Ισορροπώντας μεταξύ θρομβωτικού και αιμορραγικού κινδύνου στην ΚΜ/ΟΣΣ/PCI: τι νεώτερο από Ευρώπη & Αμερική – Δ. Αλεξόπουλος

Balancing thrombotic and hemorrhagic risk in AF/ACS/PCI: what is new from Europe & the USA – D. Alexopoulos
I, Dimitrios Alexopoulos, have received

Speaker honoraria:
AstraZeneca, Bayer, Boehringer Ingelheim, Biotronik, AMGEN

Advisory Board fees:
AstraZeneca, Boehringer Ingelheim, Bayer, Medtronic, Chiesi Hellas
FIGURE 1  Clinical Challenge in Patients With AF Undergoing PCI

- **PCI**
  - Aspirin
  - Clopidogrel
  - Prasugrel
  - Ticagrelor

- **AF**
  - AF + PCI
  - Triple Therapy

- **Stent Thrombosis**
  - DAPT > OAC

- **TIA/Stroke**
  - OAC > DAPT

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

Capodanno and Angiolillo JACC Intv 2017;10:1086
Patients With Atrial Fibrillation Undergoing Coronary Stent Placement: PIONEER AF-PCI

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

**RANDOMIZE**

- Rivaroxaban 15 mg qd*
- Clopidogrel 75 mg qd†

- **≤72 hours**
- After sheath removal

- **1,6, or 12 months**
- Pre randomization MD Choice

- **Rivaroxaban 2.5 mg bid**
- **Clopidogrel 75 mg qd†**
- **Aspirin 75-100 mg qd‡**

- **Rivaroxaban 15 mg QD**
- **Aspirin 75-100 mg qd**

- **≤1,6, or 12 months**
- Pre randomization MD Choice

- **VKA (target INR 2.0-3.0)**
- **Clopidogrel 75 mg qd†**
- **Aspirin 75-100 mg qd**

- **VKA (target INR 2.0-3.0)**
  - **Aspirin 75-100 mg qd**

**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

Gibson et al. AHA 2016
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Riva + P2Y$_{12}$ (N=709)</th>
<th>Riva + DAPT (N=709)</th>
<th>VKA + DAPT (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>
Kaplan-Meier Estimates of First Occurrence of Clinically Significant Bleeding Events

**Riva + P2Y₁₂** v. **VKA + DAPT**
- HR = 0.59 (95% CI: 0.47-0.76)
- p < 0.000013
- ARR = 9.9
- NNT = 11

**Riva + DAPT** v. **VKA + DAPT**
- HR = 0.63 (95% CI: 0.50-0.80)
- p < 0.00018
- ARR = 8.7
- NNT = 12

**No. at risk**
- **Riva + P2Y₁₂**: 696, 628, 606, 585, 543, 510, 383
- **Riva + DAPT**: 706, 636, 600, 579, 543, 509, 409
- **VKA + DAPT**: 697, 593, 555, 521, 461, 426, 329

---

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.

Clinically significant bleeding is the composite of TIMI major, TIMI minor, and BRMA.

Hazard ratios as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.

Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.
Kaplan-Meier Estimates of First Occurrence of CV Death, MI or Stroke

- **Riva + P2Y12**: 6.5%
- **Riva + DAPT**: 6.0%
- **VKA + DAPT**: 5.6%

**No. at risk**
- **Riva + P2Y12**: 694, 648, 633, 621
- **Riva + DAPT**: 704, 662, 640, 628
- **VKA + DAPT**: 695, 635, 607, 579

**Days**
- 590
- 562
- 543

**Treatment-emergent period**: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.

Composite of adverse CV events is composite of CV death, MI, and stroke.

Hazard ratios as compared to VKA group are based on the (stratified, only for the Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.

Log-Rank P-values as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/115 mg QD comparing VKA) two-sided log rank test.

Subjects were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines.

Gibson et al. AHA 2016
Riva 15mg + P2Y₁₂ vs. VKA + DAPT
HR: 0.79 (95% CI: 0.66 – 0.94), p = 0.008
ARR: 7.0%
NNT: 15

Riva 2.5mg + DAPT vs. VKA + DAPT
HR: 0.75 (95% CI: 0.62 – 0.90), p = 0.002
ARR: 10.0%
NNT: 10

Riva 15mg + P2Y₁₂

VKA + DAPT

Time in Days

No. at Risk
Riva 15mg + P2Y₁₂  696  609  582  559  496  437  322
Riva 2.5mg + DAPT  706  607  570  548  493  454  367
VKA + DAPT  697  592  540  490  422  369  272

PIONEER-AF STUDY LIMITATIONS

- The duration of DAPT was not randomized
- 15mg rivaroxaban od has not yet received approval for ACS and AF
Emerging Concepts: Dual-Pathway Inhibition (DPI)

Synergy of oral anticoagulant and antiplatelet therapy

Oral anticoagulant therapy, including direct inhibitors of factor IIa and Xa, and antiplatelet agents, such as acetylsalicylic acid and P2Y₁₂ inhibitors, synergistically target two essential components of thrombosis: coagulation and platelet activation.

Capodanno D & Angiolillo DJ. Nat Rev Cardiol. 2018; 15:480-496
Effects of Rivaroxaban on Platelet Activation and Platelet–Coagulation Pathway Interaction: In Vitro and In Vivo Studies

Perzborn E. et al. J Cardiov Pharm Therap 2015;20:554
Study Design: Multicenter, randomized, open-label trial following a PROBE design

- Patients with AF undergoing PCI with stenting
  - Randomization ≤120 hours post-PCI*
  - N=2725

  - 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

*Study drug should be administered 6 hours after sheath removal and no later than ≤120 hrs post-PCI (≤72 hrs is preferable). PROBE, prospective, randomized, open, blinded end-point; R, randomization; BMS, bare metal stent; DES, drug-eluting stent. ClinicalTrials.gov: NCT02164864; Cannon et al. Clin Cardiol 2016
Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

HR: 0.52 (95% CI: 0.42–0.63)  
Non-inferiority \( P < 0.0001 \)  
\( P < 0.0001 \)  

**Warfarin triple therapy**

HR: 0.72 (95% CI: 0.58–0.88)  
Non-inferiority \( P < 0.0001 \)  
\( P = 0.002 \)  

**Warfarin triple therapy**

**Dabigatran 110 mg dual therapy**

**Dabigatran 150 mg dual therapy**

Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (\(<70 \text{ or } >70 \text{ in Japan and } <80 \text{ or } >80 \text{ years old elsewhere} \)). For the dabigatran 150 mg vs warfarin comparison, an unstratified model is used, elderly patients outside the USA are excluded. Non-inferiority \( P \) value is one sided (alpha=0.025). Wald two-sided \( P \) value from (stratified) Cox proportional-hazard model (alpha=0.05).
Time to death or thromboembolic event, or unplanned revascularization

HR: 1.04 (95% CI: 0.84–1.29)
Non-inferiority P=0.0047

<table>
<thead>
<tr>
<th>Patients with outcome event (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran (combined dose) dual therapy (n=1744)</td>
</tr>
<tr>
<td>Warfarin triple therapy (n=981)</td>
</tr>
</tbody>
</table>

Non-inferiority P value is one sided (alpha=0.025). Results presented are Step 3 of hierarchical testing procedure, testing non-inferiority of dabigatran dual therapy (combined doses) to warfarin triple therapy in death or thromboembolic event and unplanned revascularization.
Hazard ratio, 1.04 (95% CI, 0.84–1.29)
P=0.005 for noninferiority

With a 8.5% control event rate, NIM=2%, \( \beta=90\% ; \alpha=0.05 \), 6,698 pts would be needed to show non-inferiority (x2 REDUAL)

Included TVR which may be unrelated with the anti-thrombotic regimen
Sample size for stent thrombosis

- Considering a 1-year rate of stent thrombosis of \( \approx 1\% \), a NIM of 0.3\%, with \( \alpha = 0.05 \) and \( \beta = 80\% \) a trial sample size of approximately 26,000 patients would be needed to declare non inferiority of one antithrombotic strategy toward the other.
Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials

**Figure 2** Thrombolysis in Myocardial Infarction (TIMI) major or minor bleeding. Data are n/N unless otherwise indicated. Hazard ratio <1 favours dual antithrombotic therapy and hazard ratio >1 favours triple antithrombotic therapy. CrI, credible interval; DAT, dual antithrombotic therapy; TAT, triple antithrombotic therapy.
Take home figure  Summary of bleeding and ischaemic risks for dual versus triple antithrombotic therapy.
2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS)
Patients with an indication for oral anticoagulation\(^1\) undergoing PCI\(^2\)

Concerns about ischaemic risk\(^3\) prevailing

Concerns about bleeding risk\(^4\) prevailing

Time from treatment initiation:

- 1 month
- 3 months
- 6 months
- 12 months
- Beyond 12 months

1 month Triple Therapy

- Class Ila B

3 months

- Triple Therapy up to 6 months
- Class Ila B

6 months

- Dual Therapy up to 12 months
- Class Ila A

12 months

- Dual Therapy up to 12 months
- Class Ila A

Beyond 12 months

- OAC monotherapy
- Class Ila B

\(A\) = Aspirin
\(C\) = Clopidogrel
\(O\) = Oral anticoagulation\(^1\)
The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

Jan Steffel¹*, Peter Verhamme², Tatjana S. Potpara³, Pierre Albaladejo⁴, Matthias Antz⁵, Lien Desteghe⁶, Karl Georg Haeusler⁷, Jonas Oldgren⁸, Holger Reinecke⁹, Vanessa Roldan-Schilling¹⁰, Nigel Rowell¹¹, Peter Sinnaeve², Ronan Collins¹², A. John Camm¹³, and Hein Heidbüchel⁶,¹⁴
Factors to shorten combination therapy:
- (Uncorrectable) high bleeding risk
- Low atherothrombotic risk (by REACH or SYNTAX score if elective; GRACE ≥140 if ACS)

Factors to lengthen combination therapy:
- First-generation DES
- High atherothrombotic risk (scores as above; stenting of the left main, proximal LAD, proximal bifurcation; recurrent MIs; stent thrombosis etc.) and low bleeding risk

Figure II Long-term treatment of patients on non-vitamin K antagonist oral anticoagulant therapy after elective percutaneous coronary intervention.
2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a joint consensus document of the European Heart Rhythm Association (EHRA), European Society of Cardiology Working Group on Thrombosis, European Association of Percutaneous Cardiovascular Interventions (EAPCI), and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA)

Gregory Y.H. Lip (Chair)¹,²,³, Jean-Phillippe Collet (Co-Chair)⁴, Michael Haude (Chair)⁵, and the EHRA Working Group on Thrombosis
Figure 2 Management algorithm for AF patients presenting with elective PCI or ACS undergoing PCI.

Lip G et al. Europace 2018
2018 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

Authors/Task Force Members: Franz-Josef Neumann* (ESC Chairperson)
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended that periprocedural aspirin and clopidogrel are administered to patients undergoing coronary stent implantation.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>In patients treated with coronary stent implantation, triple therapy with aspirin, clopidogrel, and an OAC should be considered for 1 month, irrespective of the type of stent used.&lt;sup&gt;755&lt;/sup&gt;</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Triple therapy with aspirin, clopidogrel, and an OAC for longer than 1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics, which outweigh the bleeding risk.&lt;sup&gt;755&lt;/sup&gt;</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Dual therapy with clopidogrel 75 mg/day and an OAC should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk. &lt;sup&gt;754,756,757&lt;/sup&gt;</td>
<td>IIa</td>
<td>A</td>
</tr>
</tbody>
</table>
### The North American Perspective – 2018 Update

**Management of antiplatelet therapy in patients with AF undergoing PCI treated with an OAC**

<table>
<thead>
<tr>
<th>Time from PCI</th>
<th>Default strategy</th>
<th>Patients at high ischemic/thrombotic and low bleeding risks</th>
<th>Patients at low ischemic/thrombotic or high bleeding risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peri-PCI</td>
<td>Triple Therapy (OAC + DAPT)</td>
<td>Triple Therapy (OAC + DAPT)</td>
<td>Triple Therapy (OAC + DAPT)</td>
</tr>
<tr>
<td>1 month</td>
<td>Double Therapy up to 12 months (OAC + SAPT)</td>
<td>Triple Therapy up to 1 month (OAC + DAPT)</td>
<td>Double Therapy up to 6 months (OAC + SAPT)</td>
</tr>
<tr>
<td>3 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>OAC</td>
<td>OAC</td>
<td>OAC</td>
</tr>
</tbody>
</table>

**Note:**
- OAC: prefer a NOAC over VKA if no contraindications
- SAPT: prefer a P2Y₁₂ inhibitor over aspirin
- Clopidogrel is the P2Y₁₂ inhibitor of choice; ticagrelor may be considered in patients at high ischemic/thrombotic and low bleeding risks; avoid prasugrel
- Consider SAPT in addition to OAC after >12 mo. only in select patients at high ischemic/thrombotic and low bleeding risks

### Summary of key changes between 2016 and 2018 Expert Consensus on Antithrombotic Management of AF patients undergoing PCI

<table>
<thead>
<tr>
<th></th>
<th>2016 Expert Consensus</th>
<th>2018 Expert Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Choice of anticoagulant</strong></td>
<td>VKA or NOAC may be both considered, with choice of agent at the discretion of the treating physician and taking into consideration patient preference</td>
<td>A NOAC (rather than a VKA) should generally be preferred in most patients unless contraindicated</td>
</tr>
<tr>
<td><strong>Choice of P2Y$_{12}$ inhibitor</strong></td>
<td>Clopidogrel is the P2Y$_{12}$ inhibitor of choice; avoid prasugrel or ticagrelor</td>
<td>Clopidogrel is the P2Y$_{12}$ inhibitor of choice; ticagrelor may represent a reasonable treatment option in patients at high ischemic/thrombotic and low bleeding risk; avoid prasugrel</td>
</tr>
<tr>
<td><strong>Strategy</strong></td>
<td>DAPT in adjunct to OAC (i.e., triple-therapy) should not extend to a full 12 months; consider SAPT (preferably clopidogrel and dropping aspirin) in adjunct to OAC (i.e., double-therapy) as early as possible (0 to 6 months post-stenting) depending on the ischemic/thrombotic and bleeding risk profile</td>
<td>A double-therapy regimen (OAC plus P2Y$_{12}$ inhibitor) immediately after hospital discharge should be considered for most patients, while extending the use of aspirin beyond hospital discharge (i.e., triple-therapy) should be considered only for patients at high ischemic/thrombotic and low bleeding risks and for a limited period of time (e.g., 1 month)</td>
</tr>
</tbody>
</table>

Short Review

Antithrombotic treatment in atrial fibrillation patients undergoing PCI: Is dual therapy the winner?

Christos Mantis\textsuperscript{a}, Dimitrios Alexopoulos\textsuperscript{b, *}

\textsuperscript{a} Cardiology Department, Konstantopoulio General Hospital, Athens, Greece
\textsuperscript{b} 2nd Department of Cardiology, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece
In order to assess the magnitude of the problem
How common is an increased HAS-BLED score ≥ 3

PIONNER AF-PCI and RE-DUAL PCI: 69% and 66% of patients had HAS-BLED score ≥ 3, respectively.

In a post hoc analysis of two randomized trials, which included 3,665 patients, a HAD-BLED score ≥ 3 was observed in 71% of the patients.

Data from real life and observational studies, in 28-35% of patients

This would help physicians to understand what to expect in real life practice and whether DAT should be a default strategy.

Conclusion

Assessment of bleeding and ischemic risk profile is a *sine qua non*.

In anticipation of new data, this can be the safest way to choose the right antithrombotic strategy for every individual patient with AF undergoing PCI, as with the current evidence, it may be too early to declare DAT or TAT as a winner.
<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients with AF at increased risk of stroke (based on CHA₂DS₂-VASc risk score of 2 or greater) who have undergone PCI with stenting for ACS, double therapy with a P2Y₁₂ inhibitor (clopidogrel or ticagrelor) and dose-adjusted vitamin K antagonist is reasonable to reduce the risk of bleeding as compared with triple therapy. <strong>NEW</strong>: New RCT data and data from 2 registries and a retrospective cohort study are available.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients with AF at increased risk of stroke (based on CHA₂DS₂-VASc risk score of 2 or greater) who have undergone PCI with stenting for ACS, double therapy with P2Y₁₂ inhibitors (clopidogrel) and low-dose rivaroxaban 15 mg daily is reasonable to reduce the risk of bleeding as compared with triple therapy. <strong>NEW</strong>: New published data are available.</td>
</tr>
</tbody>
</table>
## Recommendations for AF Complicating ACS

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients with AF at increased risk of stroke (based on CHA$_2$DS$<em>2$-VASc risk score of 2 or greater) who have undergone PCI with stenting for ACS, double therapy with a P2Y$</em>{12}$ inhibitor (clopidogrel or ticagrelor) and dose-adjusted vitamin K antagonist is reasonable to reduce the risk of bleeding as compared with triple therapy. <strong>NEW</strong>: New RCT data and data from 2 registries and a retrospective cohort study are available.</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients with AF at increased risk of stroke (based on CHA$_2$DS$<em>2$-VASc risk score of 2 or greater) who have undergone PCI with stenting for ACS, double therapy with P2Y$</em>{12}$ inhibitors (clopidogrel) and low-dose rivaroxaban 15 mg daily is reasonable to reduce the risk of bleeding as compared with triple therapy. <strong>NEW</strong>: New published data are available.</td>
</tr>
</tbody>
</table>
### Recommendations for AF Complicating ACS

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-R</td>
<td>In patients with AF at increased risk of stroke (based on CHA$_2$DS$<em>2$-VASc risk score of 2 or greater) who have undergone PCI with stenting for ACS, double therapy with a P2Y$</em>{12}$ inhibitor (clopidogrel) and dabigatran 150 mg twice daily is reasonable to reduce the risk of bleeding as compared with triple therapy. <strong>NEW</strong>: New published data are available.</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>If triple therapy (oral anticoagulant, aspirin, and P2Y$_{12}$ inhibitor) is prescribed for patients with AF who are at increased risk of stroke (based on CHA$_2$DS$<em>2$-VASc risk score of 2 or greater) and who have undergone PCI with stenting (drug eluting or bare metal) for ACS, a transition to double therapy (oral anticoagulant and P2Y$</em>{12}$ inhibitor) at 4 to 6 weeks may be considered. <strong>NEW</strong>: New published data are available.</td>
</tr>
</tbody>
</table>
Contemporary Antithrombotic Treatment in Patients with Non-valvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention: Rationale and Design of the Greek AntiPlatElet Atrial Fibrillation (GRAPE-AF) Registry

Ioanna Xanthopoulou · Vasiliki-Maria Dragaon · Periklis Davlouros · Costas Tsioufas · Efthathios Iliodromitis · Dimitrios Alexopoulos · for the GRAPE-AF Investigators

© Springer Science+Business Media, LLC, part of Springer Nature 2018

Abstract

Background Approximately 5 to 7% of patients undergoing percutaneous coronary intervention (PCI) for the treatment of coronary artery disease require chronic oral anticoagulation (OAC) on top of aspirin and a P2Y12 receptor antagonist, mainly due to non-valvular atrial fibrillation (AF). The advent of non-vitamin K antagonist oral anticoagulants (NOACs) increased treatment options, while there is cumulative evidence that dual combination of a NOAC and a P2Y12 receptor antagonist attenuates risk of bleeding, compared to traditional triple therapy, consisting of a vitamin K antagonist (VKA), aspirin, and a P2Y12 receptor antagonist, without significantly compromising efficacy.

Study Design Greek AntiPlatElet Atrial Fibrillation (GRAPE-AF, NCT 03362788) is an observational, nationwide study of non-valvular AF patients undergoing PCI, planning to enroll over 1-year period > 500 participants in 25 tertiary and non-tertiary PCI centers in Greece. Key data to be collected pre-discharge include demographics, detailed past medical history, and antithrombotic and concomitant treatment. Patients will be followed up at 1, 6, and 12 months post hospital discharge. At each follow-up visit, data on antithrombotic treatment, ischemic, bleeding, and adverse events will be collected. Study’s primary endpoint is clinically significant bleeding (Bleeding Academic Research Consortium, BARC ≥2) at 12 months, between VKAs and NOACs-treated patients, analyzed using Cox proportional hazards models, by an intention-to-treat principle. An independent endpoint committee will adjudicate all clinical events.

Conclusions This study aims at providing “real-world” information on current antithrombotic treatment patterns and clinical outcome of patients with non-valvular AF undergoing PCI.