Antithrombotic Strategy Variability In ATrial Fibrillation and Obstructive Coronary Disease Revascularized with PCI

THE AVIATOR-2 INTERNATIONAL REGISTRY

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on behalf of the AVIATOR-2 Investigators

SCAI  
Society for Cardiovascular Angiography & Interventions

Mount Sinai Heart
Disclosures

Honoraria – AstraZenca; Boston Scientific

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Patients with atrial fibrillation (AF) undergoing percutaneous coronary intervention (PCI) present unique challenges given the number of potential antithrombotic strategies, treatment durations and overlap in ischemic and bleeding risk.

Existing tools to estimate risk (CHA$_2$DS$_2$VASc and HAS BLED) were developed in AF cohorts that are distinct from PCI populations.

Therapeutic approaches and factors influencing clinical decisions in a contemporary AF/PCI cohort are not well characterized.
Index PCI

• All-comer PCI
• Non-valvular AF
• Multicenter, multinational

Study Schema

**Physician Questionnaire**

- What is your subjectively perceived risk of adverse ischemic cardiac outcome for your patient?
  - Very low
  - Low
  - Intermediate
  - High
  - Very High

- What is your subjectively perceived risk of adverse bleeding outcome for your patient?
  - Very low
  - Low
  - Intermediate
  - High
  - Very High

**Patient Questionnaire**

- With my heart condition, I am most worried about:
  - a) Stent related problem
  - b) Heart attack
  - c) Stroke
  - d) Major Bleeding
  - e) Frequent blood testing
  - f) Death

- I am convinced of the importance of my prescription medication:
  - Disagree Completely
  - Disagree Mostly
  - Not Sure
  - Agree Mostly
  - Agree Completely

**One year f/u MACCE BARC 2-5**
Study Aims & Objectives

• **Baseline**
  - To profile antithrombotic strategies in a contemporary AF/PCI cohort
  - To examine the level of agreement between subjective and empiric assessments of risk
  - Identify factors influencing choice of antithrombotic therapy.

• **Longitudinal**
  - Characterize adherence patterns over time and in relation to treatment strategy
  - Quantify the predictive value of risk scales on discriminating composite ischemic (MACCE - all-cause death, MI, def/prob ST, stroke, CD-TLR) and bleeding events.

Statistical Considerations

• **Analytic Approach**
  • Patients groups according to antithrombotic regimen at discharge
  • One-year event rates estimated using the KM method
  • ROC curves to assess risk discrimination. Ordinal logistic regression to model association between risk scale and antithrombotic strategy

• **Sample Size and Power**
  • Power calculation required total sample of 2500 patients to detect a HR for non-triple Rx versus triple Rx of 0.73
  • Study stopped enrollment due to lack of funding, resulting in a final cohort of 514 patients

## Baseline Characteristics – Overall

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>514</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>73.09 ± 9.01</td>
</tr>
<tr>
<td><strong>Female Sex</strong></td>
<td>132 (25.7%)</td>
</tr>
<tr>
<td><strong>Caucasian Race</strong></td>
<td>450 (87.5%)</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
<td>199 (38.7%)</td>
</tr>
<tr>
<td><strong>eGFR &lt; 60 ml/min/1.73m²</strong></td>
<td>232 (45.1%)</td>
</tr>
<tr>
<td><strong>Previous MI</strong></td>
<td>136 (26.5%)</td>
</tr>
<tr>
<td><strong>Previous Stroke</strong></td>
<td>14 (2.7%)</td>
</tr>
<tr>
<td><strong>ACS presentation</strong></td>
<td>261 (50.8%)</td>
</tr>
<tr>
<td><strong>CHA₂DS₂-VASc</strong></td>
<td>4.23 ± 1.32</td>
</tr>
<tr>
<td><strong>HASBLED</strong></td>
<td>2.99 ± 0.7</td>
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</tbody>
</table>
Selected Survey Responses

**Physician Questionnaire**

*Which risk scores influenced your decision?*

- **ANY**: 84.8%
- **CHA²DS²-VASc**: 73.9%
- **HASBLED**: 40.7%
- **CHADS²**: 13.0%

**Patient Questionnaire**

*I am convinced about the importance of my therapy*

- **Disagree Completely**: 0.6%
- **Disagree Mostly**: 1.2%
- **Not Sure**: 5.1%
- **Agree Mostly**: 30.2%
- **Agree Completely**: 62.8%
Selected Survey Responses

**Physician Questionnaire**

Which 2 factors were the most important in making your decision

- Safety: 93.8%
- Efficacy: 89.9%
- Familiarity: 6.2%
- Availability: 3.9%
- Cost: 2.5%
- Frequency: 2.5%

**Patient Questionnaire**

With my heart condition, I am most worried about (Select 2)

- Heart Attack: 63.4%
- Stroke: 50.6%
- Death: 47.5%
- Stent Related Problems: 19.1%
- Major Bleeding: 14.8%
- Frequent Testing: 5.8%
**Pharmacotherapy at Discharge**

**ENROLLED**

\[N = 514\]

- **Triple Therapy**
  \[(OAC + \text{P2Y}_{12} + \text{ASA}) = 338 \text{ (66.5\%)}\]

- **Dual Therapy**
  \[(OAC + \text{P2Y}_{12}) = 65 \text{ (12.8\%)}\]

- **DAPT**
  \[(\text{ASA} + \text{P2Y}_{12}) = 105 \text{ (20.7\%)}\]

*6 patients were discharged on monotherapy with Dabigatran and are not included in this analysis.*
Empiric and Subjective Risk Agreement

**ISCHEMIC RISK**

Among patients with CHA$_2$DS$_2$VASc $>2$ (465), clinicians perceived 231 (50%) as high/very high ischemic risk

Concordance: 139 (27.0%)

**BLEEDING RISK**

Among patients with HASBLED $\geq$3 (405), clinicians perceived 149 (37%) as high/very high bleeding risk

Concordance: 197 (38.4%)
Subjective vs. Empiric Ischemic Risk & Discharge Rx

Risk Estimation

<table>
<thead>
<tr>
<th>Risk Estimation</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHA₂DS₂VASc</td>
<td>1.08 (0.91-1.27)</td>
<td>0.39</td>
</tr>
<tr>
<td>MD Perception</td>
<td>0.68 (0.52-0.88)</td>
<td>0.003</td>
</tr>
</tbody>
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Models adjusted for region, race, smoking status, ACS, B2C lesion, stent length, paroxysmal AF, PVD
Subjective vs. Empiric Bleeding Risk & Discharge Rx

Risk Estimation

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<tbody>
<tr>
<td>HASBLED</td>
<td>0.99 (0.74-1.31)</td>
<td>0.92</td>
</tr>
<tr>
<td>MD Perception</td>
<td>0.85 (0.67-1.07)</td>
<td>0.17</td>
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</tbody>
</table>

Models adjusted for region, race, smoking status, ACS, B2C lesion, stent length, paroxysmal AF, PVD
Medication Adherence Over Time

30 DAYS

DAPT (N=105)

- ASA = 98.1%
- P2Y₁₂ = 100%

DUAL (N=65)

- P2Y₁₂ = 98.4%
- DOAC = 98.5%
- VKA = 100%

TRIPLE (N=338)

- ASA = 92.5%
- P2Y₁₂ = 99.7%
- DOAC = 98.8%
- VKA = 99.4%
Medication Adherence Over Time

30 DAYS
- DAPT (N=105): 98.1%
- DUAL (N=65): 96.9%
- TRIPLE (N=338): 90.4%

6 MONTHS
- DAPT (N=105): 94.1%
- DUAL (N=65): 88.8%
- TRIPLE (N=338): 41%

Observations:
- ASA = 96.1%
- P2Y_{12} = 98%

- P2Y_{12} = 90.4%
- DOAC= 96.8%
- VKA = 100%

- ASA = 49.3%
- P2Y_{12} = 93.2%
- DOAC= 95.4%
- VKA = 97.3%
Medication Adherence Over Time

30 DAYS
- DAPT (N=105): 98.1%
- DUAL (N=65): 96.9%
- TRIPLE (N=338): 90.4%

6 MONTHS
- DAPT: 94.1%
- DUAL: 88.8%
- TRIPLE: 41%

1 YEAR
- DAPT: 82.9%
- DUAL: 76.6%
- TRIPLE: 31%

ASA:
- 30 DAYS: 91.7%
- 6 MONTHS: 88.8%
- 1 YEAR: 82.9%

P2Y12:
- 30 DAYS: 76.5%
- 6 MONTHS: 95.3%
- 1 YEAR: 98.6%

DOAC:
- 30 DAYS: 96.8%
- 6 MONTHS: 94.6%
- 1 YEAR: 76.6%

VKA:
- 30 DAYS: 98.1%
- 6 MONTHS: 95.3%
- 1 YEAR: 95.3%
One-Year Event Rates

MACCE
15.3% (76)

BARC 2,3,5
13.8% (68)
Ischemic Risk Prediction

MACCE vs. Subjective risk assessment

\[ p\text{-trend} = 0.004 \]

MACCE vs. CHA\textsubscript{2}DS\textsubscript{2}VASc risk assessment

\[ p\text{-trend} = 0.01 \]

C-statistic

- 0.594: MD perceived risk
- 0.591: CHA\textsubscript{2}DS\textsubscript{2}VASc Score
Bleeding Risk Prediction

BARC 2,3,5 vs. Subjective risk assessment

\[ p\text{-trend} = 0.02 \]

- Low: 8.2%
- Intermediate: 11.2%
- High: 19.7%
- Very High: 11.1%

BARC 2,3,5 vs. HASBLED risk assessment

\[ p\text{-trend} = 0.35 \]

- (1,2): 11.7%
- (3): 13.7%
- (4): 11.4%
- (≥5): 15.4%

\[ c\text{-statistic} \]

- 0.600: MD perceived risk
- 0.534: HASBLED Score

1 - Specificity
Limitations

• Registry-based cohort does not allow for causal inference

• Follow-up limited to 1-year

• Specialized centers may limit generalizability

• Insufficient power to detect differences in clinical outcomes
Conclusions

• Antithrombotic choices in AF/PCI patients are highly variable with greater adherence to OAC versus antiplatelet drugs

• Novel tools to accurately quantify risk and inform clinical decisions are needed in complex patients with AF requiring PCI

• Validated tools to quantify ischemic and bleeding risk in AF cohorts perform poorly in AF/PCI patients
<table>
<thead>
<tr>
<th>Role</th>
<th>Name and Position</th>
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<tbody>
<tr>
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<td>Medical Lead –</td>
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<td>Project Management –</td>
<td>Clayton Snyder and Alyssa Ramkissoon</td>
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<td>AP design –</td>
<td>Dr. Ashish Atreja- Chief Innovation officer, Icahn School of Medicine</td>
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<td>Biometrics –</td>
<td>Dr. Usman Baber- lead, Melissa Aquino- Biostatistics</td>
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<td>Clinical Events Committee –</td>
<td>Emma Woodoff-Leith (lead)</td>
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