AF & CAD

Management and prognosis

Maria Agelaki

Cons. Cardiologist
Red Cross GN Hosp.
AF and CAD share in common...

Most common arrhythmia and cardiovascular disease respectively

High prevalence in general population

<table>
<thead>
<tr>
<th>age</th>
<th>ANGINA</th>
<th>AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-64 y</td>
<td>5-7%</td>
<td>Up to 4%</td>
</tr>
<tr>
<td>65-84 y</td>
<td>10-14%</td>
<td></td>
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<tr>
<td>&gt;80 y</td>
<td></td>
<td>14%</td>
</tr>
</tbody>
</table>

Associated risk factors

HTN, DM, S. APNEA, OBESITY, SMOKING

Inflammation plays a causative role in both
What is the prevalence of CAD in AF pts

ROCKET AF & RELY trials estimated at 17%

13% with stable CAD ➔ 21% requiring intervention

46%

What is the prevalence of AF in CAD pts

0.2% to 5%
one half of first-ever documented AF cases after AMI are developed in the first month

Prognostic implications

![Graph showing odds ratios for various cardiovascular events]

- Stroke
- Congestive Heart Failure
- Cardiogenic Shock
- Death
- 30 Day Readmission

Odds Ratio

AF may cause AMI through 

Thromboembolic mechanism  

Type II MI in AF with rapid ventricular response  

AF after CABG

Occurs in 20-40% of the cases  
Associated with thromboembolic events, stroke and prolonged hospitalization  
Management of patients with AF and CAD in the setting of ...

1. First diagnosed AF

2. ACS in AF pts

3. Stable CAD in AF pts
Work up of newly diagnosed AF...

Do we need to screen for CAD?

No on regular basis

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG documentation is required to establish the diagnosis of AF.</td>
<td>I</td>
<td>B</td>
<td>349</td>
</tr>
<tr>
<td>A full cardiovascular evaluation, including an accurate history, careful clinical examination, and assessment of concomitant conditions, is recommended in all AF patients.</td>
<td>I</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Transthoracic echocardiography is recommended in all AF patients to guide management.</td>
<td>I</td>
<td>C</td>
<td>339</td>
</tr>
<tr>
<td>Long-term ECG monitoring should be considered in selected patients to assess the adequacy of rate control in symptomatic patients and to relate symptoms with AF episodes.</td>
<td>IIa</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

ST depression was seen in 38% of the patients with rapid AF and half of them had CAD at angiography

4% of the patients without ST depression during rapid AF had positive noninvasive tests for myocardial ischemia and CAD at angiography

Troponin release in 15% of AF patients with symptoms of myocardial ischemia, usually in the absence of CAD at angiography

E. Michniewicz et al. / Advances in Medical Sciences 63 (2018) 30–35
Management of patients with AF and ACS

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

<table>
<thead>
<tr>
<th>Acute rate control of AF</th>
<th>Cardioversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous beta-blockers are indicated for rate control if necessary and there are no clinical signs of acute heart failure or hypotension.</td>
<td>Immediate electrical cardioversion is indicated when adequate rate control cannot be achieved promptly with pharmacological agents in patients with AF and ongoing ischaemia, severe haemodynamic compromise, or heart failure.</td>
</tr>
<tr>
<td>Intravenous amiodarone is indicated for rate control if necessary in the presence of concomitant acute heart failure and no hypotension.</td>
<td>Intravenous amiodarone is indicated to promote electrical cardioversion and/or decrease risk for early recurrence of AF after electrical cardioversion in unstable patients with recent onset AF.</td>
</tr>
<tr>
<td>Intravenous digitalis should be considered for rate control if necessary in the presence of concomitant acute heart failure and hypotension.</td>
<td>Digoxin is ineffective in converting recent onset AF to sinus rhythm and is not indicated for rhythm control.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Classification</th>
<th>Evidence Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>IIA</td>
<td>B</td>
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<tr>
<td>III</td>
<td>A</td>
</tr>
<tr>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>
A patient with AF due to AMI provided that he is re-vascularized completely, does he need anticoagulation on long term basis?

In patients with documented de novo AF during the acute phase of STEMI, long-term oral anticoagulation should be considered depending on CHA2DS2-VASc score and taking concomitant antithrombotic therapy into account.\textsuperscript{5,444}

**Figure 5** Cumulative event rate for ischaemic stroke according to pattern occurrence of atrial fibrillation (AF). SR, sinus rhythm.

Management of patients with AF and ACS

- Atrial Fibrillation (ACTIVE W): The combination of aspirin and clopidogrel is not as effective as warfarin in patients with AF

However

- Stenting (STARS): The combination of aspirin and clopidogrel is more effective than warfarin in patients with coronary stents

Danish Registry in pt with MI

Risk of bleeding with antithrombotic therapies

In the CathPCI registry, analysing data from 3.3 million PCI procedures (2004–11):

- Risk difference = 3.39% (95% CI: 3.20–3.59) P<0.001

**AF**
- Anticoagulant therapy
  - For prevention of stroke in patients with additional risk factors

**PCI**
- Antiplatelet therapy
  - For prevention of stent thrombosis following PCI
  - Dual antiplatelet therapy superior to ASA alone

**AF and PCI**
- **DUAL THERAPY:** anticoagulant and single antiplatelet?
- **OR**
- **TRIPLE THERAPY:** anticoagulant and dual antiplatelet therapy?

Chhatriwalla et al. JAMA 2013
WOEST Trial
Study Design

- Primary outcome measure: combination of TIMI and GUSTO minor and major bleeding up to 30 days and 1 year
- Secondary outcome measure: MACE

Death, MI, Stroke, Target-Vessel Revascularization, and Stent Thrombosis
2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS
PIONEER AF-PCI compared regimens of rivaroxaban with single or dual antiplatelet therapy

**Multicentre, randomized, open-label trial**

Paroxysmal, persistent or permanent AF, undergoing PCI (with stent placement)

N=2124

Primary endpoint: clinically-significant bleeding

**Composite of bleeding events**

- **Group 1**
  - Rivaroxaban 15 mg /10 mg OD + clopidogrel

- **Group 2**
  - Rivaroxaban 2.5 mg BID + DAPT*
  - Rivaroxaban 15 mg/10 mg OD + low-dose ASA

- **Group 3**
  - VKA (INR 2.0–3.0) + DAPT*
  - VKA + low-dose ASA

End of treatment (12 months)
High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction.

Bleeding risk can be estimated by HAS-BLED or ABC score.

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

Patients with an indication for oral anticoagulation undergoing PCI

- Concerns about ischaemic risk prevailing
- Concerns about bleeding risk prevailing

Time from treatment initiation:

- 1 mo.
- 3 mo.
- 6 mo.
- 12 mo.
- Beyond 12 mo.

**ACO**

1 mo. Triple Therapy
Class Ila B

3 mo.

ACO
Triple Therapy up to 6 mo.
Class Iia B

ACO

Dual Therapy up to 6 mo.
Class Ila A

**ACO**

Dual Therapy up to 12 mo.
Class Ila A

**ACO**

OAC alone
Class Ila B

**A** = Aspirin  
**C** = Clopidogrel  
**O** = Oral anticoagulation
RE-DUAL PCI tested the safety and efficacy of two regimens of dual therapy with dabigatran without ASA vs triple therapy with warfarin.

Patients with AF undergoing PCI with stenting

N=2725

Randomization
post-PCI*

Dabigatran 150 mg BID + P2Y12 inhibitor

Dabigatran 110 mg BID + P2Y12 inhibitor

Warfarin (INR 2.0–3.0) + P2Y12 inhibitor + ASA

Primary endpoint: ISTH major or CRNM bleeding

6-month minimum treatment duration, maximum treatment duration 30 months (mean follow-up ~14 months)

P value

<0.001

0.002

<0.001

0.02

0.06

0.047

0.005*

0.30

0.44

**Bleeding events: ACS vs non-ACS**

<table>
<thead>
<tr>
<th></th>
<th>D110-DT n/N (%)</th>
<th>Warfarin-TT n/N (%)</th>
<th>P interaction</th>
<th>D150-DT n/N (%)</th>
<th>Warfarin-TT n/N (%)</th>
<th>P interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ISTH Major/CRNM Bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>75/509 (14.7)</td>
<td>132/475 (27.8)</td>
<td>0.34</td>
<td>ACS</td>
<td>80/391 (20.5)</td>
<td>100/369 (27.1)</td>
</tr>
<tr>
<td>Non-ACS</td>
<td>76/472 (16.1)</td>
<td>132/505 (26.1)</td>
<td></td>
<td>Non-ACS</td>
<td>74/372 (19.9)</td>
<td>96/394 (24.4)</td>
</tr>
<tr>
<td><strong>ISTH Major Bleeding</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>26/509 (5.1)</td>
<td>55/475 (11.6)</td>
<td>0.14</td>
<td>ACS</td>
<td>25/391 (6.4)</td>
<td>40/369 (10.8)</td>
</tr>
<tr>
<td>Non-ACS</td>
<td>23/472 (4.9)</td>
<td>35/505 (6.9)</td>
<td></td>
<td>Non-ACS</td>
<td>18/372 (4.8)</td>
<td>24/394 (6.1)</td>
</tr>
<tr>
<td><strong>TIMI Major Bleeding</strong></td>
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<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>ACS</td>
<td>7/509 (1.4)</td>
<td>23/475 (4.8)</td>
<td>0.30</td>
<td>ACS</td>
<td>9/391 (2.3)</td>
<td>19/369 (5.1)</td>
</tr>
<tr>
<td>Non-ACS</td>
<td>7/472 (1.5)</td>
<td>14/505 (2.8)</td>
<td></td>
<td>Non-ACS</td>
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<td>11/394 (2.8)</td>
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**Death and thromboembolic events: ACS vs non-ACS**

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<thead>
<tr>
<th></th>
<th>D110-DT n/N (%)</th>
<th>Warfarin-TT n/N (%)</th>
<th>P interaction</th>
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<th>P interaction</th>
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<tbody>
<tr>
<td><strong>DTE or Unplanned Revascularization</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>ACS</td>
<td>92/509 (18.1)</td>
<td>70/475 (14.7)</td>
<td>0.38</td>
<td>ACS</td>
<td>41/391 (10.5)</td>
<td>52/369 (14.1)</td>
</tr>
<tr>
<td>Non-ACS</td>
<td>57/472 (12.1)</td>
<td>61/505 (12.1)</td>
<td></td>
<td>Non-ACS</td>
<td>49/372 (13.2)</td>
<td>46/394 (11.7)</td>
</tr>
<tr>
<td><strong>Myocardial infarction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>32/509 (6.3)</td>
<td>16/475 (3.4)</td>
<td>0.20</td>
<td>ACS</td>
<td>13/391 (3.3)</td>
<td>11/369 (3.0)</td>
</tr>
<tr>
<td>Non-ACS</td>
<td>12/472 (2.5)</td>
<td>13/505 (2.6)</td>
<td></td>
<td>Non-ACS</td>
<td>13/372 (3.5)</td>
<td>11/394 (2.8)</td>
</tr>
<tr>
<td><strong>All-cause Death</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>34/509 (6.7)</td>
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ACS, acute coronary syndrome; D, dabigatran; DT, dual therapy; DTE, death or thromboembolic event (myocardial infarction, stroke or systemic embolism); TT, triple therapy.
A treatment interaction was seen between CrCl and treatment for dabigatran 150 mg dual therapy versus warfarin triple therapy. A favorable effect with lower bleeding rates was seen with dabigatran 150 mg dual therapy for patients with a CrCl level ≥ 80 mL/min for ischemic outcomes, and a trend toward lower bleeding in 51–80 mL/min. A similar effect on bleeding as with warfarin triple therapy was seen in patients with a baseline CrCl level of 30–50 mL/min receiving dabigatran 150 mg dual therapy.
Original Article

Dabigatran versus vitamin K antagonist: an observational across-cohort comparison in acute coronary syndrome patients with atrial fibrillation


Kaplan-Meier Curves for MACE Endpoint

Survival without MACE (%) vs. Follow-up (months)

- VKA (N MACE = 38)
- Dabigatran (N MACE = 58)

Cumulative incidence (%) vs. Follow-up (months)

- Ischemic event VKA (N=17)
- Ischemic event Dabigatran (N=40)
- Death VKA
- Death Dabigatran

p=0.0009

p=0.0004

p=NS
The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

Factors to shorten combination therapy
- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE ≥140 if ACS)

Factors to lengthen combination therapy
- First-generation DES
- High atherothrombotic risk (scores as above ; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk
Many more to expect

**AUGUSTUS Trial**

Inclusion
- AF (prior, persistent, or > 6 h duration)
- Physician decision that OAC is indicated
- ACS and/or PCI with planned P2Y₁₂ inhibitor for 6 months

Apixaban 5 mg twice daily

- Aspirin
- Placebo

Warfarin

- Aspirin
- Placebo

Primary outcome: major/clinically relevant bleeding (through 6 months)
Secondary objective: death, MI, stroke, stent thrombosis

- P2Y₁₂ inhibitor for all patients x 6 months
- Aspirin for all on the day of ACS or PCI
- Aspirin vs placebo after randomization

Management of patients with AF and stable CAD (>1y from acute episode)

Risk of Bleeding

- Elective PCI with newer generation DES
- ACS with PCI

All cause mortality

(Circulation. 2014;129:1577-1585.)
What about AF itself?

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

Rhythm control strategy is indicated for symptom relief despite adequate rate control
Conclusion

• AF and CAD share many things in common.

• AF has a huge impact on the prognosis and management of CAD pts.

• more and more clinical data suggest that we need to revise our preview clinical practice.