Management of antithrombotic therapy in AF patients presenting with ACS and/or undergoing PCI

A Summary of the 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)

Since publication of the 2014 joint consensus document dealing with the management of antithrombotic therapy in atrial fibrillation (AF) patients presenting with acute coronary syndrome (ACS) and/or undergoing percutaneous coronary (PCI) or valve interventions, which represented an effort of the European Society of Cardiology Working Group (ESC) on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA), 1 endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS) there have been additional data from observational cohorts, randomized controlled trials and advances in percutaneous interventions.

New guidelines have also been published, as well as new drugs, devices, and interventional techniques in AF, ACS management, and PCI.2,3 Atrial fibrillation management has also evolved towards a more integrated or holistic approach that includes the following components:

- ‘A’ Avoid stroke with Anticoagulation;
- ‘B’ Better symptom management, with patient centred decisions on rate or rhythm control; and
- ‘C’ Cardiovascular and comorbidity risk management, including lifestyle changes.4

In recognizing this new information since the last consensus document, a Task Force was convened by EHRA, WG Thrombosis, EAPCI, and ACCA, with additional contribution from HRS, APHRS, Latin America Heart Rhythm Society (LAHRS), and Cardiac Arrhythmia Society of Southern Africa (CASSA), to produce an updated consensus document, with the remit of comprehensively reviewing the available evidence and providing up-to-date consensus recommendations for use in clinical practice.

The consensus document has been written by 16 authors, chaired by Gregory Y.H. Lip (UK) and co-chaired by Jean-Philippe Collet (France), Michael Haude (Germany), and Kurt Huber (Austria). In addition, a group of 22 reviewers co-ordinated by Tatjana Potpara (Serbia) revised the manuscript introducing many suggestions and criticisms, which contributed to the quality and comprehensiveness of the manuscript.

The full version of this important consensus document is published in EP Europace.5 We hope this consensus document is user-friendly, based on ranking using the EHRA ‘coloured hearts’ system that should allow physicians to easily assess the current status of the evidence and offer consequent guidance. The ultimate aim of the Task Force was to prepare an expert consensus and evidence-based document reviewing the best available scientific evidence on this growing issue, and to update the current knowledge in this field, not only for the cardiology community but also for other specialists who see patients with AF and acute or stable coronary artery disease, particularly cardiologists, general internists, and general practitioners, which have to make daily decisions on such patients in clinical routine.
Main consensus statements

General management considerations

- The period of triple antithrombotic therapy (TAT) should be as short as possible, followed by OAC plus a single antiplatelet agent (clopidogrel 75 mg once a day (o.d.), or alternatively, aspirin 75–100 mg o.d.]
- The duration of TAT is dependent on acute vs. elective procedures, bleeding risk (as assessed by the HAS-BLED score), as well as on type of stent (with a preference for new-generation drug eluting stent (DES) or bare metal stent (BMS)).
- In AF patients, stroke risk must be assessed using the CHA2DS2-VASc score, and bleeding risk assessed using the HAS-BLED score.
- Suboptimal stent placement should be avoided in selected cases by use of intracoronary imaging techniques.
- An initial period of triple therapy should be used in most AF patients undergoing PCI, depending on presentation (ACS vs. elective), stroke vs. bleeding risk, and procedural considerations (e.g. stent type, disease severity etc.)
- Dual therapy with oral anticoagulant (OAC) plus one P2Y12 inhibitor (usually clopidogrel) may be considered in patients who are predisposed to excessive bleeding risk and have low thrombotic risk.
- Dual therapy with rivaroxaban or dabigatran and a P2Y12 inhibitor is associated with a lower risk of bleeding than triple therapy with warfarin, but none have been sufficiently evaluated with respect to efficacy.
- When dabigatran is used as part of dual therapy, the standard doses of 150 mg twice a day (b.i.d.) should be used to reduce the risk of ischaemic events
- dabigatran 110 mg b.i.d. can be considered in elderly patients, concomitant when Pgp inhibitors (e.g. verapamil) are used, and in patients with high bleeding risk.
- When rivaroxaban is used as part of dual therapy, reduced dose 15 mg o.d. should be considered, especially in patients with moderate renal impairment or those at high-bleeding risk.
- When apixaban or edoxaban are used as part of triple or dual therapy, the standard dose (5 mg b.i.d. and 60 mg o.d. respectively, unless label-guided dose reduction is indicated) should be selected pending results of ongoing trials (studies still ongoing).
- When a vitamin K antagonist (VKA) is given in combination with clopidogrel and/or low-dose aspirin, the dose intensity of VKA should be carefully regulated, with a target INR range of 2.0–2.5.
- Good quality anticoagulation is recommended, with a high time in therapeutic range (TTR >65–70%) aimed for.
- In patients on VKA undergoing coronary angiography and/or PCI, an uninterrupted VKA strategy is at least as safe as interrupted VKA, and seems to be much safer than interrupted VKA with bridging anticoagulation.
- In anticoagulated patients, pre-treatment with antiplatelet therapy is appropriate if VKA is planned but avoid pre-treatment with P2Y12 inhibitors if the coronary anatomy is not known.
- Clopidogrel is the P2Y12 inhibitor of choice in anticoagulated patients; prasugrel and ticagrelor should be avoided due to their higher bleeding risk.
- Novel oral anticoagulants (NOACs) as part of triple or dual therapy are safer than VKA (e.g. warfarin) with respect to bleeding risk, and are the preferred option in the absence of contraindications to use of these drugs.
- Atrial fibrillation patients with CHA2DS2-VASc score ≥2 treated with a NOAC should continue their NOAC with addition of antiplatelets after PCI/ACS up to 12 months.
- Inpatients with AF and stable vascular disease (arbitrarily defined as being free from any acute ischaemic event or repeat revascularization for >1 year) the patient should be managed with OAC alone.
- Radial access should be considered as the default approach for coronary angiography/intervention to minimize the risk of access-related bleeding depending on operator expertise and preference.
- Gastric protection with proton pump inhibitors (PPIs) should be considered in all patients with OAC plus antiplatelet therapy.

Elective or stable coronary artery disease (CAD)

- For NOAC-treated patients undergoing elective PCI, timed cessation (e.g. >12–48 h) before intervention may be considered, depending on the agent and renal function and use of standard local anticoagulation practices peri-procedurally.
- Early after PCI, such as the same evening or the next morning, NOAC therapy should be restarted.
- In patients with stable CAD and AF undergoing PCI at low bleeding risk (HAS-BLED ≤2), triple therapy (OAC, aspirin 75–100 mg daily, clopidogrel 75 mg daily) should be given for a minimum of 4 weeks (and no longer than 6 months) after PCI following which dual therapy with OAC and clopidogrel 75 mg/day (or alternatively, aspirin 75–100 mg/day) should be continued for up to 6–12 months.
- In patients with stable CAD and AF undergoing PCI at high bleeding risk (HAS-BLED ≥3), triple therapy ([N]OAC, aspirin 75–100 mg daily, and clopidogrel 75 mg daily) or dual therapy consisting of ([N]OAC and clopidogrel 75 mg/day should be given for 1 month after PCI following which dual therapy with OAC and clopidogrel 75 mg/day (or alternatively, aspirin 75–100 mg/day) should be continued for up to 6 months, beyond which patients would be managed on ([N]OAC alone.
- In patients with stable CAD and AF undergoing PCI at very high bleeding risk (e.g. recent bleeding event), aspirin may be omitted, and dual therapy with a NOAC and clopidogrel 75 mg/day continued for 3–6 months, beyond which patients would be managed on ([N]OAC alone.
- Long-term antithrombotic therapy with OAC monotherapy (beyond 12 months) is recommended in all patients, but combination OAC plus single antiplatelet therapy (i.e. aspirin) may be considered in very selected cases with an increased ongoing ischaemic risk.
When the procedures require interruption of OAC for longer than 48 h in high-risk patients (i.e. TAVI or other non-PCI procedures at high bleeding risk), enoxaparin may be administered subcutaneously, although the efficacy of this strategy is uncertain. (Based on pharmacodynamic data enoxaparin might be a better option than unfractionated heparin, because of the more predictable and stable level of anticoagulation.)

Such 'bridging' therapies may actually be associated with an excess bleeding risk, possibly due to dual modes of anticoagulation in the overlap periods. When NOACs are used, timing of any bridging therapy should be tailored on the basis of renal function and the pharmacokinetics of the specific NOAC.

NSTE-ACS including unstable angina and NSTEMI

- In patients on OAC developing a NSTE-ACS, aspirin loading should be as in STEMI, and clopidogrel is again the P2Y12 inhibitor of choice.
- Pre-treatment with P2Y12 receptor antagonists may be withheld until the time of coronary angiography in case of an early invasive strategy within 24 h.
- An early invasive strategy (within 24 h) should be preferred among AF patients with moderate to high-risk NSTE-ACS in order to expedite treatment allocation (medical vs. PCI vs. CABG) and to determine the optimal antithrombotic regimen.
- The use of ticagrelor or prasugrel in combination with OAC may only be considered under certain circumstances (e.g. definite stent thrombosis while on clopidogrel, aspirin, and OAC; known clopidogrel resistance).
- Triple therapy is still the recommended initial treatment for the first month after PCI or an ACS in AF patients with a high-ischaemic risk and a low bleeding risk.
- In AF patients with ACS at low risk of bleeding (HAS-BLED 0–2), the initial use of triple therapy [(N)OAC, aspirin, and clopidogrel] should be considered for 3–6 months following PCI irrespective of stent type; this should be followed by long-term therapy (up to 12 months) with OAC and clopidogrel 75 mg/day (or alternatively, aspirin 75–100 mg/day).
- In patients with ACS and AF at high risk of bleeding (HAS-BLED ≥3), the initial use of triple therapy [(N)OAC, aspirin, and clopidogrel] should be considered for 4 weeks following PCI irrespective of stent type; this should be followed by long-term therapy (up to 12 months) with (N)OAC and clopidogrel 75 mg/day (or alternatively, aspirin 75–100 mg/day).
- In patients at very high bleeding risk (e.g. recent bleeding event), aspirin may be omitted, and dual therapy with a (N)OAC and clopidogrel 75 mg/day continued for 3–6 months, beyond which patients would be managed on (N)OAC alone.
- Long-term antithrombotic therapy (beyond 12 months) is recommended with OAC (VKA or a NOAC) in all patients.
- Long-term combination OAC plus single antiplatelet therapy (i.e. aspirin) may be considered in very selected cases, e.g. stenting of the left main, proximal left anterior descending, proximal bifurcation, recurrent MIs etc.

Primary PCI

- When anticoagulated patients present with a STEMI, they should be triaged for primary PCI regardless of the anticipated time to PCI-mediated reperfusion.
- In the setting of STEMI, radial access for primary PCI is the best option to avoid procedural bleeding depending on operator expertise and preference.
- In patients with STEMI and AF at low risk of bleeding (HAS-BLED 0–2), the initial use of triple therapy [(N)OAC, aspirin, and clopidogrel] should be considered for 6 months following PCI irrespective of stent type; this should be followed by long-term therapy (up to 12 months) with (N)OAC and clopidogrel 75 mg/day (or alternatively, aspirin 75–100 mg/day).
- In patients with STEMI and AF at high risk of bleeding (HAS-BLED ≥3), the initial use of triple therapy [(N)OAC, aspirin, and clopidogrel] should be considered for 4 weeks following PCI irrespective of stent type; this should be followed by long-term therapy (up to 12 months) with (N)OAC and clopidogrel 75 mg/day (or alternatively, aspirin 75–100 mg/day).
- In patients at very high bleeding risk (e.g. recent bleeding event), aspirin may be omitted, and dual therapy with a (N)OAC and clopidogrel 75 mg/day continued for 3–6 months, beyond which patients would be managed on (N)OAC alone.
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References

References are available as supplementary material at European Heart Journal online.