III convegno di anticoagulazione.it
"Anticoagulazione: Attualità cliniche e di laboratorio. Aspetti sociali."

Bologna, Savoia Regency Hotel
25-26 gennaio 2018

SESSIONE 3
Le terapie anticoagulanti e il paziente fragile
Parte 1: Il paziente anziano con Fibrillazione Atriale (FA)

La terapia anticoagulante nell'anziano con Fibrillazione Atriale (FA): dati della vita reale.

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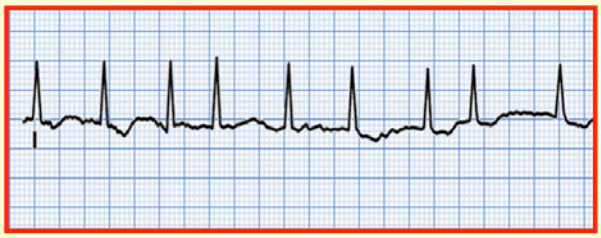
Atrial Fibrillation



The prevalence of atrial fibrillation among elderly (>75 years) is 10%

Elderly

The prevalence tends to increase with age with 1.7% in people aged 60-64 years increasing to 17.8% in those aged ≥ 85 years

Eur Heart J 2006;27:949-53

Patients aged ≥75 years

RCT	DOAC	Warfarin
Re-Ly (Dabigatran)	4828	2360
ROCKET AF (Rivaroxaban)	3073	3077
Aristotle (Apixaban)	2743	2752

Major bleeding

RCT	OR	IC 95 %
Re-Ly (Dabigatran 150)	1.07	0.90-1.28
ROCKET AF (Rivaroxaban)	0.65	0.49-0.87
Asristotle (Apixaban)	0.61	0.49-0.76

Stroke or systemic embolism

RCT	OR	IC 95 %
Re-Ly (Dabigatran)	0.75	0.58-0.96
ROCKET AF (Rivaroxaban)	0.80	0.63-1.02
Asristotle (Apixaban)	0.72	0.54-0.97

DOAC: good performance in the elderly

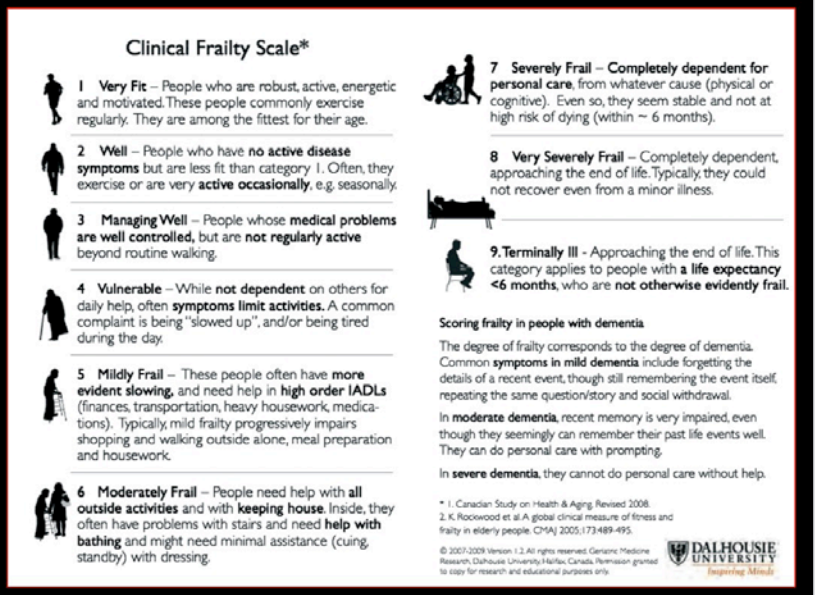
J Am Geriatr Soc 2014; 62: 857-64

Clinical frailty is independently associated with non-prescription of anticoagulants in older patients with atrial fibrillation.

A total of 419 patients with known AF were included. 215 were not anticoagulated (51.3%).

Non-anticoagulated individuals were older (median age 87 years vs 83 years P < 0.001),

more likely to be frail (81.4% vs 52.5%, P < 0.001)



Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house.** Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

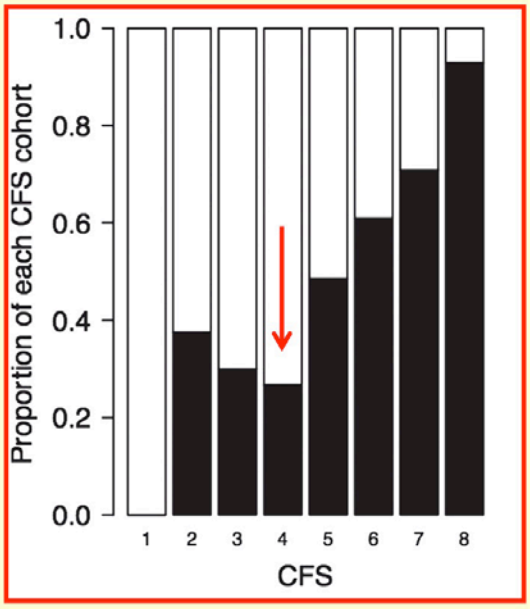
In **severe dementia**, they cannot do personal care without help.

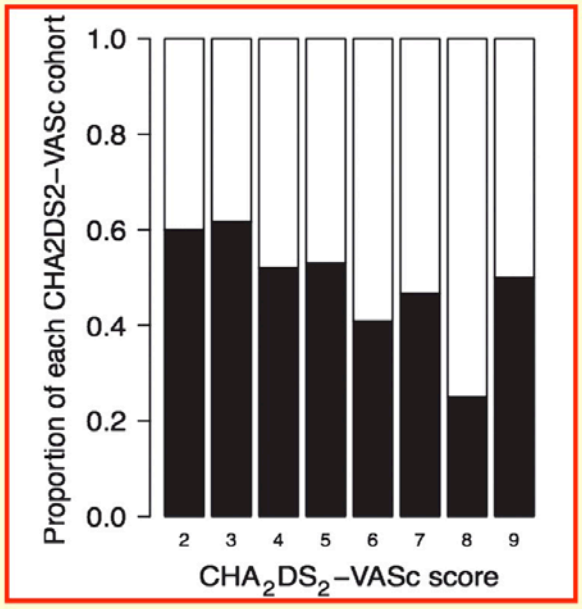
* 1. Canadian Study on Health & Aging. Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

DALHOUSIE UNIVERSITY Inspiring Minds

Geriatr Gerontol Int 2017;17: 2178-83

CFS: Clinical Frailty Scale





Anticoagulated

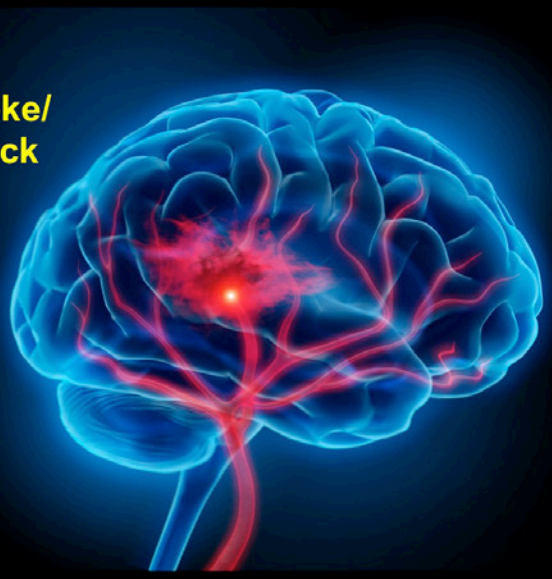
Non Anticoagulated

Geriatr Gerontol Int 2017;17: 2178-83

Underuse of oral anticoagulants in atrial fibrillation

29 studies

Patients with prior stroke/ transient ischemic attack



Oral anticoagulation treatment below 60% (range 19%-81%)

Am J Med 2010;123:638-645

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

A cross-sectional study was conducted in 682 hospitalized patients aged 80 years and older with AF

a) 70 % of octogenarians with AF received anticoagulation therapy (n = 475).

b) A high risk of stroke (CHADS2 = 3 compared with CHADS2 = 1, odds ratio [OR], 3.58; 95% confidence interval [CI], 1.09-11.77) associated to anticoagulants.

c) The absence of severe frailty (CFS < 7; OR, 3.41; 95% CI, 1.84-6.33) was independently associated with anticoagulant use.

d) High risk of bleeding (HAS-BLED score ≥ 3; OR, 0.33; 95% CI, 0.12-0.86) was associated with the absence of anticoagulation.

Warfarin 69 %
DOAC 20 %

Can J Cardiol 2016;32:169-76.

Burden of atrial fibrillation: a retrospective review of patients presenting to acute medical services.

751 patients with AF

Only 38.8% of patients with a CHA_2DS_2 -VASc score ≥2 were discharged after anticoagulation

The mean CHA_2 DS_2 –VASc score was 4.03 (SD = 1.94). The CHA_2DS_2-VASc score was not associated with being started on anticoagulation, odds ratio 1.16 (95% CI=0.83-1.61)

Age by decade older was associated with a reduced likelihood of being started on anticoagulation, odds ratio 0.61 (95% CI = 0.41-0.89)

The thromboembolic rate in patients discharged without anticoagulation within 3 months of presentation to acute medical services was 7/330 (2.1%).

Intern Med J 2016;46:1166-1171

Burden of atrial fibrillation: a retrospective review of patients presenting to acute medical services.

Reasons not to initiate anticoagulation

Fall risk or frailty: 7.2%

Primary care physician: 15.6%

High bleeding risk, 6.6%.

No reason was documented in 56.9%

Intern Med J 2016;46:1166-1171

Direct Oral Anticoagulant- or Warfarin-Related Major Bleeding

Characteristics, Reversal Strategies, and Outcomes From a Multicenter Observational Study

Among 19,061 records screened, 2,002 (460 receiving DOAC, 1,542 receiving warfarin) were eligible.

Red blood cell transfusions occurred more often in DOAC bleeding events than in warfarin events (52.0% vs 39.5%; adjusted relative risk [aRR], 1.32; 95% CI, 1.19-2.47).

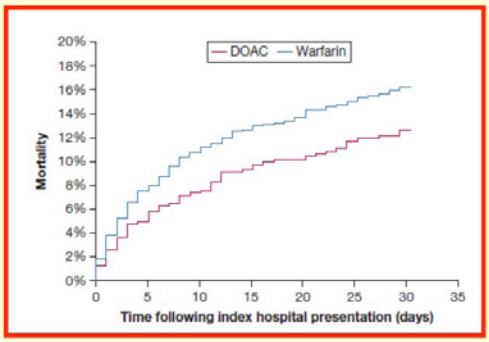
CHEST 2017; 152:81-91

Direct Oral Anticoagulant- or Warfarin-Related Major Bleeding

Characteristics, Reversal Strategies, and Outcomes From a Multicenter Observational Study

In-hospital mortality was lower following DOAC bleeding events (9.8% vs 15.2%; aRR, 0.66; 95% CI, 0.49-0.89),

Differences in 30-day mortality did not reach statistical significance (12.6% vs 16.3%; aRR, 0.79; 95% CI, 0.61-1.03).



Event	DOAC (n=460)	Warfarin (n=1542)	p
Intracranial Hemorrhage	97 (21.1%)	460 (29.8 %)	<0.001
Gastrointestinal	284 (61.7 %)	656 (42.5 %)	<0.001
Upper GI	101 (22.0 %)	301 (19.5 %)	0.260
Lower GI	143 (31.3 %)	266 (17.3 %)	<0.001

CHEST 2017; 152:81-91

Outcomes in a Warfarin-Treated Population With Atrial Fibrillation

Outcomes	Warfarin (n=34851) and AF
Any thromboembolism	2.12 % (1.99-2.24)
Arterial	1.54 % (1.44-1.5
Venous	0.12 % (0.09-0

2,0 % ~

Outcomes	Warfarin (n=34851) and A
Any major bleeding	2.04 % (1.92-2.16)
Intracranial	0.41 % (0.35-0.46)
GI tract	0.67 % (0.60-0.74)

JAMA Cardiol. 2016;1(2):172-180.

Outcomes in a Warfarin-Treated Population With Atrial Fibrillation

1.6 % ~

	Warfarin TTR ≥ 70 n=22185	Warfarin TTR <70 % n=19428
Major bleeding	1.61, 1.49-1.73 %	3.81, 3.51- 4.11 %
Intracranial	0.34, 0.28-0.39 %	0.72, 0.59-0.85 %
GI bleeding	0.56, 0.49-0.63 %	1.26, 1.09-1.43 %

An optimal management of the therapy induces a low bleeding risk

JAMA Cardiol. 2016;1(2):172-180.

>65 y: 78 %

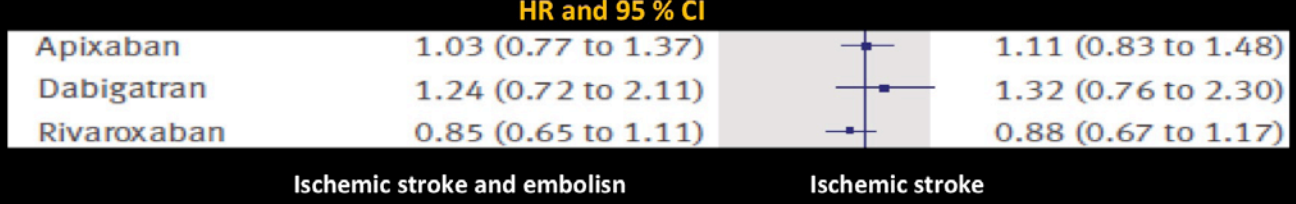
Comparative effectiveness and safety of non-vitamin K antagonist oral anticoagulants and warfarin in patients with atrial fibrillation: propensity weighted nationwide cohort study

Torben Bjerregaard Larsen,[1,2] Flemming Skjøth,[2,3] Peter Brønnum Nielsen,[2] Jette Nordstrøm Kjældgaard,[2] Gregory Y H Lip[2,4]

>75 y: 33 %

61 678 patients with non-valvular atrial fibrillation who were naïve to oral anticoagulants.

When the analysis was restricted to systemic embolism and stroke and to ischaemic stroke, NOACs were not significantly different from warfarin.



BMJ 2016;353:i3189

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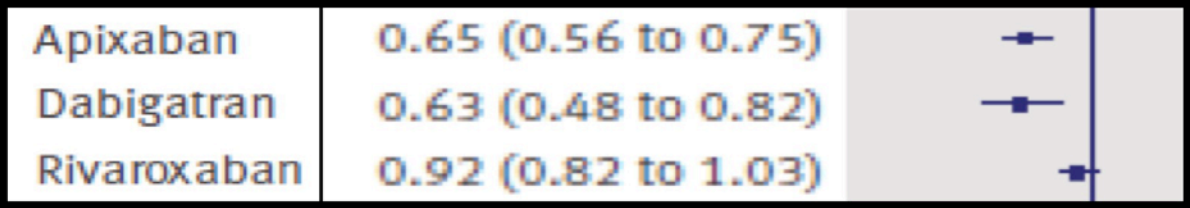
Annual risk of death:
significantly lower with Apixaban (5.2%), Dabigatran (2.7%), compared with warfarin (8.5%)
but not with rivaroxaban (7.7%)

HR and 95 % CI



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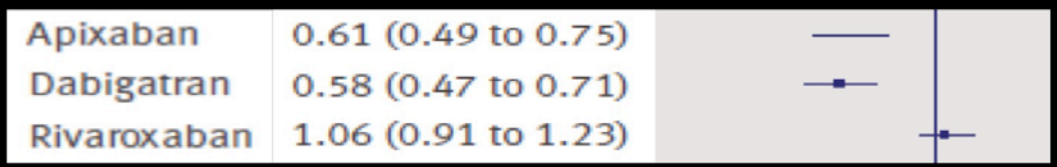
2.4-5.3 % ~

Any bleeding:
igatran (2.4%) was significantly lower than for warfarin (5.0%).
n (5.3%) had comparable annual bleeding rates

HR and 95 % CI



Comment
Warfarin 5 %:
Too high percentage if VKA well managed

BMJ 2016;353:i389

Intracranial bleeding

Apixaban	0.72 (0.42 to 1.24)
Dabigatran	0.40 (0.25 to 0.65)
Rivaroxaban	0.56 (0.34 to 0.90)

Warfarin 0.6 % year

Warfarin (Trials): 0.38 - 0.70 %

BMJ 2016;353:i3189

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

Retrospective observational cohort study

Individuals aged 75 and older with AF admitted to the hospital from October 2010 through September 2015 (N = 6,568, 50% female, 15% non-white).

NOAC use increased over time in all age groups (75-79, 80-84, 85-89) except aged 90 and older.

Fewer than 45% of participants were prescribed an anticoagulant.

Younger age, white race, female sex, higher hemoglobin, higher creatinine clearance, being on a medical service, hypertension, stroke or transient ischemic attack, no history of intracranial hemorrhage, and a HAS-BLED score of less than 3 increased the likelihood of receiving NOACs.

J Am Geriatr Soc 2017; 65:2405-2412

Anticoagulant	Major Bleeding	ICH
Dabigatran 150 mg	3.11	0.10
Dabigatran 110 mg	2.71	0.12
Warfarin	3.36	0.38
Rivaroxaban 20 mg	3.60	0.50
Warfarin 2.0-3.0 INR	3.40	0.70
Apixaban 5 mg	2.13	0.24
Warfarin	3.09	0.47
Edoxaban 60 mg	2.75	0.26
Edoxaban 30 mg	1.61	0.16
Warfarin	3.43	0.47

	ISCOAT 2016	ISCOAT 1996
Major bleeding n. (% annually) [fatal]	123 (1.38)	28 (1.39)
Fatal	10 (0.11)	5 (0.25)
ICH	38 (0.43) [7]	9 (0.45) [5]
Gastrointestinal	29 (0.32) [3]	7 (0.35) [/]
Other	56 (45.5) [/]	12 (0.60) [/]
Major + NMCRB events occurring during the first 90 days of treatment n/N (%)	78/267 (29.2)	62/153 (40.5)

Palareti G et al
Int Emerg Med
2017;12:1109-1119

DOAC and Internal Medicine ward

Schirru P, Moledda V, Mameli A, Porru M, Barcellona D, Marongiu F (unpublished)

Aim of the study:

evaluation for DOAC prescription in consecutively hospitalized patients in our internal medicine ward from 1 January, 2015 to November 30, 2017.

DOAC: Exclusion criteria

a)MDRD <30ml/min
b)Platelet count < 100.000/mm3
c)AST e ALT > 3 times normal values
d)Hb < 10 g/dl
e)Active cancer
f)Unreliable adherence and persistance
g)Pathologic condition of GI tract at risk of bleeding
h)Cardiac mechanic prosthesis
i)Splancnic Thrombosis
j)Anti-phospholipid Syndrome
k)Severe mitral stenosis

Patients admitted to the clinical ward: 2041

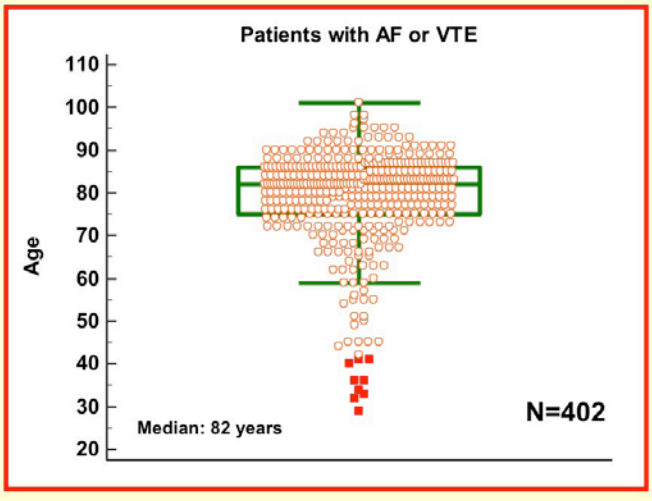
402 (19.7 %) patients with a clear indication to Oral Anticoagulation

Men 193 (48.1 %), Women 209 (51.9 %)

Age: 82, 29-101 years

Atrial Fibrillation: 333 (82.8 %)

Venous thromboembolism and heart prosthesis: 69 (17.2 %)



Diagnosis already known: 315

New diagnosis of AF and VTE: 87

Not in anticoagulant therapy: 62	
With aspirin or other anti-platelet drugs 26	Without aspirin or other antiplatelet drugs 36

On anticoagulant therapy: 253		
Heparins 10	VKA 166	DOAC 77*

*Apixaban 27, Xarelto 25, Pradaxa 24, Lixiana 1

Discharge

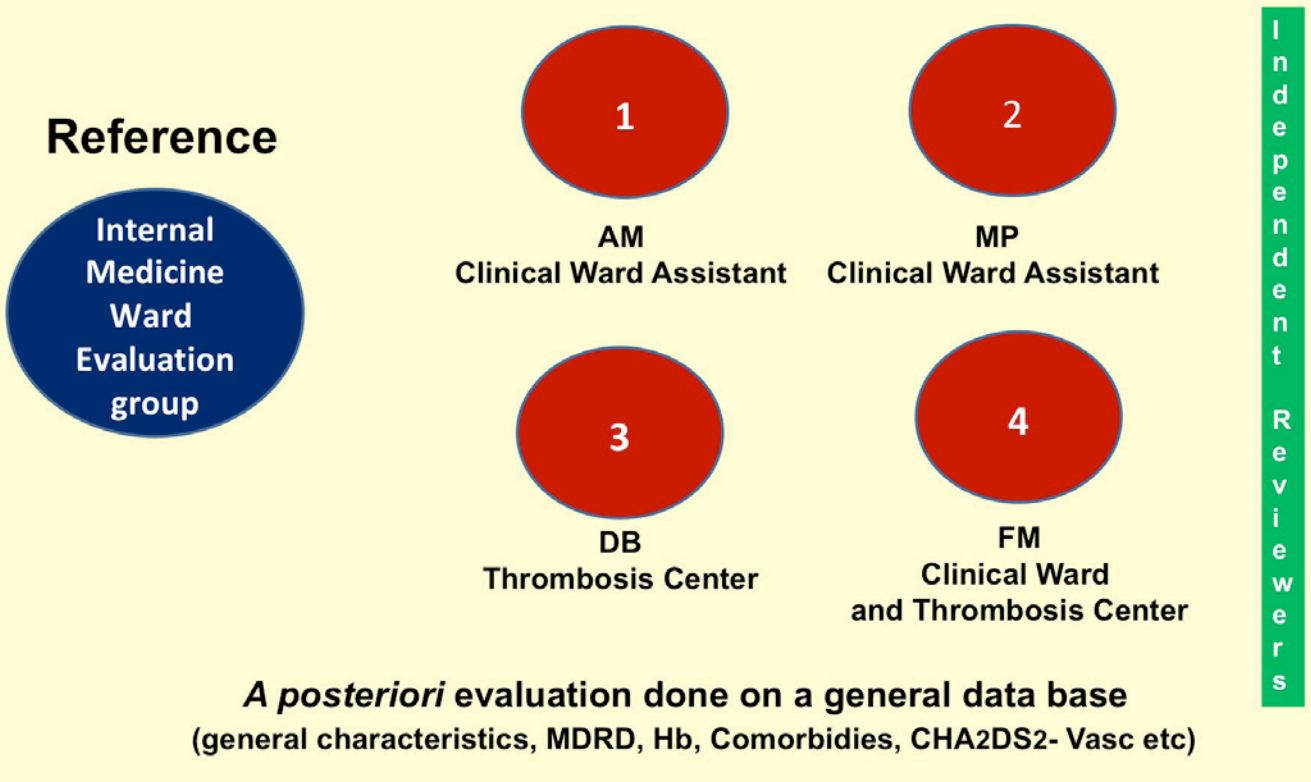
Patients		DOAC Yes	DOAC no*
402		182 (45,3 %)	220 (54,7 %)
Atrial Fibrllation	333	159 (47.7 %)	174 (52.2 %)
TEV	69	23 (33.3 %)	46 (66.7 %)

Evaluation at the Internal Medicine Ward on the basis of criteria previously shown

* No anticoagulant therapy N=44

Patients already with AVK	Can be switched to DOAC	Cannot be switched to DOAC
166	62 (37,3 %)	104 (62,7 %)

TTR unknown



Intraclass correlation coefficient

	Interclass correlation	95 % Confidence Intervals
Average measures *	0.881	0.862 to 0.898

* Estimates the reliability of averages of *k* ratings

Value of K	Strength of agreement
< 0.20	Poor
0.21 - 0.40	Fair
0.41 - 0.60	Moderate
0.61 - 0.80	Good
0.81 - 1.00	Very good

MEDCALC
Statistical Software

Multivariate statistical analysis

Variable	DOAC NO Odds Ratio	95% CI
CHA2Ds2-VASc ≥4	0,6537	0,3609 to 1,1841
Age (82 years old)	0,8493	0,5315 to 1,3572
HASBLED ≥ 4	3,0542	1,7835 to 5,2303
MDRD ≤ 60	1,5237	0,9397 to 2,4705
Comorbidities ≥ 3	2,7312	1,5015 to 4,9681

Stepwise

Variable	DOAC NO Odds Ratio	95% CI
HASBLED ≥ 4	3,015	1,792 to 5,071
Comorbidities ≥ 3	2,509	1,453 to 4,332

MEDCALC
Statistical Software

Conclusions

1 Oral anticoagulants are underused in the elderly.

2 We hope DOAC will increase anticoagulation in the elderly.

3 DOAC not for all patients, however.

4 Less close criteria could extend the use if DOAC in the future.