la terapia anticoagulante nell'anziano: luci e ombre
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CREDITI ECM
Il corso ha ottenuto nr. 7 crediti ECM per Medico Chirurgo, Specialità: Cardiologia, Geriatria, Medicina Interna, MMG, Medicina di Urgenza
OBIETTIVO FORMATIVO.
Epidemiologia – Prevenzione e promozione della salute con acquisizione di nozioni tecnico-strumentali

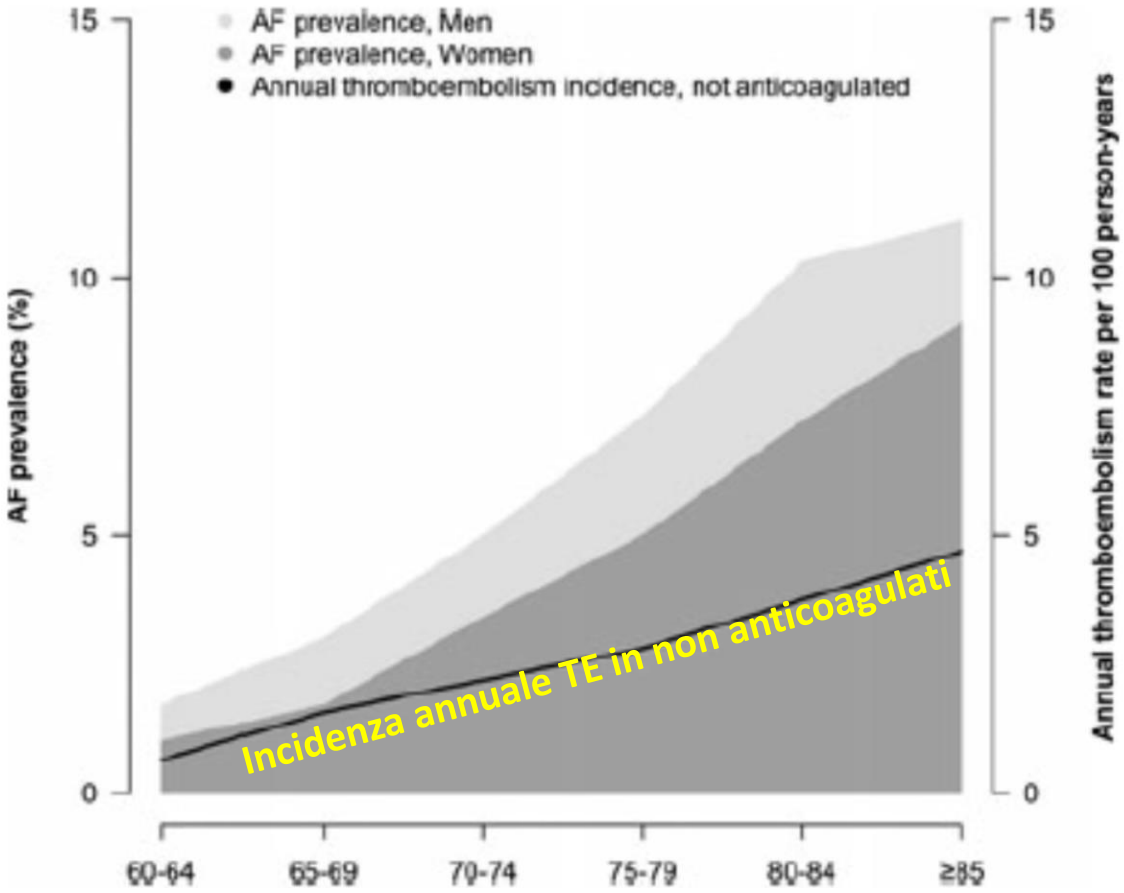
CON IL CONTRIBUTO INCONDIZIONATO DI

BAYER

LA FIBRILLAZIONE ATRIALE E LA TERAPIA ANTICOAGULANTE NELL'ANZIANO

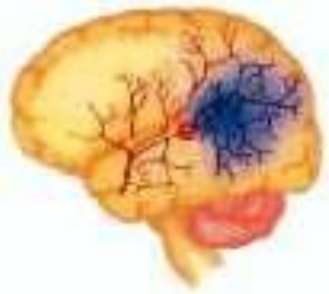
2/3 MARZO 2018
POLLENZO

ALBERGO DELL'AGENZIA - VIA FOSSANO, 21



Sex-stratified prevalence of AF according to age and annualized incidence of systemic thromboembolism in non anticoagulated subjects.

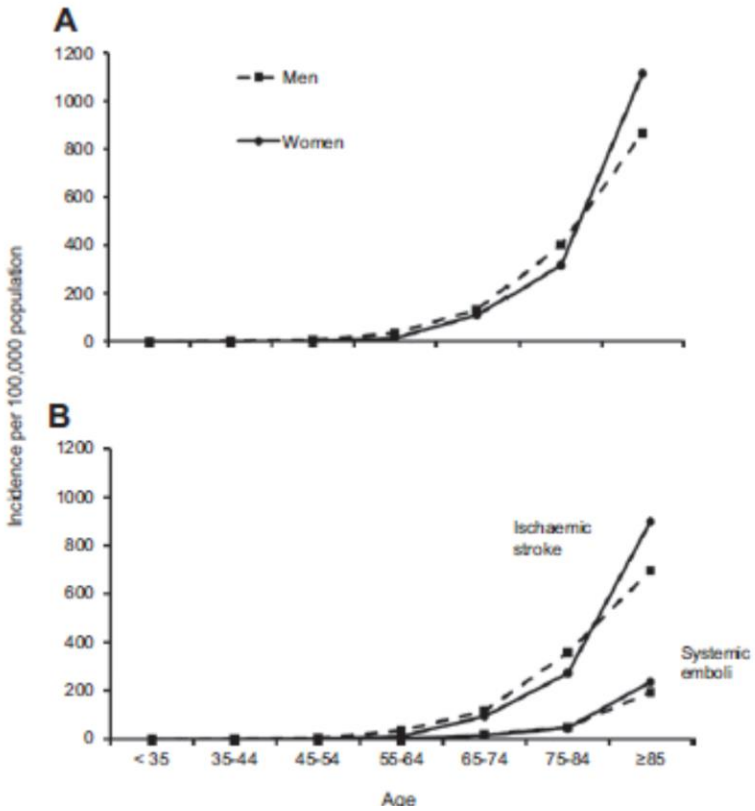
Mortalità a 30 gg ictus CE: 25%



Age-Specific Incidence, Outcome, Cost, and Projected Future Burden of Atrial Fibrillation–Related Embolic Vascular Events

(*Circulation*. 2014;130:1236-1244.) **A Population-Based Study**

Age-specific incidence, outcome, and cost of all AF-related incident strokes (ISs) and systemic embolisms (SEs) from 2002 to 2012 in the OXVASC study.



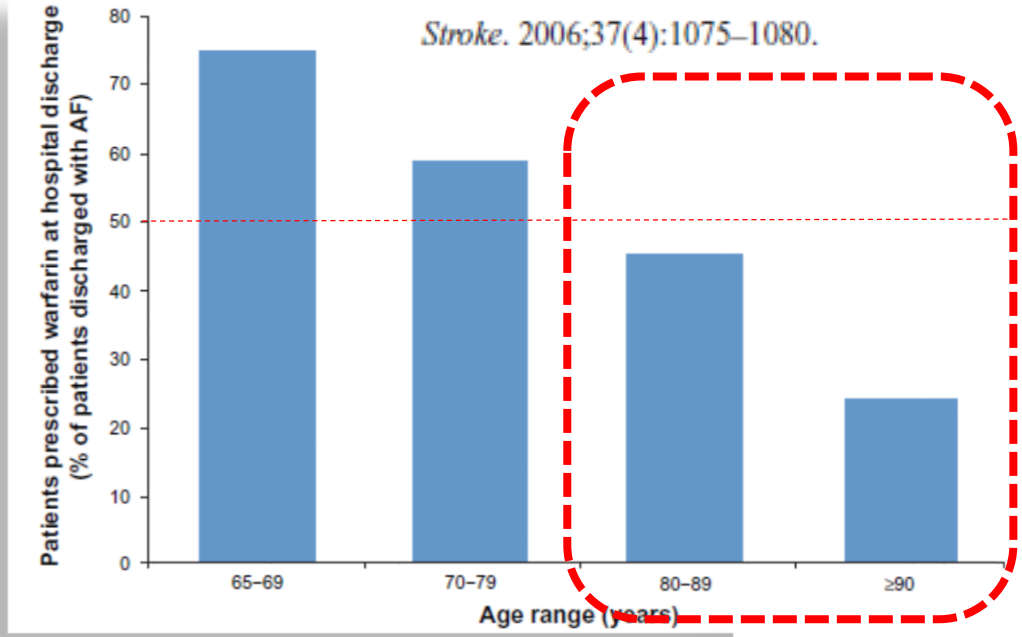
Age and sex-specific rates (per 100.000/year) for all **incident AF-related IS and SE**

60% degli **stroke ischemici** in pazienti di **80+ anni**.

43.9% degli stroke fatali o disabilitanti sono FA-relati

Il numero degli stroke da FA nei soggetti di **80+ anni si è triplicato** dal **1981-1986** al **2002-2012**, e questo numero **è ulteriormente destinato a triplicare** entro il 2050, quando **più dell'80% degli eventi embolici si verificheranno in questa fascia di età**

La TAO nell'anziano con FA, prima dei NAO



Di Pasquale G, Int J Cardiol 2013

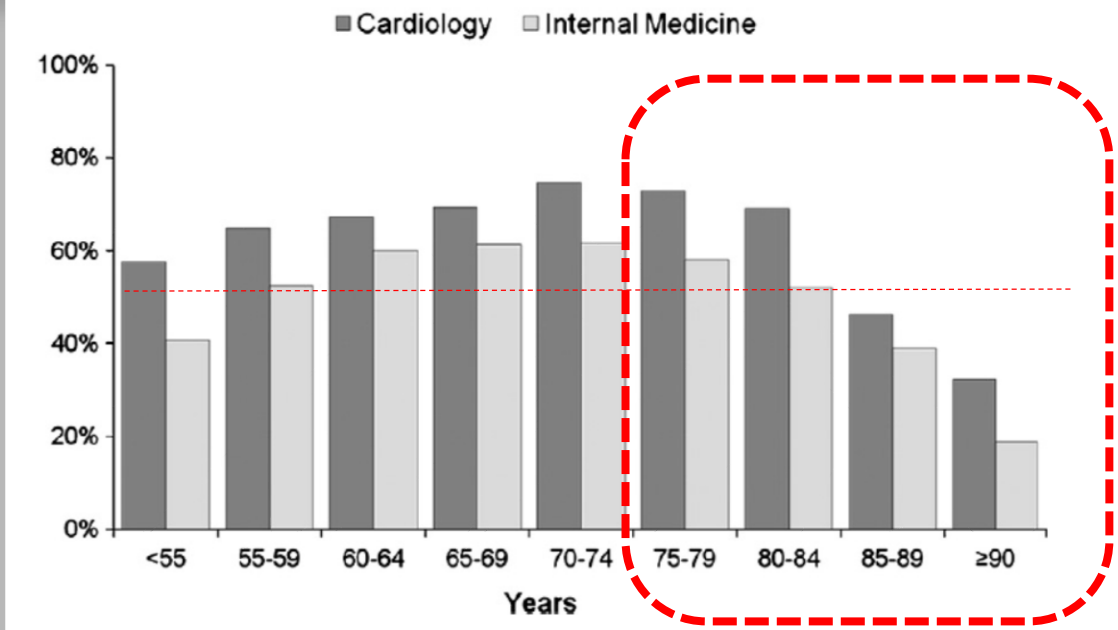


Fig. 5. OAC prescription at discharge from cardiology and internal medicine patients according to the age.

(Am J Cardiol 2017;120:786–791)

Changes in Use of Anticoagulation in Patients With Atrial Fibrillation Within a Primary Care Network Associated With the Introduction of Direct Oral Anticoagulants

Adult patients with AF cared for in an 18-practice primary network between 2010 and 2015

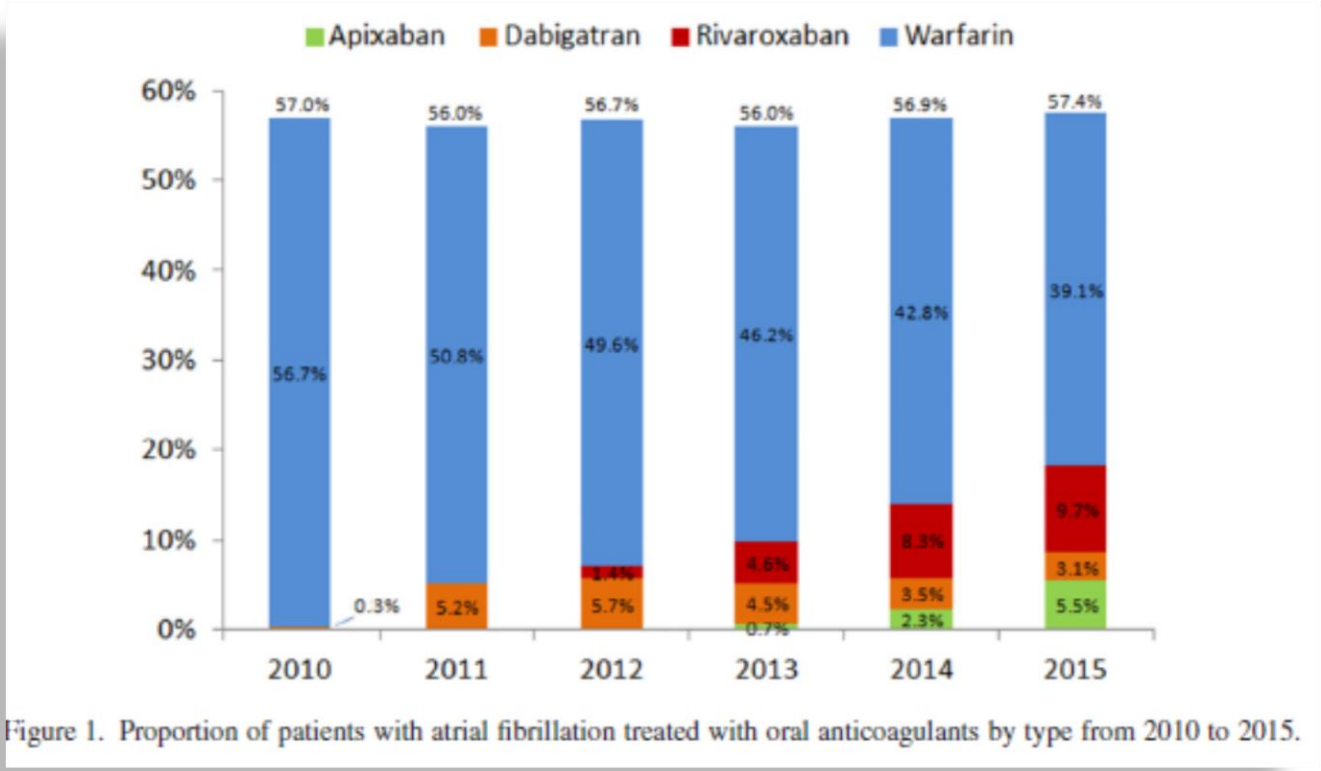


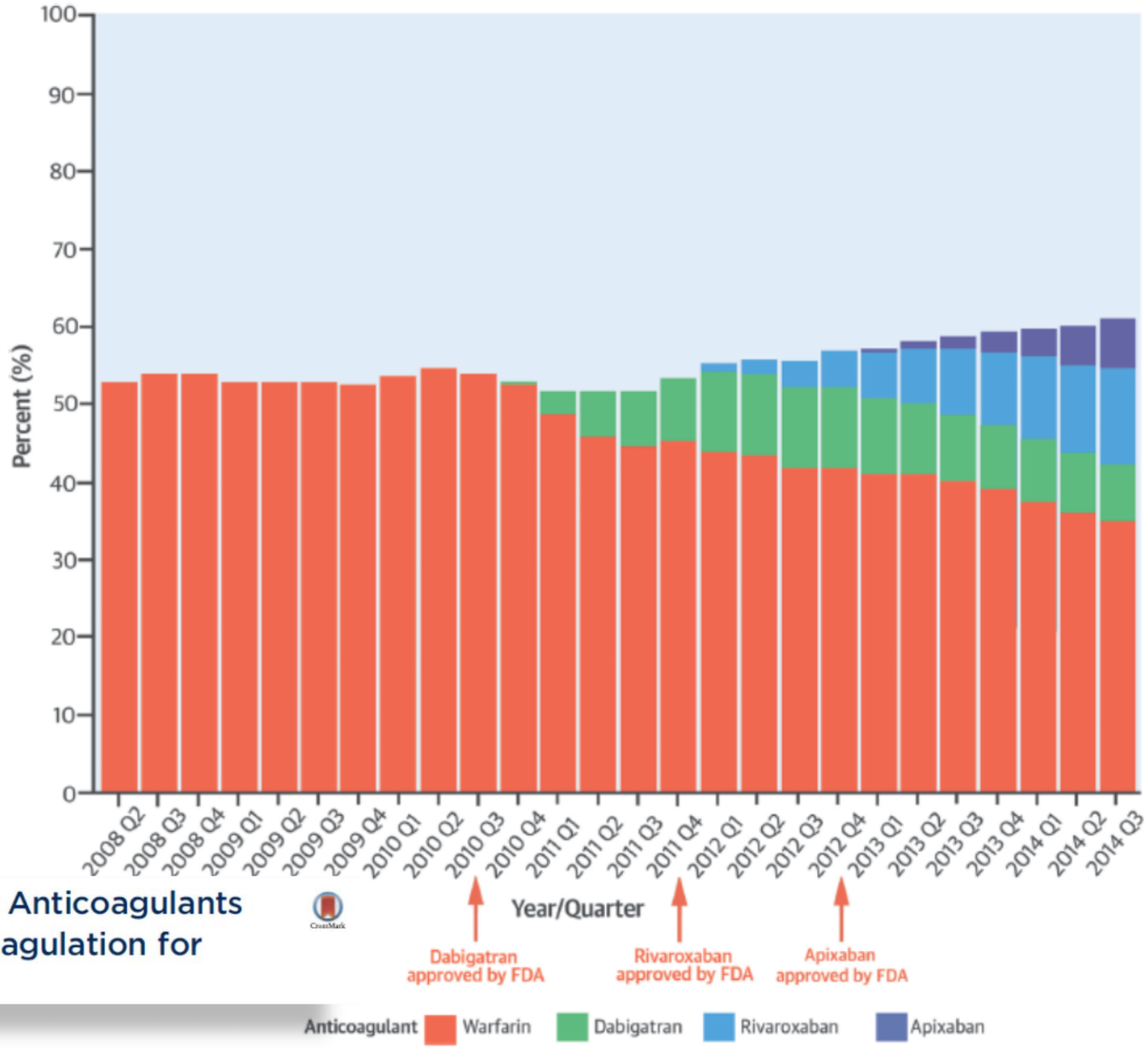
Figure 1. Proportion of patients with atrial fibrillation treated with oral anticoagulants by type from 2010 to 2015.

…The use of DOACs increased over time; however, the proportion of patients treated with OAC did not increase over time…

Patients prescribed DOACs were younger, with lower risk of stroke.

655000 patients with NVAF and CHADS2VASC2>1 enrolled in the **PINNACLE registry** between april 1, 2008 and september 30, 2014

CENTRAL ILLUSTRATION Introduction of Direct Oral Anticoagulants Is Associated With Increase in Overall Rates of Oral Anticoagulation for Atrial Fibrillation



Influence of Direct Oral Anticoagulants on Rates of Oral Anticoagulation for Atrial Fibrillation

Marzec, L.N. et al. J Am Coll Cardiol. 2017;69(20):2475-84.

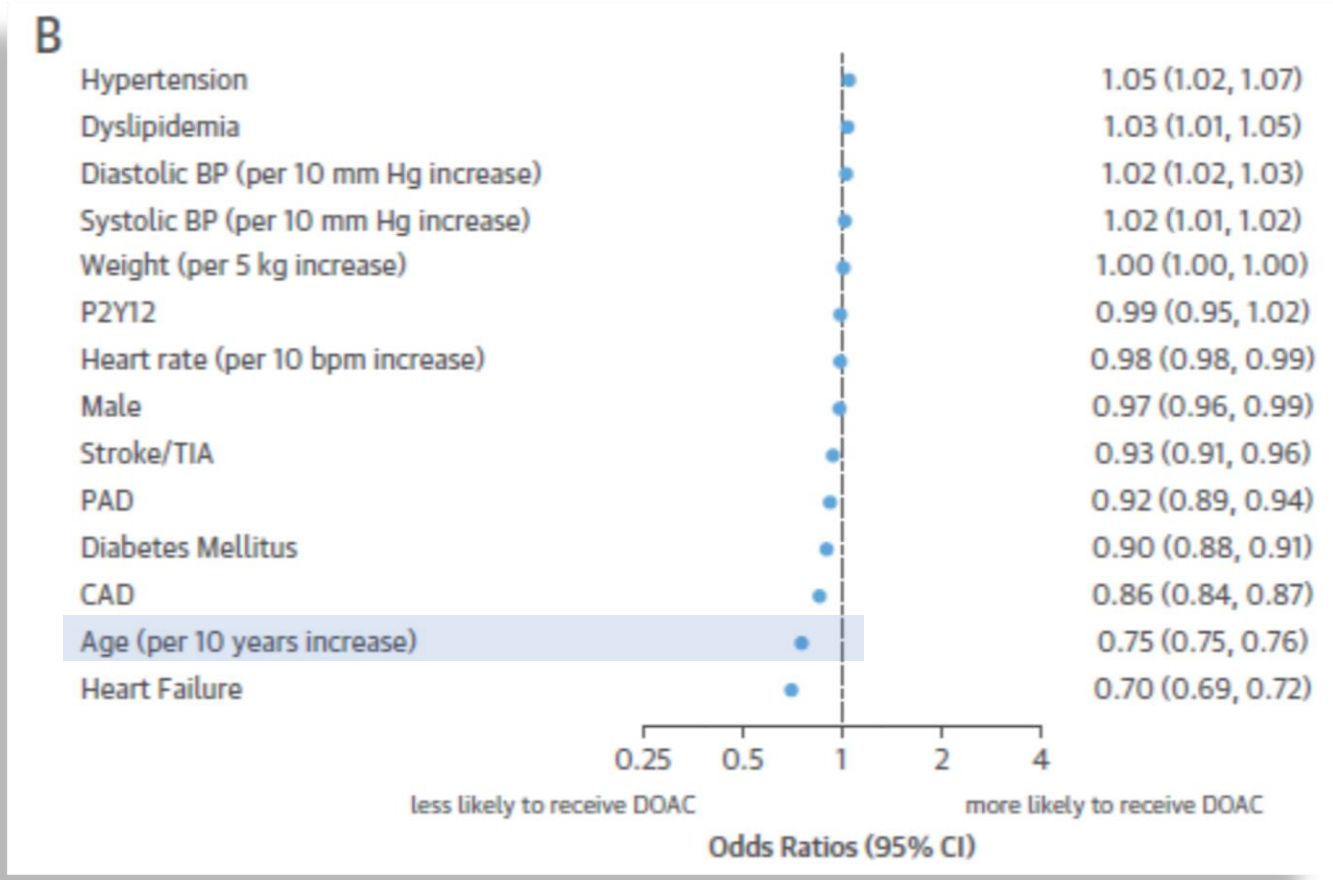
Influence of Direct Oral Anticoagulants on Rates of Oral Anticoagulation for Atrial Fibrillation

655000 patients with NVAF and CHADS2VASC2>1 enrolled in the **PINNACLE registry** between april 1, 2008 and september 30, 2014

Age and **OAC prescription**:

Warfarin	76.2 (10.2)
Dabigatran	72.8 (10.5)
Rivaroxaban	72.9 (10.4)
Apixaban	74.2 (10.2)
None	73.2 (13.3)

P<0.001



Adjusted Patient Factors Associated With Overall OAC Use and DOAC Use in the Primary Analysis Cohort

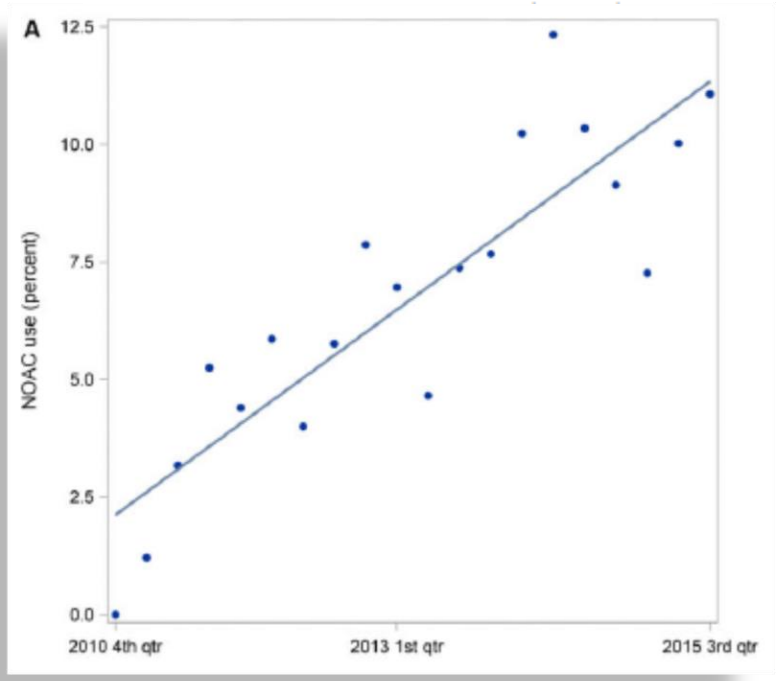
Effect of New Oral Anticoagulants on Prescribing Practices for Atrial Fibrillation in Older Adults

J Am Geriatr Soc 2017.

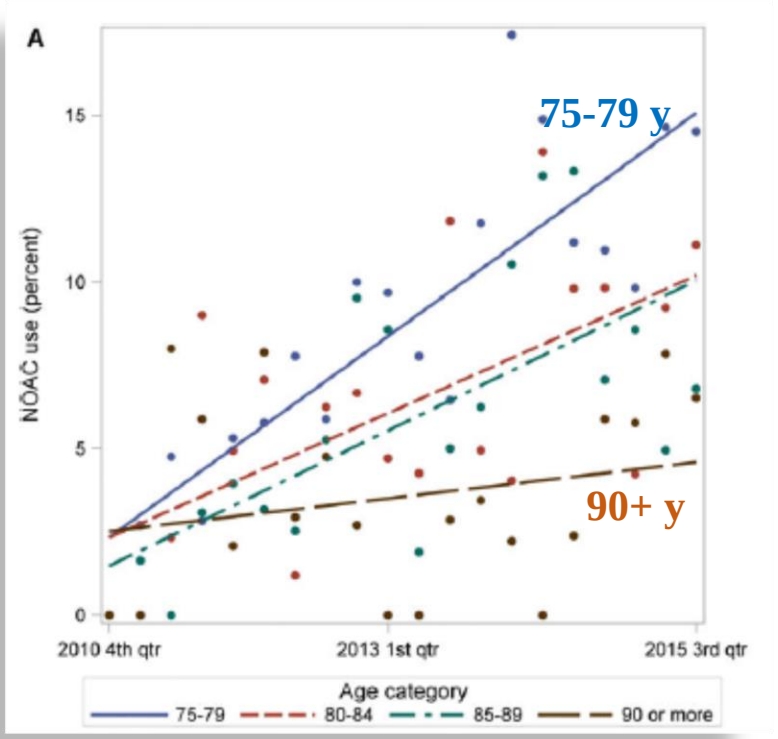
Raymond B. Fohtung, MD, Eric Novak, MS, and Michael W. Rich, MD

Retrospective study; **6568 patients aged 75+ years** with AF admitted to hospital from Oct 2010 to Sept 2015

(A) Quarterly trend in novel oral anticoagulant use



(A) Quarterly trends in novel oral anticoagulant use according to age group:



CONCLUSION …Nonetheless, despite high risk of stroke, **fewer than 45%** of participants were **discharged on an anticoagulant**





Perché spesso gli anziani con FA non ricevono terapia anticoagulante?

E’ giusto non dare la terapia anticoagulante nell’anziano? O, in alternativa, si possono identificare i pazienti anziani ai quali è meglio non dare la terapia anticoagulante?





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Health status, geriatric syndromes and prescription of oral anticoagulant therapy in elderly medical inpatients with atrial fibrillation

Geriatr Gerontol Int 2017; **17:** *416–423*

Mario Bo,[1] Irene Sciarrillo,[1] Guido Maggiani,[1] Yolanda Falcone,[1] Marina Iacovino,[1] Enrica Grisoglio,[1] Gianfranco Fonte,[1] Simon Grosjean[1] and Fiorenzo Gaita[2]

Studio retrospettico su **1078** pazienti con FA dimessi 2010-2013 (**83.4** anni, 60.3% femmine); 26.8% dipendenti ADL, 37.3% dipendenti IADL, cognitive impairment in 56.2%; CHA_2DS_2-VASC medio 4.8; HAS-BLED medio 2.1

Patients without contraindications to VKA	OR	95% CI
Discharge in medium-/long-term facilities	0.4181	0.20–0.87
Permanent/persistent AF	7.1269	4.02–12.63
Hemoglobin	1.2229	1.08–1.39
ADL score	1.6603	1.18–2.33
Age	0.9223	0.89–0.96
No. drugs at discharge	1.1824	1.07–1.31
CHA_2DS_2-VASc score	1.7966	1.47–2.20

Table 4 Variables associated with prescription of oral anticoagulants (vitamin K antagonists) at discharge: multivariate analysis

Archives of Gerontology and Geriatrics 65 (2016) 248–254

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

The role of comprehensive geriatric assessment and functional status in evaluating the patterns of antithrombotic use among older people with atrial fibrillation

A. Mazzone[a,b,1], M. Bo[d], A. Lucenti[a,e], S. Galimberti[a,e], G. Bellelli[a,b,c,*], G. Annoni[a,b,c]

399 patients (83 years) consecutively admitted to a GU, undergoing CGA; 55.7% discharged with OAT

Factors associated with OAC underuse at discharge.

Characteristics		No OAC/n	% No OAC	Multivariate Analysis		
				OR	95%CI	p-value
Age:	<90 yrs	101/245	41.2	1		
	>90 yrs	34/60	56.7	2.57	1.28–5.16	0.008
Severe functional impairment:	No	48/75	64.0	1		
	Yes	87/230	37.8	3.38	1.63–7.01	0.001
Polypharmacy (≥5):	No	93/221	42.1	1		
	Yes	42/84	50.0	2.07	1.1–3.86	0.023
HASBLED score:				1.64	1.09–2.47	0.019
Contraindication to OAC:	No	66/205	32.2	1		
	Yes	64/91	70.3	5.01	2.68–9.34	<0.001
Discharge to Nursing home:	No	113/269	42.0	1		
	Yes	22/36	61.1	2.22	0.97–5.01	0.059

Warfarin Treatment and All-Cause Mortality in Community-Dwelling Older Adults with Atrial Fibrillation: A Retrospective Observational Study

J Am Geriatr Soc 64:1416–1424, 2016.

Alberto Pilotto, MD, Pietro Gallina, MD,† Massimiliano Copetti, PhD,‡ Andrea Pilotto, MD,§ Francesco Marcato, MSc,† Anna M. Mello, MD,* Matteo Simonato, MD,† Giancarlo Logroscino, MD, PhD,¶** Alessandro Padovani, MD, PhD,§ Luigi Ferrucci, PhD,†† and Francesco Panza, MD, PhD,‡¶ on behalf of the Multidimensional Prognostic Index_Age Project Investigators*[1]

Retrospective observational study in 1827 community-dwelling individuals with AF aged 65 and older

Risk of **mortality estimated** using the **MPI** (Multidimensional Prognostic Index) based on information collected using the Standardized Multidimensional Assessment Schedule for Adults and Aged Persons (SVaMA)

Characteristic	All, N = 1,827, 100%	MPI-SVaMA-1 (Mild Risk), n = 705, 38.6%	MPI-SVaMA-2 (Moderate Risk), n = 634, 34.7%	MPI-SVaMA-3 (Severe Risk), n = 488, 26.7%	*P* for Trend
Age, mean ± SD	84.4 ± 7.1	83.8 ± 7.1	85.0 ± 6.4	83.2 ± 7.5	.74
Male, n (%)	653 (35.7)	164 (23.3)	218 (34.4)	271 (55.5)	<.001
Activities of Daily Living, mean ± SD	43.5 ± 18.4	31.6 ± 18.5	52.7 ± 11.1	48.9 ± 16.3	<.001
Cognitive Status, mean ± SD	5.5 ± 3.6	4.6 ± 3.4	6.7 ± 3.3	5.3 ± 3.9	<.001
Nursing Care Needs, mean ± SD	7.6 ± 8.2	2.9 ± 4.8	7.9 ± 6.6	14.1 ± 9.5	<.001
Mobility, mean ± SD	30.0 ± 11.7	23.2 ± 12.5	36.8 ± 5.9	34.5 ± 9.8	<.001
Participants starting warfarin, n (%)	798 (43.7)	380 (53.9)	245 (38.6)	173 (35.5)	<.001
		53.9%	**38.6%**	**35.5%**	





Health status, geriatric syndromes and prescription of oral anticoagulant therapy in elderly medical in-patients with atrial fibrillation: a prospective observational study

International Journal of Cardiology 187 (2015) 123–125

M. Bo [a], F. Li Puma [a], M. Badinella Martini [a], Y. Falcone [a,*], M. Iacovino [a], E. Grisoglio [a], M. Bonetto [a], G. Isaia [b], G. Ciccone [a], G.C. Isaia [a], F. Gaita [c]

. Advanced age, very short life expectancy, difficult or impossible management of therapy, perceived fear of bleeding and harm greater than benefit were the most common reasons why physicians withhold OAs.




JAMA Internal Medicine | Original Investigation JAMA Intern Med. 2016;176(8):1176-1183.

Risk of Bleeding and Thrombosis in Patients 70 Years or Older Using Vitamin K Antagonists

3313 patients using VKAs (70% for AF)

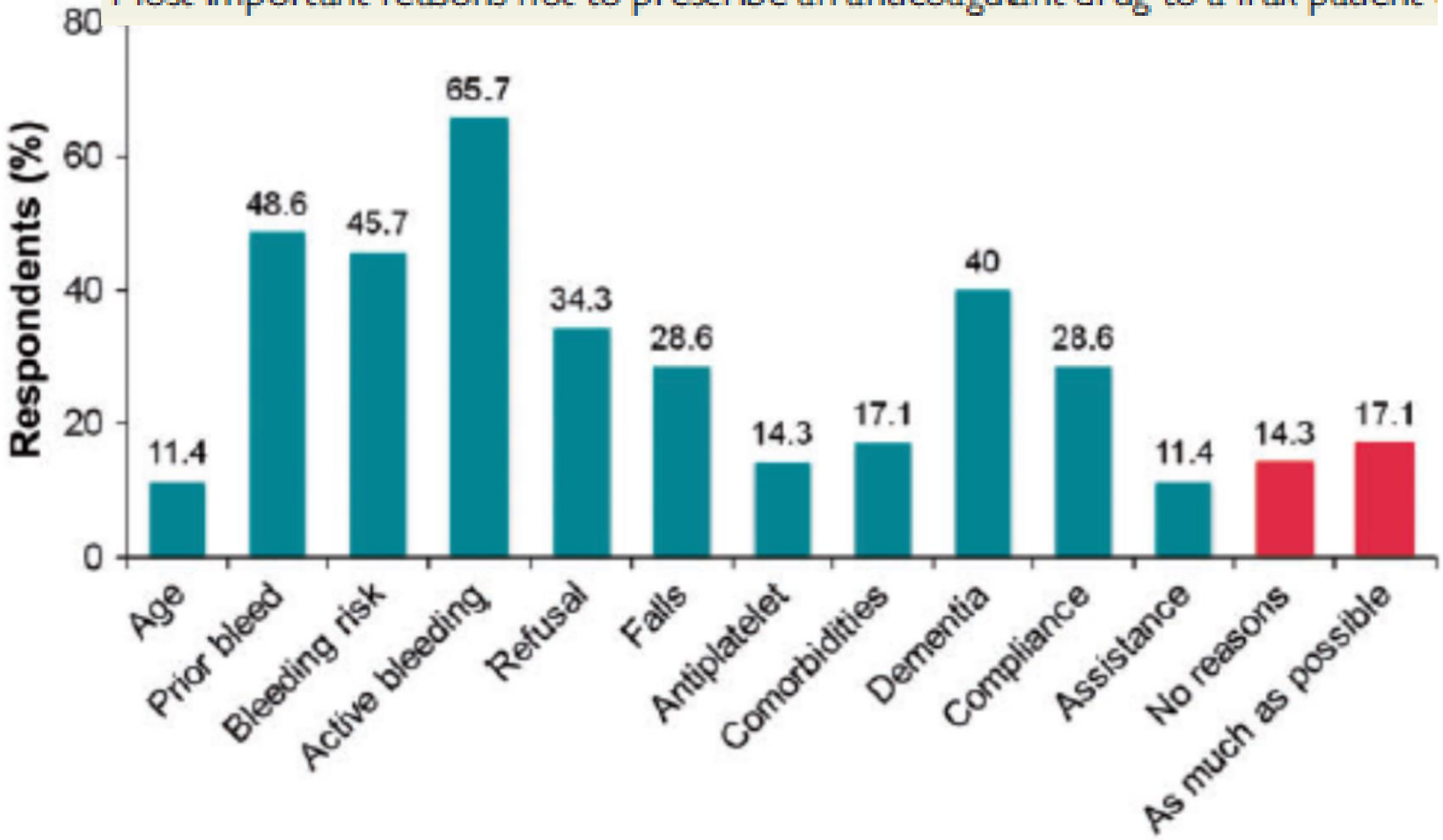
	Risk of bleeding	Major bleeding	Risk of thrombosis
1104 pazienti **70-79** anni	**1**	**1**	**1**
1100 pazienti **80-89** anni	1.07 (0.89-1.27)	1.07 (0.89-1.27)	1.75 (1.002-3.05)
1109 pazienti **90+** anni	1.26 (1.05-1.50)	1.20 (0.65-2.22)	**2.14 (1.22-3.75)**

Frailty syndrome: an emerging clinical problem in the everyday management of clinical arrhythmias. The results of the European Heart Rhythm Association survey

Europace (2017) **19**, 1896–1902

Stefano Fumagalli[1]*, Tatjana S. Potpara[2], Torben Bjerregaard Larsen[3], Kristina H. Haugaa[4], Dan Dobreanu[5], Alessandro Proclemer[6], and Nikolaos Dagres[7]

Most important reasons not to prescribe an anticoagulant drug to a frail patient



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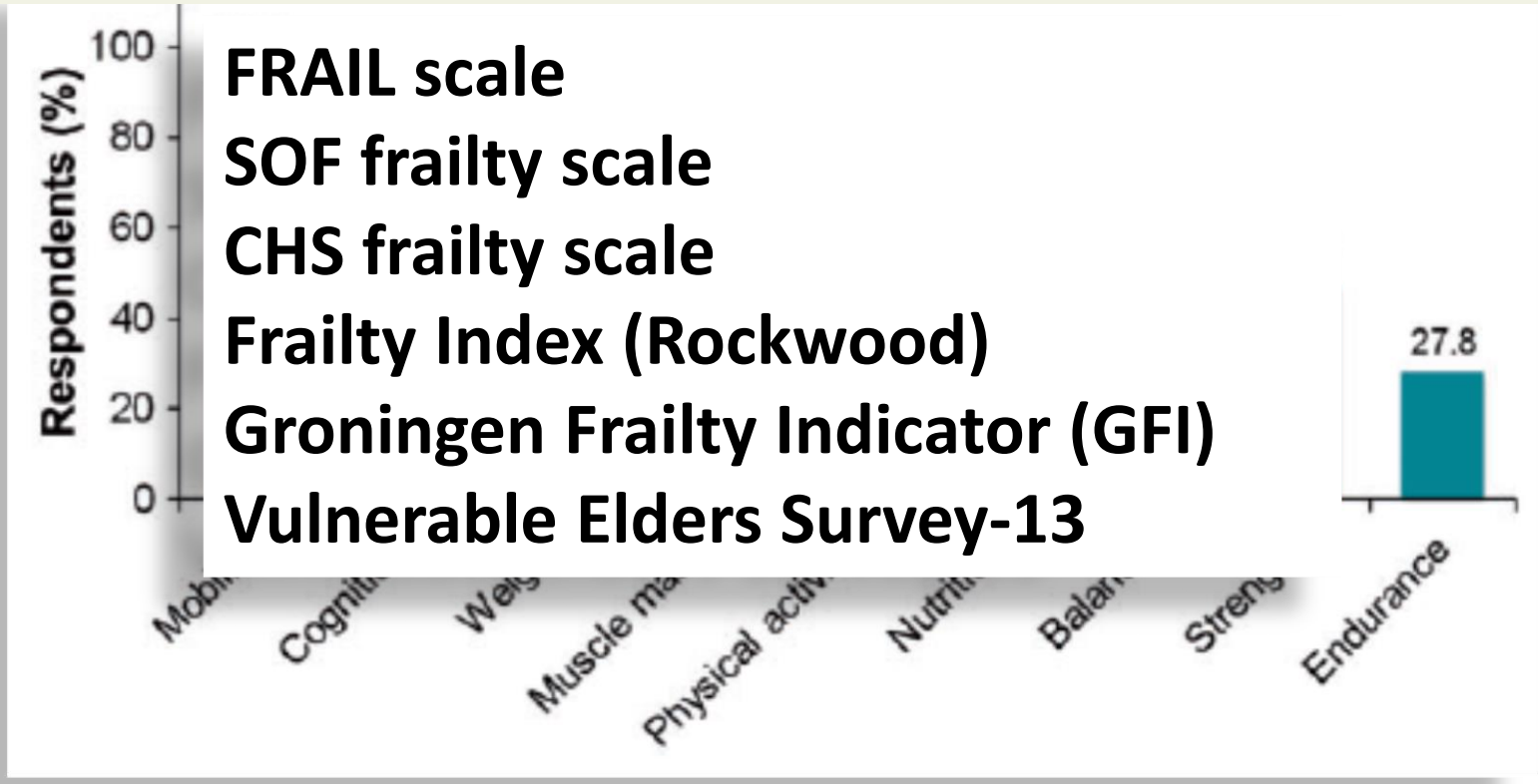
La **FRAGILITA'** nell'anziano: brevissimo lessico **«geriatrico»** per evitare fraintesi…con i **CARDIOLOGI!**

Features that characterize frailty syndrome according to the participants' opinion.



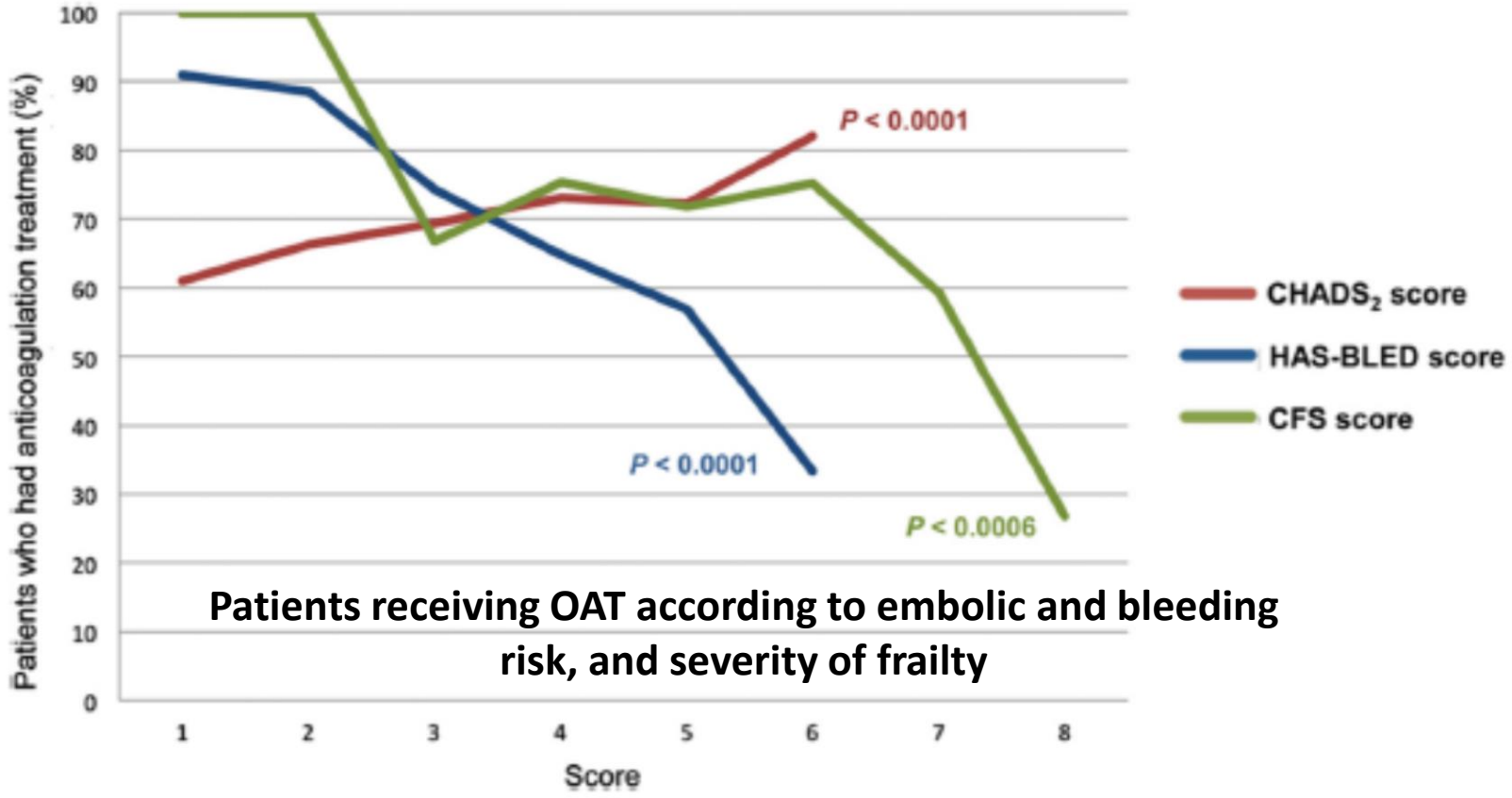
FRAIL scale
SOF frailty scale
CHS frailty scale
Frailty Index (Rockwood)
Groningen Frailty Indicator (GFI)
Vulnerable Elders Survey-13

Canadian Journal of Cardiology 32 (2016) 169–176

Clinical Research

The Effect of Bleeding Risk and Frailty Status on Anticoagulation Patterns in Octogenarians With Atrial Fibrillation: The FRAIL-AF Study

682 hospitalized patients aged 80 years and older



Patients receiving OAT according to embolic and bleeding risk, and severity of frailty

A global clinical measure of fitness and frailty in elderly people

Kenneth Rockwood, Xiaowei Song, Chris MacKnight, Howard Bergman, David B. Hogan, Ian McDowell, Arnold Mitnitski

FRAILTY INDEX
(INDICE PROGNOSTICO)

Appendix 1: List of variables used by the Canadian Study of Health and Aging to construct the 70-item CSHA Frailty Index

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls
- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease
- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmomental reflex
- Other medical history

SCORE PROGNOSTICO di mortalità ad 1 anno

Table 1. MPI Score Assigned to Each Domain Based on the Severity of the Problems

	Problems		
	No	Minor	Severe
Assessment	(Value=0)	(Value=0.5)	(Value=1)
ADL*	6–5	4–3	2–0
Instrumental ADL*	8–6	5–4	3–0
Short portable mental status questionnaire†	0–3	4–7	8–10
Comorbidity index (cumulative illness rating scale-CI)‡	0	1–2	≥3
Mini nutritional assessment§	≥24	17–23.5	<17
Exton-smith scale¶	16–20	10–15	5–9
No. of medications	0–3	4–6	≥7
Social support network	Living with family	Institutionalized	Living alone

*No. of active functional activities.
†No. of errors.
‡No. of diseases.
§Mini Nutritional Assessment score: ≥24, satisfactory nutritional status; 17–23.5, at risk of malnutrition; <17, malnutrition.
¶Exton-Smith Scale score: 16–20, minimum risk; 10–15, moderate risk; 5–9 high risk of developing scores.

Basso rischio

(≤ 0,33)

Medio rischio

(≥ 0,33 ≤ 0,66)

Alto rischio

(≥ 0,67)

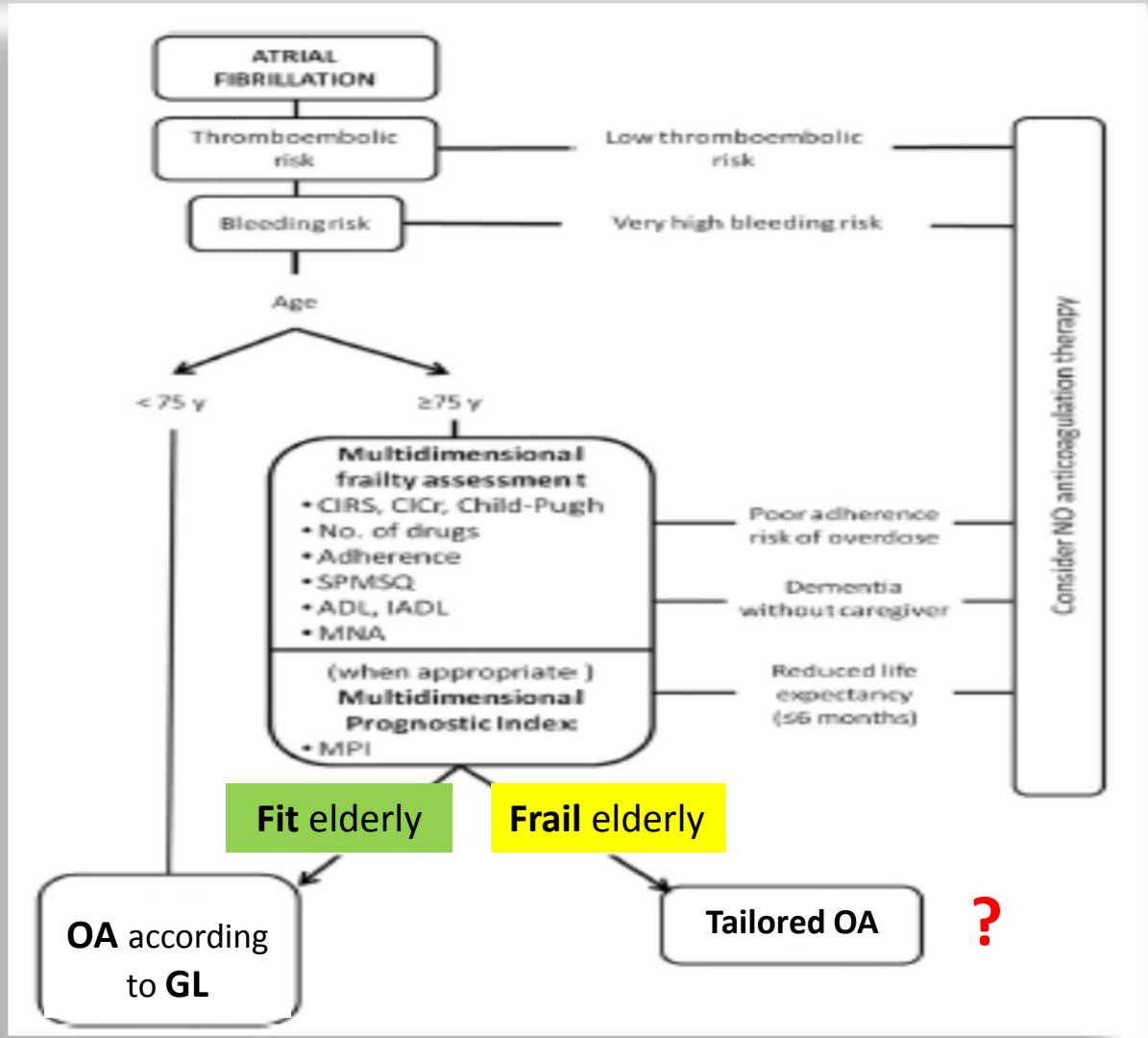
Pilotto A. et Al. Circ.Heart Fail.2010;3.14-20

Review Article

Thromboembolic Prevention in Frail Elderly Patients With Atrial Fibrillation: A Practical Algorithm

Serena Granziera MD [a,b,*], Alexander T. Cohen MD [c], Giovanni Nante MD [a], Enzo Manzato MD, PhD [a], Giuseppe Sergi MD [a,*]

JAMDA 16 (2015) 358–364



Journal of Gerontology: MEDICAL SCIENCES
2001, Vol. 56A, No. 3, M146–M156

Frailty in Older Adults: Evidence for a Phenotype

Linda P. Fried,[1] Catherine M. Tangen,[2] Jeremy Walston,[1] Anne B. Newman,[3] Calvin Hirsch,[4] John Gottdiener,[5] Teresa Seeman,[6] Russell Tracy,[7] Willem J. Kop,[8] Gregory Burke,[9] and Mary Ann McBurnie[2] for the Cardiovascular Health Study Collaborative Research Group

Increasingly, geriatricians define frailty as a biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes (9–13). This concept distinguishes frailty from disability (9,10,14,15). There is a growing consensus that markers of frailty include age-associated declines in lean body mass, strength, endurance, balance, walking performance, and low activity (9,10,14–17), and that multiple components must be present clinically to constitute frailty

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Linda P. Fried,[1] Catherine M. Tangen,[2] Jeremy Walston,[1] Anne B. Newman,[3] Calvin Hirsch,[4]

Table 1. Operationalizing a Phenotype of Frailty

A. *Characteristics of Frailty*	B. *Cardiovascular Health Study Measure**
Shrinking: Weight loss (unintentional) Sarcopenia (loss of muscle mass)	Baseline: >10 lbs lost unintentionally in prior year
Weakness	Grip strength: lowest 20% (by gender, body mass index)
Poor endurance; Exhaustion	"Exhaustion" (self-report)
Slowness	Walking time/15 feet: slowest 20% (by gender, height)
Low activity	Kcals/week: lowest 20% males: <383 Kcals/week females: <270 Kcals/week
	C. *Presence of Frailty*
	Positive for frailty phenotype: ≥3 criteria present
	Intermediate or prefrail: 1 or 2 criteria present

*See Appendix.

CHS

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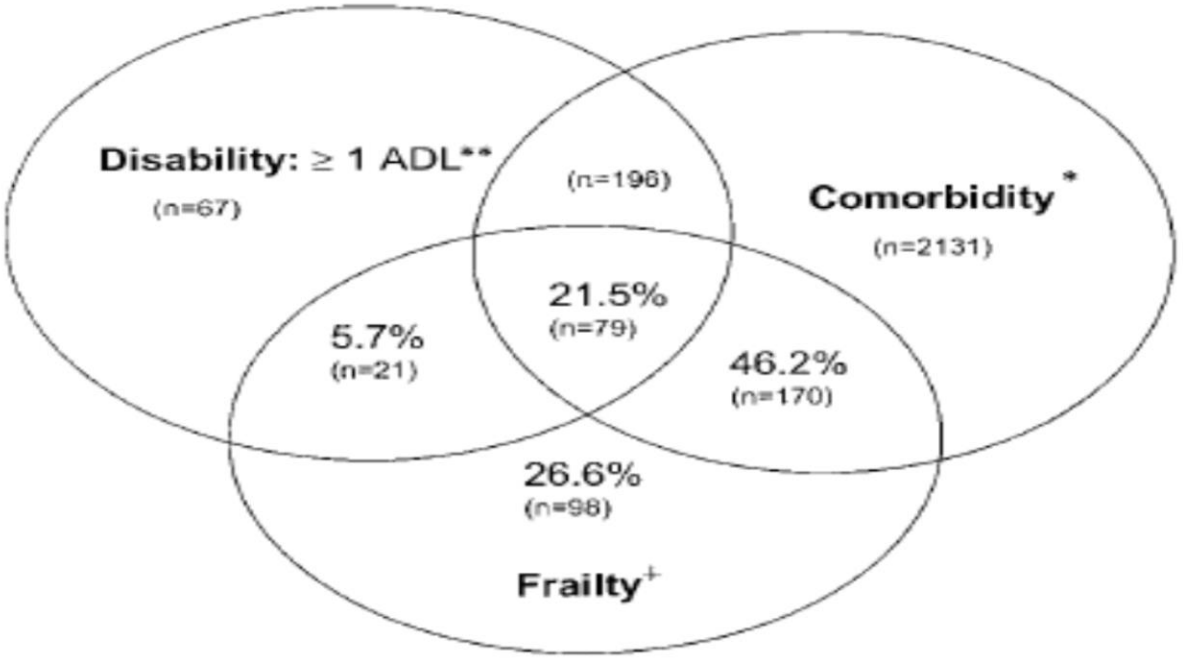
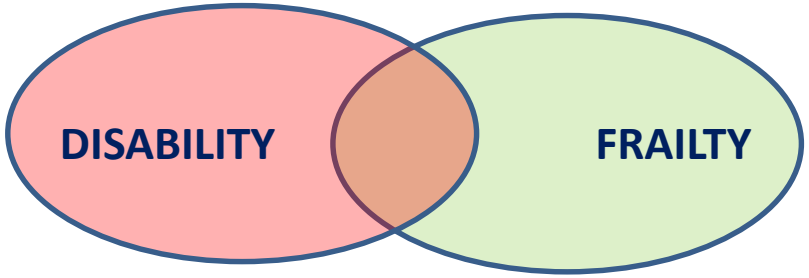
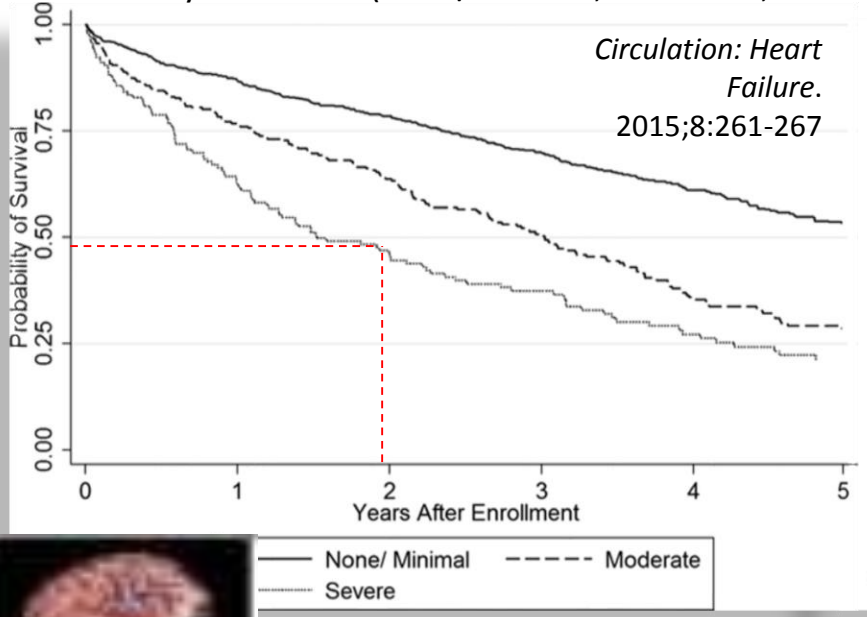


Figure 3. Venn diagram displaying extent of overlap of frailty with ADL disability and comorbidity (≥2 diseases). Total represented: 2,762 subjects who had comorbidity and/or disability and/or frailty. *n* of each subgroup indicated in parentheses. + Frail: overall $n = 368$ frail subjects (both cohorts). *Comorbidity: overall $n = 2,576$ with 2 or more out of the following 9 diseases: myocardial infarction, angina, congestive heart failure, claudication, arthritis, cancer, diabetes, hypertension, COPD. Of these, 249 were also frail. **Disabled: overall $n = 363$ with an ADL disability; of these, 100 were frail.

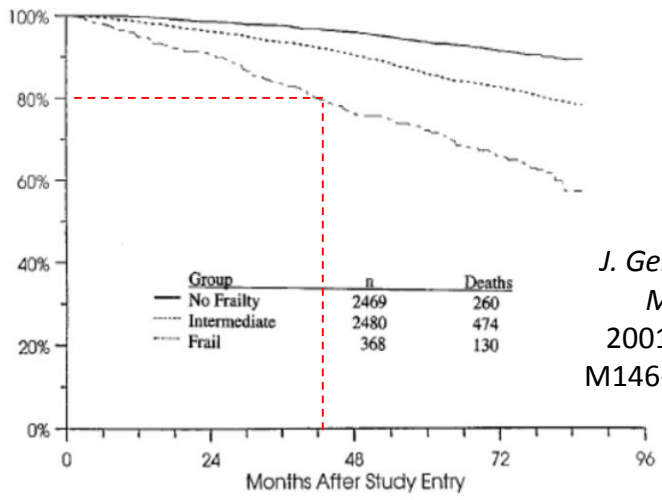


Time to death in patients with HF according to their level of difficulty with **ADLs** (none/minimal, moderate, severe)



Circulation: Heart Failure. 2015;8:261-267

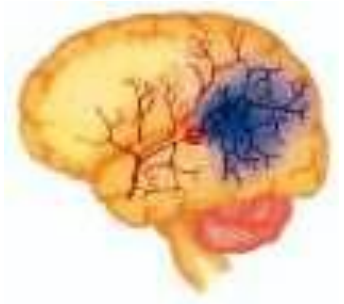
Survival curve estimates according to **FRAILTY** status



J. Gerontol: Med Sci 2001;56 A: M146-M156

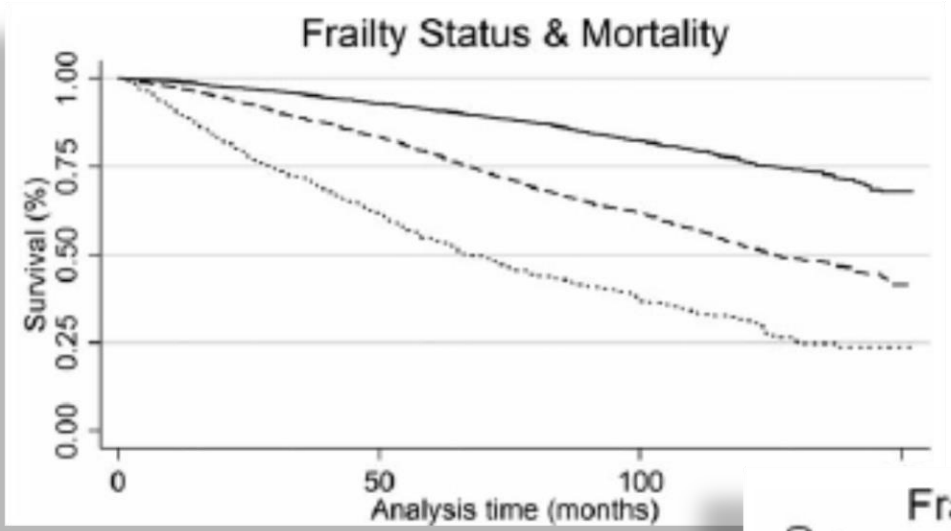
Figure 4. Survival curve estimates (unadjusted) over 72 months of follow-up by frailty status at baseline: Frail (3 or more criteria termediate (1 or 2 criteria present); Not frail (0 criteria present). (Data are from both cohorts.)

….**fragilità** e **disabilità** devono essere «pesate» in modo diverso quando si prenda in considerazione una terapia (anticoagulante) volta primariamente a prevenire la **disabilità conseguente ad un ictus cardio-embolico**….

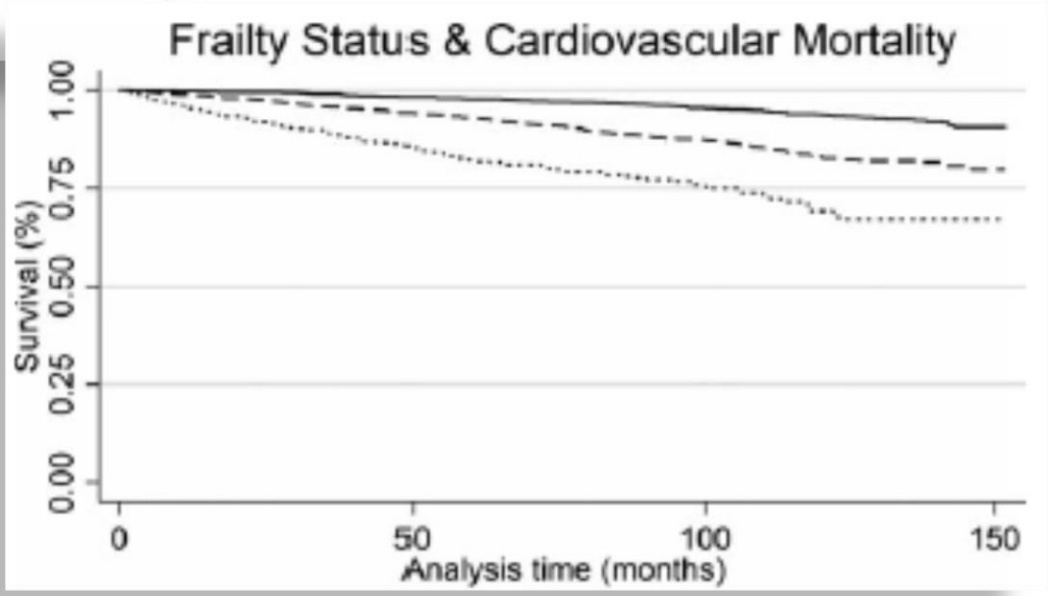


Mortality Risk Along the Frailty Spectrum: Data from the National Health and Nutrition Examination Survey 1999 to 2004

J Am Geriatr Soc 2018.



CONCLUSION: Frailty and prefrailty are associated with increased risk of death. Demonstrating the association between prefrail status and mortality is the first step to identifying potential targets of intervention in future studies.



Mortality Risk Along the Frailty Spectrum: Data from the National Health and Nutrition Examination Survey 1999 to 2004

J Am Geriatr Soc 2018.

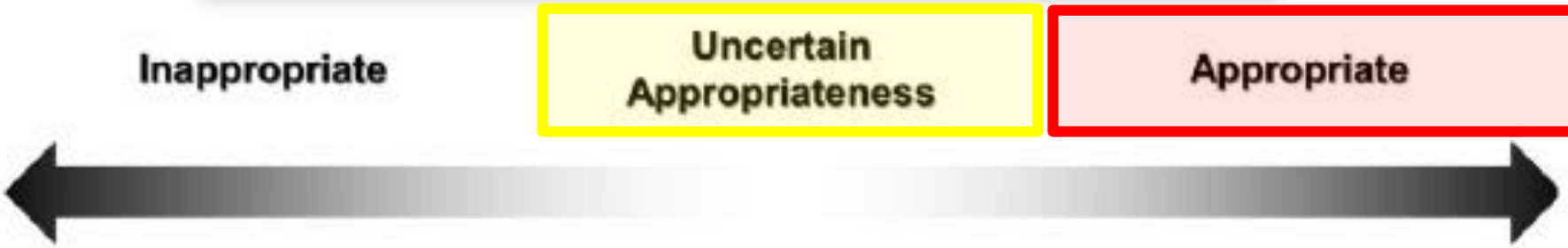
Table 3. Association Between Frailty and Overall and Cardiovascular Mortality

	Model 1	Model 2	Model 3
Mortality	Hazard Ratio (95% Confidence Interval)		
Overall			
Prefrail	2.40 (2.16–2.67)	1.79 (1.60–2.01)	1.64 (1.45–1.85)
Frail	4.97 (4.34–5.69)	3.89 (3.36–4.51)	2.79 (2.35–3.30)
Cardiovascular			
Prefrail	2.82 (2.28–3.48)	2.07 (1.65–2.60)	1.84 (1.45–2.34)
Frail	3.72 (2.85–4.87)	4.79 (3.61–6.34)	3.39 (2.45–4.70)

E’ possibile che almeno parte di questo eccesso di mortalità CV e totale nei soggetti FRAGILI possa essere addebitato al mancato uso degli anticoagulanti orali per la FA (o di altri farmaci indicati per il trattamento o la prevenzione della malattie CV) in ragione della loro «fragilità»?

(Am Heart J 2014;168:239-247.e1.)

Addressing barriers to optimal oral anticoagulation use and persistence among patients with atrial fibrillation: Proceedings, Washington, DC, December 3-4, 2012



Reasons for unsuitability for oral anticoagulation among patients with AF and CHADS ≥1 and/or CHADS-VASc ≥2. *Applicable to VKA only.

THE AMERICAN JOURNAL of MEDICINE®

Risk of Falls and Major Bleeds in Patients on Oral Anticoagulation Therapy

The American Journal of Medicine (2012) 125, 773-778

Studio prospettico su 515 pazienti dimessi in TAO; 308 pazienti (59.8%) ad alto rischio di cadute; outcome: tempo al primo sanguinamento maggiore; follow-up: 12 mesi

Rischio di sanguinamento maggiore non significativamente aumentato nei pazienti ad alto rischio di cadute rispetto agli altri (8,0 vs 6,8/100/anno, p=.64). Il rischio di sanguinamento maggiore è risultato indipendentemente associato al sesso femminile ed alla politerapia ma non all'alto rischio di cadute. Solo 3 sanguinamenti maggiori conseguenza diretta di caduta (0.6/100/anno)

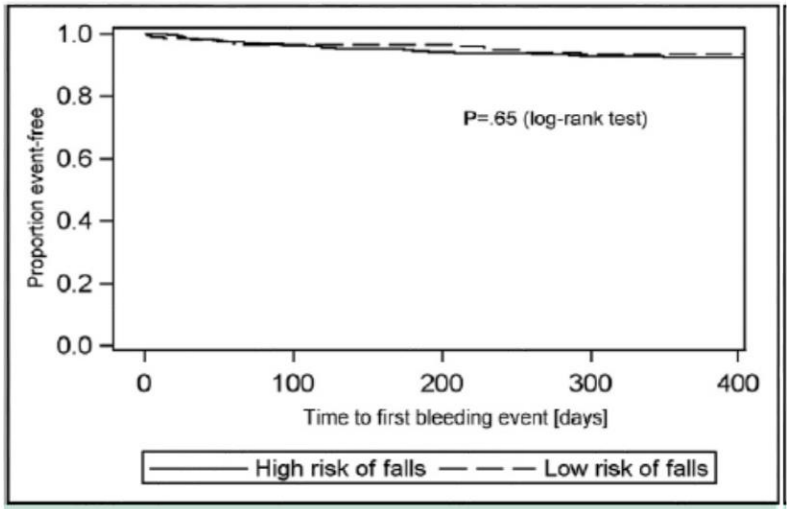


Figure Unadjusted time to first major bleeding event curves according to risk of falls (n = 515).

- The incidence rate of major bleeding in patients on oral anticoagulants is low overall, and fall-related bleeds are rare in these patients.
- A high falls risk is not statistically significantly associated with a risk of major bleeds (hazard ratio 1.09; 95% confidence interval, 0.54-2.21), suggesting that being at risk of falls is not a valid reason to avoid oral anticoagulants in medical patients.

The American Journal of Medicine (2005) 118, 612–617

ELSEVIER

THE AMERICAN JOURNAL of MEDICINE®

Incidence of intracranial hemorrhage in patients with atrial fibrillation who are prone to fall

METHODS: Quality improvement organizations identified 1245 Medicare beneficiaries who were documented in the medical record to be at high risk of falls and 18 261 other patients with atrial fibrillation. The patients were elderly (mean 80 years), and 48% were prescribed warfarin at hospital discharge. The primary endpoint was subsequent hospitalization for an intracranial hemorrhage, based on ICD-9 codes.

Table 3 Multivariate Cox regression showing hazard ratios (HR) of independent predictors of intracranial hemorrhage

Factor	HR (95% CI)	*P* Value
High-risk for falls	1.9 (1.3–2.9)	0.002
Prior stroke	2.2 (1.7–2.8)	<0.0001
Prior bleed	1.8 (1.4–2.4)	<0.0001
Neuropsychiatric impairment	1.4 (1.0–1.9)	0.055

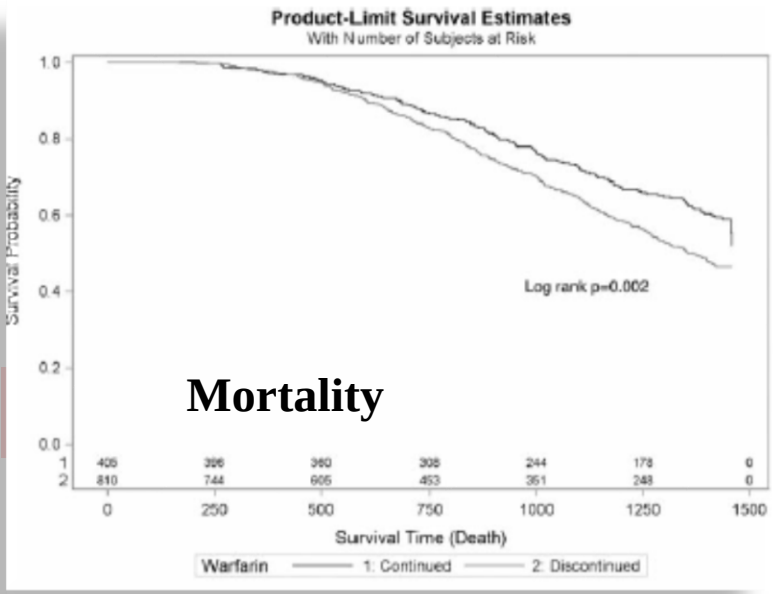
Table 4 Hazard ratio of warfarin for composite outcome—out-of-hospital death or hospitalization for stroke, myocardial infarction, or hemorrhage—in 1245 patients at high risk for falls

$CHADS_2$ score	Hazard ratio (95% CI)	*P* value	Recommended antithrombotic therapy
0–1	0.98 (0.56,1.72)	0.94	Aspirin or nil
2–6	0.75 (0.61,0.91)	0.004	Anticoagulant

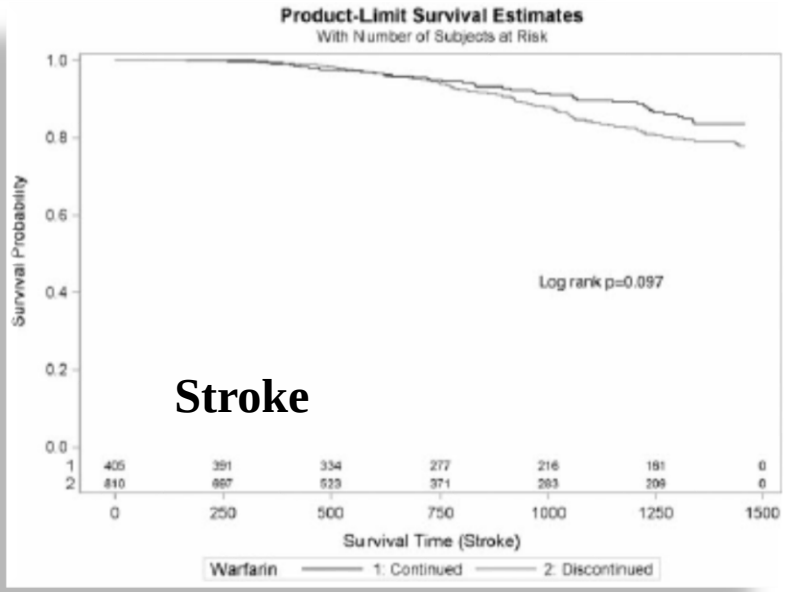
CONCLUSION: Patients at high risk for falls with atrial fibrillation are at substantially increased risk of intracranial hemorrhage, especially traumatic intracranial hemorrhage. However, because of their high stroke rate, they appear to benefit from anticoagulant therapy if they have multiple stroke risk factors.

Continued Use of Warfarin in Veterans with Atrial Fibrillation After Dementia Diagnosis

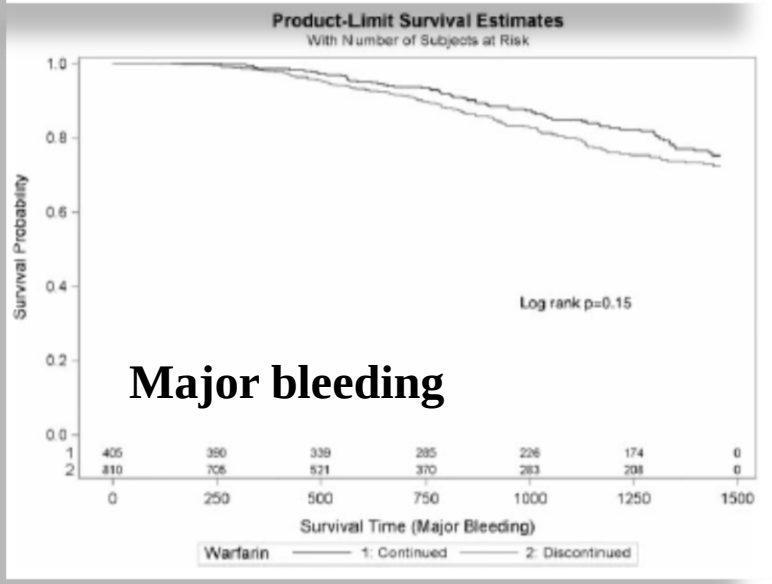
J Am Geriatr Soc 65:249–256, 2017.



Mortality



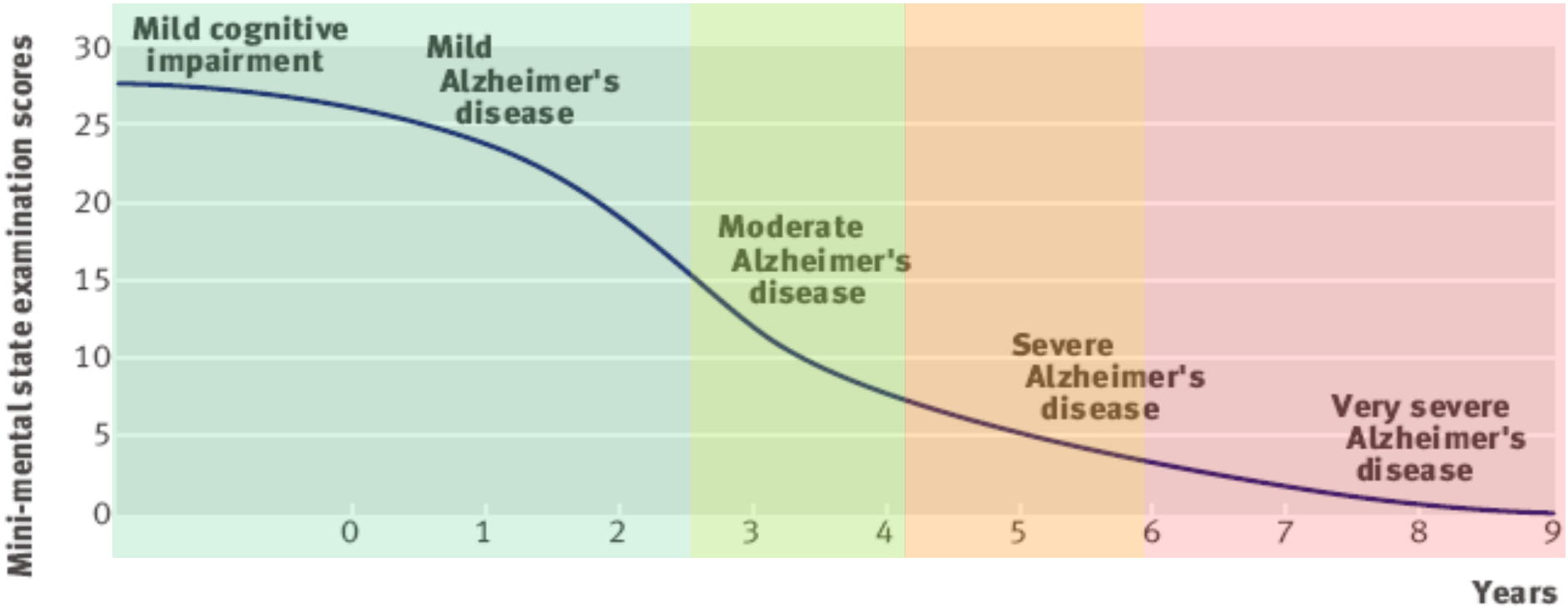
Stroke



Major bleeding

Using propensity score matching, the protective effect of continuing warfarin persisted in prevention of stroke (HR = 0.74, 95% CI = 0.54–0.996, $P = .047$) and mortality (HR = 0.72, 95% CI = 0.60–0.87, $P < .001$), with no statistically significant decrease in risk of major bleeding (HR = 0.78, 95% CI = 0.61–1.01, $P = .06$).

CONCLUSION: Discontinuing warfarin after a diagnosis of dementia is associated with a significant increase in stroke and mortality. **J Am Geriatr Soc 65:249–256, 2017.**



Mild cognitive impairment: Complaints of memory loss, intact activities of daily living, no evidence of Alzheimer's disease

Mild Alzheimer's disease: Forgetfulness, short term memory loss, repetitive questions, hobbies, interests lost, impaired activities of daily living

Moderate Alzheimer's disease: Progression of cognitive deficits, dysexecutive syndrome, further impaired activities of daily living, transitions in care, emergence of behavioural and psychological symptoms of dementia

Severe Alzheimer's disease: Agitation, altered sleep patterns, assistance required in dressing, feeding, bathing, established behavioural and psychological symptoms of dementia

Very severe Alzheimer's disease: Bedbound, no speech, incontinent, basic psychomotor skills lost





Perché spesso gli anziani con FA non ricevono terapia anticoagulante?

E’ giusto non dare la terapia anticoagulante nell’anziano? O, in alternativa, si possono identificare i pazienti anziani ai quali è meglio non dare la terapia anticoagulante?



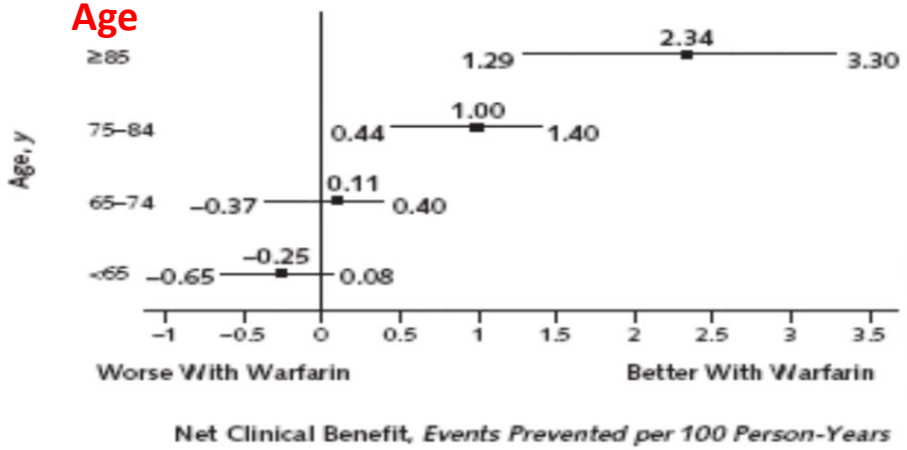

Annals of Internal Medicin Ann Intern Med. 2009;151:297-305. | ARTICLE

The Net Clinical Benefit of Warfarin Anticoagulation in Atrial Fibrillation

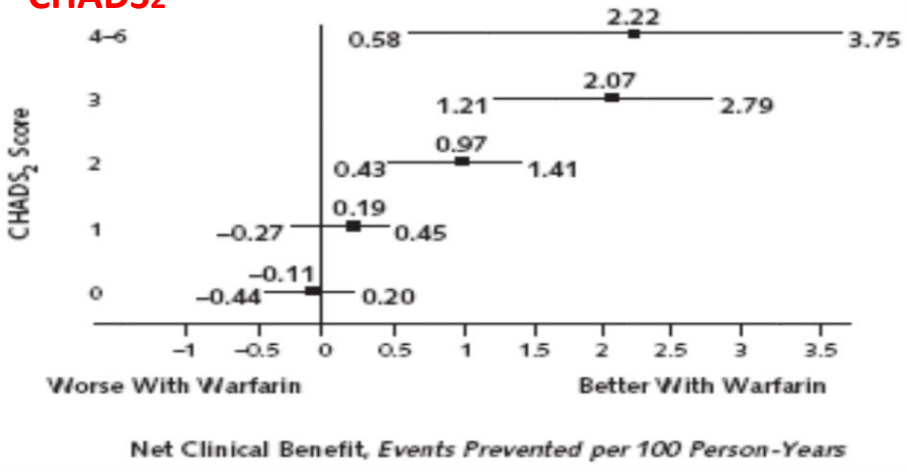
Daniel E. Singer, MD; Yuchiao Chang, PhD; Margaret C. Fang, MD, MPH; Leila H. Borowsky, MPH; Niela K. Pomernacki, RD; Natalia Udaltsova, PhD; and Alan S. Go, MD

Figure. **The net clinical benefit of warfarin, by age (*top*) and $CHADS_2$ score (*bottom*).**

Age



CHADS2



Obiettivo: *quantificare* ***il beneficio clinico netto del warfarin*** *in 13559 pazienti con FA (****6141 età>75 anni****; 45% femmine); studio misto retrospettico e prospettico su pazienti consecutivi con FA dal 1996 al 2003*

Benefit minus harm (net treatment benefit) was highest in patients with:
-previous stroke
-age older than 84 years
-others with high stroke risk

Age and Ageing 2018; **47:** 9–17

Effectiveness and safety of oral anticoagulants in older patients with atrial fibrillation: a systematic review and meta-regression analysis

Key points

- Warfarin use was superior to warfarin non-use, aspirin and no antithrombotic therapy in reducing the risk of stroke/TE in older patients with AF.
- The non-vitamin K antagonist oral anticoagulants (NOACs) were superior to warfarin for stroke/TE prevention with reduced risk of major bleeding in older AF patients.
- This study adds to the evidence suggesting that NOACs should be preferred to warfarin as oral anticoagulants for stroke prevention in older people with AF.

(Am J Cardiol 2016;117:590–595)

Effects of Oral Anticoagulant Therapy in Medical Inpatients ≥65 Years With Atrial Fibrillation

Mario Bo, PhD[a], Irene Sciarrillo, MD[a], Federica Li Puma, MD[a], Marco Badinella Martini, MD[a], Yolanda Falcone, MD[a,*], Marina Iacovino, MD[a], Enrica Grisoglio, MD[a], Elena Menditto, MD[a], Gianfranco Fonte, MD[a], Enrico Brunetti, MD[a], Guido Maggiani, MD[a], Giovanni Carlo Isaia, MD[a], and Fiorenzo Gaita, PhD[b]

Studio retrospettico su **980** pazienti con FA dimessi 2010-2013 (**83.4** anni, 60.3% femmine); 37.3 dipendenti ADL, 37.3% dipendenti IADL, cognitive impairment in 56.2%; CHA_2DS_2-VASC 4.8; HAS-BLED medio 2.1

Baseline characteristics and outcome clinical events of the cohorts, before and after propensity score matching by treatment group

Baseline clinical variables	Before propensity score matching			After propensity score matching		
	Oral Anticoagulant Therapy		p Value	Oral Anticoagulant Therapy		p Value
	YES (n=384)	NO (n=596)		YES (n=201)	NO (n=201)	
Age (years)	81.8± 6.1	84.7±6.8	0.000	83.7±5.8	83.6±6.7	0.943
Female gender	230 (59.9%)	363 (60.9%)	0.753	117 (58.2%)	114 (56.7%)	0.267
Length of stay (mg/dl, median [25°-75°])	7 (4-12)	8 (5-13)	0.162	8 (5-14)	8 (5-12)	0.128
ADL dependent	165 (42.9%)	384 (64.4%)	0.000	114 (56.7%)	114 (56.7%)	0.999
IADL dependent	238 (52.0%)	455 (76.4%)	0.000	146 (72.6%)	146 (72.6%)	0.999
Moderate-severe cognitive impairment	179 (46.6%)	117 (19.6%)	0.000	111 (55.2%)	114 (56.7%)	0.852
Charlson comorbidity index (m±sd)	7.0±2.0	7.6± 2.2	0.000	7.3±2.0	7.3±2.3	0.774
CHA_2DS_2-VASc (m±sd)	4.9±1.3	4.7±1.4	0.252	4.9±1.3	4.7±1.4	0.257
HAS-BLED (m±sd)	2.0 (1-2)	2.0 (2-3)	0.000	2.0 (1-3)	2.0 (1-3)	0.306
Hemoglobin (g/dl, m±sd)	12.3±1.9	11.7±2.1	0.000	12.0±1.9	12.0±2.0	0.849
Creatinine (mg/dl, median [25°-75°])	1.02 (0.88-1.41)	1.1 (0.9-1.5)	0.000	1.1 (0.87-1.42)	1.1 (0.9-1.57)	0.262
Home-discharge	349 (90.9%)	444 (74.5%)	0.001	172 (85.6%)	169 (84.1%)	0.771
Permanent atrial fibrillation	319 (83.1%)	401 (67.3%)	0.001	147 (73.1%)	144 (71.6%)	0.822
Clinical outcomes						
Overall mortality	140 (36.5%)	365 (61.2%)	0.000	90 (44.8%)	120 (59.7%)	0.008
Ischemic stroke	22 (6.8%)	60 (10.1%)	0.075	17 (8.5%)	19 (9.5%)	0.864
Hemorrhagic stroke	6 (1.6%)	7 (1.3%)	0.776	3 (1.5%)	1 (0.5%)	0.625
Major extracranial hemorrhagic events	18 (4.7%)	25 (4.2%)	0.861	11 (5.5%)	8 (4.0%)	0.629

Effects of oral anticoagulant therapy in older medical in-patients with atrial fibrillation: a prospective cohort observational study

Mario Bo[1] · Federica Li Puma[1] · Marco Badinella Martini[1] · Yolanda Falcone[1] · Marina Iacovino[1] · Enrica Grisoglio[1] · Elena Menditto[1] · Gianfranco Fonte[1] · Enrico Brunetti[1] · Giovanni Carlo Isaia[1] · Fabrizio D'Ascenzo[2] · Fiorenzo Gaita[2]

Aging Clin Exp Res
DOI 10.1007/s40520-016-0569-7

CrossMark

	β	SE	p	OR
Mortality				
Oral anticoagulant therapy at discharge	−0.6223	0.2281	0.0064	0.5367
ADL ≥2—dependent	0.8625	0.2440	0.0004	2.3691
Groningen ≥4—frailty	1.0194	0.3339	0.0023	2.7716
Serum albumin <3 g/dl	0.7286	0.2936	0.0131	2.0722
Readmission	0.5340	0.2258	0.0180	1.7058
Ischemic stroke				
Oral anticoagulant therapy at discharge	−1.3594	0.6067	0.0250	0.2568
MNA ≤11—at risk of malnutrition	−1.8109	0.5471	0.0009	0.1635
Readmission	1.6421	0.6160	0.0077	5.1658
Bedridden	1.9165	0.7256	0.0083	6.7973
Number of falls in the last year	1.4635	0.5572	0.0086	4.3212
Hemorrhagic stroke	–	–	–	–
Major bleeding events				
Readmissions	2.3434	0.6177	0.0001	10.4161
Presence of a caregiver	−0.8652	0.4226	0.0406	0.4210

Warfarin Treatment and All-Cause Mortality in Community-Dwelling Older Adults with Atrial Fibrillation: A Retrospective Observational Study

J Am Geriatr Soc 64:1416–1424, 2016.

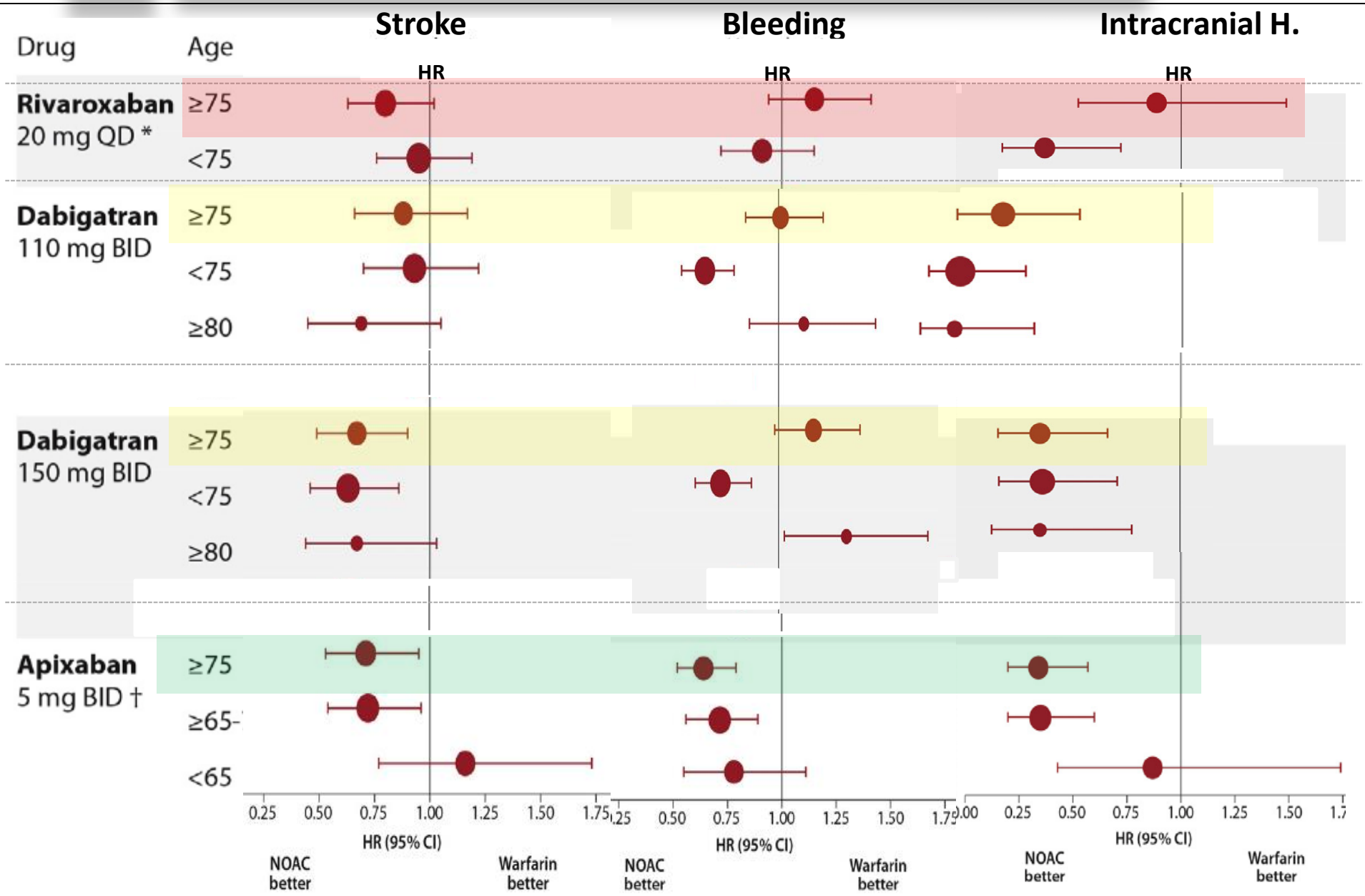
Alberto Pilotto, MD, Pietro Gallina, MD,† Massimiliano Copetti, PhD,‡ Andrea Pilotto, MD,§ Francesco Marcato, MSc,† Anna M. Mello, MD,* Matteo Simonato, MD,† Giancarlo Logroscino, MD, PhD,¶** Alessandro Padovani, MD, PhD,§ Luigi Ferrucci, PhD,†† and Francesco Panza, MD, PhD,‡¶ on behalf of the Multidimensional Prognostic Index_Age Project Investigators*[1]

Retrospective observational study in 1827 community-dwelling individuals with AF aged 65 and older

MPI Based on the SVaMA Risk	n		Mortality (Events per 100 Person-Years)				Hazard Ratio (95% Confidence Interval) *P*-Value	
				Warfarin Use				
	Events	Participants	All	No	Yes	Change[b]	Multivariable[a]	Adjusted for Propensity Score Quintile
1 year								
1 (mild)	141	705	23.3	33.7	15.4	−18.3	0.5 (0.3–0.7) <.001	0.5 (0.4–0.7) <.001
2 (moderate)	240	634	50.8	65.5	31.7	−33.8	0.5 (0.4–0.7) <.001	0.5 (0.4–0.7) <.001
3 (severe)	301	488	104.6	147.2	54.9	−92.3	0.4 (0.3–0.5) <.001	0.4 (0.3–0.5) <.001
All	682	1,827	49.9	71.8	28.0	−43.8	0.4 (0.4–0.5) <.001	0.5 (0.4–0.6) <.001
2 years								
1 (mild)	240	705	22.8	31.5	16.5	−15.0	0.6 (0.4–0.8) <.001	0.6 (0.4–0.8) <.001
2 (moderate)	347	634	45.5	56.1	32.2	−23.9	0.6 (0.5–0.8) <.001	0.7 (0.5–0.8) <.001
3 (severe)	396	488	96.7	126.9	64.6	−62.3	0.5 (0.4–0.6) <.001	0.5 (0.4–0.7) <.001
All	983	1,827	44.2	59.8	29.5	−30.3	0.6 (0.5–0.6) <.001	0.6 (0.5–0.7) <.001
3 years								
1 (mild)	303	705	22.2	29.2	17.2	−12.0	0.6 (0.5–0.8) <.001	0.6 (0.5–0.8) <.001
2 (moderate)	404	634	43.3	52.8	31.9	−20.9	0.7 (0.5–0.8) <.001	0.7 (0.6–0.9) <.001
3 (severe)	418	488	91.4	119.6	61.8	−57.8	0.5 (0.4–0.6) <.001	0.6 (0.4–0.7) <.001
All	1,125	1,827	40.8	54.5	28.4	−26.1	0.6 (0.5–0.7) <.001	0.6 (0.6–0.7) <.001

New oral anticoagulants in elderly patients

Barco S. Best Pract Res Clin Haematol 2013



Contents lists available at ScienceDirect

European Journal of Internal Medicine

European Journal of Internal Medicine 41 (2017) 18–27

Oral anticoagulant therapy for older patients with atrial fibrillation: a review of current evidence

Mario Bo [a], Enrica Grisoglio [a], Enrico Brunetti [a,*], Yolanda Falcone [a], Niccolò Marchionni [b]

Efficacy and safety outcomes in patients >=75 years

Efficacy and safety outcomes in patients ≥ 75 years from sub-analysis of Phase III RCTs on DOACs.
Abbreviations: y = years; n = number; TTR = time in therapeutic range; N.A. = not available; SD = standard deviation; IQR = interquartile range; SE = systemic embolism; HR = hazard ratio; CI = confidence interval; IC = intracranial; GI = gastrointestinal.

	RE-LY [74]		ROCKET AF [75]	ARISTOTLE [76]	AVERROES [77]	ENGAGE AF-TIMI 48 [78]	
Patients ≥ 75 y/total (%)	7258/18,113 (40.1%)		6229/14,264 (43.7%)	5678/18,201 (31.2%)	1898/5599 (33.9%)	8474/21,105 (40.2%)	
TTR in patients ≥ 75 y control arm	TTR according to age group N.A.		TTR higher in patients ≥ 75 y 56.9 ± 21.6% (mean ± SD)	TTR higher in patients ≥75 y Median: 67.2% (IQR: 53.7%–77.4%)	N.A.	TTR higher in patients ≥ 75 y Median: 69.6% (IQR: 57.1%–78.3%)	
Dose	**Dabigatran 150 mg**	**Dabigatran 110 mg**	**Rivaroxaban**	**Apixaban**	**Apixaban**	**Edoxaban High dose**	**Edoxaban Low dose**
Stroke/SE	0.67	0.88	0.80	0.71	0.33	0.83	1.12
HR (95% CI)	(0.49–0.90)	(0.66–1.17)	(0.63–1.02)	(0.53–0.95)	(0.19–0.54)	(0.67–1.04)	(0.91–1.40)
Major bleeding	1.18	1.01	1.11	0.64	1.21	0.83	0.47
HR (95% CI)	(0.98–1.42)	(0.83–1.23)	(0.92–1.34)	(0.52–0.79)	(0.69–2.12)	(0.70–0.99)	(0.38–0.58)
IC bleeding	0.42	0.37	0.80	0.34	0.81	0.40	0.31
HR (95% CI)	(0.25–0.70)	(0.21–0.64)	(0.50–1.28)	(0.20–0.57)	(0.28–2.35)	(0.26–0.62)	(0.19–0.49)
GI bleeding	1.79	1.39	N.A.	N.A.	N.A.	1.32	0.72
HR (95% CI)	(1.35–2.37)	(1.03–1.98)				(1.01–1.72)	(0.53–0.98)

Suárez Fernández *et al. BMC Cardiovascular Disorders* (2015) 15:143 and on behalf of Grupo de trabajo de Riesgo vascular de la SEMI

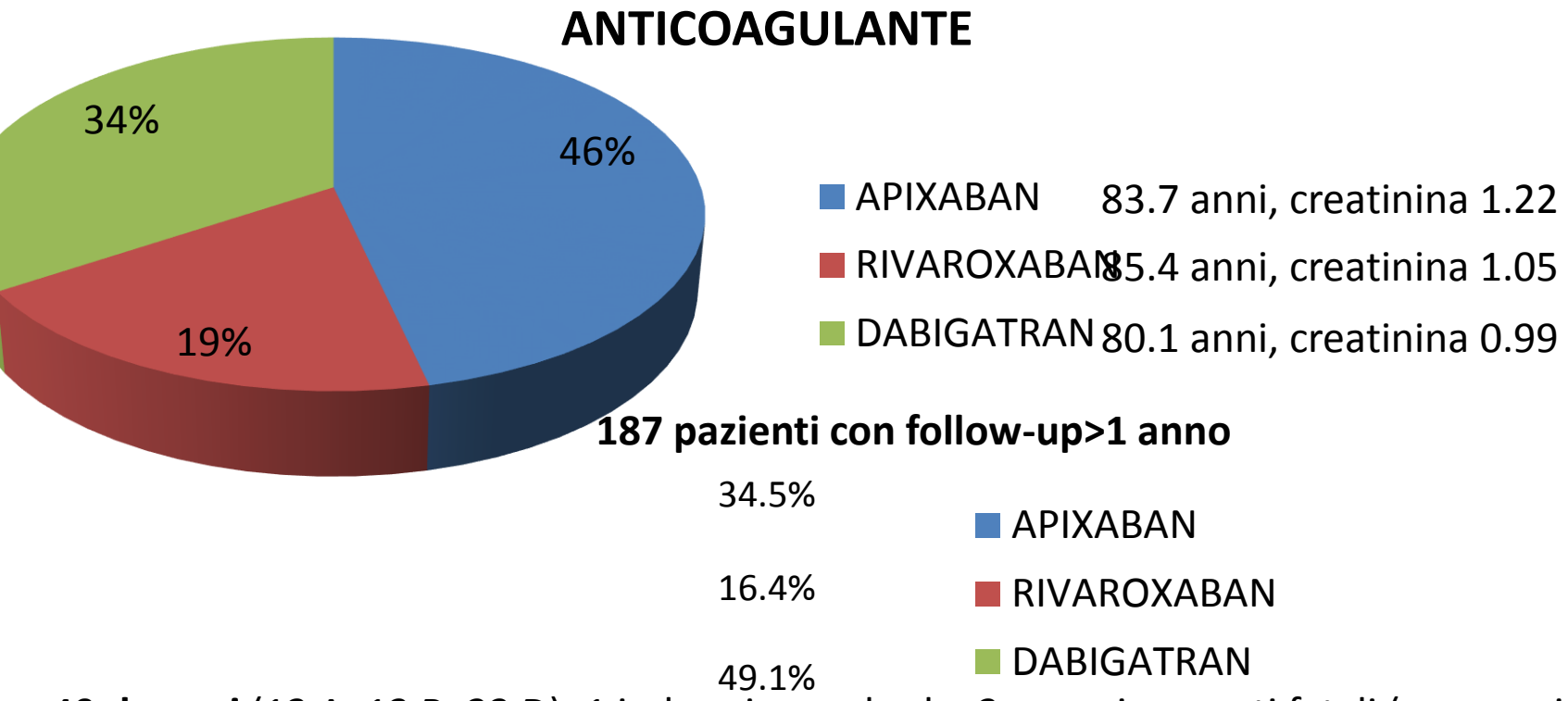
Antithrombotic treatment in elderly patients with atrial fibrillation: a practical approach

CONTRAINDICATIONS

Comorbidities or frailty do not contraindicate anticoagulation…life expectancy, functionality and cognitive impairment should be considered… **Age, risk of falls, previous bleedings** (particularly when the cause has been eliminated), **need for antiplatelet treatment should not be considered contraindications to anticoagulation**

Quindi, sebbene la TAO sia tradizionalmente vista come una terapia "impegnativa" per l'anziano polipatologico, non vi è evidenza di dover arbitrariamente negare questa opzione in assenza di controindicazioni o comorbilità associate ad una cattiva prognosi a breve e, soprattutto, in presenza di una conservata autonomia funzionale.

372 pazienti dimessi con NAO (F 56%, 82.8 anni), CHA2DS2-VASC 4.5 (1.4), HAS-BLED 1.9 (0.8)



187 pazienti con follow-up>1 anno

49 **decessi** (13 A, 13 R, 23 D): 1 ischemia cerebrale, 3 sanguinamenti fatali (emorragie da perforazione intestinale), 7 neoplasie, 6 CAD, 7 HF, 11 cause infettive, 15 demenza & marasmi

8 **sanguinamenti maggiori** non fatali prevalentemente gastrointestinali (3 in concomitante uso di FANS, 3 in presenza di peggioramento funzionalità renale)

297 pazienti ambulatoriali con NAO (F 51%, 80.1 anni), CHA2DS2-VASC 4.3 (1.2), HAS-BLED 1.7 (0.8) con follow-up >1 anno: 35 **decessi** (nessuno riconducibile a NAO), 7 **sanguinamenti maggiori non fatali**

Età avanzata/pazienti fragili

- Il trattamento anticoagulante nei pazienti anziani è sottoutilizzato? Se sì, quali le principali motivazioni?
- Le sotto analisi degli studi di fase III confermano la sicurezza e l'efficacia dei NOAC nel paziente anziano? I dati di real world sono discordanti dai trial clinici?
- Quali i dati nel grande anziano (≥85 aa)?
- Esistono dati sufficienti nei pazienti a rischio di caduta? Come identificarli?
- Esistono differenze tra i NOAC?

Età avanzata/pazienti fragili

A global clinical measure of fitness and frailty in elderly people

CMAJ 2005;173(5):489-95

Kenneth Rockwood, Xiaowei Song, Chris MacKnight, Howard Bergman, David B. Hogan, Ian McDowell, Arnold Mitnitski

Box 1: The CSHA Clinical Frailty Scale

1 *Very fit* — robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age

2 *Well* — without active disease, but less fit than people in category 1

3 *Well, with treated comorbid disease* — disease symptoms are well controlled compared with those in category 4

4 *Apparently vulnerable* — although not frankly dependent, these people commonly complain of being "slowed up" or have disease symptoms

5 *Mildly frail* — with limited dependence on others for instrumental activities of daily living

6 *Moderately frail* — help is needed with both instrumental and non-instrumental activities of daily living

7 *Severely frail* — completely dependent on others for the activities of daily living, or terminally ill

Note: CSHA = Canadian Study of Health and Aging.

Table 3: Receiver operating characteristic (ROC) analyses for adverse outcomes within 70 months

	Area under the ROC curve	
Assessment tool	Death	Entry into an institution
Cumulative Illness Rating Scale	0.58	0.62
Modified Mini-Mental State Examination	0.64	0.69
CSHA rules-based definition of frailty	0.66	0.70
CSHA Function Scale	0.68	0.80
CSHA Frailty Index	0.69	0.72
CSHA Clinical Frailty Scale	0.70	0.75

Note: CSHA = Canadian Study of Health and Aging.

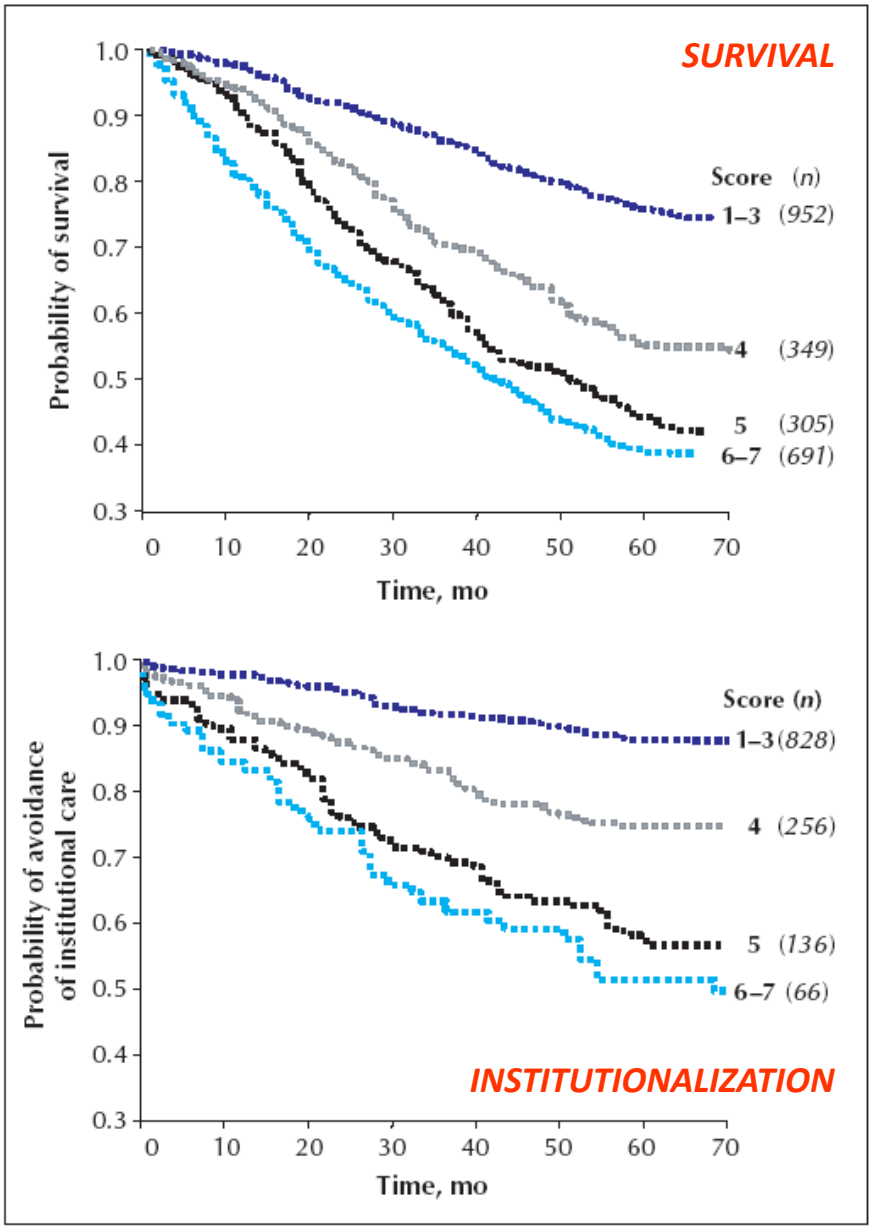


Fig. 1: Kaplan–Meier curves, adjusted for age and sex, for study participants (*n*) over the medium term (5–6 years), according to their scores on the CSHA Clinical Frailty Scale. Some scores were grouped. Top: Probability of survival. Bottom: Probability of avoidance of institutional care.

Età avanzata/pazienti fragili

- Il trattamento anticoagulante nei pazienti anziani è sottoutilizzato? Se sì, quali le principali motivazioni?

Età avanzata/pazienti fragili

- Le sotto analisi degli studi di fase III confermano la sicurezza e l'efficacia dei NOAC nel paziente anziano? I dati di real world sono discordanti dai trial clinici?

Postapproval Observational Studies of Non-Vitamin K Antagonist Oral Anticoagulants in Atrial Fibrillation

Tatjana S. Potpara, MD, PhD, FESC; Gregory Y. H. Lip, MD

JAMA March 21, 2017 Volume 317, Number 11

MAJOR BLEEDING (per 100 patient-years) IN POST-OBSERVATIONAL STUDIES COMPARED WITH PHASE III RCTS

	OBSERVATIONAL STUDIES	PHASE III TRIALS
APIXABAN	2.29-2.38	2.13
DABIGATRAN	2.04-3.60*	3.11 (150 mg) 2.17 (110 mg)
RIVAROXABAN	2.90-6.00**	3.60

*Lower rates with 150 mg bid than with 110 or 75 mg bid
**Highest rate for rivaroxaban 15 mg od

3. Larsen TB, Skjøth F, Nielsen PB, Kjældgaard JN, Lip GY. Comparative effectiveness and safety of non-vitamin K antagonist oral anticoagulants and warfarin in patients with atrial fibrillation. *BMJ*. 2016;353:i3189.

4. Yao X, Abraham NS, Sangaralingham LR, et al. Effectiveness and safety of dabigatran, rivaroxaban, and apixaban vs warfarin in nonvalvular atrial fibrillation. *J Am Heart Assoc*. 2016;5(6):pii e003725.

5. Lip GY, Keshishian A, Kamble S, et al. Real-world comparison of major bleeding risk among non-valvular atrial fibrillation patients initiated on apixaban, dabigatran, rivaroxaban, or warfarin. *Thromb Haemost*. 2016;116(5):975-986.

6. Staerk L, Fosbol EL, Lip GY, et al. Ischaemic and haemorrhagic stroke associated with non-vitamin K antagonist oral anticoagulants and warfarin use in patients with atrial fibrillation [published online October 14, 2016]. *Eur Heart J*. doi:10.1093/eurheartj/ehw496

7. Graham DJ, Reichman ME, Wernecke M, et al. Stroke, bleeding, and mortality risks in elderly Medicare beneficiaries treated with dabigatran or rivaroxaban for nonvalvular atrial fibrillation. *JAMA Intern Med*. 2016;176(11):1662-1671.

8. Gorst-Rasmussen A, Lip GY, Bjerregaard Larsen T. Rivaroxaban vs warfarin and dabigatran in atrial fibrillation. *Pharmacoepidemiol Drug Saf*. 2016;25:1236-1244.

9. Maura G, Blotiere PO, Bouillon K, et al. Comparison of the short-term risk of bleeding and arterial thromboembolic events in nonvalvular atrial fibrillation patients newly treated with dabigatran or rivaroxaban vs vitamin k antagonists. *Circulation*. 2015;132:1252-1260.

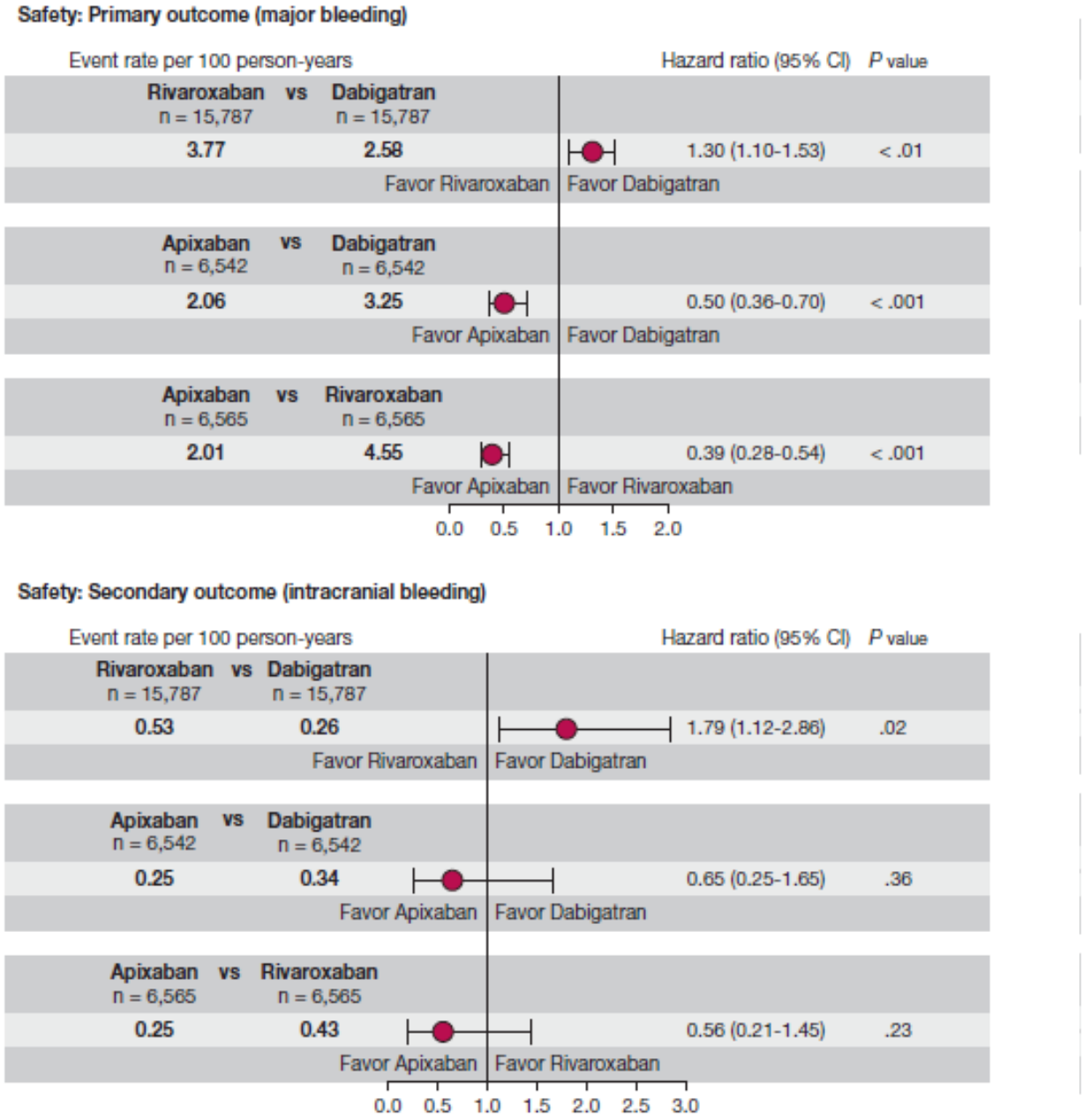


Figure 3 – *Forest plot depicting the event rates per 100 person-years and the hazard ratio for each pairwise propensity-matched medication comparison for major bleeding and intracranial bleeding.*

Età avanzata/pazienti fragili

- Quali i dati nel grande anziano (≥85 aa)?

Età avanzata/pazienti fragili

- Esistono dati sufficienti nei pazienti a rischio di caduta? Come identificarli?

Clinical Outcomes and History of Fall in Patients with Atrial Fibrillation Treated with Oral Anticoagulation: Insights From the ARISTOTLE Trial

THE AMERICAN JOURNAL of MEDICINE®

PURPOSE: We assessed outcomes among anticoagulated patients with atrial fibrillation and a history of falling, and whether the benefits of apixaban vs warfarin are consistent in this population.

METHODS: Of the 18,201 patients in the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) study, 16,491 had information about history of falling–753 with history of falling and 15,738 without history of falling. The primary efficacy outcome was stroke or systemic embolism; the primary safety outcome was major bleeding.

RESULTS: When compared with patients without a history of falling, patients with a history of falling were older, more likely to be female and to have dementia, cerebrovascular disease, depression, diabetes, heart failure, osteoporosis, fractures, and higher CHA_2DS_2-VASc (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, prior Stroke or TIA or thromboembolism, Vascular disease, Age 65-74 years, Sex category female) and HAS-BLED (Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile international normalized ratio, Elderly, Drugs or alcohol) scores. Patients with a history of falling had higher rates of major bleeding (adjusted hazard ratio [HR] 1.39; 95% confidence interval [CI], 1.05-1.84; $P = .020$), including intracranial bleeding (adjusted HR 1.87; 95% CI, 1.02-3.43; $P = .044$) and death (adjusted HR 1.70; 95% CI, 1.36-2.14; $P < .0001$), but similar rates of stroke or systemic embolism and hemorrhagic stroke. There was no evidence of a differential effect of apixaban compared with warfarin on any outcome, regardless of history of falling. Among those with a history of falling, subdural bleeding occurred in 5 of 367 patients treated with warfarin and 0 of 386 treated with apixaban.

CONCLUSIONS: Patients with atrial fibrillation and a history of falling receiving anticoagulation have a higher risk of major bleeding, including intracranial, and death. The efficacy and safety of apixaban compared with warfarin were consistent, irrespective of history of falling.

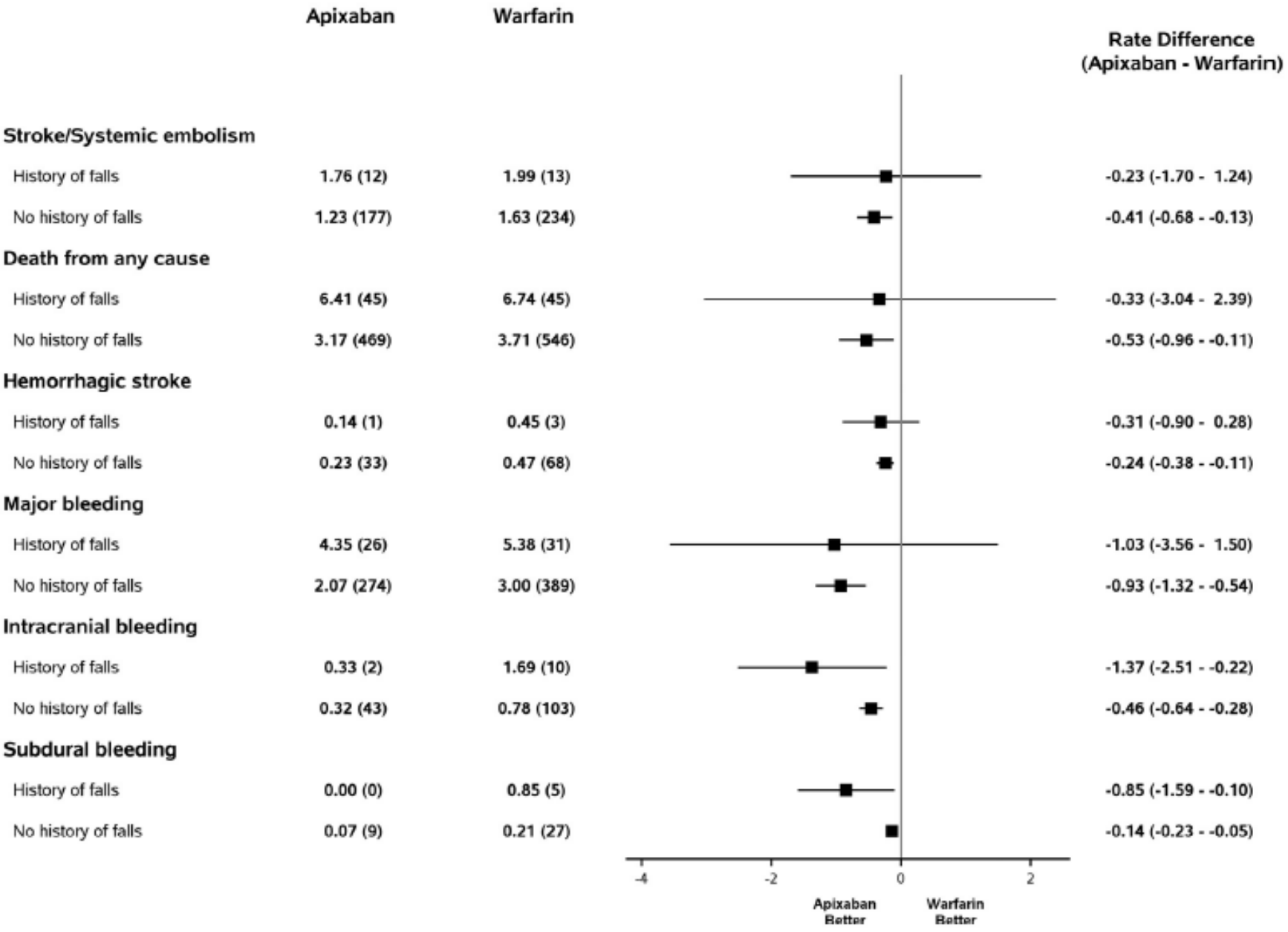
Characteristics	Fall(s) Within 1 Year		*P*-Value
	Yes (n = 753)	No (n = 15,738)	
Age, median (25th, 75th), years	75 (67, 79)	70 (63, 76)	< .0001
Age ≥75 years, n (%)	379 (50.3%)	4787 (30.4%)	< .0001
Female sex, n (%)	357 (47.4%)	5438 (34.6%)	< .0001
BMI, median (25th, 75th), kg/m^2	29.1 (25.6, 33.8)	28.4 (25.2, 32.4)	< .001
CHA_2DS_2-VASc score, mean (SD)	4.19 (1.65)	3.43 (1.51)	< .0001
CHA_2DS_2-VASc score distribution, n (%)			< .0001
≤1	23 (3.1%)	1370 (8.7%)	
2	94 (12.5%)	3261 (20.7%)	
≥3	636 (84.5%)	11,107 (70.6%)	
Prior stroke, TIA, or SE, n (%)	213 (28.3%)	3287 (20.9%)	< .0001
HAS-BLED score, mean (SD)	2.40 (1.07)	1.77 (1.05%)	< .0001
HAS-BLED score distribution, n (%)			< .0001
≤1	155 (20.6%)	6469 (41.1%)	
2	244 (32.4%)	5690 (36.2%)	
≥3	354 (47.0%)	3579 (22.7%)	
Prior bleeding, n (%)	264 (35.1%)	2525 (16.0%)	< .0001
Comorbidities at randomization, n (%)			
Dementia	20 (2.7%)	76 (0.5%)	< .0001
Depression	163 (21.6%)	1023 (6.5%)	< .0001
Cerebrovascular disease	221 (29.4%)	2934 (18.6%)	< .0001
Peripheral vascular disease	86 (11.7%)	907 (6.3%)	< .0001
Pulmonary disease	137 (18.6%)	2106 (14.5%)	< .01
Renal disease	216 (29.3%)	3168 (21.9%)	< .0001
Gastrointestinal disease	286 (38.8%)	3001 (20.7%)	< .0001
Hematological disease	242 (32.8%)	2416 (16.7%)	< .0001
Malignancy	108 (14.6%)	1045 (7.2%)	< .0001
Thyroid disease	145 (19.7%)	1633 (11.3%)	< .0001
Diabetes	272 (36.1%)	3944 (25.1%)	< .0001
Hypertension	638 (86.6%)	12,554 (86.9%)	.82
Congestive heart failure	166 (22.5%)	3897 (26.9%)	< .01
Prior MI	126 (16.7%)	2250 (14.3%)	.06
Moderate/severe valvular heart disease	171 (23.2%)	2625 (18.1%)	< .001
Osteoporosis	124 (16.5%)	784 (5.0%)	< .0001
Fractures	110 (14.7%)	931 (5.9%)	< .0001

Table 2 Association Between History of Fall(s) and Outcome

Event	Fall(s) Within 1 Year: Yes (n = 753) Rate (Events)	Fall(s) Within 1 Year: No (n = 15,738) Rate (Events)	Unadjusted HR (95% CI)	Adjusted 1* HR (95% CI)	Interaction *P*-Value	Adjusted 2* HR (95% CI)	Interaction *P*-Value
Stroke or SE	1.87 (25)	1.43 (411)	1.30 (0.87-1.95)	1.21 (0.80-1.82)	.370	1.12 (0.72-1.72)	.618
Major bleeding	4.86 (57)	2.53 (663)	1.91 (1.46-2.51)	1.39 (1.05-1.84)	.020	1.30 (0.98-1.74)	.071
Major or CRNM bleeding	8.98 (101)	4.92 (1262)	1.81 (1.48-2.21)	1.36 (1.10-1.68)	.004	1.27 (1.03-1.58)	.028
Any bleeding	36.59 (316)	21.56 (4652)	1.64 (1.46-1.83)	1.25 (1.11-1.41)	<.001	1.19 (1.05-1.34)	.005
Hemorrhagic stroke	0.30 (4)	0.35 (101)	0.85 (0.31-2.31)	0.92 (0.33-2.53)	.869	0.77 (0.24-2.46)	.659
Intracranial bleeding	1.00 (12)	0.55 (146)	1.82 (1.01-3.27)	1.87 (1.02-3.43)	.044	1.96 (1.06-3.61)	.032
Subdural bleeding	0.42 (5)	0.14 (36)	3.06 (1.20-7.81)	2.45 (0.92-6.52)	.072	2.27 (0.83-6.20)	.111
Cardiovascular death	2.92 (40)	1.77 (522)	1.65 (1.20-2.28)	1.64 (1.17-2.31)	.004	1.59 (1.26-2.00)	<.0001
All-cause death	6.57 (90)	3.44 (1015)	1.91 (1.54-2.37)	1.70 (1.36-2.14)	<.0001	1.50 (1.06-2.13)	.023
Stroke/SE/Major bleeding	6.29 (81)	3.59 (1012)	1.74 (1.39-2.19)	1.29 (1.02-1.64)	.036	1.22 (0.95-1.56)	.113
Stroke/SE/Major bleeding/Death	11.69 (151)	6.36 (1796)	1.84 (1.55-2.17)	1.47 (1.23-1.75)	.004	1.37 (1.15-1.64)	.001

Table 3 Treatment Effect of Apixaban and Warfarin on Study Outcomes in Patients with a History of Fall Compared with Those Without a History of Fall

Event	Fall(s) Within 1 Year: Apixaban (n = 386) Rate (Events)	Fall(s) Within 1 Year: Warfarin (n = 367) Rate (Events)	HR (95% CI)	No Fall(s) Within 1 Year: Apixaban (n = 7867) Rate (Events)	No Fall(s) Within 1 Year: Warfarin (n = 7871) Rate (Events)	HR (95% CI)	Interaction *P*-value
Stroke or SE	1.76 (12)	1.99 (13)	0.88 (0.40-1.93)	1.23 (177)	1.63 (234)	0.75 (0.62-0.91)	.69
Major bleeding	4.35 (26)	5.38 (31)	0.81 (0.48-1.36)	2.07 (274)	3.00 (389)	0.69 (0.59-0.81)	.57
Major or CRNM bleeding	8.81 (50)	9.15 (51)	0.95 (0.65-1.41)	3.88 (506)	5.98 (756)	0.65 (0.58-0.73)	.06
Any bleeding	28.86 (135)	45.72 (181)	0.65 (0.52-0.81)	17.85 (2014)	25.64 (2638)	0.71 (0.67-0.75)	.46
Hemorrhagic stroke	0.14 (1)	0.45 (3)	0.32 (0.03-3.09)	0.23 (33)	0.47 (68)	0.48 (0.32-0.73)	.72
Intracranial bleeding	0.33 (2)	1.69 (10)	0.19 (0.04-0.88)	0.32 (43)	0.78 (103)	0.41 (0.29-0.59)	.35
Subdural bleeding	0.00 (0)	0.85 (5)	–	0.07 (9)	0.21 (27)	0.33 (0.15-0.69)	–
Cardiovascular death	3.42 (24)	2.40 (16)	1.43 (0.76-2.70)	1.60 (237)	1.94 (285)	0.83 (0.70-0.99)	.11
All-cause death	6.41 (45)	6.74 (45)	0.96 (0.63-1.44)	3.17 (469)	3.71 (546)	0.86 (0.76-0.97)	.63
Stroke/SE/Major bleeding	5.82 (38)	6.79 (43)	0.85 (0.55-1.32)	3.10 (440)	4.07 (572)	0.76 (0.67-0.86)	.62
Stroke/SE/Major Bleeding/Death	11.41 (75)	11.98 (76)	0.95 (0.69-1.31)	5.75 (817)	6.96 (979)	0.83 (0.75-0.91)	.40


Apixaban
Warfarin
Rate Difference
(Apixaban - Warfarin)
Stroke/Systemic embolism
History of falls
1.76 (12)
1.99 (13)
-0.23 (-1.70 - 1.24)
No history of falls
1.23 (177)
1.63 (234)
-0.41 (-0.68 - -0.13)
Death from any cause
History of falls
6.41 (45)
6.74 (45)
-0.33 (-3.04 - 2.39)
No history of falls
3.17 (469)
3.71 (546)
-0.53 (-0.96 - -0.11)
Hemorrhagic stroke
History of falls
0.14 (1)
0.45 (3)
-0.31 (-0.90 - 0.28)
No history of falls
0.23 (33)
0.47 (68)
-0.24 (-0.38 - -0.11)
Major bleeding
History of falls
4.35 (26)
5.38 (31)
-1.03 (-3.56 - 1.50)
No history of falls
2.07 (274)
3.00 (389)
-0.93 (-1.32 - -0.54)
Intracranial bleeding
History of falls
0.33 (2)
1.69 (10)
-1.37 (-2.51 - -0.22)
No history of falls
0.32 (43)
0.78 (103)
-0.46 (-0.64 - -0.28)
Subdural bleeding
History of falls
0.00 (0)
0.85 (5)
-0.85 (-1.59 - -0.10)
No history of falls
0.07 (9)
0.21 (27)
-0.14 (-0.23 - -0.05)
-4
-2
0
2
Apixaban Better
Warfarin Better

CONCLUSION

Patients with atrial fibrillation and a history of falling who are treated with anticoagulation have a higher risk of major bleeding, including intracranial bleeding, major or clinically relevant nonmajor bleeding, cardiovascular death, and all-cause death. The efficacy and safety benefits of apixaban compared with warfarin were consistent, irrespective of history of falling.

CLINICAL SIGNIFICANCE

- Patients with atrial fibrillation and a history of falling receiving anticoagulation had a higher risk of major bleeding, including intracranial bleeding, and death, but similar rates of stroke or systemic embolism and hemorrhagic stroke.
- Benefits of apixaban over warfarin were preserved, with an 80% reduction in intracranial bleeding; thus, apixaban appears to be a better alternative than warfarin for anticoagulation in patients with a history of falling.

VALUTAZIONE ORIENTATA ALLA PERFORMANCE DEI PROBLEMI DI MOBILITA': TINETTI	
Scala CONLEY	
Cut off point	Esperienza e giudizio clinico. >18 (versione breve) è indicato come cut off point predittore di cadute (Tinetti 1986)
Conclusioni	Vengono valutati molti aspetti sia dell'equilibrio che della performance. Lunga da somministrare e gravosa per i pazienti.

SCALA CONLEY

ISTRUZIONI: le prime tre domande devono essere rivolte solo al paziente. Possono essere rivolte ad un familiare o al caregiver o all'infermiere solo se il paziente ha gravi deficit cognitivi e fisici che gli impediscono di rispondere. Barrare il valore corrispondente alla risposta fornita, Sommare i valori positivi. La risposta "Non so" è da considerare come risposta negativa.

Precedenti cadute (domande al paziente/caregiver/infermiere)	SI	NO
C1 - E' caduto nel corso degli ultimi tre mesi?	2	0
C2 - Ha mai avuto vertigini o capogiri? (negli ultimi 3 mesi)	1	0
C3 - Le è mai capitato di perdere urine o feci mentre si recava in bagno? (negli ultimi 3 mesi)	1	0
Deterioramento cognitivo (osservazione infermieristica)		
C4 - Compromissione della marcia, passo strisciante, ampia base d'appoggio, marcia instabile.	1	0
C5 - Agitato (Definizione: eccessiva attività motoria, solitamente non finalizzata ed associato ad agitazione interiore. Es: incapacità a stare seduto fermo, si muove con irrequietezza, si tira i vestiti, ecc.).	2	0
C6 - Deterioramento della capacità di giudizio / mancanza del senso del pericolo.	3	0
Punteggio 0 = nessun rischio **Punteggio 8 = massimo rischio** **Punteggio di Cut-off = 2**	**TOTALE**	_____

Età avanzata/pazienti fragili

- Esistono differenze tra i NOAC?

	DABIGATRAN	RIVAROXABAN	APIXABAN	EDOXABAN
BIOAVAILABILITY, %	**6%**	66 fasting 80-100 with food	50	**62%**
HALF-LIFE, hours	12-17	5-13	9-14	10-14
RENAL EXCRETION, %	**80%**	33%	27%	**50%**
DOSE, mg	150 /110 bid	20 OD	5 BID	60 / 30 OD
DOSE REDUCTION		15 if CrCl 30-49 ml/min	2.5 BID if at **least 2 of**: age>=80, BW<60kg, creat>1.5	30 / 15 OD if **any of**: eGFR 30-50 ml/min, BW<60 kg, Verap, Droned, Quinid
EXCLUSION for CKD	CrCl<30ml/min	CrCl<30ml/min	CrCl<25ml/min	CrCl<30ml/min
% with CKD	20% CrCl 30-49	21% Cr Cl 30-49	15% Cr Cl 30-50	19% CrCl <50

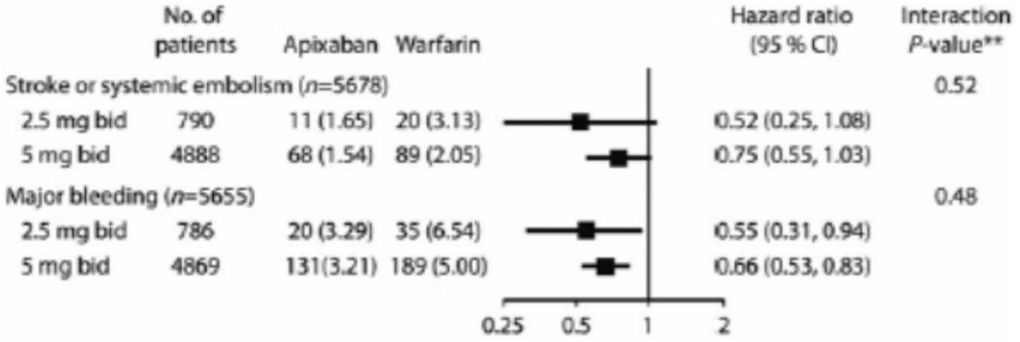
2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Health status, geriatric syndromes and prescription of oral anticoagulant therapy in elderly medical in-patients with atrial fibrillation: a prospective observational study

International Journal of Cardiology 187 (2015) 123–125

M. Bo [a], F. Li Puma [a], M. Badinella Martini [a], Y. Falcone [a,*], M. Iacovino [a], E. Grisoglio [a], M. Bonetto [a], G. Isaia [b], G. Ciccone [a], G.C. Isaia [a], F. Gaita [c]

Advanced age, very short life expectancy, difficult or impossible management of therapy, perceived fear of bleeding and harm greater than benefit were the most common reasons why physicians withhold OAs.



A reduced dose of 2.5 mg twice daily or placebo were administered to a total of 831 patients; 790 of these patients were ≥75 years.
** Interaction among treatment, age and dose based on randomized or treated population

Figure 3 The effect of apixaban vs. warfarin on stroke or systemic embolism and major bleeding in patients ≥75 years in relation to apixaban dose.

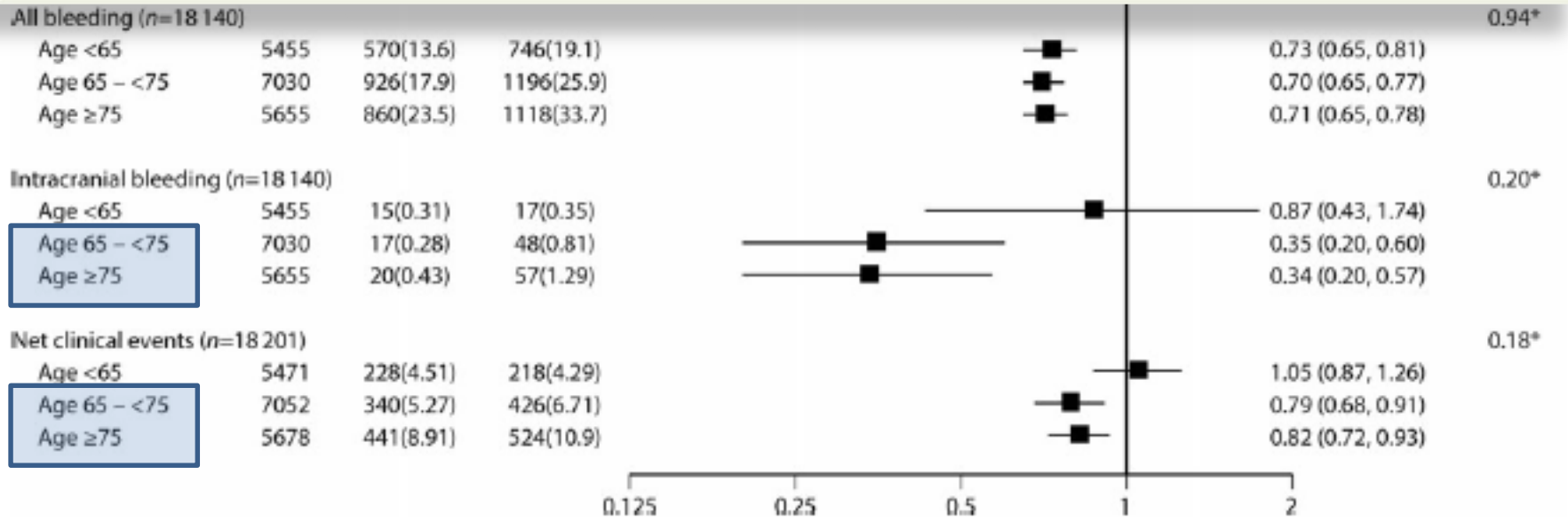
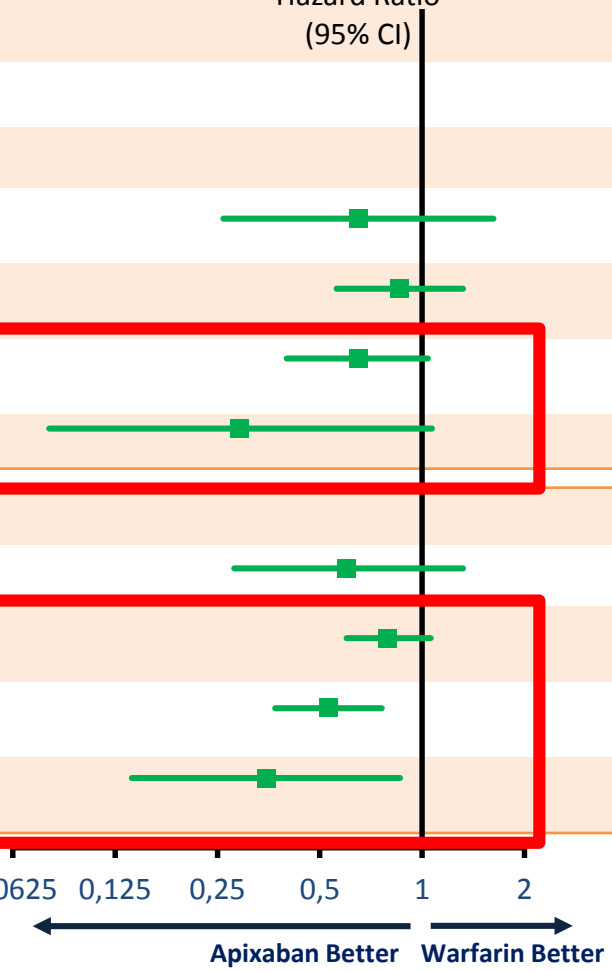


Figure 2 The effect of apixaban vs. warfarin on major study outcomes according to age. *Interaction *P*-values are based on continuous age.

Efficacy and safety outcomes of Apixaban in elderly patients (≥ 75 years) across the range of eGFR (ARISTOTLE study)

	No. of **patients ≥ 75** years	**Apixaban** %/yr (n)	**Warfarin** %/yr (n)	Hazard Ratio (95% CI)	P Value for Interaction
Stroke/SE					0.4954
Cockcroft-Gault (eGFR mL/min)					
>80	597	1.41 (8)	2.16 (11)		
>50–80	2922	1.45 (39)	1.70 (45)		
> 30-50	1906	1.74 (28)	2.69 (44)		
≤ 30	222	1.70 (3)	5.57 (9)		
Major Bleeding					0.1635
>80	596	2.10 (11)	3.39 (15)		
>50–80	2912	3.53 (85)	4.45 (104)		
> 30-50	1898	3.32 (47)	6.27 (87)		
≤ 30	221	4.64 (7)	13.4 (17)		



NOTE: Patients with calculated creatinine clearance of <25 ml /minute were excluded from ARISTOTLE

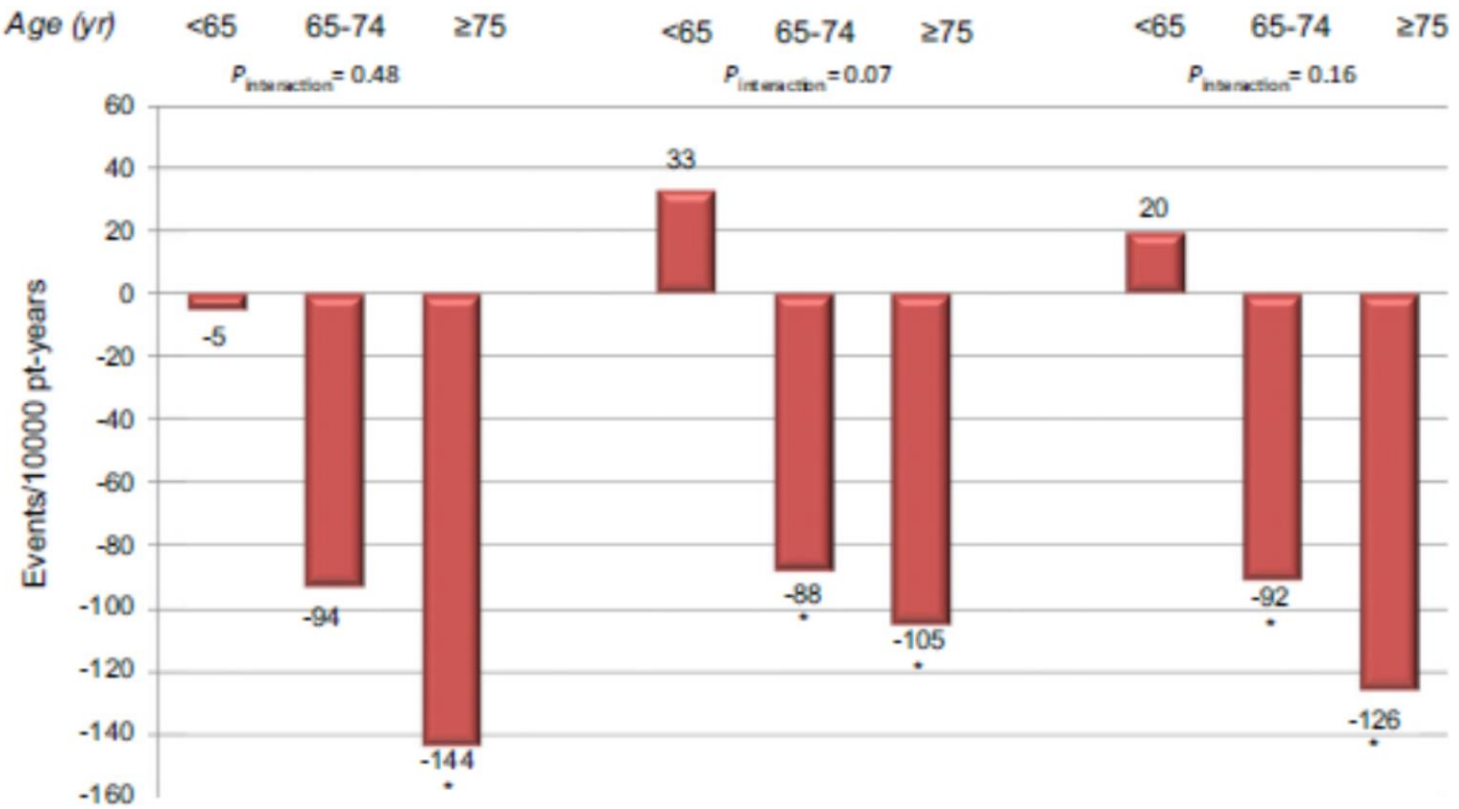
CI, confidence interval; eGFR, estimated glomerular filtration rate; HR hazard ratio; SE, systemic embolism

Adapted from Halvorsen S et al. European Heart J doi:10.1093/eurheartj/ehu046 epub February 2014.

(*J Am Heart Assoc.* 2016;5: e003432 doi: 10.1161/JAHA.116.003432)

Efficacy and Safety of Edoxaban in Elderly Patients With Atrial Fibrillation in the ENGAGE AF–TIMI 48 Trial

Stroke/SE/MB/death | **Disabling Stroke/life - threatening Bl/death** | **Stroke/SE/L-T Bl/death**



Event rates (%/yr)

Age (yr)	<65	65-74	≥75	<65	65-74	≥75	<65	65-74	≥75
Warfarin	4.9	7.3	11.2	3.0	4.8	7.2	3.6	5.5	8.2
HDER	4.8	6.4	9.7	3.3	3.9	6.1	3.8	4.6	7.0

European Heart Journal Advance Access published February 4, 2016

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

Non-vitamin K oral anticoagulants and age

First choice	In patients older than 75 years, we suggest apixaban 5 mg twice daily [2.5 mg if ≥2 of the following: age ≥80 years, body weight ≤60 kg, or creatinine ≥1.5 mg/dL (133 μmol/L)]
Second choice	Dabigatran 110 mg twice daily, rivaroxaban 20 mg once daily, or edoxaban 60 mg once daily

COMORBILITA'

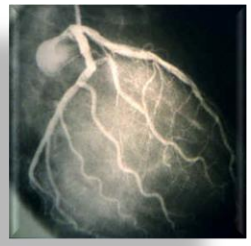
Demenza
IRC
Osteoartrite
Depress
Osteop
Disequi
BPCO
Incontr
urinaria
Vasculo
Diabete
Iperten
Deficit
Disturb
Stipsi
Anemia

SINDROMI GERIATRICHE

Fragilità
Impairment cognitivo
Dipendenza funzionale

Sebbene la TAO sia tradizionalmente vista come una terapia "impegnativa" per l'anziano polipatologico, non vi sono evidenze che ne scoraggino l'uso in ragione dell'età avanzata, in assenza di controindicazioni o comorbilità associate ad una cattiva prognosi a breve. Vi sono discrete evidenze che i DOACs, ed in particolare Apixaban, possano essere una valida alternativa al warfarin in questi pazienti

& ADRs



Maggior prevalenza di FAC rispetto a FAP
Maggior rimodellamento atriale
Minor efficacia terapia antiaritmica
Maggior prevalenza e severità cardiopatia

Dimissione del **20/2/18**:
CM, femmina, 91 anni
Ipertensione arteriosa
Pregresso IMA rivascolarizzato (2010)
Ischemia ponto cerebellare
Portatrice di PM dal 2006: registrati eventi di FA rapida asintomatici al PM
Riscontro clinico di FAP nel gennaio 2017
Terapia all'ingresso: Clopidogrel 75, Carvedilolo 6.25 ½ bid, Amlodipina 10, Simvastatina 10, Indapamide 2.5, Ranitidina 150, Zoloft, Allopurinolo, Risedronato, calcio-Vitamina D, Vertiserc, Voltaren ab

Vive sola, senza aiuti
Cognitivamente integra (SPMSQ 0/10), autonoma (ADL 1/6 IADL 11/14) MPI 0.67
Deambulazione autonoma in schemi
Crea 0.78 (eGFR 56 ml/min)
CHADSVASC: 6 HAS-BLED: 2