Current guideline for atrial fibrillation patients who underwent PCI

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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)

WHITE PAPER

Antithrombotic Therapy in Patients With Atrial Fibrillation Treated With Oral Anticoagulation Undergoing Percutaneous Coronary Intervention
A North American Perspective–2018 Update
2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy

Antithrombotic Therapy for Atrial Fibrillation
CHEST Guideline and Expert Panel Report

2018 Korean Guideline of Atrial Fibrillation Management

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

ESC European Society of Cardiology

Europace (2019) 21, 192–193
doi:10.1093/europace/euy174

EHRA CONSENSUS DOCUMENT

The Heart Center of CHOSUN UNIVERSITY HOSPITAL
**Interventionist vs. Non-interventionist**

**Circulation**

**ORIGINAL RESEARCH ARTICLE**

Open-Label Randomized Trial Comparing Oral Anticoagulation With and Without Single Antiplatelet Therapy in Patients With Atrial Fibrillation and Stable Coronary Artery Disease Beyond 1 Year After Coronary Stent Implantation

OAC-ALONE Study

<table>
<thead>
<tr>
<th>End Points</th>
<th>OAC Alone (N=344)</th>
<th>Combined OAC and APT (N=346)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Noninferiority</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ischemic end point</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A composite of cardiovascular death, myocardial infarction, ischemic stroke, or systemic embolism</td>
<td>36 (10.5/4.2)</td>
<td>31 (9.0/3.6)</td>
<td>1.17 (0.73–1.91)</td>
<td>0.32</td>
<td>0.51</td>
</tr>
<tr>
<td><strong>Myocardial infarction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 (2.3/0.93)</td>
<td>4 (1.2/0.46)</td>
<td>2.03 (0.64–7.59)</td>
<td>0.23</td>
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<tr>
<td><strong>Stent thrombosis</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>2 (0.58/0.23)</td>
<td>0 (0.0/0.0)</td>
<td>NA*</td>
<td>0.15†</td>
<td></td>
</tr>
<tr>
<td><strong>TIMI major bleeding</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17 (4.9/1.9)</td>
<td>29 (8.4/3.4)</td>
<td>0.57 (0.31–1.03)</td>
<td>0.07</td>
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</tr>
</tbody>
</table>

JACC interv 2017;10:1086

Circulation 2019;139:604
Concerned more stent than bleeding (My opinion)

<table>
<thead>
<tr>
<th>입원</th>
<th>2016-12-21 05:44</th>
<th>2017-01-17 10:24</th>
<th>신경외과</th>
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<td>순환기내과</td>
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<td>2016-10-21 10:53</td>
<td>순환기내과</td>
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</tbody>
</table>

2016.10.19 UAP : pmLAD, dLCX PCI
2016.12.21 brain CT : ICH in Rt. thalamus

<table>
<thead>
<tr>
<th>입원</th>
<th>2017-03-15 12:08</th>
<th>2017-03-16 12:14</th>
<th>순환기내과</th>
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<td>외래</td>
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<td>입원</td>
<td>2017-02-28 00:33</td>
<td>2017-03-03 10:39</td>
<td>순환기내과</td>
</tr>
</tbody>
</table>

2017.02.28 NSTEMI : pmLAD PCI
2017.03.15 massive Gl bleeding → embolization
→ expire d/t multi-organ failure

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>입원</td>
<td>2012-07-13 09:41</td>
<td>2012-07-19 11:23</td>
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</tbody>
</table>

2012.07.16 NSTEMI : mLAD PCI
2019.05.30 STEMI : stent thrombosis
self-initiated interruption, neoatherosclerosis

How could I know the bleeding events?
1. Consult from other department
2. Study enrolled patient
## Korean data about AF + PCI

<table>
<thead>
<tr>
<th></th>
<th>Asan-PCI registry</th>
<th>Korean NHIS</th>
<th>KAMIR-NIH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients category</strong></td>
<td>all IHD</td>
<td>PCI, AF code</td>
<td>NSTEMI, STEMI</td>
</tr>
<tr>
<td><strong>Publication</strong></td>
<td>JACC Interv 2017</td>
<td>Am J Cardiol 2019</td>
<td>Unpublished</td>
</tr>
<tr>
<td><strong>Number of AF (%)</strong></td>
<td>711 (7.1%)</td>
<td>8,891 (NA)</td>
<td>763 (5.6%)</td>
</tr>
<tr>
<td>No OAC during 1 year</td>
<td>90.5%</td>
<td>85.4%</td>
<td>83.1%</td>
</tr>
<tr>
<td>OAC only after 1 year</td>
<td>NA</td>
<td>9.9%</td>
<td>21.1%</td>
</tr>
</tbody>
</table>
Contents

✓ Guideline 에서 권고가 비슷한 부분

✓ Guideline 에서 차이가 있는 부분

✓ Cases about AF + PCI
Contents

✓ Guideline 에서 권고가 비슷한 부분

✓ Guideline 에서 차이가 있는 부분

✓ Cases about AF + PCI
The first RCT about dual therapy: WOEST

15 sites in the Netherlands and Belgium
2008.11 – 2011.11
PCI: 75% stenosis or FFR < 0.8
DES 65%, ACS ~25%

Lancet 2013;381:1107
Powerful 2 RCTs – PIONEER, RE-DUAL PCI

Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI

C. Michael Gibson, M.D., Roxana Mehran, M.D., Christoph Bode, M.D., Jonathan Halperin, M.D., Freek W. Verheugt, M.D., Peter Wildgoose, Ph.D., Mary Birmingham, Pharm.D., Juliana Ianus, Ph.D., Paul Burton, M.D., Ph.D., Martin van Eickels, M.D., Serge Korjian, M.D., Yazen Daaboul, M.D., Gregory Y.H. Lip, M.D., Marc Cohen, M.D., Steen Husted, M.D., Eric D. Peterson, M.D., M.P.H., and Keith A. Fox, M.B., Ch.B.

NEJM 2016;375:2423

Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation


NEJM 2017;377:1513
PIioneer-AF PCI: less bleeding, similar ischemic events

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

Bleeding events

Ischemic events

Gibson et al. AHA 2016
RE-DUAL PCI: less bleeding!! reduce dosage?

**Dabigatran 150 mg BID + P2Y12 inhibitor**

- ISTH major bleeding event: HR: 0.52 (95% CI: 0.37–0.74), P<0.001
- TIMI major bleeding event: HR: 0.64 (95% CI: 0.43–0.94), P=0.02

**Dabigatran 110 mg BID + P2Y12 inhibitor**

- ISTH major bleeding event: HR: 1.04 (95% CI: 0.84–1.29), P<0.74 (0.005 for noninferiority)
- TIMI major bleeding event: HR: 1.13 (95% CI: 0.90–1.43), P=0.30

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

- ISTH major bleeding event: HR: 1.17 (95% CI: 0.90–1.53), P<0.25 (0.11 for noninferiority)
- TIMI major bleeding event: HR: 1.30 (95% CI: 0.98–1.73), P=0.07

**End Point**

- **Composite efficacy endpoint:** thromboembolic events, death, or unplanned revascularization
  - Combined Dual-Therapy Group (N=1744): 239 (13.7)
  - Triple-Therapy Group (N=981): 131 (13.4)
  - Hazard Ratio (95% CI): 1.04 (0.84–1.29), P=0.74 (0.005 for noninferiority)

- **Thromboembolic events or death**
  - Combined Dual-Therapy Group (N=1744): 168 (9.6)
  - Triple-Therapy Group (N=981): 83 (8.5)
  - Hazard Ratio (95% CI): 1.17 (0.90–1.53), P=0.25 (0.11 for noninferiority)

- **Death**
  - Combined Dual-Therapy Group (N=1744): 55 (5.6)
  - Triple-Therapy Group (N=981): 48 (4.9)
  - Hazard Ratio (95% CI): 1.12 (0.76–1.65), P=0.56

- **Myocardial infarction**
  - Combined Dual-Therapy Group (N=1744): 44 (4.5)
  - Triple-Therapy Group (N=981): 29 (3.0)
  - Hazard Ratio (95% CI): 1.51 (0.94–2.41), P=0.09

- **Stroke**
  - Combined Dual-Therapy Group (N=1744): 17 (1.7)
  - Triple-Therapy Group (N=981): 13 (1.3)
  - Hazard Ratio (95% CI): 1.30 (0.63–2.67), P=0.48

- **Definite stent thrombosis**
  - Combined Dual-Therapy Group (N=1744): 15 (1.5)
  - Triple-Therapy Group (N=981): 8 (0.8)
  - Hazard Ratio (95% CI): 1.86 (0.79–4.40), P=0.15

N=2725
**NOAC > VKA, Dual therapy reasonable**

### 2018 North America Perspective

<table>
<thead>
<tr>
<th>Choice of anticoagulant</th>
<th>2016 Expert Consensus</th>
<th>2018 Expert Consensus Update</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Both VKAs and NOACs may be considered, with choice of agent at the discretion of the treating physician and taking into consideration patient preference</td>
<td>An NOAC (rather than a VKA) should generally be preferred in most patients unless contraindicated</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Choice of P2Y₁₂ inhibitor</th>
<th>2016 Expert Consensus</th>
<th>2018 Expert Consensus Update</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel is the P2Y₁₂ inhibitor of choice; avoid prasugrel or ticagrelor</td>
<td>Clopidogrel is the P2Y₁₂ inhibitor of choice; ticagrelor may represent a reasonable treatment option in patients at high ischemic/thrombotic and low bleeding risks; avoid prasugrel</td>
<td></td>
</tr>
</tbody>
</table>

### 2018 ESC/EACTS

In patients with non-valvular AF requiring anticoagulation and antiplatelet treatment, a NOAC should be preferred over VKAs.\(^{758-760}\)

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.\(^{754,756,757}\)
Questions after 2 RCTs

✓ Ischemic events < bleeding events
  - PIONEER AF PCI: 5~6% vs. 20~30%
  - RE-DUAL PCI: 5~10% vs. 10~20%
  ➔ If larger trial, triple > dual in ischemic events?

✓ Reducing bleeding events
  - by NOAC instead of VKA?
  - by early discontinuation of aspirin?
  ➔ What was the major factor of reducing bleeding?

From NEJM editorial for AUGUSTUS trial
Study Design of AUGUSTUS

**INCLUSION**
- Atrial fibrillation (prior, persistent, >6 hr)
  - Physician decision for OAC
- Acute coronary syndrome or PCI
  - Planned P2Y$_{12}$ inhibitor for ≥6 months

**EXCLUSION**
- Contraindication to DAPT
- Other reason for VKA
  (prosthetic valve, moderate / severe mitral stenosis)

Randomize n=4600 patients

Apixaban 5 mg BID
Apixaban 2.5 mg BID in selected patients

Open Label

VKA (INR 2–3)

Aspirin for all on the day of ACS or PCI
Aspirin versus placebo after randomization

Aspirin
Double Blind
Placebo

Aspirin
Double Blind
Placebo

Primary outcome: ISTH major / CRNM bleeding
Secondary outcome(s): death / hospitalization, death / ischemic events


PIONEER AF PCI : n= 2100
RE-DUAL PCI : n=2725

PIONEER AF PCI : Rivaloxaban 15mg (reduced) QD, 2.5mg bid
RE-DUAL PCI : Pradaxa 150mg, 110mg (random)
Results 1. Apixaban >> VKA

**Major / CRNM Bleeding**
Apixaban vs. VKA

- **HR 0.69, 95% CI 0.58–0.81**
- P<0.001 for non-inferiority
- P<0.001 for superiority
- ARR=4.2%
- NNT=24

**Death / Hospitalization**
Apixaban vs. VKA

- **HR 0.83, 95% CI 0.74–0.93**
- P=0.002
- ARR=3.9%
- NNT=26

### Endpoint Comparison

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Apixaban (N=2306)</th>
<th>VKA (N=2308)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death / Ischemic Events (%)</td>
<td>6.7</td>
<td>7.1</td>
<td>0.93 (0.75–1.16)</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3.3</td>
<td>3.2</td>
<td>1.03 (0.75–1.42)</td>
</tr>
<tr>
<td>CV Death (%)</td>
<td>2.5</td>
<td>2.3</td>
<td>1.05 (0.72–1.52)</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>0.6</td>
<td>1.1</td>
<td>0.50 (0.26–0.97)</td>
</tr>
<tr>
<td>Myocardial Infarction (%)</td>
<td>3.1</td>
<td>3.5</td>
<td>0.89 (0.65–1.23)</td>
</tr>
<tr>
<td>Definite or Probable Stent Thrombosis (%)</td>
<td>0.6</td>
<td>0.8</td>
<td>0.77 (0.38–1.56)</td>
</tr>
<tr>
<td>Urgent Revascularization (%)</td>
<td>1.7</td>
<td>1.9</td>
<td>0.90 (0.59–1.38)</td>
</tr>
<tr>
<td>Hospitalization (%)</td>
<td>22.5</td>
<td>26.3</td>
<td>0.83 (0.74–0.93)</td>
</tr>
</tbody>
</table>
Results 2. Aspirin: bleeding without definite benefits

Major / CRNM Bleeding
Aspirin vs. Placebo

HR 1.89, 95% CI 1.59–2.24
P<0.001
ARI=7.1%
NNH=14

Aspirin: 16.1%
Placebo: 9.0%

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Aspirin (N=2307)</th>
<th>Placebo (N=2307)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death / Ischemic Events (%)</td>
<td>6.5</td>
<td>7.3</td>
<td>0.89 (0.71–1.11)</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3.1</td>
<td>3.4</td>
<td>0.91 (0.66–1.26)</td>
</tr>
<tr>
<td>CV Death (%)</td>
<td>2.3</td>
<td>2.5</td>
<td>0.92 (0.63–1.33)</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>0.9</td>
<td>0.8</td>
<td>1.06 (0.56–1.98)</td>
</tr>
<tr>
<td>Myocardial Infarction (%)</td>
<td>2.9</td>
<td>3.6</td>
<td>0.81 (0.59–1.12)</td>
</tr>
<tr>
<td>Definite or Probable Stent Thrombosis (%)</td>
<td>0.5</td>
<td>0.9</td>
<td>0.52 (0.25–1.08)</td>
</tr>
<tr>
<td>Urgent Revascularization (%)</td>
<td>1.6</td>
<td>2.0</td>
<td>0.79 (0.51–1.21)</td>
</tr>
<tr>
<td>Hospitalization (%)</td>
<td>25.4</td>
<td>23.4</td>
<td>1.10 (0.98–1.24)</td>
</tr>
</tbody>
</table>
Bleeding events in AUGUSTUS

VKA + Aspirin (18.7%)
Apixaban + Aspirin (13.8%)
VKA + Placebo (10.9%)
Apixaban + Placebo (7.3%)

Apixaban + Placebo vs. VKA + Aspirin: 11.4% absolute risk reduction (NNT=9)
If VKA is chosen, INR target?

2018 North America Perspective
2018 CCS/CAIC guideline

If VKA is chosen, maintain INR at the lower end of the therapeutic range (e.g., 2.0 – 2.5).

2018 EHRA consensus document

TAT : INR 2.0-2.5 with high TTR (>65-70%)
DAT : INR 2.0-3.0 with high TTR
→ INR 2.0-2.5 + SAPT
→ INR 2.0-3.0 (OAC only)

Apixaban 5mg bid, edoxaban 60mg
Rivaroxaban 15mg
Dabigatran 110mg – discrete to physician

All RCTs (PIONEER AF, REDUAL-PCI, AUGUSTUS) – INR 2.0-3.0
Contents

✓ Guideline 에서 권고가 비슷한 부분

✓ Guideline 에서 차이가 있는 부분

✓ Cases about AF + PCI
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and an OAC.

**2018-2019 guidelines summary**

2018 ESC/EACTS, 2018 CHEST, 2018 Korea

**Patients with an indication for oral anticoagulation**

- Concerns about ischemic risk prevailing
- Concerns about bleeding risk prevailing

**2018 North America Perspective**

- **Time from PCI**
  - Peri-PCI
  - 1 month
  - 3 months
  - 6 months
  - 12 months
  - >12 months

- **Default strategy**
  - Triple Therapy (OAC + DAPT)
  - Double Therapy up to 12 months (OAC + SAPT)
  - OAC

- **Patients at high ischemic/thrombotic and low bleeding risks**
  - Triple Therapy (OAC + DAPT)
  - Double Therapy up to 1 month (OAC + SAPT)
  - OAC

- **Patients at low ischemic/thrombotic or high bleeding risks**
  - Triple Therapy (OAC + DAPT)
  - Double Therapy up to 6 months (OAC + SAPT)

**SAPT: prefer a P2Y12 inhibitor over aspirin**

- *Duration of triple in dual group*
- RE-DUAL PCI: 5 days
- PIONEER-AF PCI: 3 days
- AUGUSTUS: Random within 14 days

Clopidogrel is the P2Y12 inhibitor of choice; ticagrelor may represent a reasonable treatment option in patients at high ischemic/thrombotic and low bleeding risks; avoid prasugrel.
2018-2019 guidelines summary

2018 CCS/CAIC : practical guideline

AF and elective PCI without high-risk features

Age < 65 and CHADS₂ = 0
ASA + Clopidogrel
Duration: at least 1 month for BMS and at least 3 months for DES (and up to 12 months)
ASA +/- P₂Y₁₂ inhibitor

Age ≥ 65 or CHADS₂ = 1
OAC² + Clopidogrel
Duration: at least 1 month for BMS and at least 3 months for DES (and up to 12 months)
OAC⁴ +/- SAPT

AF and PCI for ACS or high-risk elective PCI

Age < 65 and CHADS₂ = 0
ASA + P₂Y₁₂ inhibitor² (ticagrelor, prasugrel preferred over clopidogrel for ACS)
Duration after PCI: Up to 12 months
ASA +/- P₂Y₁₂ inhibitor

Age ≥ 65 or CHADS₂ ≥ 1* Reduced OAC⁴ + ASA + clopidogrel
ASA: stop 1 day post PCI or any time up to 6 months² Followed by: clopidogrel + OAC
Duration after PCI: Up to 12 months
OAC⁶ +/- SAPT

* High risk features in CCS 2018
DM, prior ACS, prior stent thrombosis
CKD, current smoker
multi-vessel disease, multiple stents
total stent length > 60mm
bifurcation, CTO, BVS

* High risk features in EHRA 2018
Elective PCI: Syntax score
ACS: GRACE score > 140
LM, pLAD, bifurcation
Prior MI, prior stent thrombosis
Bleeding events mostly within 1 month

2000-2009 Denmark registry

Lamberts et al. Circulation 2012;126:1185
1. Longer triple duration: evidence (1)

**Stroke risk for patients with AF**

<table>
<thead>
<tr>
<th>CHADS2 score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>&gt;5</th>
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<tr>
<td></td>
<td>5</td>
<td>37</td>
<td>79</td>
<td>76</td>
<td>36</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(2.0)</td>
<td>(14.6)</td>
<td>(31.1)</td>
<td>(29.9)</td>
<td>(14.2)</td>
<td>(5.9)</td>
<td>(2.3)</td>
</tr>
</tbody>
</table>

**Differences:** mostly occurred within 6 weeks

**ACS:** 32% - STEMI 0.8%, NSTEMI 14.8%, UAP 16.4%

More history of CABG, more LM disease

CHADS2 score >3, 6 weeks group 22.4%, 6 months group 14.5%

**CONCLUSIONS**

The ISAR-TRIPLE trial did not show that 6 weeks of triple therapy was superior to 6 months with regard to the net clinical outcome. These results suggest that physicians should weigh the trade-off between ischemic and bleeding risk when choosing the shorter or longer duration of triple therapy.

1. Longer triple duration: evidence (1)

**Primary endpoint**
- Death, myocardial infarction, stent thrombosis, stroke or major bleeding
  - 6-week group: 6 (2.1)
  - 6-month group: 14 (4.7)
  - Hazard ratio (95% CI): 0.44 (0.17 - 1.12)
  - p value: 0.09

**Secondary endpoints**
- Cardiac death, myocardial infarction, stent thrombosis or ischemic stroke
  - 6-week group: 2 (0.7)
  - 6-month group: 6 (2.0)
  - Hazard ratio (95% CI): 0.34 (0.07 - 1.56)
  - p value: 0.19

**Landmark Analysis 6 weeks to 6 months**

<table>
<thead>
<tr>
<th>Landmark Analysis 6 weeks to 6 months</th>
<th>6-week group</th>
<th>6-month group</th>
<th>Hazard ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Death, myocardial infarction, stent</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>thrombosis, stroke or major bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (2.1)</td>
<td>14 (4.7)</td>
<td>0.44 (0.17 - 1.12)</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death, myocardial infarction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>stent thrombosis or ischemic stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (0.7)</td>
<td>6 (2.0)</td>
<td>0.34 (0.07 - 1.56)</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>Any BARC bleeding</td>
<td>31 (13.1)</td>
<td>55 (21.8)</td>
<td>0.57 (0.37 - 0.88)</td>
<td>0.01</td>
</tr>
<tr>
<td>BARC 1</td>
<td>19 (7.1)</td>
<td>27 (9.7)</td>
<td>0.72 (0.40 - 1.29)</td>
<td>0.27</td>
</tr>
<tr>
<td>BARC 2</td>
<td>4 (1.4)</td>
<td>14 (4.9)</td>
<td>0.28 (0.10 - 0.79)</td>
<td>0.03</td>
</tr>
<tr>
<td>BARC 3a</td>
<td>4 (1.4)</td>
<td>6 (2.1)</td>
<td>0.67 (0.19 - 2.36)</td>
<td>0.54</td>
</tr>
<tr>
<td>BARC 3b</td>
<td>4 (1.4)</td>
<td>8 (2.7)</td>
<td>0.51 (0.16 - 1.65)</td>
<td>0.27</td>
</tr>
<tr>
<td>BARC 3c</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARC 4</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARC 5a</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARC 5b</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARC bleeding ≥ 2</td>
<td>12 (4.5)</td>
<td>28 (10.3)</td>
<td>0.43 (0.22 - 0.82)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Non-adherent of clopidogrel (6 months) – DES

Primary end point: 6-week group 16.0% vs. 6-month group 7.7%
1. Longer triple duration: evidence (2)

Bern PCI registry, JACC Interv 2016;9:1473
1. Comments from 2019 AHA/ACC/HRS

8. 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$_2$-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$_{12}$ inhibitor) at 4 to 6 weeks may be considered (S7.4-9, S7.4-10).

NEW: New published data are available.

8. The ISAR-TRIPLE (Triple Therapy in Patients on Oral Anticoagulation After Drug Eluting Stent Implantation) trial (S7.4-9) was a randomized, open-label trial of patients receiving anticoagulation who underwent PCI with drug-eluting stents. Patients received concomitant anticoagulant and aspirin and were randomized to 6 weeks versus 6 months of clopidogrel. There was no difference between the 2 groups in terms of the primary composite endpoint of death, MI, definite stent thrombosis, stroke, or TIMI major bleeding or in terms of the secondary bleeding endpoint of TIMI major bleeding at 9 months (S7.4-9). The Bern PCI Registry (S7.4-10) is a prospective registry of consecutive patients who have undergone PCI for stable coronary artery disease or ACS at Bern University Hospital since 2009. Among patients who were discharged on triple therapy, there was no difference between ≤1 month versus >1 month of triple therapy in the primary composite endpoint of cardiac death, MI, stroke, definite stent thrombosis, or TIMI major bleeding at 1 year (S7.4-10). Although both the ISAR-TRIPLE trial and the Bern PCI Registry have limitations, the consistent finding in both patients with ACS and patients with stable ischemic heart disease suggests that with current drug-eluting stents, selecting bare metal stents to shorten the duration of DAPT is no longer indicated. Of the patients treated with triple therapy for 1 month in the Bern PCI Registry, 60% were treated with a current-generation drug-eluting stent.
2. OAC monotherapy after 1-year?

Table 3: Summary of main recommendations in recent guidelines

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>ESC myocardial revascularization 2017 (143)</th>
<th>ESC AF 2016(2)</th>
<th>ACC/AHA 2016 combined OAC/APT (144)</th>
<th>ESC 2017 DAPT update(5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of periprocedural aspirin and clopidogrel</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>++</td>
</tr>
<tr>
<td>Preferred use of DES</td>
<td>++</td>
<td>—</td>
<td>—</td>
<td>n/a</td>
</tr>
<tr>
<td>Recommendations according to the type of platform (DES vs. BMS)</td>
<td>n/a</td>
<td>—</td>
<td>++</td>
<td>n/a</td>
</tr>
<tr>
<td>Use of ticagrelor or prasugrel</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Use of specific score for ischaemic or bleeding risks</td>
<td>++</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>DAPT as an alternative to TAT in CHA2DS2-VASc score ≤ 1</td>
<td>++</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>DAT as an alternative to initial TAT</td>
<td>+</td>
<td>+</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>1–6 months as the default strategy in ACS patients</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Use of NOAC</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Stopping aspirin rather than clopidogrel</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Stopping all antiplatelet therapy after 1 year</td>
<td>n/a</td>
<td>++</td>
<td>n/a</td>
<td>++</td>
</tr>
</tbody>
</table>

++, recommended; +, may be considered; −, not recommended by the relevant guideline; ACS, acute coronary syndrome; BMS, bare-metal stent; DAT, dual therapy; DES, drug-eluting stent; n/a, box means not stated; NOAC, non-vitamin K antagonist oral anticoagulant; TAT, triple therapy.

Discontinuation of antiplatelet treatment in patients treated with OAC should be considered at 12 months.753
Evidence of OAC monotherapy (1)

2002-2011 Denmark registry, 8,700 stable coronary artery disease
(No event during 1-year after AF MI or PCI)

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>MI/coronary death</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA plus aspirin plus clopidogrel</td>
<td></td>
<td>1.76 [1.05-2.94]</td>
</tr>
<tr>
<td>VKA plus clopidogrel</td>
<td></td>
<td>1.53 [0.93-2.52]</td>
</tr>
<tr>
<td>VKA plus aspirin</td>
<td></td>
<td>1.12 [0.94-1.34]</td>
</tr>
<tr>
<td>VKA</td>
<td></td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Aspirin plus clopidogrel</td>
<td></td>
<td>2.24 [1.76-2.84]</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td></td>
<td>1.73 [1.27-2.34]</td>
</tr>
<tr>
<td>Aspirin</td>
<td></td>
<td>1.73 [1.48-2.02]</td>
</tr>
</tbody>
</table>

Hazard Ratio
(Horizontal bars indicate 95% confidence interval)

Lamberts et al. Circulation 2014;129:1577
Evidence of OAC monotherapy (1)

2002-2011 Denmark registry, 8,700 stable coronary artery disease
(No event during 1-year after AF MI or PCI)

Bleeding events

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA plus aspirin plus clopidogrel</td>
<td>2.81 [1.82-4.33]</td>
</tr>
<tr>
<td>VKA plus clopidogrel</td>
<td>1.84 [1.11-3.06]</td>
</tr>
<tr>
<td>VKA plus aspirin</td>
<td>1.50 [1.23-1.82]</td>
</tr>
<tr>
<td>VKA</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Aspirin plus clopidogrel</td>
<td>1.04 [0.76-1.42]</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>1.12 [0.75-1.65]</td>
</tr>
<tr>
<td>Aspirin</td>
<td>0.72 [0.59-0.87]</td>
</tr>
</tbody>
</table>

Hazard Ratio
(Horizontal bars indicate 95% confidence interval)

Lamberts et al. Circulation 2014;129:1577
Evidence of OAC monotherapy (1)

2002-2011 Denmark registry, 8,700 stable coronary artery disease
(No event during 1-year after AF MI or PCI)

Thromboembolism

<table>
<thead>
<tr>
<th>Treatment regimen</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA plus aspirin plus clopidogrel</td>
<td>1.31 [0.66-2.59]</td>
</tr>
<tr>
<td>VKA plus clopidogrel</td>
<td>1.56 [0.84-2.90]</td>
</tr>
<tr>
<td>VKA plus aspirin</td>
<td>0.86 [0.67-1.09]</td>
</tr>
<tr>
<td>VKA</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Aspirin plus clopidogrel</td>
<td>1.77 [1.32-2.38]</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>1.73 [1.18-2.53]</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1.34 [1.13-1.70]</td>
</tr>
</tbody>
</table>

Lamberts et al. Circulation 2014;129:1577
Evidence of OAC monotherapy (2)

2010.2-2011.4 CORONOR study, 4,184 stable coronary artery disease
Previous MI 62.4%, previous PCI 85.9%, stroke 7.4%  JACC 2014;64:1430

Ischemic event: similar

JACC 2014;64:1437
large randomised trials done in patients who survived after myocardial infarction to compare oral anticoagulation with aspirin in the prevention of reinfarction and stroke. Lower recurrence rates but higher risks of bleeding were associated with oral anticoagulation.\(^{16,17}\)

Thus, oral anticoagulation was at least as good as aspirin in protecting patients from thrombotic events. The

Nevertheless, this study was not powered to detect differences in the occurrence of thrombotic events, such as stent thrombosis, when aspirin was omitted, and this feature would need to be studied in a larger trial. A very large trial, however, is unlikely to be done because of lack of interest to sponsors. Therefore, on the basis of
1st RCT about OAC monotherapy – All Okay

OAC–ALONE: No Clear Answer for Best Therapy Beyond 1 Year After PCI in A–fib Patients

Slow enrollment led to a premature end to the study, making it difficult to draw firm conclusions.

By Todd Neale | September 24, 2018

<table>
<thead>
<tr>
<th>End Points</th>
<th>OAC Alone (N=344)</th>
<th>Combined OAC and APT (N=346)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Noninferiority</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point</td>
<td>No. of Patients With Event (Crude Incidence Rate/Annualized Event Rate, %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A composite of all-cause death, myocardial infarction, stroke, or systemic embolism</td>
<td>54 (15.7/6.4)</td>
<td>47 (13.6/5.5)</td>
<td>1.16 (0.79–1.72)</td>
<td>0.20</td>
<td>0.45</td>
</tr>
<tr>
<td>Major secondary end point</td>
<td>A composite of all-cause death, myocardial infarction, stroke, systemic embolism, or ISTH major bleeding</td>
<td>67 (19.5/8.1)</td>
<td>67 (19.4/8.2)</td>
<td>0.99 (0.71–1.39)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Bhatt said that even though practice should not be altered on the basis of this trial, OAC–ALONE could serve as a platform on which to build future studies. “The question is important, but it would really require a well–designed trial to nail it down,” he commented.

Asked whether the trial—which was limited by the premature stop, the lack of statistical power, the failure to establish noninferiority for the primary endpoint, and differences in INR targets between Japan and other parts of the world—is likely to induce US doctors to change their practice, Bhatt said it might.
Recent guidelines – tone down

Long-term antithrombotic therapy (beyond 12 months) is recommended with OAC in all patients.

- Combination OAC plus single antiplatelet therapy (i.e. aspirin) may sometimes be continued in very selected cases, e.g. stenting of the left main, proximal bifurcation, recurrent MI etc.

2018 EHRA expert consensus

*31. For patients with AF and stable coronary artery disease (e.g., no acute coronary syndrome within the previous year) and who choose oral anticoagulation, we suggest OAC with either an NOAC or adjusted-dose VKA therapy alone (target international normalized ratio [INR] range, 2.0-3.0) rather than the combination of OAC and aspirin (Weak recommendation, low quality evidence).

2018 CHEST guideline

2018 North America Perspective

- Discontinue SAPT at 1 year in most patients; consider earlier SAPT discontinuation (e.g., 6 months) in patients at low ischemic or high bleeding risks and prolonging SAPT (>1 year) for select patients with high ischemic and low bleeding risks.
3. Same data, EU: both no/US: ticagrelor OK

Regular Article

Concomitant use of warfarin and ticagrelor as an alternative to triple antithrombotic therapy after an acute coronary syndrome

Oscar Ø. Braun 4, Besim Bico 4, Uzma Chaudhry 5, Henrik Wagner 5, Sasha Koul 4, Patrik Tydén 4, Fredrik Scherstén 6, Stefan Jovinge 6, Peter J. Svensson 6, J. Gustav Smith 6, Jesper van der Pals 4

Departments of Cardiology, Sahlgrenska University Hospital, Lund University, Lund and Malmö, Sweden

Department of Internal Medicine, Helsingborg Hospital, Lund University, Lund and Helsingborg, Sweden

Department for Cardiology, Sahlgrenska University Hospital, Lund University, Lund and Malmö, Sweden

Table 1

<table>
<thead>
<tr>
<th>Characteristic, n (%)</th>
<th>TT (n = 159)</th>
<th>DT (n = 107)</th>
<th>p-value</th>
</tr>
</thead>
</table>

TT: aspirin, clopidogrel, warfarin, DT: ticagrelor, warfarin

JACC 2013:61:2060

More bleeding in prasugrel

- Patient-reported bleeding
- Similar rehospitalized

11,756 PCI-treated acute MI patients discharged on either dual antiplatelet or triple antithrombotic therapy

Triple-C (n=526)  Triple-P (n=91)  Dual-C (n=7715)  Dual-P (n=3424)

Rehospitalized bleeding

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Rate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple-C vs. dual-C</td>
<td>46 (10.9) vs. 217 (3.4)</td>
<td>3.13 (1.97-4.96) &lt; 0.0001</td>
</tr>
<tr>
<td>Triple-P vs. dual-P</td>
<td>6 (9.7) vs. 71 (2.8)</td>
<td>4.91 (1.36-17.7) 0.0150</td>
</tr>
<tr>
<td>Triple-P vs. triple-C</td>
<td>4 (7.8) vs. 16 (7.8)</td>
<td>0.62 (0.20-1.93) 0.4127</td>
</tr>
</tbody>
</table>
Guideline에서 권고가 비슷한 부분

Guideline에서 차이가 있는 부분

Cases about AF + PCI
Case 1. 64-year-old male in OPD

C/C  Chest pain (2 months ago, CCS 2 → 3)

P/H  renal infarction with atrial fibrillation (5 months ago)

med : rivaroxaban 20mg, rosuzet 10/5mg, bisoprolol 1.25mg, perindopril 2mg
Coronary angiogram

LM with 3 vessel disease – multiple stents, long segment stents
CABG recommend → patient refuse
PCI for LCX, LM bifurcation, LAD, RCA
Final angiogram

LAD 3.0x38mm + 2.75x24mm/LCX 2.5x38mm + 2.75x22mm/RCA 2.75x26mm

5 stents, total stent length 148mm
This patient → LM with 3vv, 64yr, renal infarction

- High ischemic risk with relatively low bleeding risk
  - Cr 1.52, CrCl 49.3ml/min

- 2 weeks triple therapy → dual
  - aspirin + clopidogrel + apixaban 5mg bid
  - clopidogrel 75mg + apixaban 5mg bid

- Planned apixaban 5mg bid + aspirin 100mg after 1 year
Case 2. 84-year-old male in ER 18.12.29

C/C Chest pain (3 hours ago)

P/H Benign prostate hypertrophy – repetitive operation
Urgent coronary angiogram
Urgent coronary angiogram

No significant stenosis in left coronary artery
Thrombotic near total occlusion in RCA ostium
PCI for RCA ostium
 PCI for RCA ostium

Xience Sierra 3.5x15mm
EKG after PCI
This patient → RCA STEMI, AF, 84 years

✓ Embolic > plaque rupture

  : relatively no atherosclerotic changes in other vessel, lesion..

✓ 41kg (<60kg), 145cm, Cr 1.6 (>1.5) (GFR 20 ml/min)

✓ Concerns more about bleeding & embolic stroke

  : aspirin, clopidogrel, heparinization for 7 days

  clopidogrel + apixaban 2.5mg bid change before discharge

✓ No events during 6 months FU
Thank you For Listening!!

No greater opportunity, responsibility, or obligation can fall to the lot of a human being than to become a physician. In the care of the suffering he needs technical skill, scientific knowledge, and human understanding. He who uses these with courage, with humility, and with wisdom will provide a unique service for his fellow man, and will build an enduring edifice of character within himself. The physician should ask of his destiny no more than this; he should be content with no less.

Page 1, paragraph 1, Edition 1, Harrison’s Introduction, Harrison’s Principles of Internal Medicine, 1950.

human understanding.... Tact, sympathy, and understanding are expected of the physician, for the patient is no mere collection of symptoms, signs, disordered functions, damaged organs, and disturbed emotions. [The patient] is human, fearful, and hopeful, seeking relief, help, and reassurance.

—Harrison’s Principles of Internal Medicine, 1950