NAO NELLA FIBRILLAZIONE ATRIALE DELL’ANZIANO: DAI TRIAL AL MONDO REALE

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Sex Differences and Similarities in Atrial Fibrillation Epidemiology, Risk Factors, and Mortality in Community Cohorts

Cumulative incidence curves for AF by gender, with death as a competing risk (left); gender-related all-cause mortality with AF (Cox model; right)

Interaction $P = 0.70$

HR = 3.51 (3.26-3.78)
HR = 3.59 (3.27-3.95)

N=79793 from 4 community-based European studies
Age: 50 (24-98) years
FU: 12.6 years
Frailty syndrome: an emerging clinical problem in the everyday management of clinical arrhythmias: results of the European Heart Rhythm Association survey

Comorbidities most frequently associated to the frailty syndrome

Fumagalli S et Al., EP Europace 2017
Real-world characteristics of hospitalized frail elderly patients with atrial fibrillation: can we improve the current prescription of anticoagulants?

Annoni G, J Geriatr Cardiol 2016

The Most Common Chronic Comorbid Conditions in Patients with Atrial Fibrillation Admitted to an Acute Geriatric Unit (N=403/1619, 24.9%; 2012-4)

Age: 85±6 years

P<0.001

Prevalence (%) of different comorbid conditions in patients with and without AF.

- HF: 36.5%
- Dementia: 31.3%
- CVD: 30%
- Diabetes: 25.8%
- COPD: 24.3%
- CAD: 22.1%
- CKD: 20.6%
- AF Multimorbidity (>3 conditions): 71%
- No-AF Multimorbidity: 29%
Model-predicted 3MSE score trajectories in CHS participants with and without incident AF (74.4 vs. 72.9 years)

**3MSE:** Modified Mini-Mental State Examination - Scores range from 0 (worst) to 100 (best)

*The Cardiovascular Health Study*
5150 participants (1989-1993)
Incident AF: n=552 (10.7%); FU: 7 years

![Graph showing model-predicted 3MSE score trajectories with and without incident AF (74.4 vs. 72.9 years).](image-url)
Atrial fibrillation and physical function decline in an Italian elderly population: the InCHIANTI Study experience

SPPB trends by presence of AF
(N=267; AF prevalence: 4.9%; age - AF: 81±6 vs. NO AF: 77±6 years, p<0.01)

β = -1.369±0.507; p=0.007

Fumagalli S, EHRA 2017
Lone Atrial Fibrillation Is Associated With Impaired Left Ventricular Energetics That Persists Despite Successful Catheter Ablation

Schematic representation of the relationships between lone atrial fibrillation, subtle left ventricular dysfunction and upstream cardiomyopathy, and the effect of ablation

Baseline

A

Occult cardiomyopathy

Impaired energetics

“Lone” AF

Subtle LV dysfunction

Adverse haemodynamics

After AF ablation

B

Occult cardiomyopathy

Catheter ablation

Impaired energetics

Sinus rhythm ↓ AF burden

Subtle LV dysfunction

Wijesurendra RS, 2016
Relazione fra comorbilità, disabilità e fragilità secondo il Phenotype Frailty Index

Disabilità (n=67)

Comorbilità (n=2131)

Fragilità (n=170)

Fragilità (n=98)

Disabilità (n=196)

Comorbilità (n=170)

Disabilità (n=79)

Comorbilità (n=21)

Disabilità (n=21)

26.6% (n=98)

46.2% (n=170)

21.5% (n=79)

5.7% (n=21)

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

Reasons not to prescribe OAs to a frail patient with AF (light green bars indicate responses that are in favour of the use of OAs)

Fumagalli S et al., EP Europace 2017
NAO: outcome principali in SPAF

**Stroke/ SE**

<table>
<thead>
<tr>
<th>Drug</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban ARISTOTLE</td>
<td>0.80 (0.67–0.95)</td>
</tr>
<tr>
<td>Dabigatran 150mg RE-LY</td>
<td>0.66 (0.53–0.82)</td>
</tr>
<tr>
<td>Edoxaban 60mg ENGAGE AF-TIMI 48</td>
<td>0.88 (0.75–1.02)</td>
</tr>
<tr>
<td>Rivaroxaban ROCKET AF</td>
<td>0.88 (0.75–1.03)</td>
</tr>
<tr>
<td>Combined (random)</td>
<td>0.81 (0.73–0.91)</td>
</tr>
</tbody>
</table>

**Major bleeding**

<table>
<thead>
<tr>
<th>Drug</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban ARISTOTLE</td>
<td>0.71 (0.61–0.81)</td>
</tr>
<tr>
<td>Dabigatran 150mg RE-LY</td>
<td>0.94 (0.82–1.07)</td>
</tr>
<tr>
<td>Edoxaban 60mg ENGAGE AF-TIMI 48</td>
<td>0.80 (0.71–0.90)</td>
</tr>
<tr>
<td>Rivaroxaban ROCKET AF</td>
<td>1.03 (0.90–1.18)</td>
</tr>
<tr>
<td>Combined (random)</td>
<td>0.86 (0.73–1.00)</td>
</tr>
</tbody>
</table>

Modified from Ruff et al. Lancet 2014;383:955-62

New Oral Anticoagulants in Elderly Adults: Evidence from a Meta-Analysis of Randomized Trials

Patients aged more than 75 years: Stroke or systemic embolism

**Odds Ratio**

**Rivaroxaban**
- ROCKET-AF
- Subtotal

**Apixaban**
- ARISTOTLE
- AVERROES
- Subtotal

**Dabigatran**
- RE-LY
- Subtotal

**Total**
- NOAC: 3.3 vs. C: 4.7%
- OR=0.65 – NNT=71
- 95%CI=0.48-0.87

New oral anticoagulants vs. conventional therapy for participants aged >75 years

NOAC – N: 11562
Control – N: 9177

NNT: number needed to treat

Sardar P, 2014
New Oral Anticoagulants in Elderly Adults: Evidence from a Meta-Analysis of Randomized Trials

Patients aged more than 75 years: Major or clinically relevant bleeding

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study</th>
<th>NOAC – N: 13625</th>
<th>Control – N: 11083</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban</td>
<td>EINSTEIN PE, EINSTEIN,</td>
<td></td>
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<tr>
<td></td>
<td>EINSTEIN-Extension, ROCET-AF</td>
<td></td>
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</tr>
<tr>
<td>Apixaban</td>
<td>ARISTOTLE, AVERROES</td>
<td></td>
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</tr>
<tr>
<td>Dabigatran</td>
<td>RE-LY</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

New oral anticoagulants vs. conventional therapy for participants aged >75 years

$$\text{OR} = 1.02, 95\% \text{CI} = 0.73 - 1.43$$

Sardar P, 2014
Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated With Dabigatran or Warfarin for Nonvalvular Atrial Fibrillation

Outcome Incidence in New-User Cohorts of Dabigatran and Warfarin

**Hemorrhages**

<table>
<thead>
<tr>
<th>Hemorrhage</th>
<th>Dabigatran - N=67207</th>
<th>Warfarin - N=67207</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>HR=0.80 (0.67-0.96)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Major</td>
<td>HR=0.97 (0.88-1.07)</td>
<td>p=0.50</td>
</tr>
<tr>
<td>GI</td>
<td>HR=1.28 (1.14-1.44)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>IC</td>
<td>HR=0.34 (0.26-0.46)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>AMI</td>
<td>HR=0.92 (0.78-1.08)</td>
<td>p=0.29</td>
</tr>
<tr>
<td>Mortality</td>
<td>HR=0.86 (0.77-0.96)</td>
<td>p=0.006</td>
</tr>
</tbody>
</table>

**Incidence rate** (1000 person-years)

- **Stroke**: 11.3, 13.9
- **Major**: 42.7, 43.9
- **GI**: 34.2, 26.5
- **IC**: 3.3, 9.6
- **AMI**: 15.7, 16.9
- **Mortality**: 32.6, 37.8

**Incidence in New-User Cohorts**

- Medicare patients (2010-2012): 75-84 years: 43%, >85 years: 16%
Contemporary stroke prevention strategies in 11 096 European patients with atrial fibrillation: a report from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Long-Term General Registry

Proportions of patients treated with antithrombotic drugs by CHA\textsubscript{2}DS\textsubscript{2}-VASc score

Boriani G, Europace EP 2017
Contemporary stroke prevention strategies in 11 096 European patients with atrial fibrillation: a report from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Long-Term General Registry

Antithrombotic treatments at discharge/after consultation (Age; 71 (63-77) years; 250 Centres, 27 European Countries; 2013-6)

All P values <0.001
OAC: 84.9%; None: 6.4%
Effect of New Oral Anticoagulants on Prescribing Practices for Atrial Fibrillation in Older Adults

Quarterly trend in anticoagulants use (N=6568; age ≥75 years) (the Clinical Investigation Data Exploration Repository - CIDER, Washington University)

- **NOAC use (%)**
  - 2010 qtr 4: 0%
  - 2013 qtr 3: 10%
  - 2015 qtr 3: 15%
  - $R = 0.87$, $p < 0.001$

- **Warfarin use (%)**
  - 2010 qtr 4: 30%
  - 2013 qtr 3: 28%
  - 2015 qtr 3: 26%
  - $R = -0.16$, $p = 0.50$

- **<45%**
  - 2010 qtr 4: 30%
  - 2013 qtr 3: 35%
  - 2015 qtr 3: 40%
  - $R = 0.68$, $p = 0.001$

Fohung RB et al, JAGS 2017
Nuovi utilizzatori (incidenti) di AVK e NAO in Umbria

Fonte: Elaborazione Iss su dati SSR Umbria
L’uso di AVK e NAO a livello regionale nel 2016

Fonte: Elaborazione Iss su dati Ministero salute (tracciabilità del farmaco)
Caratteristiche degli utilizzatori incidenti

Uso di anticoagulanti orali per classe e gruppo di età

AVK – N=10202 (58%)
Età: 74±12; Donne: 50%

NAO – N=7468 (42%)
Età: 77±12; Donne: 52%

Fonte: Elaborazione Iss su dati SSR Umbria
Fattori predittivi prescrizione di NAO

Fonte: Elaborazione Iss su dati SSR Umbria
Clinical frailty is independently associated with non-prescription of anticoagulants in older patients with atrial fibrillation

The proportion of individuals not taking anticoagulants (black) compared with those taking anticoagulants (white), by Clinical Frailty Scale, CHA₂DS₂-VASc and HAS-BLED scores (N=419; anticoagulated No/Yes: 215/204)

Anticoagulated
Yes – Frailty: 52.5%
No – Frailty: 81.4%
P<0.001

Anticoagulated
Yes – CHA₂DS₂-VASc: 5
No – CHA₂DS₂-VASc: 4
P<0.001

Anticoagulated
Yes – Age: 83
No – Age: 87
P<0.001

Multivariate predictors
OR Frailty = 0.77, p<0.001
OR Bleeding Risk = 0.85, p=0.02
OR Age = 0.98, p<0.001

Induruwa I et Al, Geriatr Gerontol Int 2017
The Effect of Bleeding Risk and Frailty Status on Anticoagulation Patterns in Octogenarians With Atrial Fibrillation: The FRAIL-AF Study

Anticoagulant use in 682 hospitalized patients ≥80 years with AF/AFI (Age: 85.9; 3 academic hospitals; Montreal, Quebec; 2012-2013)

The most common reasons for not prescribing an OA:
1. Hx of bleeding (15.5%)
2. Active bleeding (15.5%)
3. Risk of falls (14%)
4. Patient refusal (8.7%)
5. No justification provided (15%)
### ARISTOTLE: Adverse Events in Each Comorbidity Group Treated With Apixaban vs. Warfarin

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Apixaban Rate (Events)</th>
<th>Warfarin Rate (Events)</th>
<th>HR (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke / SE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 2 comorbidities</td>
<td>1.03 (59)</td>
<td>1.36 (77)</td>
<td>0.76 (0.54 to 1.06)</td>
<td>0.7367</td>
</tr>
<tr>
<td>3 to 5 comorbidities</td>
<td>1.39 (109)</td>
<td>1.87 (144)</td>
<td>0.74 (0.58 to 0.95)</td>
<td></td>
</tr>
<tr>
<td>6+ comorbidities</td>
<td>1.64 (31)</td>
<td>1.77 (34)</td>
<td>0.93 (0.57 to 1.51)</td>
<td></td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 2 comorbidities</td>
<td>2.21 (129)</td>
<td>2.96 (172)</td>
<td>0.75 (0.59 to 0.94)</td>
<td>0.2205</td>
</tr>
<tr>
<td>3 to 5 comorbidities</td>
<td>3.69 (297)</td>
<td>3.86 (305)</td>
<td>0.96 (0.81 to 1.12)</td>
<td></td>
</tr>
<tr>
<td>6+ comorbidities</td>
<td>6.95 (135)</td>
<td>7.93 (156)</td>
<td>0.88 (0.70 to 1.11)</td>
<td></td>
</tr>
<tr>
<td><strong>Major Bleed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 2 comorbidities</td>
<td>1.61 (86)</td>
<td>2.58 (135)</td>
<td>0.62 (0.48 to 0.82)</td>
<td>0.4857</td>
</tr>
<tr>
<td>3 to 5 comorbidities</td>
<td>2.30 (164)</td>
<td>3.34 (231)</td>
<td>0.69 (0.56 to 0.84)</td>
<td></td>
</tr>
<tr>
<td>6+ comorbidities</td>
<td>3.98 (66)</td>
<td>4.94 (79)</td>
<td>0.81 (0.58 to 1.12)</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- **0-2 comorbidities** – N=6087
- **3-5 comorbidities** – N=8491
- **6+ comorbidities** – N=2196

Alexander KP et al, AHA Congress 2017
Absolute Risk Reduction of HD Edoxaban Regimen Compared With Warfarin in Patients at Increased Versus Not at Increased Fall Risk

- **Hemorrhagic S**: NNT 157 vs. 500
- **ICH**: NNT 152 vs. 293
- **Bleed Life-Threatening**: NNT 157 vs. 500
- **All-Cause Death**: NNT 152 vs. 293
### ARISTOTLE: History of Falls

**Endpoints**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Apixaban Rate [%/year] (number of events)</th>
<th>Warfarin Rate [%/year] (number of events)</th>
<th>HR (95% CI)</th>
<th>Interaction P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke/Systemic embolism</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of falls</td>
<td>1.76 (12)</td>
<td>1.99 (13)</td>
<td>0.88 (0.40 – 1.93)</td>
<td>0.69</td>
</tr>
<tr>
<td>No history of falls</td>
<td>1.23 (177)</td>
<td>1.63 (234)</td>
<td>0.75 (0.62 – 0.91)</td>
<td></td>
</tr>
<tr>
<td><strong>Death from any cause</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of falls</td>
<td>6.41 (45)</td>
<td>6.74 (45)</td>
<td>0.96 (0.63 – 1.44)</td>
<td>0.63</td>
</tr>
<tr>
<td>No history of falls</td>
<td>3.17 (469)</td>
<td>3.71 (546)</td>
<td>0.86 (0.76 – 0.97)</td>
<td></td>
</tr>
<tr>
<td><strong>Hemorrhagic stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of falls</td>
<td>0.14 (1)</td>
<td>0.45 (3)</td>
<td>0.32 (0.03 – 3.09)</td>
<td>0.72</td>
</tr>
<tr>
<td>No history of falls</td>
<td>0.23 (33)</td>
<td>0.47 (68)</td>
<td>0.48 (0.32 – 0.73)</td>
<td></td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of falls</td>
<td>4.35 (26)</td>
<td>5.38 (31)</td>
<td>0.81 (0.48 – 1.36)</td>
<td>0.57</td>
</tr>
<tr>
<td>No history of falls</td>
<td>2.07 (274)</td>
<td>3.00 (389)</td>
<td>0.69 (0.59 – 0.81)</td>
<td></td>
</tr>
<tr>
<td><strong>Intracranial bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of falls</td>
<td>0.33 (2)</td>
<td>1.69 (10)</td>
<td>0.19 (0.04 – 0.88)</td>
<td>0.35</td>
</tr>
<tr>
<td>No history of falls</td>
<td>0.32 (43)</td>
<td>0.78 (103)</td>
<td>0.41 (0.29 – 0.59)</td>
<td></td>
</tr>
<tr>
<td><strong>Subdural bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of falls</td>
<td>0.00 (0)</td>
<td>0.85 (5)</td>
<td>0.33 (0.15 – 0.69)</td>
<td></td>
</tr>
<tr>
<td>No history of falls</td>
<td>0.07 (9)</td>
<td>0.21 (27)</td>
<td>0.33 (0.15 – 0.69)</td>
<td></td>
</tr>
</tbody>
</table>
Non-Vitamin K Antagonist Oral Anticoagulant Dosing in Patients With Atrial Fibrillation and Renal Dysfunction

Prevalence of Inappropriate NOAC Dosing (OptumLabs Data Warehouse and Medicare Advantage, 2010-2015; N=14865)

Yao X et al., J Am Coll Cardiol 2017

- Appropriately dosed (No renal indication for dose reduction)
- Renal indication for reduced dose: Over-dosed
- No renal indication for reduced dose: Under-dosed
- Age: 71±11 years
- Women: 42.6%
- GFR - No renal / Renal indication: 73 / 38 mL/min/1.73 m²
- CHA₂DS₂-VASc - No renal / Renal indication: 4 / 5
Non-Vitamin K Antagonist Oral Anticoagulant Dosing in Patients With Atrial Fibrillation and Renal Dysfunction

Outcomes Associated With Overdosing

<table>
<thead>
<tr>
<th>Event rate (100 p-years)</th>
<th>Reduced</th>
<th>Standard</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/SE</td>
<td>1.85</td>
<td>2.32</td>
<td>1.66 (0.40-6.88)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>5.06</td>
<td>11.29</td>
<td>2.19 (1.07-4.46)</td>
</tr>
</tbody>
</table>

Favor Standard Dose       Favor Reduced Dose
Non-Vitamin K Antagonist Oral Anticoagulant Dosing in Patients With Atrial Fibrillation and Renal Dysfunction

Outcomes Associated With Underdosing

<table>
<thead>
<tr>
<th></th>
<th>Reduced</th>
<th>Standard</th>
<th>HR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Apixaban</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>550</td>
<td>550</td>
<td></td>
</tr>
<tr>
<td>S/SE</td>
<td>2.57</td>
<td>0.54</td>
<td>4.87 (1.30-18.26)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>6.01</td>
<td>4.64</td>
<td>1.29 (0.48-3.42)</td>
</tr>
<tr>
<td><strong>Dabigatran</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>412</td>
<td>412</td>
<td></td>
</tr>
<tr>
<td>S/SE</td>
<td>1.64</td>
<td>1.75</td>
<td>0.92 (0.30-2.87)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>4.99</td>
<td>5.54</td>
<td>0.91 (0.45-1.85)</td>
</tr>
<tr>
<td><strong>Rivaroxaban</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>815</td>
<td>815</td>
<td></td>
</tr>
<tr>
<td>S/SE</td>
<td>1.23</td>
<td>1.65</td>
<td>0.71 (0.24-2.09)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>5.42</td>
<td>4.90</td>
<td>1.09 (0.63-1.87)</td>
</tr>
</tbody>
</table>
Effetto dell’età sul dosaggio (prima prescrizione)

![Bar chart showing the effect of age on dosage (first prescription).](chart.png)

**Fonte:** Elaborazione Iss su dati SSR Umbria
Persistence With Dabigatran Therapy at 2 Years in Patients With Atrial Fibrillation

Therapy Persistence With Dabigatran Etexilate (DE): Kaplan-Meier Curve of Time to Treatment Discontinuation Over 2 Years (the GLORIA-AF Registry, Phase II; N=2932; age: 70 years; DE discontinuation – N=828)

Discontinuation for:
AE/SAE: 7.5/7.7%
Bleeding: 7.0%
Dementia: 0.5%
Other: 59.8%

HR <75 vs. ≥75 years = 0.95 (0.80-1.12)

Paquette M, JACC 2017
Unbound Dabigatran levels and reversal of anticoagulation with idarucizumab
(RE-VERSE AD, Group B, “Emergency surgery or procedure”, N=196, Age: 77 years)

Idarucizumab, a monoclonal antibody fragment, binds dabigatran with approximately 350 times the avidity with which thrombin binds dabigatran.

Median time to surgery: 1.6 h
Normal hemostasis: 93%

Time post-idarucizumab
Clinical characteristics of patients with bleeding (year 2015; people potentially referring to the ED: N=3.000.000)

- All bleeding – N=1977
- All other accesses – N=95993
- All other bleeding – N=1962
- Bleeding due to NOAC – N=15

Bleeding types:
- Genitourinary: 5
- Gastrointestinal: 2
- ICH: 5
- Mixed: 3

Other characteristics:
- Age: 77±11 years
- CHA₂DS₂-VASc: 4
- HAS-BLED: 2

Hospitalization – N=11/15 (73%)
Mortality – 3/15 (20%)

Salzano A, Eur J Intern Med 2017
A Randomized, Open-Label, Blinded Outcome Assessment Trial Evaluating the Efficacy and Safety of LMWH/Edoxaban Versus Dalteparin for Venous Thromboembolism Associated with Cancer: Hokusai VTE-Cancer Study

Raskob GE, Late-Breaking Abstracts Session, 2017

Primary outcome and survival by treatment
(Edoxaban - N=522; Dalteparin - N=524; FU: up to 12 months; 2015-6)

P=0.0056 for non-inferiority

Edoxaban 60 mg; Dalteparin 200 U/Kg (30 d), 150 U/Kg (thereafter)

Primary outcome – first recurrent VTE or major bleeding event
Conclusioni

- La FA è l’aritmia più frequente nel paziente anziano.
- I paziente anziani con FA sono generalmente complessi, spesso fragili, con una più alta mortalità.
- La terapia anticoagulante è sempre più utilizzata nei pazienti con FA.
- Dati di “mondo reale” sembrano dimostrare che i NOACs sono più efficaci e sicuri, soprattutto nei pazienti anziani, e si associano ad una più alta persistenza del trattamento. Tuttavia, proprio nei soggetti più complessi e fragili, l’anticoagulazione, se utilizzata, si basa soprattutto sugli antagonisti della Vit. K.
- Dati italiani dimostrano che esiste un’ampia disomogeneità regionale nella prescrizione dei NOACs.
- I NOACs devono essere prescritti con il dosaggio appropriato.
Uso di farmaci* negli utilizzatori incidenti

* 12 mesi precedenti la prima prescrizione di anticoagulanti

Fonte: Elaborazione Iss su dati SSR Umbria
**Patologie*** negli utilizzatori incidenti

<table>
<thead>
<tr>
<th>Patologia</th>
<th>AVK</th>
<th>NAO</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrillazione atriale</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Infarto miocardico</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Cardiopatia ischemica</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Scompenso cardiaco</td>
<td></td>
<td></td>
<td>p=0,63</td>
</tr>
<tr>
<td>Malattie cerebrovascolari</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Diabete</td>
<td></td>
<td></td>
<td>p=0,03</td>
</tr>
<tr>
<td>Tumore</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Embolia/Trombosi arteriosa e venosa</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Ipertensione</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Vasculopatie</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Psicosi</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Alzheimer e demenze</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
<tr>
<td>Insufficienza renale cronica</td>
<td></td>
<td></td>
<td><strong>p&lt;0,01</strong></td>
</tr>
</tbody>
</table>

* 24 mesi precedenti la prima prescrizione di anticoagulanti

Fonte: Elaborazione Iss su dati SSR Umbria
La probabilità di andare incontro a uno switch (periodo 2015-2016)

Fonte: Elaborazione Iss su dati SSR Umbria
Knowledge Gaps in Cardiovascular Care of the Older Adult Population

Ten Most Common Chronic Comorbid Conditions Among Medicare Beneficiaries With AF (Beneficiaries ≥65 y of Age; N=2,426,865)

- Hypertension: 83%
- Hyperlipidemia: 64%
- HF: 62%
- Anemia: 51%
- Arthritis: 42%
- DM: 40%
- CKD: 36%
- COPD: 32%
- Cataract: 23%
- Median N of Conditions = 6
Effect of New Oral Anticoagulants on Prescribing Practices for Atrial Fibrillation in Older Adults

Quarterly trend in anticoagulant use by age groups (N=6568; age ≥ 75 years) (the Clinical Investigation Data Exploration Repository - CIDER, Washington University)

Anticoagulants
Dementia – OR=0.51, p<0.001
Falls – OR=0.60, p<0.001

OR: Adjusted value for independent predictors of anticoagulant use

Fohling RB et Al, JAGS 2017
Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial

973 patients aged ≥75 years (mean age: 81.5 ± 4.2 years)

Follow-up = 2.7 ± 1.2 years

Primary endpoint: fatal / disabling stroke (ischemic / hemorrhagic), intracranial hemorrhage, or clinically significant arterial embolism

Warfarin
N = 24 / 488
1.8% per year

Aspirin
N = 48 / 485
3.8% per year

RR Warfarin vs. ASA = 0.48
95%CI = 0.28 - 0.80 - P = 0.003
Real-world characteristics of hospitalized frail elderly patients with atrial fibrillation: can we improve the current prescription of anticoagulants?

Assessment of Frailty in Patients with Atrial Fibrillation Admitted to an Acute Geriatric Unit (N=403/1619, 24.9%; 2012-4)

Frailty by Robinson’s criteria

- impaired cognition (Mini-Cog ≤ 3)
- recent falls (≥1 in the previous 6 m)
- impaired mobility (NMS ≤ 6)
- Anemia (due to chronic disease, Htc < 35%)
- functional dependence in ≥1 ADL
- poor nutrition (MNA-SF ≤ 8 or a serum albumin level <3.4 g/dL)
- comorbidity (CCI ≥ 3)

Values as percentages

Frail – >4
Pre-Frail – 2-3
Non Frail – 0-1

57
29
14
Contemporary stroke prevention strategies in 11 096 European patients with atrial fibrillation: a report from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Long-Term General Registry

Oral anticoagulant treatment distribution and VKA / NOAC ratio at discharge by region

All ORs and P values derive from multivariable model

VKA/NOAC ratio

<table>
<thead>
<tr>
<th>Region</th>
<th>VKA/NOAC Ratio</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern Europe</td>
<td>0.64</td>
<td>1.33</td>
<td>0.0073</td>
</tr>
<tr>
<td>Western Europe</td>
<td>1</td>
<td>1.31</td>
<td>0.0018</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>2.32</td>
<td>Ref</td>
<td>1</td>
</tr>
<tr>
<td>Southern Europe</td>
<td>2.28</td>
<td>0.75</td>
<td>0.0005</td>
</tr>
</tbody>
</table>
Age-Specific Incidence, Outcome, Cost and Projected Future Burden of Atrial Fibrillation-Related Embolic Vascular Events: A Population-Based Study

Age-specific rates of first ever AF-related incident ischaemic stroke and systemic embolism in the Oxford Vascular Study (2002-2012; N=92728; 9 general practices - about 100 family doctors)

Stroke: Ischaemic stroke
SE: Systemic embolism

Yiin GSC, 2014
Baseline functional status as the strongest predictor of in-hospital mortality in elderly patients with non-valvular atrial fibrillation: Results of the NONAVASC registry

Mortality proportion observed according to the different associated factors (N=804; Age; 85±5 years; Mortality: N=81 -10.1%; 2014-5)

ARF: acute renal failure at admission
Dependency:
Total – BI ≤20
Severe – BI 21-40
Moderate – BI 41-60
Mild – BI 61-99
Impact of Renal Function on Outcomes With Edoxaban in the ENGAGE AF-TIMI 48 Trial

Primary efficacy and safety end points by exploratory CrCl subgroups

**Stroke or SE**

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Absolute Rates (%/year)</th>
<th>P interaction = 0.08</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-50</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>&gt;50-95</td>
<td>1.9</td>
<td></td>
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<tr>
<td>&gt;95</td>
<td>0.8</td>
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</tbody>
</table>

\[ P = 0.019 \]

**Major Bleeding**

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Absolute Rates (%/year)</th>
<th>P interaction = 0.11</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-50</td>
<td>5.3</td>
<td></td>
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<tr>
<td>&gt;50-95</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>&gt;95</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

\[ P = 0.036 \]

Bohula EA, 2016