NAVIGATING THROMBOSIS AND BLEEDING AT THE INTERSECTION OF ATRIAL FIBRILLATION AND CORONARY STENTING

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Objectives

- Design an evidence-based antithrombotic regimen in a patient with atrial fibrillation (AF) and acute coronary syndrome (ACS)

- Analyze the risks of bleeding and thrombosis in patients with AF and ACS based on published literature

- Discuss the current guideline recommendations for using antithrombotic therapy in patients with AF and ACS
Patient Case

- BA is a 63-year-old man who presents with worsening chest pain over the past week.
- At PCP office – ECG suggestive of ischemia
- Transferred to emergency department
  - Troponin T: 0.12 ng/mL
- Admitted or NSTEMI and possible PCI
- PMH and Medications:
  - Dyslipidemia: Atorvastatin 40 mg daily
  - Hypertension: Losartan 100 mg daily, Amlodipine 5 mg daily
  - Diabetes: Metformin 1000 mg BID, Aspirin 81 mg daily
  - Atrial Fibrillation: Warfarin, INR: 2.3
Patient Case

• Following morning, BA is taken for cardiac catheterization
  • Found to have 80% stenosis in his mid-LAD
    • Stented with Drug-eluting stent (DES)

• How do we manage his long-term antithrombotic therapy?
  • ACS + PCI with DES to mid-LAD
  • AF: previously taking warfarin
Which of the following would you recommend for AF stroke prevention therapy for BA?

a) Oral anticoagulation with Warfarin
b) Oral anticoagulation with a DOAC
c) Dual Antiplatelet Therapy (DAPT)
d) Aspirin monotherapy
Which of the following would you recommend for preventing recurrent MI and stent thrombosis for BA’s DES?

a) Aspirin monotherapy
b) Oral anticoagulation monotherapy
c) Aspirin + Oral anticoagulation
d) Aspirin + P2Y\textsubscript{12} inhibitor
How would you manage his overall antithrombotic therapy?

a) Aspirin 81 mg daily + Clopidogrel 75 mg daily + Warfarin
b) Aspirin 81 mg daily + Prasugrel 10 mg daily + Warfarin
c) Aspirin 81 mg daily + Rivaroxaban 20 mg daily
d) Clopidogrel 75 mg daily + Dabigatran 150 mg BID
The AF and ACS Cross Over

ACS/ Stenting
1 - 2 million people

Stent + Afib

Atrial Fibrillation
~ 7 million people
What’s the Antithrombotic Challenge?

ACS/PCI

Stent Thrombosis Recurrent MI

DAPT: ASA + P2Y$_{12}$ Inhibitor

Thrombotic Complication?

AF

Stroke

Oral Anticoagulation

Drug Therapy?
P2Y₁₂ inhibitor therapy should be **given for at least 1 year** to post-PCI patients treated with coronary stents for ACS, using the following maintenance doses:

- Clopidogrel 75 mg daily; or
- Prasugrel 10 mg daily; or
- Ticagrelor 90 mg twice a day

Continuation of DAPT beyond 12 months may be considered in patients undergoing DES placement.

Clopidogrel should be given to patients receiving drug-eluting stents for a non-ACS indication for at least 12 months if the patients are not at high risk of bleeding; or in patients receiving bare metal stents for a non-ACS indication for a minimum of 1 month, but ideally for 12 months:

- If the patient received a bare metal stent and is at increased risk of bleeding then clopidogrel should be given for a minimum of 2 weeks

2018 Chest Guidelines: Antithrombotic Therapy for AF

- CHADS-VASc = 0 (1 in females): No Therapy

- CHADS-VASc = 1 (2 in females): Oral Anticoagulation preferred over ASA, DAPT

- CHADS-VASc = 2 (≥ 3 in females): Oral Anticoagulation preferred over ASA, DAPT

*** Prefer DOACs over Warfarin***

** When using warfarin: goal TTR ≥ 70%

ASPIRIN AND WARFARIN IN ACS
## Aspirin and Warfarin in ACS

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects, n</th>
<th>ASA alone</th>
<th>Warfarin alone</th>
<th>ASA + Warfarin</th>
<th>HR (95%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAMP†</td>
<td>5059</td>
<td>31.4</td>
<td>30.9</td>
<td>1.01</td>
<td>(0.9-1.14)</td>
<td>NS</td>
</tr>
<tr>
<td>ASPECT-2†</td>
<td>993</td>
<td>9</td>
<td>5</td>
<td>5</td>
<td>0.52</td>
<td>(0.28-0.98)</td>
</tr>
<tr>
<td>APRICOT-2*</td>
<td>274</td>
<td>34</td>
<td>14</td>
<td></td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>WARIS-II†</td>
<td>3630</td>
<td>20</td>
<td>16.7</td>
<td>15</td>
<td>0.71</td>
<td>0.001</td>
</tr>
</tbody>
</table>

WARIS-II: Major bleeding was 0.62% for warfarin vs. 0.17% for Aspirin (p<0.001)
Minor bleeding was 2.14% for warfarin vs. 0.84% for Aspirin
- Target INR 2.8 – 4.2 in the warfarin alone group

†= death, MI, or stroke; *= Death, reinfarction, revascularization

DAPT IN ATRIAL FIBRILLATION
ACTIVE Trials

Adults in AF or 2 AF episodes in last 6 months

Active A
- Aspirin
- Aspirin + Clopidogrel

Active W
- Aspirin + Clopidogrel
- VKA

1° Outcome: Composite of stroke, non-CNS systemic embolism, MI, CV death
2° Outcome: Stroke; individual outcomes of composite, bleeding, net clinical benefit

Connolly SJ, et al. NEJM 2009; 360: 2066-78
<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel/ASA n (%/yr)</th>
<th>Warfarin n (%/yr)</th>
<th>RR (95%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ischemic events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Outcome</td>
<td>234 (5.6)</td>
<td>165 (3.93)</td>
<td>1.44 (1.18-1.76)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Stroke</td>
<td>100 (2.39)</td>
<td>59 (1.4)</td>
<td>1.72 (1.24-2.37)</td>
<td>0.001</td>
</tr>
<tr>
<td>MI</td>
<td>36 (0.86)</td>
<td>23 (0.55)</td>
<td>1.58 (0.94-2.67)</td>
<td>0.09</td>
</tr>
<tr>
<td>Non-CNS embolism</td>
<td>18 (0.43)</td>
<td>4 (0.1)</td>
<td>4.66 (1.58-13.8)</td>
<td>0.005</td>
</tr>
<tr>
<td>Death</td>
<td>159 (3.8)</td>
<td>158 (3.76)</td>
<td>0.93 (0.45-1.94)</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Bleeding Events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>101 (2.42)</td>
<td>93 (2.21)</td>
<td>1.10 (0.83-1.45)</td>
<td>0.53</td>
</tr>
<tr>
<td>Minor</td>
<td>568 (13.58)</td>
<td>481 (11.45)</td>
<td>1.23 (1.09-139)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Any Bleeding</td>
<td>644 (15.40)</td>
<td>555 (13.21)</td>
<td>1.21 (1.08-1.35)</td>
<td>0.001</td>
</tr>
<tr>
<td>Net clinical benefit</td>
<td>316 (7.56)</td>
<td>229 (5.45)</td>
<td>1.41 (1.19-1.67)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Triple Therapy

- Triple therapy is defined as dual-antiplatelet therapy (DAPT) with concomitant oral anticoagulation.

- Commonly used in patients who have indications for both DAPT and OAC
  - Atrial Fibrillation (AF)
  - ACS and/or PCI with stenting
Triple Therapy: Risks

• Major bleeding is higher!

• Numerous published data have demonstrated that compared with dual therapies:
  • Patients with DAPT + OAC have much higher rates of major bleeding
## Danish National Patient Registry

<table>
<thead>
<tr>
<th></th>
<th>Patients treated for AF</th>
<th>Patients treated for MI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence (% per person-yr)</td>
<td>Unadjusted risk ratio (95% CI)</td>
</tr>
<tr>
<td>ASA alone</td>
<td>3.7</td>
<td>0.96 (0.95 – 0.96)</td>
</tr>
<tr>
<td>Clopidogrel Alone</td>
<td>5.6</td>
<td>1.45 (1.22 – 1.66)</td>
</tr>
<tr>
<td>VKA alone</td>
<td>3.9</td>
<td>Reference</td>
</tr>
<tr>
<td>ASA/Clopidogrel</td>
<td>7.4</td>
<td>1.91 (1.59 – 2.21)</td>
</tr>
<tr>
<td>ASA/VKA</td>
<td>6.9</td>
<td>1.75 (1.71 – 1.79)</td>
</tr>
<tr>
<td>Clopidogrel/VKA</td>
<td>13.9</td>
<td>3.57 (2.88 – 4.22)</td>
</tr>
<tr>
<td>Triple Therapy</td>
<td>15.7</td>
<td>4.03 (3.22 – 4.78)</td>
</tr>
</tbody>
</table>

Risk of Bleeding Event – includes admissions for bleeding diagnoses, nonfatal bleeding episodes, or bleeding listed as cause of death

WOEST: Can we do better?

Age 18-80 years old with an indication for PCI and a clear need for ≥ one year oral anticoagulation

Warfarin, Clopidogrel, ASA

Warfarin and Clopidogrel

WOEST

• Primary Endpoint:
  • Bleeding rates (TIMI, GUSTO, BARC)

• Secondary Endpoint:
  • Composite of death, MI, stroke, target vessel revascularization, and stent thrombosis
  • Each item individually

Primary Endpoint:
Total number of TIMI bleeding events

Primary Endpoint: Bleeding events TIMI classification

- TIMI Minimal: 6.5% (p<0.001)
- TIMI Minor: 16.7% (p=0.159)
- TIMI Major: 11.2% (p<0.001)
- Any TIMI bleeding: 27.2% (p<0.001)
- Double therapy group: 3.3% (p<0.001)
- Triple therapy group: 5.8% (p<0.001)

Percentages show a significant difference between the double therapy and triple therapy groups in terms of TIMI bleeding events.
WOEST: Secondary Endpoint

<table>
<thead>
<tr>
<th>Event</th>
<th>Double therapy group</th>
<th>Triple therapy group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2.6</td>
<td>6.4</td>
<td>0.027</td>
</tr>
<tr>
<td>MI</td>
<td>3.3</td>
<td>4.7</td>
<td>0.382</td>
</tr>
<tr>
<td>TVR</td>
<td>2.6</td>
<td>6.8</td>
<td>0.876</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.1</td>
<td>2.9</td>
<td>0.128</td>
</tr>
<tr>
<td>ST</td>
<td>1.5</td>
<td>3.2</td>
<td>0.165</td>
</tr>
</tbody>
</table>
WOEST: Conclusions

• First randomized trial to address the optimal antiplatelet therapy in patients on OAC undergoing coronary stenting
  • OAC plus clopidogrel causes less bleeding than triple antithrombotic therapy
  • Secondary endpoint was met: with double therapy there is no excess of thrombotic/thromboembolic events
  • Less all-cause mortality with double therapy
• The study was powered to show superiority on the primary bleeding endpoint, but not to show non-inferiority on the secondary endpoint
PREVENTION OF BLEEDING IN PATIENTS WITH ATRIAL FIBRILLATION UNDERGOING PCI: PIONEER AF-PCI

Gibson CM, Mehran R, Bode C et al.
Pioneer AF-PCI: Objectives

• To evaluate the risks and benefits of using 2 different Rivaroxaban dosing strategies in patients with AF who present for coronary stent placement
PIONEER AF-PCI: Trial Design + Interventions

- 2100 patients with NVAF
- Coronary stenting
- No prior stroke/TIA, GI bleeding, Hb<10, CrCl<30

**Primary endpoint:** TIMI major + minor + bleeding requiring medical attention

**Secondary endpoint:** CV death, MI, and stroke *(Ischemic, Hemorrhagic, or Uncertain Origin)*

* Rivaroxaban dosed at 10 mg once daily in patients with CrCl of 30 to <50 mL/min.
† Alternative P2Y₁₂ inhibitors: 10 mg once-daily prasugrel or 90 mg twice-daily ticagrelor.
‡ Low-dose aspirin (75-100 mg/d). ∆ Open label VKA
Pioneer AF-PCI: Inclusion and Exclusion

**Inclusion Criteria**
- Men and Women aged 18 years or older
- Patients with AF who required OAC
- PCI with stent placement

**Exclusion Criteria**
- Pts with a h/o Stroke or TIA
- Clinically significant GI Bleeding within 12 months of randomization
- CLcr < 30 mL/min
- Anemia: Hgb < 10 g/dL
PIONEER AF-PCI: Endpoints

• Primary Endpoint: SAFETY
  • 1\textsuperscript{st} occurrence of clinically significant bleeding
    • Composite of TIMI major or minor bleeding

• Secondary Endpoints:
  • Incidence of bleeding for the individual components of bleeding
  • Major Adverse Cardiovascular Events (MACE)
    • Composite: Death, MI, Stroke
How is TIMI Major and Minor bleeding defined?

TIMI Major:
- Any symptomatic intracranial hemorrhage
- Clinically overt signs of hemorrhage (including imaging) associated with a drop in hemoglobin of ≥ 5 g/dL, -or-
- Absolute drop in hematocrit of ≥ 15%

TIMI Minor:
- Clinically overt sign of hemorrhage (including imaging) with a fall in hemoglobin concentration of 3 to < 5 g/dL, -or-
- Drop in hematocrit of 9 - < 15%
## PIONEER AF-PCI: Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Riva + SAPT (N=709)</th>
<th>Riva + DAPT (N=709)</th>
<th>Triple Therapy (N=706)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, mean ± SD</strong></td>
<td>70.4 ± 9.1</td>
<td>70.0 ± 9.1</td>
<td>69.9 ± 8.7</td>
</tr>
<tr>
<td><strong>Sex, female, n (%)</strong></td>
<td>181 (25.5%)</td>
<td>174 (24.5%)</td>
<td>188 (26.6%)</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus, n (%)</strong></td>
<td>204 (28.8%)</td>
<td>199 (28.1%)</td>
<td>221 (31.1%)</td>
</tr>
<tr>
<td><strong>Type of Index Event, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSTEMI</td>
<td>130 (18.5%)</td>
<td>129 (18.4%)</td>
<td>123 (17.8%)</td>
</tr>
<tr>
<td>STEMI</td>
<td>86 (12.3%)</td>
<td>97 (13.8%)</td>
<td>74 (10.7%)</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td>145 (20.7%)</td>
<td>148 (21.1%)</td>
<td>164 (23.7%)</td>
</tr>
<tr>
<td>Stable Angina</td>
<td>340 (48.5%)</td>
<td>329 (46.8%)</td>
<td>330 (47.8%)</td>
</tr>
<tr>
<td>Drug-eluting stent, n (%)</td>
<td>464 (65.4%)</td>
<td>471 (66.8%)</td>
<td>468 (66.5%)</td>
</tr>
<tr>
<td><strong>Type of Atrial Fibrillation, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent</td>
<td>146 (20.6%)</td>
<td>146 (20.6%)</td>
<td>149 (21.1%)</td>
</tr>
<tr>
<td>Permanent</td>
<td>262 (37.0%)</td>
<td>238 (33.6%)</td>
<td>243 (34.5%)</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>300 (42.4%)</td>
<td>325 (45.8%)</td>
<td>313 (44.4%)</td>
</tr>
</tbody>
</table>
PIioneer AF-PCI: Results

- **Primary Endpoint Major Bleeding MACE**
  - Riva+SAPT: 16.8%
  - DAPT + RIVA: 2.1%
  - Triple: 6.5%
  - p < 0.001

- **Major Bleeding**
  - Riva+SAPT: 2.1%
  - DAPT + RIVA: 1.9%
  - Triple: 3.3%
  - p = NS

- **MACE**
  - Riva+SAPT: 6.5%
  - DAPT + RIVA: 5.6%
  - Triple: 6%
  - p = NS
PIioneer AF-PCI: Conclusions

- Compared with triple therapy:
  - RIVA + SAPT was associated with a significant reduction in bleeding
  - RIVA + SAPT did not appear to be associated with an increased risk of MACE
PIONEER AF-PCI: Additional Thoughts

- PIONEER and WOEST differ in some key ways:
  - WOEST had 69% AF patients vs. 100% in PIONEER
  - WOEST had 66% of patients receive triple therapy for 1 year
    - PIONEER had 22%
  - Even with these differences, the safety difference is impressive in PIONEER
  - PIONEER mimics WOEST in the overall impression that for 1 year, OAC + SAPT (P2Y₁₂ inhibitor) appears to be safer without compromising efficacy
RE-DUAL PCI: dual antithrombotic therapy with dabigatran after percutaneous coronary intervention in patients with atrial fibrillation

RE-DUAL: Study Design

Patients with AF undergoing PCI with stenting

N=2725

Randomization ≤120 hours post-PCI*

**Dabigatran 150 mg BID + P2Y12 inhibitor**

**Dabigatran 110 mg BID + P2Y12 inhibitor**

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

6-month minimum treatment duration with visits every 3 months for the first year, then visits and telephone contact alternating every 3 months and a 1-month post-treatment visit

**Mean duration of follow-up:** ~14 months

Dabigatran (110 or 150 mg) P2Y12 inhibitor

Warfarin P2Y12 inhibitor

1 month of ASA (BMS) 3 months of ASA (DES)

*Study drug should be administered 6 hours after sheath removal and no later than ≤120 hrs post-PCI (≤72 hrs is preferable).

RE-DUAL: Enrollment Criteria

**Key inclusion criteria**

- Patients aged ≥18 years with paroxysmal, persistent or permanent NVAF
- ACS successfully treated by PCI and stenting (BMS or DES)
- Stable CAD with ≥1 lesion eligible for PCI that was successfully treated by elective PCI and stenting (BMS or DES)

**Key exclusion criteria**

- Cardiogenic shock during current hospitalization
- Use of fibrinolytics within 24 hrs of randomization that, in the investigator's opinion, will put patient at high risk of bleeding
- Stroke or major bleeding event within 1 month prior to screening visit
- Severe renal impairment (CrCl <30mL/min)

ACS, acute coronary syndrome; CAD, coronary artery disease; CrCl, creatinine clearance

RE-DUAL: Study objective and design

RE-DUAL PCI tests the safety and efficacy of two regimens of dual therapy with dabigatran without aspirin vs. triple therapy with warfarin

- The primary endpoint was time to first ISTH major or clinically relevant non-major bleeding
- Secondary endpoints: MACE
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Dabi 110 mg dual therapy (n=981)</th>
<th>Warfarin triple therapy (n=981)</th>
<th>Dabi 150 mg dual therapy (n=763)</th>
<th>Corresponding Warfarin triple therapy (n=764)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean</td>
<td>71.5</td>
<td>71.7</td>
<td>68.6</td>
<td>68.8</td>
</tr>
<tr>
<td>≥80 (US, ROW), ≥70 (Japan), %</td>
<td>22.9</td>
<td>22.9</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>&lt;80 (US, ROW), &lt;70 (Japan), %</td>
<td>77.1</td>
<td>77.1</td>
<td>99.0</td>
<td>99.0</td>
</tr>
<tr>
<td>Male, %</td>
<td>74.2</td>
<td>76.5</td>
<td>77.6</td>
<td>77.7</td>
</tr>
<tr>
<td>Baseline CrCl, mL/min, mean</td>
<td>76.3</td>
<td>75.4</td>
<td>83.7</td>
<td>81.3</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>36.9</td>
<td>37.8</td>
<td>34.1</td>
<td>39.7</td>
</tr>
<tr>
<td>CHA2DS2-VASc score (mean)</td>
<td>3.7</td>
<td>3.8</td>
<td>3.3</td>
<td>3.6</td>
</tr>
<tr>
<td>Modified HAS-BLED score at baseline (mean)</td>
<td>2.7</td>
<td>2.8</td>
<td>2.6</td>
<td>2.7</td>
</tr>
<tr>
<td>ACS indication for PCI, %</td>
<td>51.9</td>
<td>48.4</td>
<td>51.2</td>
<td>48.3</td>
</tr>
<tr>
<td>DES only, %</td>
<td>82.0</td>
<td>84.2</td>
<td>81.4</td>
<td>83.5</td>
</tr>
</tbody>
</table>

Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

HR: 0.52 (95% CI: 0.42–0.63)  P<0.0001

ARR: 11.5%

Dabigatran 110 mg dual therapy (n=981)

Warfarin triple therapy (n=981)

HR: 0.72 (95% CI: 0.58–0.88)  P=0.002

ARR: 5.5%

Dabigatran 150 mg dual therapy (n=763)

Warfarin triple therapy (n=764)

## RE-DUAL: thromboembolic endpoints

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran 110 mg dual therapy (n=981) n (%)</th>
<th>Warfarin triple therapy (n=981) n (%)</th>
<th>D110 DT vs. warfarin TT HR (95% CI) P value</th>
<th>Dabigatran 150 mg dual therapy (n=763) n (%)</th>
<th>Warfarin triple therapy (n=764) n (%)</th>
<th>D150 DT vs. warfarin TT HR (95% CI) P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause death</td>
<td>55 (5.6)</td>
<td>48 (4.9)</td>
<td>1.12 (0.76–1.65) 0.56</td>
<td>30 (3.9)</td>
<td>35 (4.6)</td>
<td>0.83 (0.51–1.34) 0.44</td>
</tr>
<tr>
<td>Stroke</td>
<td>17 (1.7)</td>
<td>13 (1.3)</td>
<td>1.30 (0.63–2.67) 0.48</td>
<td>9 (1.2)</td>
<td>8 (1.0)</td>
<td>1.09 (0.42–2.83) 0.85</td>
</tr>
<tr>
<td>Unplanned revascularization</td>
<td>76 (7.7)</td>
<td>69 (7.0)</td>
<td>1.09 (0.79–1.51) 0.61</td>
<td>51 (6.7)</td>
<td>52 (6.8)</td>
<td>0.96 (0.65–1.41) 0.83</td>
</tr>
<tr>
<td>MI</td>
<td>44 (4.5)</td>
<td>29 (3.0)</td>
<td>1.51 (0.94–2.41) 0.09</td>
<td>26 (3.4)</td>
<td>22 (2.9)</td>
<td>1.16 (0.66–2.04) 0.61</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>15 (1.5)</td>
<td>8 (0.8)</td>
<td>1.86 (0.79–4.40) 0.15</td>
<td>7 (0.9)</td>
<td>7 (0.9)</td>
<td>0.99 (0.35–2.81) 0.98</td>
</tr>
</tbody>
</table>

OAC + SAPT: Questions remain

• While focusing on bleeding is important
  • Why not have MACE as the primary endpoint?
    • Stroke, MI, Stent thrombosis are also very important events

• Rivaroxaban 2.5 mg BID dose fit into practice?
  • Currently not FDA approved, but might be soon....
  • Is that “enough” OAC intensity to prevent stroke in AF chronically?

• Dabigatran 110 mg BID dose?
  • Currently not approved for stroke prevention in AF in the US

• What about the other DOACs?

• What about the more potent P2Y12 inhibitors?
  • How do those impact bleeding rates?
  • Choice of OAC
Apixaban Versus Warfarin in Patients with AF and ACS or PCI: The AUGUSTUS Trial

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

**Exclusion**
- Contraindication to DAPT
- Other reason for warfarin (prosthetic valve, mod/sev MS)

Randomize n = 4,600 Patients

- Apixaban: ASA, placebo
- Warfarin: ASA, placebo

Primary outcome: major/clinically relevant bleeding (through 6 months)
Secondary objective: Death, MI, stroke, stent thrombosis
ENTRUST-AF-PCI Study Design

PROBE design: prospective, randomized, open label, blinded evaluation edoxaban based regimen vs VKA based regimen in N ≥ 1500 AF patients

12 months: end of treatment

Inclusion Criteria:
- OAC indication for AF for at least 12 months
- Successful PCI with stent placement (goal of at least 25% ACS)

RANDOMIZE

EDOxaban 60 mg/day*
- P2Y₁₂ antagonist**
  (without ASA)

Vitamin K Antagonist***
- P2Y₁₂ antagonist
  (ASA 1 - 12 months)****

* Edoxaban dose reduction to 30 mg OD
  + if CrCL<50 ml/min
  + BW>50 kg
  + certain P-gp inhibitors

** Clopidogrel 75mg once-daily or if documented need prasugrel 5 or 10mg once-daily or ticagrelor 90mg twice-daily. Predeclared at randomization

*** VKA, target INR 2-3

**** ASA 100mg OD for 1-12 months guided by clinical presentation (ACS or stable CAD), CHA₂DS-VASc₂ and HAS_BLED

Primary outcome: ISTH major and clinically relevant non-major bleeding

ClinicalTrials.gov Identifier: NCT02866175
North American Consensus White Paper

Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention, Volume: 138, Issue: 5, Pages: 527-536, DOI: (10.1161/CIRCULATIONAHA.118.034722)
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How to identify risk?

**Bleeding Risks:**
- HAS-BLED score
- Recent or previous history of major bleeding
- Concomitant anemia
- Poorly controlled hypertension

**Thrombotic Risks:**
- Left-main stenting
- Proximal LAD stenting
- Multiple Stents
- PCI complications
- History of embolic events (stroke, VTE)
- History of stent thrombosis
- DAPT score > 2 points
Key take home points

• OAC + SAPT ($P2Y_{12}$ inhibitor) preferred over triple therapy in patients with AF + ACS
  • Clopidogrel is the preferred $P2Y_{12}$ inhibitor
    • Limited data with Ticagrelor; Prasugrel currently not recommended
  • DOACs are preferred over warfarin
    • Rivaroxaban 10 – 15 mg once daily (based on CLcr)
    • Dabigatran 150 mg BID

• Consider bleeding and thrombotic risk when considering choice of agents and duration of therapy
  • High bleeding risk = OAC + SAPT x 6 months, then OAC alone
  • High thrombotic risk = OAC + SAPT x 12 months, then OAC alone
    • Can consider triple therapy (OAC + DAPT) x 1 month
How would you manage BA’s antithrombotic therapy?

a) Aspirin 81 mg daily + Clopidogrel 75 mg daily + Warfarin
b) Aspirin 81 mg daily + Prasugrel 10 mg daily + Warfarin
c) Aspirin 81 mg daily + Rivaroxaban 20 mg daily
d) Clopidogrel 75 mg daily + Dabigatran 150 mg daily
e) None of these