Fibrillation auriculaire et stents coronaires: que faire?

Edoardo De Benedetti
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www.edebenedetti.com
La FA

- FA: arythmie la + commune
- 1-2% population générale
  Augmente avec l’âge
- Risque d’AVC x 5
- Etiologie de l’AVC:
  - 87% d’origine thromboembolique
  - dans 90% cas thrombus dans l’auricule gauche
- AVC sur FA → plus de sequelles
- AVC:
  1ère cause d’handicap
  3ème cause de décès chez pts en FA

1. Risque d’AVC

2. Risque d’AVC sans FA
   Risque d’AVC avec FA
   > 5 X

3.1 AVC non thrombo-embolique
   87%
   13%

3.2 Thrombus dans LAA
   90%
   10%
   Non-LAA

Heart Disease and Stroke Statistical Update: 2009 Update Circulation 1-27-09
AHA Statistical Update: Heart Disease and Stroke Statistics-2008 Update; NHLBI and ARIC Circulation 1-29-08
Hylek EM, et.al. NEJM. 2003; 349: 1019-1026
Johnson. Eur J Cardiothoracic Surg 2000;17
@ 1 Billion people in US and Europe
@ 20 Million with AF (1-2% of population)\textsuperscript{1,2}
@ 16 Million anticoagulation indicated (80%) \textsuperscript{1,2}
@ 4.8 Million have CAD as well (20%-45%) \textsuperscript{1,2}
@ 1-2 Million potential revasc (20%-25%) \textsuperscript{3,4}
Le problème

stent

FA

25% PCI
Atrial Fibrillation (ACTIVE W)\(^1\): The combination of aspirin and clopidogrel is not as effective as warfarin in patients with AF\(^1\)

However

Stenting (STARS)\(^2\): The combination of aspirin and a thienopyridine is more effective than warfarin+asa in patients with coronary stents \(^2\)

**DRUG REGIMEN**

**BEFORE:**
- Aspirin 500 mg bd
- Dipyridamole 75 mg qds
- Sulfinpyrazone 200 mg qds
- Nifedipine 10–20 mg tds

**DURING:**
- Full heparinisation
  - Urokinase ca. 100000 IU

**AFTER:**
- Aspirin 100 mg od
- Dipyridamole 75 mg qds
- Sulfinpyrazone 200 mg tds
- Nifedipine 10–20 mg tds
- Oral anticoagulants (INR < 2.3)
Angiographic follow-up after placement of a self-expanding coronary artery stent


March 86-January 88
117 wallstents in 105 patients
Angio FU in 95 patients at 5.7 mths

Pie chart: 23% occluded
Antithrombotic treatment after BMS

Death/MI/Re-intervention at 30-day

- **ISAR:** Schoemig A et al, NEJM 1996;334:1084
- **STARS:** Leon M et al, NEJM 1998;339:1665
- **FANTASTIC:** Bertrand ME et al, Circulation 1998;98:1597
- **MATTIS:** Urban P et al, Circulation 1998;98:2126
Le traitement n’est pas le même
Les options?

- Triple thérapie: AVK+DAPT
- Double thérapie: AC-antiplqt
  - NOAC vs AVK
- Nouveaux stents: BMS? DES?
- Fermeture auricule

Et combien de temps?
VKA + antiplatelets

The management of AF patients who undergo stent placement for an ACS is challenging

- Bleeding associated with antithrombotic therapy
- AF-related ischaemic stroke
- Stent thrombosis

Haemorrhagic risk  Thrombotic risk
Triple therapy after coronary stenting for ACS

2423 patients
159 on TT

GJ Smith Eurointervention 2012; 8: 672
**Triple Therapy With Aspirin, Prasugrel, and Vitamin K Antagonists in Patients With Drug-Eluting Stent Implantation and an Indication for Oral Anticoagulation**

Nikolaus Sarafoff, MD,* Amadea Martischnig, MD,† Jill Wealer, MS,† Katharina Mayer, MD,† Julinda Mehilli, MD,* Dirk Sibbing, MD,* Adnan Kastrati, MD†

**JACC 2013; 61: 2060**

HR: 1.4, 95% CI: 0.3 to 6.1], p 0.61 for ischemic events
Risque thrombotique élevé

- ACS
- AVC
- Maladie coronarienne complexe
- Résultat PCI sub-optimal
- Arrêt DAPT
- >65 ans
- IRC
Risque hémorragique élevé
Score HASBLED

- HTA
- Maladie rénale, hépatique
- AVC
- Tendance hémorragique
- INR labile
- >65 ans
- ASA ou AINS, OH

Max 9, haut risque > 3
Is ASA Necessary In Triple Therapy? The WOEST trial

Modest-scale, open-label WOEST study (N=573) compared safety outcomes with triple therapy (VKA + clopidogrel + ASA) vs dual therapy (VKA + clopidogrel). 69% of WOEST patients had AF, included prosthetic heart valves.

Safety outcomes:
- Any bleeding: 14.9% (44.9% for dual therapy)
- TIMI major: 3.3% (5.8% for dual therapy)
- TIMI major + minor: 11.2% (27.2% for dual therapy)

Efficacy outcomes:
- BMS: 30% 1 mois
- DES: 65% 1 an

* *p<0.05.
** All-cause death (CV & non-CV death p = 0.207 & 0.069)
All-Cause Mortality

Triple therapy group
Double therapy group

HR=0.39  95% CI[0.16-0.93]

p=0.027

Ce que nous dit WOEST

- Petite étude, 30 % valvulaires
- Moins de saignement si double tt

Ce que ne nous dit pas WOEST

- Si double tt est aussi efficace au niveau protection thrombotique
ISAR-TRIPLE: Study Organization

**DESIGN:**
Prospective, randomized open-label trial

**INCLUSION CRITERIA:**
DES implantation and indication for oral anticoagulation

**MAJOR EXCLUSION CRITERIA:**
Previous stent thrombosis
DES in left main coronary artery

**SPONSOR:**
Deutsches Herzzentrum Munich, (ClinicalTrials.gov # NCT00776633)

614 patients with DES implantation
3 European centers
(September 2008 – December 2013)

Aspirin and VKA

6-week Clopidogrel (n=307)
6-month Clopidogrel (n=307)

Clinical follow up at 9 months in 606 patients (98.7%)
ISAR-Triple

Primary Endpoint

Death, myocardial infarction, stent thrombosis, stroke or TIMI major bleeding

HR 1.14 (95%, CI 0.68 – 1.91), p=0.63
Secondary Endpoints

Cardiac death, myocardial infarction, stent thrombosis or ischemic stroke

HR 0.93 (0.43 - 2.05), p=0.87

TIMI major bleeding

HR 1.35 (0.64 - 2.84), p=0.44
2124 pts avec FA et PCI
1. Rivaroxaban 15 mg - plavix 12 m
2. Rivaroxaban 2x2.5 mg - DAPT 1-6-12 m
3. Warfarin-DAPT 1-6-12 m

Étude sécurité, pas puissance pour efficacité
In participants with atrial fibrillation undergoing PCI with placement of stents, the administration of either low-dose rivaroxaban plus a P2Y$_{12}$ inhibitor for 12 months or very-low-dose rivaroxaban plus DAPT for 1, 6, or 12 months was associated with a lower rate of clinically significant bleeding than was standard therapy with a vitamin K antagonist plus DAPT for 1, 6, or 12 months.

The three groups had similar efficacy rates, although the observed broad confidence intervals diminish the surety of any conclusions regarding efficacy.
A forgotten patient population

Current DAPT trend: «shorter is better»

A new polymer-free metallic stent
Prospective, double-blind randomized (1:1) trial
2466 High bleeding risk (HBR) PCI patients

BioFreedom™ DCS VS. Gazelle™ BMS

DAPT mandated for 1 month only, followed by long-term SAPT

- **Primary safety endpoint:** Composite of cardiac death, MI, definite / probable stent thrombosis at 1 year (non-inferiority then superiority)
- **Primary efficacy endpoint:** Clinically-driven TLR at 1 year (superiority)
BioFreedom™

Selectively micro-structured surface holds drug in abluminal surface structures

Hypothesis: Polymer-free drug release via porous-eluting stents may reduce late events caused by polymer stent coatings.

Potential advantage

- Avoid long term late adverse effects that might be attributable to the polymer
- Improved surface integrity since there is no polymer to be sheared or peeled away from the stent struts
- Possible shorter need of dual antiplatelet therapy
Primary EP safety (cardiac death, MI, ST)

![Graph showing cumulative percentage with event over days with DCS and BMS groups]

Number at Risk

- **DCS**
  - 1221
  - 1146
  - 1105
  - 1081
  - 1045

- **BMS**
  - 1211
  - 1115
  - 1066
  - 1037
  - 1000

*P = 0.005 for superiority*

NEJM 2015
LEADERS FREE OAC

Anticoagulant therapy at discharge

448 DCS patients

- VKA: 91%
- NOAC: 8.2%
- no OAC: 8.2%

431 BMS patients

- VKA: 82.2%
- NOAC: 9.6%
- no OAC: 8.2%
Antithrombotic Medication at Discharge

TCT 2016
LEADERS FREE OAC
(Bleeding During 12 Month Follow-up)

BARC 1-5
p = 0.85

BARC 2-5
p = 0.81

BARC 3-5
p = 0.80

TCT 2016
Guidelines ESC 2015

ACS = acute coronary syndrome; CABG = coronary artery bypass graft; CHA₂DS₂-VASc = Cardiac failure, Hypertension, Age ≥75 [2 points], Diabetes, Stroke [2 points] – Vascular disease, Age 65–74, Sex category; DAPT = dual antiplatelet therapy; NOACs = non-vitamin K antagonist oral anticoagulants; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; VKAs = vitamin K antagonists. Adapted from Lip et al.²

Dual therapy with oral anticoagulation and clopidogrel may be considered in selected patients (low ischaemic risk).

Aspirin as an alternative to clopidogrel may be considered in patients on dual therapy (i.e., oral anticoagulation plus single antiplatelet); triple therapy may be considered up to 12 months in very selected patients at high risk of ischaemic events (e.g., prior stent thrombosis on adequate antiplatelet therapy, stenting in the left main or last remaining patent coronary artery, multiple stenting in proximal coronary segments, two stents bifurcation treatment, or diffuse multivessel disease, especially in diabetic patients).

Dual therapy with oral anticoagulation and an antiplatelet agent (aspirin or clopidogrel) beyond one year may be considered in patients at very high risk of coronary events. In patients undergoing coronary stenting, dual antiplatelet therapy may be an alternative to triple or a combination of anticoagulants and single antiplatelet therapy if the CHA₂DS₂-VASc score is 1 (males) or 2 (females).
Fermeture de l’auricule gauche

Johnson, Eur J Cardiothoracic Surg 2000:17
Aspirin and Plavix® registry (ASAP)

• The ASAP registry is a non-randomized feasibility study designed to evaluate if the WATCHMAN® Device is a safe and effective treatment for people unable to take warfarin.

• AF patients who are contraindicated or intolerant of warfarin have few options for thromboembolic prophylaxis.

• Patients may be treated with aspirin and/or clopidogrel; this treatment paradigm has a higher stroke risk than warfarin.

Results

Observed rate of ischemic stroke represents a 77% reduction from the expected event rate.

Expected and Observed Stroke Rates (per 100 patient-years)

- Expected, based on CHADS2 Score
- Expected, if Clopidogrel was used throughout follow-up
- Observed rate in ASAP

ACTIVE trial AHJ 2006 151(6): 1187-93
First time therapy
Positive news to be recommended in the guidelines
Will be updated as more evidence becomes available

Patient population:
High stroke risk = CHA2DS2-VASc > 2
Contraindicated = ineligible to take long term OATs and “intolerant” patients
Mon approche

- Évaluation du risque thromb vs hém
- CHADSVASC 0-1: DAPT
- CABG vs PCI
- Biofreedom (pas de BMS)
- Si AVK → AVK (2-2.5)-clopidoo 1-12 mois
- Si NOAC → NOAC faible dose-clopidoo
- Jamais ticagrelor ou prasugrel
- Toujours IPP
- Si saigne considérer fermeture auricule
## Etudes en cours

<table>
<thead>
<tr>
<th>Trial</th>
<th>No. of Participants</th>
<th>Control</th>
<th>Intervention</th>
<th>Primary Outcome</th>
<th>ClinicalTrials.gov No.</th>
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</thead>
<tbody>
<tr>
<td>REDUAL-PCI</td>
<td>2800</td>
<td>Aspirin, P2Y₁₂ inhibitor, and vitamin K antagonist</td>
<td>Dabigatran (either 110 mg twice daily or 150 mg twice daily) plus P2Y₁₂ inhibitor</td>
<td>Major bleeding and clinically relevant nonmajor bleeding, defined according to ISTH criteria</td>
<td>NCT02164864</td>
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<tr>
<td>ENTRUST-AF-PCI</td>
<td>1500</td>
<td>Aspirin, P2Y₁₂ inhibitor, and vitamin K antagonist</td>
<td>Edoxaban (60 mg once daily) plus P2Y₁₂ inhibitor</td>
<td>Major bleeding and clinically relevant nonmajor bleeding, defined according to ISTH criteria</td>
<td>NCT02866175</td>
</tr>
<tr>
<td>AUGUSTUS</td>
<td>4600</td>
<td>Either aspirin or vitamin K antagonist (2-by-2 factorial design)</td>
<td>Either apixaban (5 mg twice daily) or placebo</td>
<td>Major bleeding and clinically relevant nonmajor bleeding, defined according to ISTH criteria</td>
<td>NCT02415400</td>
</tr>
</tbody>
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KEEP CALM AND SAY NO TO DRUGS