Guidance for the use of both an anticoagulant and an antiplatelet

This guidance has been produced in response to queries raised within primary care when patients are discharged from secondary care, having been prescribed both an antiplatelet and an anticoagulant.

Please note: *Primary care clinicians are not expected to initiate an anticoagulant plus an antiplatelet. This guidance is for information only in order to provide background for when patients are discharged from secondary care on this combination therapy.*

The optimal strategy to balance the risk of bleeding events and recurrent ischaemic events in people needing antiplatelets and anticoagulants is subject to debate as specifically designed and powered studies are not available, relying on expert consensus instead (UKMI 2015). The choice of therapy and its duration is individualised, based on atherothrombotic risk, cardioembolic risk, and bleeding risk.

Patients with atrial fibrillation (AF), mechanical heart valves or a history of pulmonary emboli are at high risk of stroke or thromboembolism and therefore require anticoagulation to prevent these events. It is important to note that a significant number of these patients also have an indication for an antiplatelet, and many patients taking an antiplatelet also have an indication for an anticoagulant:

- Around a third of patients with AF also have coronary artery disease.
- Between 6% and 21% of patients with ACS (Acute Coronary Syndrome) go on to develop AF.

This is a complex problem to manage because:

- Dual antiplatelet therapy reduces the risk of ischaemic cardiac events but not AF related thrombotic stroke.
- Anticoagulants reduce the risk of AF related thrombotic stroke but not of cardiac ischaemic events.
- The combination of dual-antiplatelet therapy plus anticoagulant (referred to as “triple oral antithrombotic therapy” or “triple therapy”) increases the risk of bleeding events by about 2-4 times compared to anticoagulant or aspirin alone.

A recent meta-analysis (Oldgren 2013) involving 30,866 patients with a recent ACS evaluated the effects of adding NOAC therapy to single (4135 patients) or dual (26,731 patients) antiplatelet therapy. The addition of a NOAC increased the bleeding risk by 79–134%, while reducing recurrent ischaemic events only marginally in patients without AF.

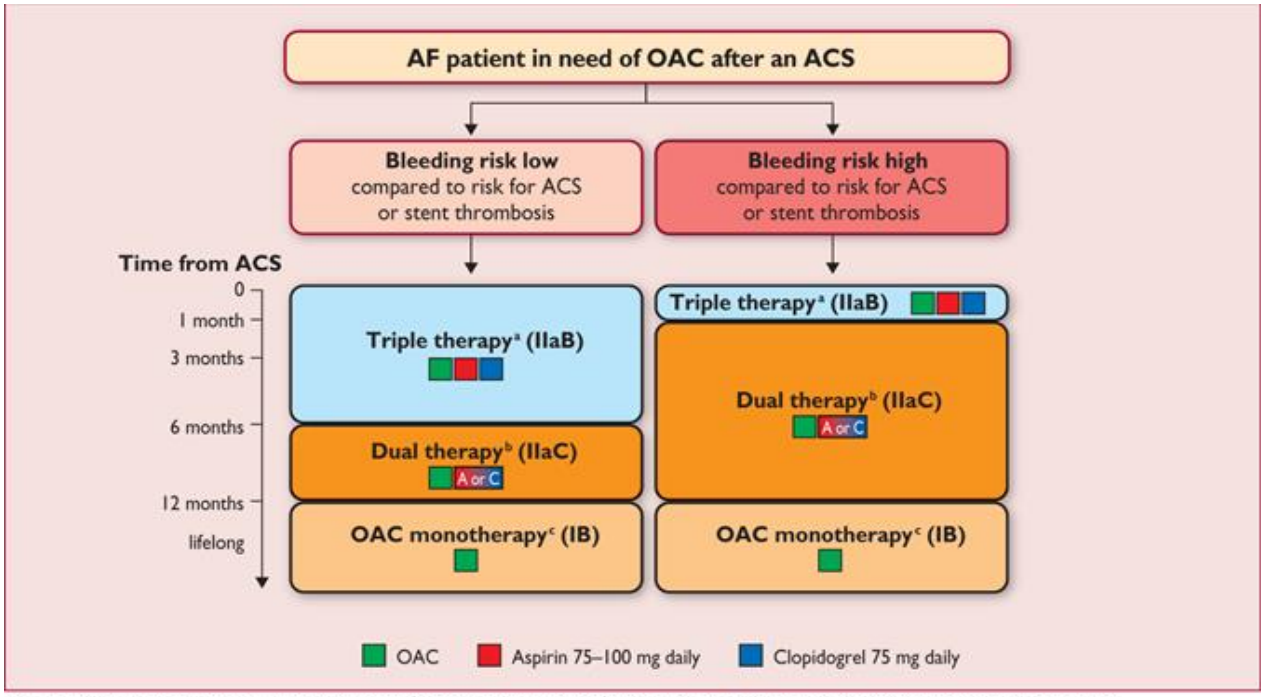
Patients on anticoagulant therapy who develop an indication for antiplatelet:
(Most commonly patients with atrial fibrillation but also includes patients with recent or recurrent deep vein thrombosis or pulmonary embolism)

Patients treated for ACS (in past 12 months) or receiving coronary stent (Sheffield 2015; ESC 2016)

- Short-term triple combination therapy of OAC, clopidogrel, and aspirin seems warranted. Triple therapy would be indicated for 4 weeks, followed by aspirin plus warfarin for up to 12 months. (See figures 1 and 2 below)
- If a NOAC is used then the lowest dose effective for stroke prevention should be considered. Please note: the combination aspirin plus clopidogrel plus low dose rivaroxaban (2.5mg twice daily) is not recommended for stroke prevention in AF). (ESC 2016)
- The use of prasugrel or ticagrelor as part of triple therapy should be avoided unless a clear need is identified (e.g. stent thrombosis on aspirin plus clopidogrel) (ESC 2016)

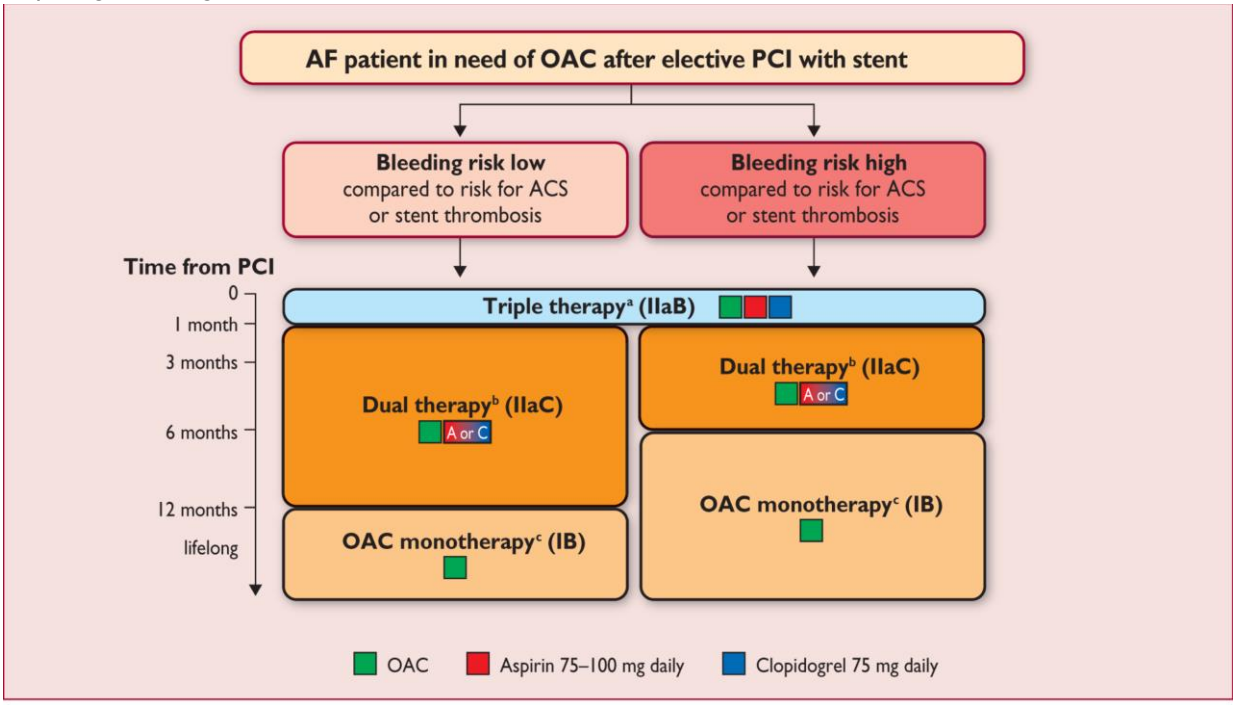
Triple therapy (two antiplatelets plus oral anticoagulant) may be indicated in certain circumstances (e.g. low bleed risk, or high stroke risk). This will be a specialist decision and should be clearly documented, the duration of triple therapy will differ and will be decided on a case by case basis. If dual antiplatelet therapy is indicated: use warfarin for anticoagulation (not NOAC).

Fig 1: Antithrombotic therapy after an acute coronary syndrome in atrial fibrillation patients requiring anticoagulation (ESC 2016)



ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.
[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients, especially those not receiving a stent or patients at a longer time from the index event.
[b]OAC plus single antiplatelet.
[c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Fig 2: Antithrombotic therapy after elective percutaneous intervention in atrial fibrillation patients requiring anticoagulation



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[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients.
[b]OAC plus single antiplatelet.
[c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Patients on antiplatelet therapy who develop an indication for warfarin:

- Patients receiving an anti-platelet agent as primary prophylaxis for CVD on developing an indication for warfarin should stop their antiplatelet agent. (Keeling 2011)
- Patients with peripheral artery disease or previous ischaemic stroke on antiplatelet therapy should stop this agent if warfarin is commenced. (Keeling 2011)
- Patients on antiplatelet as secondary prophylaxis with stable ischaemic heart disease (often defined as >12 months following ACS) should stop their antiplatelet agent while being treated with warfarin. (Keeling 2011)
- Patients with stable CHD without previous PCI should stop antiplatelets once patient is anticoagulated. (Sheffield 2015, Keeling 2011)
- Patients on a single antiplatelet agent <12 months following an ACS, who require to start warfarin therapy should continue aspirin therapy until 12 months post ACS, unless they are regarded as having a high bleeding risk.
- Patients on aspirin and clopidogrel, following an ACS or stent placement, who develop an indication for warfarin should be carefully assessed for bleeding risk and discussed with their cardiologist, with a view to introducing warfarin and minimizing the duration of triple therapy.

Assessing the bleeding risk

The HAS-BLED bleeding risk score was developed for use in patients with atrial fibrillation. There are no other assessment tools for overall bleeding risk in patients who do not have AF, therefore, the HAS-BLED bleeding risk tool is provided below to give an indication of the clinical situations which would be considered as having an increased bleeding risk.

HAS-BLED bleeding risk score

Hypertension	>160mmHg	1
Abnormal renal and liver function	Chronic dialysis, renal transplantation or creatinine >200µmol/l Chronic hepatic disease or biochemical evidence (e.g. bilirubin > 2 x ULN in association with ALT or Alk Phos > 3 x ULN)	1 or 2 (1 point each)
Stroke		1
Bleeding	Previous bleeding history and/or predisposition to bleeding e.g. bleeding diathesis, anaemia etc	1
Labile INRs	Unstable/high INRs or poor time in therapeutic range (e.g. <60%)	1
Elderly	>65	1
Drugs/alcohol	Concomitant use of drugs such as antiplatelets, NSAIDs or alcohol abuse. etc	1 or 2
≥ 3 indicates high bleeding risk		

A score of 0-2 indicates low risk.
A score of ≥ 3 indicates high risk. This suggests that the bleeding risk is such that caution and/or regular review is recommended.

Communication

If an antiplatelet is indicated, in addition to oral anticoagulation, then this must be clearly communicated between care providers, preferably by documenting the need for combination therapy in the oral anticoagulant therapy record book. The following points should be communicated:

- Indication for antiplatelet
- Indication for anticoagulant
- Duration of therapy

Development Process

This guidance has been produced by Medicines Management Team, Barnsley CCG in consultation with Cardiologists at BHNFT. This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 12th June 2017 and the LMC in August 2017.

References

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