Patients with Atrial Fibrillation and PCI or ACS Need Triple Therapy - Practical Guidance

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Antithrombotic Therapy for Atrial Fibrillation and PCI

**Anticoagulant therapy**

Low sheer stress thrombosis in left atrium

**Antiplatelet therapy**

High sheer stress thrombosis – platelet mediated in the arteries

Dual antiplatelet therapy superior to aspirin alone

**BOTH anticoagulant and dual antiplatelet therapy =**

‘triple therapy’
STARS: in PCI: Aspirin vs. Aspirin + warfarin vs. aspirin + P2Y12


Figure 1. Cumulative Incidence of the Primary End Point in the Three Treatment Groups.
ACTIVE W: In Afib: Warfarin vs. Clopidogrel + ASA: Risk of Stroke

ACTIVE W: Stroke, Non-CNS Systemic Embolism, MI & Vascular Death

NVAF and PCI: a broad spectrum of options

**Single therapy**
- ASA alone
- Clopidogrel alone
- Prasugrel alone
- Ticagrelor alone
- Warfarin alone
- NOAC alone

**Antiplatelet + OAC**
- ASA + warfarin
- Clopidogrel + warfarin
- Prasugrel + warfarin
- Ticagrelor + warfarin
- ASA + NOAC
- Clopidogrel + NOAC (low dose)
- Clopidogrel + NOAC (high dose)
- Prasugrel + NOAC
- Ticagrelor + NOAC

**Dual Antiplatelet Therapy**
- ASA + clopidogrel
- ASA + prasugrel
- ASA + ticagrelor

**Triple Therapy**
- ASA + clopidogrel + warfarin
- ASA + prasugrel + warfarin
- ASA + ticagrelor + warfarin
- ASA + clopidogrel + NOAC (low dose)
- ASA + clopidogrel + NOAC (high dose)
- ASA + prasugrel + NOAC
- ASA + ticagrelor + NOAC

NOAC = novel oral anticoagulant
Bleeding associated with warfarin, aspirin, clopidogrel in patients with AF
n=82,854

Hansen et al, Arch Intern Med, 2010;170:1433-1441
2014 ACC/AHA/HRS Guidelines for AFib

Table 5. Summary of Recommendations for Prevention of Thromboembolism in Patients With AF

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombotic therapy based on shared decision-making, discussion of risks of stroke and bleeding, and patient’s preferences</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Antithrombotic therapy selection based on risk of thromboembolism</td>
<td>I</td>
<td>B</td>
<td>(64-67)</td>
</tr>
<tr>
<td>CHA2DS2-VASc score recommended to assess stroke risk</td>
<td>I</td>
<td>B</td>
<td>(68-70)</td>
</tr>
<tr>
<td>Warfarin recommended with mechanical heart valves. Target INR intensity should be based on the type and location of prosthesis</td>
<td>I</td>
<td>B</td>
<td>(71-73)</td>
</tr>
<tr>
<td>With prior stroke, TIA, or CHA2DS2-VASc score ≥2, oral anticoagulants recommended. Options include:</td>
<td></td>
<td></td>
<td>(68-70)</td>
</tr>
<tr>
<td>• Warfarin</td>
<td>I</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>• Dabigatran, rivaroxaban, or apixaban</td>
<td>I</td>
<td>B</td>
<td>(74-76)</td>
</tr>
<tr>
<td>For PCI, * BMS may be considered to minimize duration of DAPT</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>Following coronary revascularization in patients with CHA2DS2-VASc score of ≥2, it may be reasonable to use clopidogrel concurrently with oral anticoagulants, but without aspirin</td>
<td>IIb</td>
<td>B</td>
<td>(83)</td>
</tr>
</tbody>
</table>
Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with an increased risk of bleeding and should be monitored closely.

In patients requiring warfarin, clopidogrel, and aspirin therapy after PCI, an INR of 2.0 to 2.5 is recommended with low dose aspirin (75 mg to 81 mg) and a 75-mg dose of clopidogrel.
RE-LY Antiplatelet analysis

Worldwide event-driven trial with 2840 patients per arm (Total = 8520 patients)

Paroxysmal, persistent or permanent NVAF (PCI with stenting [BMS or DES] elective or ACS)

- Dabigatran 150mg BID + P2Y12 inhibitor
- Dabigatran 110mg BID + P2Y12 inhibitor
- Warfarin (INR 2.0-3.0) + P2Y12 inhibitor + ASA*

1° End Point
Thrombotic Event Rate (Death + MI + Stroke/SE)
Plus
Clinically Relevant Bleeding Rate (ISTH Major)

*ASA will be given for 1 month post BMS and 3 months post DES
## RE-DUAL PCI: Regimens begin tested

### Single therapy
- ASA alone
- Clopidogrel alone
- Prasugrel alone
- Ticagrelor alone
- Warfarin alone
- NOAC alone

### Antiplatelet + OAC
- ASA + warfarin
- Clopidogrel + warfarin
- Ticagrelor + warfarin
- Prasugrel + warfarin
- ASA + NOAC
- Clopidogrel/Ticagrelor + Dabi 110 mg bid
- Clopidogrel/Ticagrelor + Dabi 150 mg bid
- Prasugrel + NOAC

### Triple Therapy
- ASA + clopidogrel + warfarin
- ASA + ticagrelor + warfarin
- ASA + prasugrel + warfarin
- ASA + clopidogrel + NOAC (low dose)
- ASA + clopidogrel + NOAC (high dose)
- ASA + prasugrel + NOAC
- ASA + ticagrelor + NOAC (low dose)
- ASA + ticagrelor + NOAC (high dose)

NOAC = novel oral anticoagulant
PCI in patients with NVAF: Antithrombotic therapy

- Triple therapy increases the risk of bleeding vs dual antiplatelet therapy\(^1\)
  - Bleeding after PCI is associated with higher rates of mortality and MACE\(^2,3\)
- The WOEST trial data suggest the potential benefit of a double antithrombotic regimen (OAC + clopidogrel) vs triple therapy\(^4\)
- RE-DUAL PCI™ incorporates two approaches to evaluate outcomes: \(^5\)

Two new regimens with dabigatran:
- 150 or 110 mg BID plus single antiplatelet (P2Y12 inhibitor)

‘Enhanced’ Standard of Care:
- VKA plus dual antiplatelets (but with earlier discontinuation of ASA)

ASA = acetylsalicylic acid; BID = twice daily; MACE = major adverse cardiac events; OAC = oral anticoagulant; VKA = vitamin K antagonist