Coronary Stenting and Atrial Fibrillation: what’s the right regimen for oral anticoagulation?

PD Dr. med. Giovanni Pedrazzini
Case nr. 1

- 75-year-old man with AF, stable Angina CCS III
- Previous CABG
- Previous CRT-D and MitraClip
- EF 20%, NYHA III

FA and Stable CAD
Case nr. 1

Your Strategy

- Sintrom (NOACs) + Plavix
- Sintrom (NOACs) + Aspirin + Plavix
- Sintrom + Brilique/Efient

![Images of medical procedures with percentages and stents]
Case nr. 2

- 73-year-old man with AF and STEMI
  - Previous CABG, **AVR** and LM-Stenting DES
  - EF 40%
  - Previous retroperitoneal Hematoma

Stent Thrombosis (Protected LM)

DEB + Kissing Balloon

FA (valve) and ACS
Case nr. 2

Your Strategy

- Sintrom + Plavix
- Sintrom + Aspirin + Plavix
- Sintrom + Brilique

Stent Thrombosis (Protected LM)

DEB + Kissing Balloon
Coronary stenting and atrial fibrillation

Epidemiology and outcome
Atrial fibrillation

- 7.2% in pts aged 65 years and older (with increased in men, 7.8%), **10.3%** in pts 75 years and older (Lancet 2012;379:648-61)

- AF increases the risk of stroke **fivefold** independent of other factors (Stroke, 1991)

- Overall incidence of CAD in AF >**30%** (40% >70 years); among them > 20% are revascularized either by PCI or CABG (Kralev S et al. PLoS One 2011;6: e24964)
Atrial fibrillation and coronary artery disease

- Atrial fibrillation is present in
  - 10-20% of patients with stable CAD* (varying according to comorbidities) (Rohla et al, Int J Cardiol 2015; RECENT Registry, Pol Arch Med 2015)
  - 6 to 8% of patients with ACS (AMIS Plus and own data)

In Hospital Mortality
13.2% vs 5.1%
Coronary stenting and Atrial fibrillation

The big Dilemma (or challenge?)
Coronary stenting in AF: which treatment?

The winning combination?
**THE THERAPEUTIC GOAL**

- **THROMBOTIC RISK**
  - STABLE CAD (3-6 Months)
    - ASA + Clopidogrel
  - ACS (12 Months)
    - ASA + New P2Y12 inh.

- **STROKE PREVENTION**

- **HEMORRAGIC RISK**
  - LIFELONG INDICATION
  - HAS BLED SCORE

Old patients, patients with comorbidities,…

*OAC reduce the relative risk of stroke by 64 (and all cause mortality by 26%), NOAC by 77% (Lancet, 2012)*
Coronary stenting in AF

THE MAIN ISSUES

- Dual vs triple therapy
  - Bleeding risk
  - Ischemic risk

- VKA vs NOACs
  - Bleeding risk
  - Ischemic risk
Coronary stenting and atrial fibrillation

How **safe** is to use the triple therapy? How **good** is the dual therapy?
All ACS patients - Triple therapy at discharge (ASA and AOC/NOAC and P2Y12 inhibitors) N=48'604

Increasing number of patients with triple tx at discharge since 1997

Courtesy of H. Rickli, D. Radovanovic
Trends in triple antithrombotic therapy at discharge in ACS patients with atrial fibrillation at admission (n=294)

![Bar chart showing trends in triple antithrombotic therapy from 2010 to 2014. The chart indicates the percentage of patients receiving different combinations of antithrombotic medications over the years. The categories include OAC or NOAC & Prasugrel or Ticagrelor, NOAC & ASA & Clopidogrel, OAC & ASA & Clopidogrel.

Courtesy of H. Rickli, D. Radovanovic]
How safe and how good is the triple therapy?


12'165 pts (Denish Registry)
Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial

573 pts, 69% atrial fibrillation

<table>
<thead>
<tr>
<th>Stent type</th>
<th>None</th>
<th>5 (2%)</th>
<th>4 (1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bare metal</td>
<td></td>
<td>89 (32%)</td>
<td>86 (30%)</td>
</tr>
<tr>
<td>Drug eluting</td>
<td></td>
<td>181 (65%)</td>
<td>183 (64%)</td>
</tr>
<tr>
<td>Bare metal and drug eluting</td>
<td></td>
<td>3 (1%)</td>
<td>11 (4%)</td>
</tr>
</tbody>
</table>

Many retrospective and 1 prospective analysis have compared **triple therapy** \((OAC + dual antiplatelet)\) against **dual therapy** \((OAC + one antiplatelet)\), and the results are consistent in showing an **increase in the risk of bleeding with triple therapy**, that is \(\sim 50\%\) higher compared with dual therapy and were evident for early and delayed bleeding risk as well.

Joint consensus document EAPCI, EHRA, ACCA EHJ 2014
Conclusion dual vs triple therapy

- Triple therapy consisting of ASA, Clopidogrel, and (N)OAC after PCI, should only be given in a **compelling indication exists i.e paroxismal, persistent or permanent AF with CHA2Vascc Score ≥ 2**
- Triple therapy should **be limited in duration**, depending on the clinical setting, thromboembolic and bleeding risk
- The use of prasugrel or ticagrelor as part of triple therapy **should be avoided**, given the lack of established benefit and the greater risk of major bleeding

Joint consensus document EAPCI, EHRA, ACCA EHJ 2014
ACO in Coronary stenting and Atrial fibrillation

Role of NOACs
Vitamin-K-Antagonisten und neue orale Antikoagulantien

- Rivaroxaban
- Apixaban
- Edoxaban

Dabigatran Etexilat

Vitamin-K-Antagonisten

What do we know

- Data on the effects of concomitant prescription of NOACs and antiplatelet drug derived from **post hoc analysis** of **randomised controlled** trials of NOACs in non-valvular AF patients

- **No head to head comparison** for one of the NOACS and VKA in ACS

- Paucity of data on the use of the NOACs in combination with dual with ASA and **new P2Y12 inhibitors**
Dabigatran (RE-LY) increases the risk of bleeding (lower GI tract) in the setting of ACS, and at doses below those proven to be beneficial with non significant increase in ischemic events.

Apixaban increases the risk of bleeding when added to DAPT, without an additional benefits on ischemic events (ARISTOTLE).

Rivaroxaban at low dose decreases the risk of ischemic events but increases the bleeding risk (intracranial haemorrhage).
Coronary stenting in AF: NOAC

Figure 5 Association of effects of adding an oral anticoagulant to single (aspirin) or dual (aspirin and clopidogrel) antiplatelet therapy on rate of MACE with effects on rate of clinically significant bleeding events after an acute coronary syndrome. Random-effects meta-regression, stratified on number of antiplatelet drugs. The area of a circle representing a study arm is proportional to its weight in the random-effects model. Shaded areas are 95% confidence intervals. HR, hazard ratio; MACE, major adverse cardiovascular events; Riv, rivaroxaban; Dab, dabigatran; Api, apixaban; Dar, darexaban; Xim, ximelagatran; b.i.d., twice daily; o.d., once daily; number denotes strength in milligram.
In general in the setting of ACS, *triple therapy with DAPT and NOACs* is associated with at least *doubling of the risk of major bleedings* similarly reported for OAC in the WOEST trial.

Today there is no strong evidence that NOACs behave differently to VKA in the setting of ACS or stenting.

In ACS patients who develop new-onset AF while on dual antiplatelet, OAC, either with VKA or NOAC, *should be started*.

The duration of triple therapy depends on the individual risk for ischemic/bleeding events.
ACO in Coronary stenting and Atrial fibrillation

Is there a consensus?
Coronary stenting and Atrial fibrillation
Coronary stenting and Atrial fibrillation

**STEP 1**

**Non-valvular atrial fibrillation**

- **CHA$_2$DS$_2$-VASc = 1**
  - Low to intermediate (e.g. HAS-BLED = 0–2)
  - High (e.g. HAS-BLED ≥3)

- **CHA$_2$DS$_2$-VASc ≥ 2**
  - Low to intermediate (e.g. HAS-BLED = 0–2)
  - High (e.g. HAS-BLED ≥3)

**STEP 2**

- Stable CAD
  - If PCI is performed
- ACS
  - If PCI is performed
- Stable CAD
  - If PCI is performed
- ACS
  - If PCI is performed
- Stable CAD
  - If PCI is performed
- ACS
  - If PCI is performed
Coronary stenting and Atrial fibrillation

CHADS2-VASc Score ≥ 2

= individualized treatment
Case nr. 1

Our Strategy

- Sintrom + Plavix
- Sintrom + Aspirin + Plavix
- Sintrom + Brilique

CHAD2-VASCc Score = 6, HAS BLED Score 3
Case nr. 2

Your Strategy

- Sintrom + Plavix
- **Sintrom + Aspirin + Plavix for 4-6 week, then OAC + Plavix**
- Sintrom + Brilique

Stent Thrombosis (Protected LM)

DEB + Kissing Balloon
Coronary stenting and Atrial fibrillation

What about LAA Closure

Patients with AF undergoing concomitant PCI with drug-eluting stents (DES) and LAAO with dedicated devices were consecutively entered into a prospective single-centre registry and were compared to AF patients from the Bern DES registry treated with different antithrombotic strategies. Among 379 patients with AF, 56 patients were treated with concomitant PCI and LAAO, 268 patients were treated with PCI and dual therapy (DT), and 55 patients were started on triple anti-thrombotic therapy (TT).

Figure 1: Events per treatment strategy. BARC = bleeding academic research consortium; MI = myocardial infarction.
Conclusions

- An **individualized approach** is recommended for all the patients undergoing PCI/Stenting in the clinical context of AF.
- **Triple therapy**, either with VKA or NOAC, is **feasible however needs to be carefully pondered** according to the ischemic and bleeding risk.
- In patients with a recent **ACS, the addition of NOAC to antiplatelets therapy** results in a modest reduction in CV events, but substantial increase in bleeding (most pronounced when combined with DAPT).
- **LAA closure** may represent a valid option for patients with elevated bleeding risk.
Thank you for your attention

High Camp Mera Peak, Himalaya
5900 m, 1.11.2013
Coronary stenting in AF: which treatment?

**Anticoagulants**
- VKA
- Dabigatran
- Rivaroxaban
- Apixaban
- Edoxaban

**Antiplatelet regimen**
- SAPT
  - ASS
  - Clopidogrel
  - Prasugrel
  - Ticagrelor
- DAPT
  - ASS +
  - Clopidogrel
  - Prasugrel
  - Ticagrelor

The winning combination?
Coronary stenting and Atrial Fibrillation

Patients with AF undergoing concomitant PCI with drug-eluting stents (DES) and LAAO with dedicated devices were consecutively entered into a prospective single-centre registry and were compared to AF patients from the Bern DES registry treated with different antithrombotic strategies. Among 379 patients with AF, 56 patients were treated with concomitant PCI and LAAO, 268 patients were treated with PCI and dual therapy (DT), and 55 patients were started on triple anti-thrombotic therapy (TT).

Figure 1: Events per treatment strategy. BARC = bleeding academic research consortium; MI = myocardial infarction.
Atrial Fibrillation in ACS: current approach

Study population
- December 2012 – December 2014
- ACS patients (STEMI/NSTEMI): 1245
- AF subgroup patients: 105 (8.4%)
  - paroxysmal, persistent, permanent

CCT Retrospective Analysis on 105 ACS pts with Atrial fibrillation (B. Adjbodou)
Coronary stenting in AF

Recommendations for antithrombotic treatment in patients undergoing PCI who require oral anticoagulation

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with a firm indication for oral anticoagulation (e.g. atrial fibrillation with CHA2DS2-VASc score ≥2, venous thromboembolism, LV thrombus, or mechanical valve prosthesis), oral anticoagulation is recommended in addition to antiplatelet therapy.</td>
<td>I</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>New-generation DES are preferred over BMS among patients requiring oral anticoagulation if bleeding risk is low (HAS-BLED ≤2).</td>
<td>IIA</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>In patients with SCAD and atrial fibrillation with CHA2DS2-VASc score ≥2 at low bleeding risk (HAS-BLED ≤2), initial triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of at least one month after BMS or new-generation DES followed by dual therapy with (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) continued up to 12 months.</td>
<td>IIA</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>DAPT should be considered as alternative to initial triple therapy for patients with SCAD and atrial fibrillation with a CHA2DS2-VASc score ≤1.</td>
<td>IIA</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>In patients requiring oral anticoagulation at high bleeding risk (HAS BLED ≥3), triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of one month followed by (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) irrespective of clinical setting (SCAD or ACS) and stent type (BMS or new-generation DES).</td>
<td>IIA</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

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New antithrombotic agents not recommended in triple therapy

No formal controindication for NOAC in triple therapy

However dose adjustment is recommended

2014 ESC/EACST Guidelines on Myocardial Revascularization
THANK YOU for your attention
Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial

Table 1: Clinical characteristics and treatments at baseline

<table>
<thead>
<tr>
<th></th>
<th>Double therapy (n=279)</th>
<th>Triple therapy (n=284)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication for oral anticoagulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation/atrial flutter</td>
<td>164/236 (69%)</td>
<td>162/234 (69%)</td>
</tr>
<tr>
<td>Mechanical valve</td>
<td>24/236 (10%)</td>
<td>25/234 (11%)</td>
</tr>
<tr>
<td>Other (eg, apical aneurysm, pulmonary embolus, PAD, EF &lt;30%)</td>
<td>48/236 (20%)</td>
<td>47/234 (20%)</td>
</tr>
<tr>
<td>Acute coronary syndrome at baseline</td>
<td>Yes</td>
<td>69 (25%)</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td></td>
<td>Mean (SD) at baseline (%)</td>
</tr>
<tr>
<td></td>
<td>EF &lt;30%</td>
<td>40/190 (21%)</td>
</tr>
</tbody>
</table>

Values are n (%) unless stated otherwise. Categories do not add up to 100% for all variables owing to missing values. BMI=body-mass index. CAD=coronary artery disease. PCI=percutaneous coronary intervention. CABG=coronary artery bypass graft. AF=atrial fibrillation. ACE-inhibitor=angiotensin-converting enzyme inhibitor. ARB=angiotensin-II-receptor blocker. PPI=proton-pump inhibitor. PAD=peripheral artery disease. EF=ejection fraction. *n=163 in the double-therapy group and n=161 in the triple-therapy group.
Atrial fibrillation and coronary artery disease

- Overall incidence of CAD in AF >30% (40% >70 years)
- Among them > 20% are revascularized either by PCI or CABG

AF in Stable CAD:

- Higher mortality rate (HR 1.59, 95% CI 1.26-2.00; p<0.001) and higher bleeding rate (HR 4.28, 95% CI 1.36-13.48; p=0.013) (Pilgrim Eurintervention 2013)
- 2 fold increased relative risk of death at 4.8 y FU (HR .95, 95%CI 1.27-2.99) (Rohla, Int J Cardiol 2015)

AF in ACS patients:

- In-Hospital Mortality
  - 13.2% vs 5.1% (AMIS Plus)
  - 8.4% vs 5.2% (Own data)