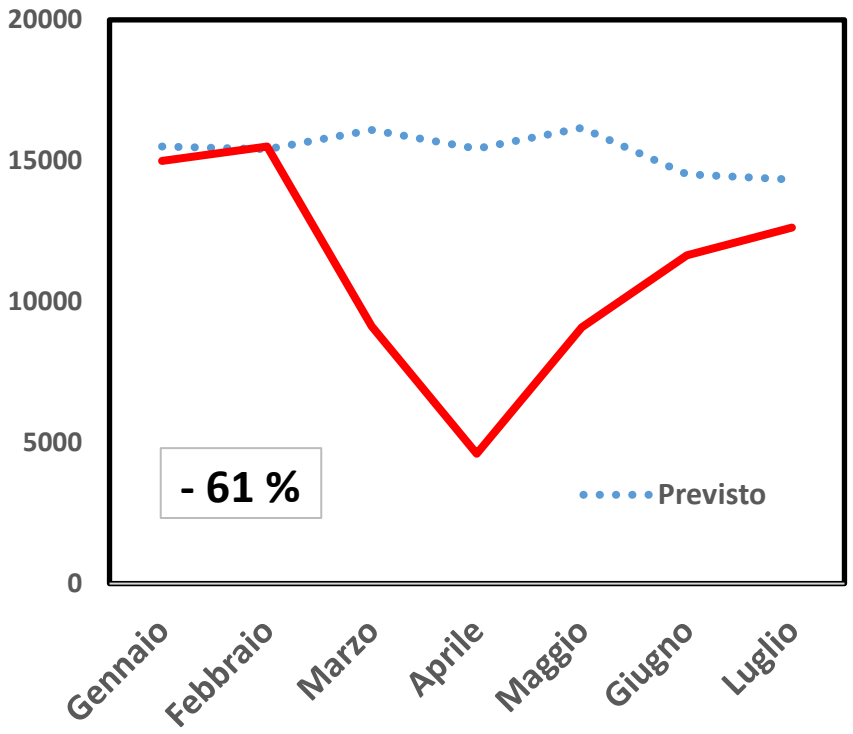
Graziano Onder [1]*, Pier Paolo Olimpieri[2†], Simone Celant[2†], Andrea Di Lenarda[3], Giuseppe Ambrosio [4], Gianpaolo Reboldi[5], Gianfranco Gensini[6], Antonietta Colatrella[2], Katie Palmer[7], Domenico Gabrielli[8], and Pierluigi Russo[2]; on behalf of AIFA Monitoring Registries Group

From June 2013 to July 2020, the AIFA NOAC registry collected data on 1,515,629 new NOAC prescriptions, including 1,312,214 (86.6%) new prescriptions for non-valvular AF, and 203,415 (13.4%) for prevention or treatment of VTE.

Nuove Prescrizioni di Anticoagulanti in Italia
Fibrillazione Atriale - Totale



Nuove Prescrizioni di Anticoagulanti in Italia
Fibrillazione Atriale - > 75 anni



Grazie per l'attenzione

ESC European Society of Cardiology
European Heart Journal (2020) 00, 1–125
doi:10.1093/eurheartj/ehaa612

Clinical pattern of AF (i.e. first detected, paroxysmal, persistent, long-standing persistent, permanent) should not condition the indication to thromboprophylaxis **III**

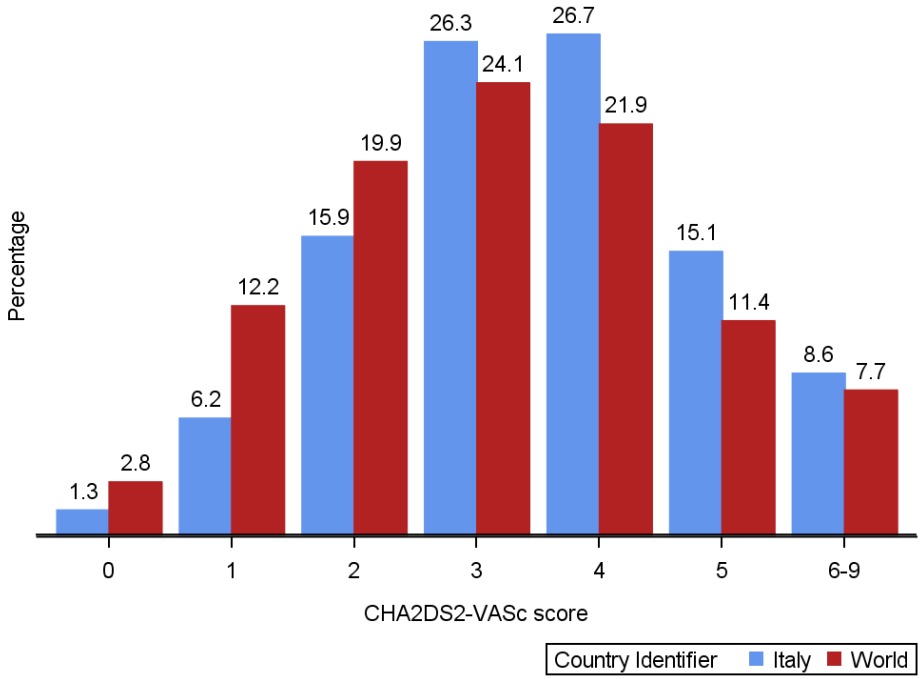
Terminology that should be abandoned:

Lone AF: A historical descriptor.
Increasing knowledge about the pathophysiology of AF shows that in every patient a cause is present.
Hence, this term is potentially confusing and should be abandoned.

Valvular/nonvalvular AF
Differentiates patients with moderate/severe mitral stenosis and those with mechanical prosthetic heart valve(s) from other patients with AF, but may be confusing and should not be used.

Baseline scores in patients with newly diagnosed AF: Italy *vs.* all countries

CHA_2DS_2-VASc



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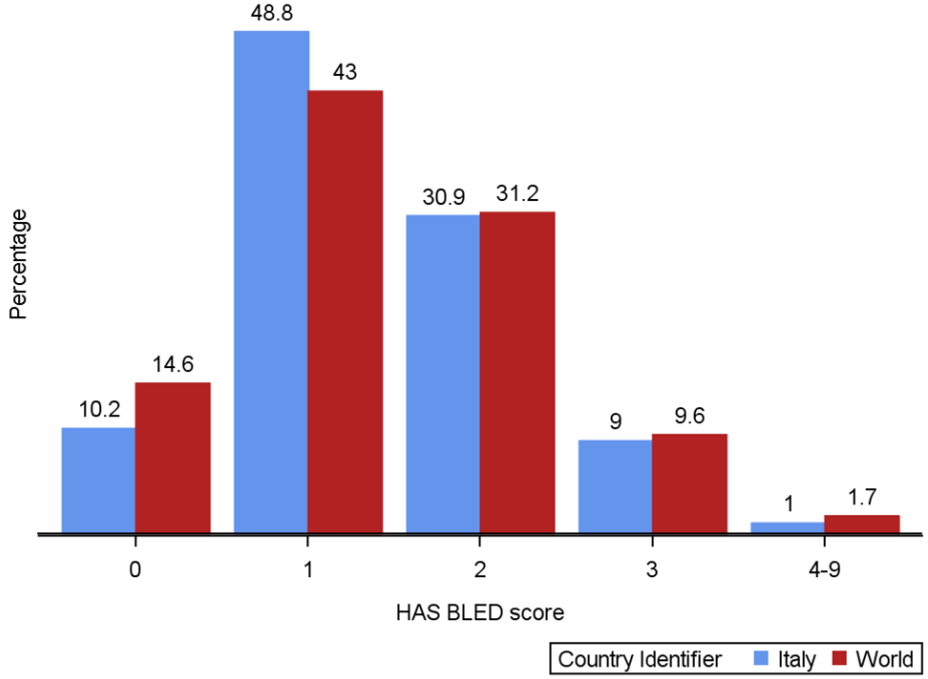


Prospective Cohorts 1–5. Italy: N=2145/2191; All countries: N=49952/51270

Monthly estimated and observed new prescriptions of Non-vitamin K Oral Anticoagulants for treatment of non-valvular atrial fibrillation by age group.

Rows identifying months characterized by the lockdown period are in grey.

	Overall			< 65 years			65-74 years			75 years or older		
Month	Estimated	Observed	Δ	Estimated	Observed	Δ	Estimated	Observed	Δ	Estimated	Observed	Δ
March	24,151	14,024	-41.9%	2,339	1,531	-34.5%	5,783	3,368	-41.8%	16,085	9,125	-43.3%
April	21,427	8,811	-58.9%	1,894	1,052	-44.5%	5,100	2,147	-57.9%	14,417	5,612	-61.1%
May	23,807	13,852	-41.8%	2,073	1,454	-29.9%	5,586	3,314	-40.7%	16,172	9,084	-43.8%
June	21,382	17,414	-18.6%	1,878	1,787	-4.8%	5,032	3,994	-20.6%	14,514	11,633	-19.9%
July	21,288	18,914	-11.2%	1,921	1,918	-0.2%	5,039	4,363	-13.4%	14,331	12,633	-11.8%
March-July	112,055	73,015	-34.8%	10,105	7,742	-23.4%	26,540	17,186	-35.2%	75,519	48,087	-36.3%

Nota 97

In considerazione delle evidenze scientifiche disponibili, relativamente all'uso prevalente nell'indicazione terapeutica FANV, i quattro DOAC (dabigatran, rivaroxaban, apixaban, edoxaban) possono essere considerati globalmente sovrapponibili

Nei 4 mega-trials, come si sono 'comportati' i singoli NAO rispetto al warfarin, nei sottogruppi di pazienti che più sembrano assomigliare al paziente che ora ho davanti a me?

Caratteristiche Del paziente	Base Razionale	Possibile Opzione
Alto rischio di sanguinamento (HAS-BLED≥ 3)	I NAO associati al più basso rischio di sanguinamento vs warfarin	Apixaban; Dabigatran 110; Edoxaban 30, 60
Pregresse emorragie gastrointestinali	I NAO associati al più basso rischio di emorragie gastrointestinali vs warfarin	Edoxaban 30
Pregresso ictus ischemico	I NAO associati al più basso rischio di ictus ischemico vs warfarin	Dabigatran 150
Card Ischemica con necessità di DAPT	I NAO testati in combinazione con ASA +clopidogrel	Dabigatran 110, 150
Card Ischemica con alto rischio di re-SCA	I NAO associati al minor rischio di SCA ricorrente vs warfarin	Rivaroxaban
Insufficienza renale (30-50 mL/min)	I NAO con accettabile rapporto efficacia/ sicurezza vs warfarin nell'insuff. renale Considerazioni cliniche e farmacocinetiche	Apixaban; Rivaroxaban 15 Edoxaban 30; Dabigatran 110
Insufficienza epatica (Child Plough B-C)	I NAO a minor metabolismo epatico	Dabigatran 110, 150
Preferenza per singola somministrazione giornaliera	I NAO testati once daily	Rivaroxaban, Edoxaban 30, 60
Fastidi/dolori epigastrici	I NAO associati al più basso rischio di fastidi/dolori epigastrici vs warfarin	Apixaban; Rivaroxaban Edoxaban 30, 60

INDICAZIONE TERAPEUTICA RCP

Prevenzione di ictus ed embolia sistemica in pazienti adulti con fibrillazione atriale non valvolare (FANV), con uno o più fattori di rischio quali:

- **Precedente ictus o attacco ischemico transitorio (TIA)**
- **Età ≥ 75 anni**
- **Insufficienza cardiaca (Classe NYHA ≥ II)**
- **Diabete mellito**
- **Ipertensione**

NOTA AIFA 97 per la prescrizione della terapia anticoagulante orale nei pazienti con Fibrillazione atriale non valvolare (FANV)

Farmaci inclusi nella Nota AIFA: AVK: ▪ **Warfarin** ▪ **Acenocumarolo** NAO/DOAC: ▪ **Dabigatran** ▪ **Apixaban** ▪ **Edoxaban** ▪ **Rivaroxaban**	La prescrizione della terapia anticoagulante orale è a carico del SSN limitatamente alla FANV e al rispetto del percorso decisionale illustrato ai punti A, B, C, D. La prescrizione dovrà essere accompagnata dalla compilazione della scheda di valutazione prescrizione e follow-up di cui all'allegato I da parte dello specialista o del Medico di Medicina Generale. Una copia della scheda dovrà essere conservata dal prescrittore e una consegnata al paziente, in previsione del successivo aggiornamento periodico in occasione del follow-up. Il regime di fornitura delle altre indicazioni di AVK e NAO/NOAC rimane invariato. **PERCORSO DECISIONALE** A. La diagnosi di FANV deve essere sempre confermata da un elettrocardiogramma e dalla valutazione clinica del paziente.

Demographics and clinical characteristics of GARFIELD-AF patients with and without history of ACS

	No ACS (N=46,916)	ACS (N=4914)
Female, %	45.5	31.7
Age at AF diagnosis (years), median	71.0	73.0
Heart failure	18.8	30.3
Coronary artery bypass graft	1.3	21.2
Hypercholesterolaemia	38.9	67.0
Vascular disease	5.7	99.0
Stenting	3.1	42.5
Diabetes mellitus	20.9	33.4

Cohorts 1–5, N=52,081

(E)	Paziente con Fibrillazione Atriale non Valvolare (FANV) *:	Sì
	Peso *:	70 kg
	Emoglobina *:	15.3 g/dl
	Creatinina sierica *:	0.7 mg/dl

Campo Obbligatorio

Sc

	(C) Scompenso cardiaco/disfunzione ventricolare sinistra (Congestive heart failure) *:	0
	(H) Ipertensione arteriosa (Hypertension) *:	1
	(A) Età >= 75 anni (Age) *:	0
	(D) Diabete mellito (Diabetes mellitus) *:	0
	(S) Pregresso Ictus cerebrale/TIA/ Episodio trombo-embolico TE (Prior Stroke or TIA) *:	0
	(V) Malattie vascolari: precedente IM, malattia arteriosa periferica o placca aortica (Vascular disease) *:	1
	(A) Età 65-74 anni (Age) *:	1
	(Sc) Sesso femminile (Sex category: female gender) *:	0
(E)	Punteggio totale:	3.0

Scala HAS-BLED

	(H) Ipertensione arteriosa (Hypertension) *:	1
	(A) Alterata funzionalità renale (Abnormal renal function): dialisi, trapianto renale, creatinina sierica > 200 µmol/L *:	0
	(A) Alterata funzionalità epatica (Abnormal liver function): cirrosi epatica, evidenza di insufficienza epatica (livelli di bilirubina di 2 volte superiori la norma, livelli di AST/ALT di 3 volte superiori la norma) *:	0
	(S) Pregresso Ictus cerebrale (Stroke in past) *:	0
	(B) Storia di sanguinamento o diatesi emorragica o anemia (Bleeding) *:	0
	(L) Labile controllo dell'INR (INR instabile con tempo in range terapeutico < 60%) *:	0
	(E) Età > 65 anni (Elderly) *:	1
	(D) Terapia farmacologica (Drug Therapy): terapia concomitante con antiaggreganti piastrinici, FANS *:	1
	(D) Etilismo cronico (Alcohol intake) *:	0
	Punteggio totale:	3.0

(E)	Il paziente è in terapia con anticoagulanti (farmaci antagonisti della vitamina K)? *:	No
	Il trattamento anticoagulante non è attuabile per difficoltà oggettive ad eseguire i controlli di INR *:	No

NOTA AIFA 97 per la prescrizione della terapia anticoagulante orale

Farmaci inclusi nella Nota AIFA: AVK: ▪ Warfarin ▪ Acenocumarolo NAO/DOAC: ▪ Dabigatran ▪ Apixaban ▪ Edoxaban ▪ Rivaroxaban	La prescrizione della terapia anticoagulante orale è a carico del SSN limitatamente alla FANV e nel rispetto del percorso decisionale illustrato ai punti A, B, C, D. La prescrizione dovrà essere accompagnata dalla compilazione della scheda di valutazione prescrizione e follow-up di cui all'allegato 1 da parte dello specialista o del Medico di Medicina Generale. Una copia della scheda dovrà essere conservata dal prescrittore e una consegnata al paziente, in previsione del successivo aggiornamento periodico in occasione del follow-up. Il regime di fornitura delle altre indicazioni degli AVK e dei NAO/NOAC rimane invariato. **PERCORSO DECISIONALE** A. La diagnosi di FANV deve essere sempre confermata da un elettrocardiogramma e dalla valutazione clinica del paziente. B. La decisione di iniziare un trattamento anticoagulante per la prevenzione primaria o secondaria di ictus ed embolia sistemica in pazienti adulti con FANV deve avvenire dopo una accurata valutazione del rischio trombo-embolico e del rischio emorragico del singolo paziente.

C. **LA TERAPIA ANTICOAGULANTE DOVRÀ ESSERE INIZIATA**

- **in tutti** i pazienti con punteggio CHA2DS2-VASc: ≥2 (se maschi) e ≥3 (se femmine).

La scelta terapeutica finale dipenderà comunque dalla valutazione clinica e dovrà considerare la presenza di fattori di rischio emorragico anche in rapporto alle loro caratteristiche.

Allegato 1. alla Nota AIFA 97

Scheda di valutazione prescrizione e follow-up della terapia anticoagulante orale con AVK e NAO/DOAC nei pazienti con FAVN

Da compilare a cura del prescrittore che seguirà il paziente nella gestione della terapia anticoagulante e del follow-up periodico (Specialista, Medico di Medicina Generale)
La scheda contiene un minimum data set di dati da raccogliere attraverso modalità decise dalle singole Regioni.

Sezione 1: scheda di valutazione e di prescrizione

Medico prescrittore _____ Tel _____ specialista in: _____

❑ U.O. _____ ❑ Az. Sanitaria _____ ❑ libero professionista

Paziente (nome e cognome) _____ Sesso: ❑ M ❑ F

Data di Nascita_____ Residenza_____Codice Fiscale _____

Verificata la presenza delle seguenti condizioni:

A diagnosi clinica e elettrocardiografica di FANV ❑

B e C risultato del bilancio fra rischio trombo-embolico e rischio emorragico: ❑ favorevole per:

Punteggio CHA2DS2-VASc _____

Rischio emorragico _____
Indicare eventuali fattori di rischio presenti

Creatinina (mg/dL) _____ VFG (mL/min) _____ Hb (g/dL) _____

D proposta di strategia terapeutica

❑ AVK : ❑ Warfarin ❑ acenocumarolo **target di INR:** _____

❑ dabigatran ❑ 150 mg x 2 /die ❑ 110 mg x 2/die _____
Motivare la riduzione della dose

❑ apixaban ❑ 5 mg x 2/die ❑ 2,5 mg x 2 /die _____
Motivare la riduzione della dose

❑ edoxaban ❑ 60 mg/die ❑ 30 mg /die _____
Motivare la riduzione della dose

❑ rivaroxaban ❑ 20 mg /die ❑ 15 mg/die _____
Motivare la riduzione della dose

Data prevista per il Follow up: _____

La validità della prima prescrizione è al massimo di 6 mesi.

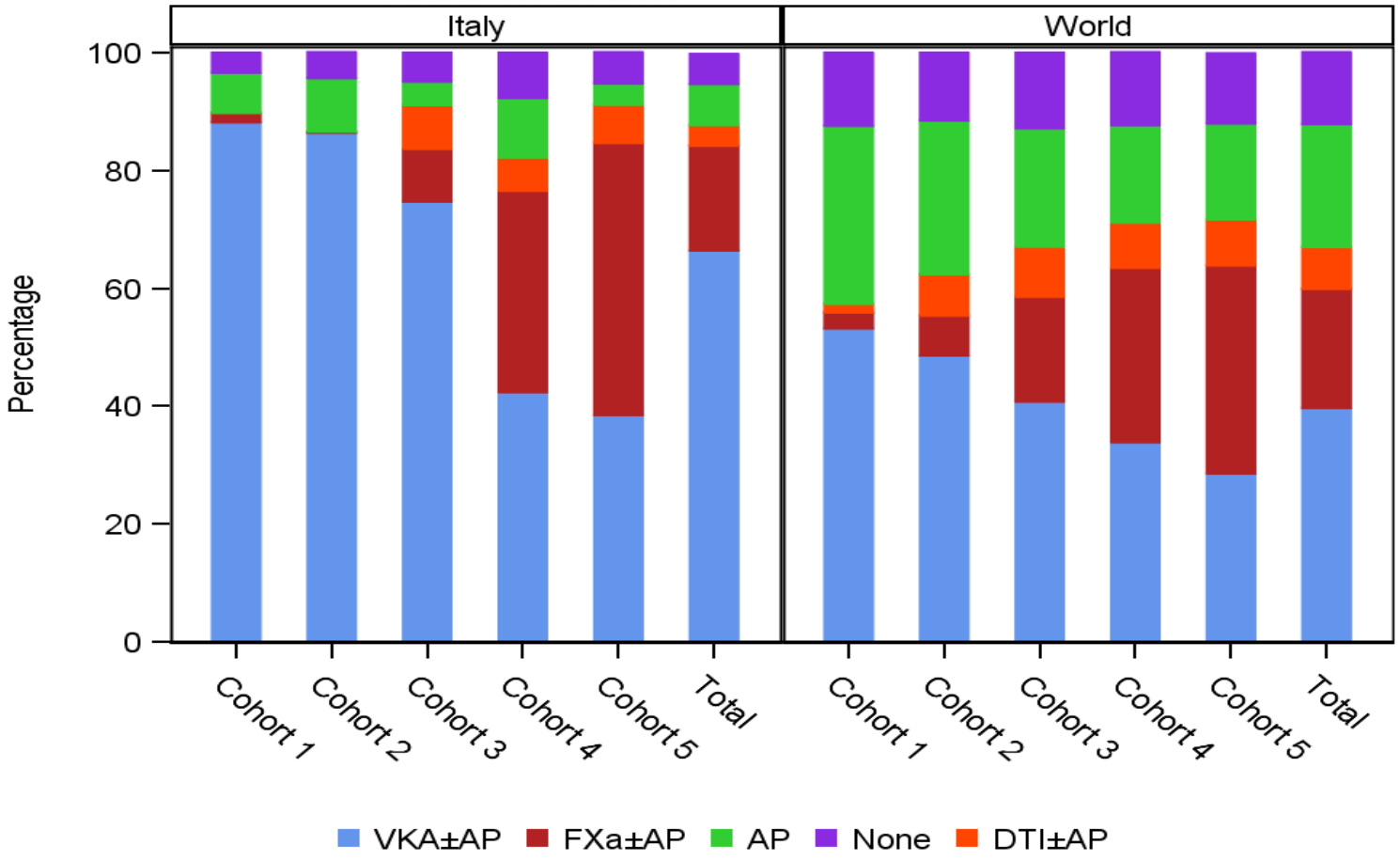
Heart Online First, published on September 19, 2016 as 10.1136/heartjnl-2016-309832

OPEN ACCESS

ORIGINAL ARTICLE

Evolving antithrombotic treatment patterns for patients with newly diagnosed atrial fibrillation

A John Camm,[1] Gabriele Accetta,[2] Giuseppe Ambrosio,[3] Dan Atar,[4,5] Jean-Pierre Bassand,[6] Eivind Berge,[7] Frank Cools,[8] David A Fitzmaurice,[9] Samuel Z Goldhaber,[10] Shinya Goto,[11] Sylvia Haas,[12] Gloria Kayani,[2] Yukihiro Koretsune,[13] Lorenzo G Mantovani,[14] Frank Misselwitz,[15] Seil Oh,[16] Alexander G G Turpie,[17] Freek W A Verheugt,[18] Ajay K Kakkar,[2,19] for the GARFIELD-AF Investigators



Prospective Cohorts 1–5. Italy: N=2175/2191; All countries: N=50643/51270

Tabella 1. Classificazione delle principali manovre diagnostiche/chirurgiche rispetto al rischio emorragico.

Rischio emorragico Basso	Rischio emorragico Alto
▪ **Estrazione dentaria (fino a 3 denti)***	▪ Anestesia lombare, epidurale
▪ **Chirurgia parodontale***	▪ Puntura lombare, neurochirurgia
▪ **Impianti odontoiatrici***	▪ Legatura varici esofagee
▪ **Interventi per cataratta o glaucoma***	▪ Polipectomia endoscopica
▪ **Chirurgia cutanea minore***	▪ Sfinterotomia e dilatazione stenosi
▪ **Endoscopie senza biopsia o resezione***	▪ Chirurgia toracica, addominale
▪ **Endoscopie con biopsia**	▪ Chirurgia ortopedica maggiore
▪ **Biopsie prostatiche o vescicali**	▪ Biopsie epatiche, renali
▪ **Studi elettrofisiologici, ablazione con radiofrequenze, angiografie**	▪ Resezione prostatica trans-uretrale
▪ **Impianto di pacemaker**	▪ Litotrissia extracorporea con ultrasuoni

* In questi casi il rischio è considerato molto basso, se è possibile una buona emostasi locale

NOTA AIFA 97 per la prescrizione della terapia anticoagulante orale nei pazienti con Fibrillazione atriale non valvolare (FANV)

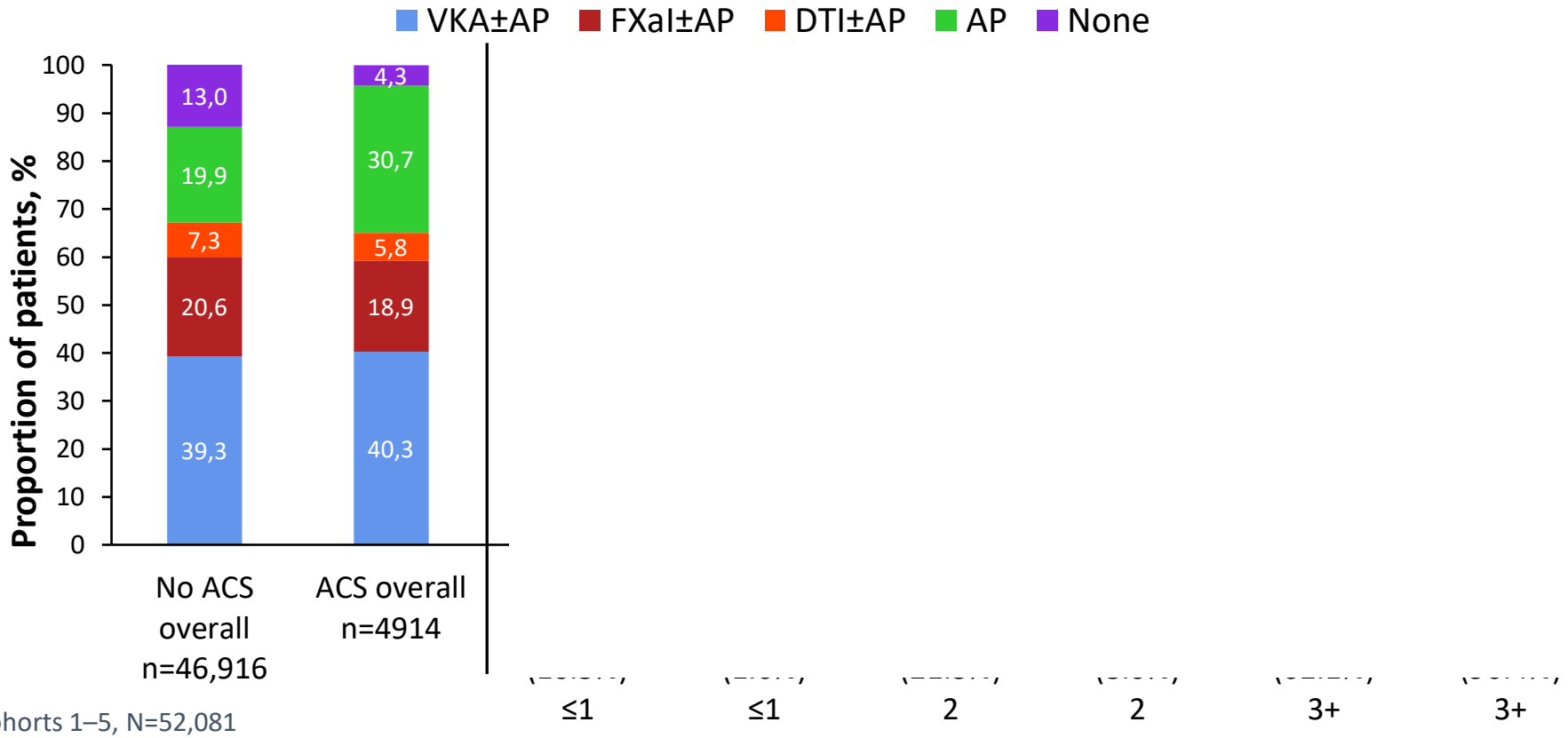
Farmaci inclusi nella Nota AIFA: AVK: ▪ **Warfarin** ▪ **Acenocumarolo** **NAO/DOAC:** ▪ **Dabigatran** ▪ **Apixaban** ▪ **Edoxaban** ▪ **Rivaroxaban**	La prescrizione della terapia anticoagulante orale è a carico del SSN limitatamente alla FANV e al rispetto del percorso decisionale illustrato ai punti A, B, C, D. La prescrizione dovrà essere accompagnata dalla compilazione della scheda di valutazione prescrizione e follow-up di cui all'allegato I da parte dello specialista o del Medico di Medicina Generale. Una copia della scheda dovrà essere conservata dal prescrittore e una consegnata al paziente, in previsione del successivo aggiornamento periodico in occasione del follow-up. Il regime di fornitura delle altre indicazioni di AVK e NAO/NOAC rimane invariato. **PERCORSO DECISIONALE** A. La diagnosi di FANV deve essere sempre confermata da un elettrocardiogramma e dalla valutazione clinica del paziente.

La diagnosi di fibrillazione atriale valvolare comprende i portatori di valvulopatia su base reumatica, sostanzialmente (sic…) la stenosi mitralica moderata o grave.

Non sembra esserci correlazione fra la scelta dell'anticoagulante e il rischio trombo embolico nella insufficienza mitralica e nella valvulopatia aortica.

… protesi valvolari meccaniche ….

Antithrombotic therapy at diagnosis in patients with and without history of ACS



Cohorts 1–5, N=52,081

AP, antiplatelet; DTI, direct thrombin inhibitor; FXaI, factor Xa inhibitor; VKA, vitamin K antagonist