Composing Antiplatlet Drugs and Oral Anticoagulant Therapy in Atrial Fibrillation: Acute Coronary Syndromes and/or Percutaneous Coronary Intervention/Stenting Revisited

To the Editor:

We agree with Gorelic	extsuperscript{1} that there is little evidence that combination aspirin and oral anticoagulant (OAC) therapy among patients with atrial fibrillation (AF) improves stroke prevention but, instead, increases risk of major bleeding. The latter should come as little surprise, given the mode of action of both drugs.

Indeed, the efficacy of OAC compared with aspirin in this condition is overwhelmingly supported by data from clinical trials.\textsuperscript{2} However, AF commonly associates with (cardio)vascular disease, and frequently AF patients are still prescribed both OAC and antiplatelet therapies in combination. In the setting of AF and acute coronary syndromes (ACS) or coronary angioplasty/stents, it is not infrequent for patients to be prescribed ‘triple therapy’ with OAC, aspirin and clopidogrel.

Gorelick\textsuperscript{1} provides a critique on the recent article by Flaker et al.,\textsuperscript{3} but broad similar conclusions were reported from the FFAACS trial,\textsuperscript{4} where fluindione (an OAC) plus aspirin was compared with fluindione alone, and no difference in thromboembolism rate was reported between the 2 arms, although combination therapy did significantly increase bleeding rate (13.1\% versus 1.2\%, \textit{P}=0.003).

Given the rising prevalence of AF and coexistent vascular disease, as well as increasing application of percutaneous coronary angioplasty/stenting, the coprescription of OAC and antiplatelet agents is likely to surge. The ACC/AHA/ESC\textsuperscript{5} 2006 Guidelines for the Management of Patients with AF\textsuperscript{5} suggest that after angioplasty/stenting, low-dose aspirin (<100 mg/d) and/or clopidogrel (75 mg/d) may be given concurrently with anticoagulation to prevent myocardial ischemic events, but acknowledges these strategies have not been thoroughly evaluated and are associated with an increased risk of bleeding. These recommendations do not give a differential management strategy in relation to an ACS presentation or the perceived bleeding risk.

Given recent concerns over late stent thrombosis with drug eluting stents, the likelihood of some AF patients at high risk of stroke being coprescribed OAC plus aspirin plus clopidogrel for 12 months (or more) by some cardiologists is real, with the associated high bleeding risk.\textsuperscript{6} Other practical management guidance for AF patient presenting with ACS and/or need angioplasty/stenting have tried to relate the approach to stroke risk, associated ACS presentation, bleeding risk and/or type of stent used\textsuperscript{7} (Table). The choice of warfarin plus clopidogrel long-term\textsuperscript{8} may seem an ‘evidence free’ zone, but given data demonstrating that the combination of OAC plus aspirin is inadequate to prevent coronary stent thrombosis,\textsuperscript{9} and that OAC alone is marginally different from ‘OAC plus aspirin’ in ACS for reducing coronary events but increases bleeding,\textsuperscript{7,9} more prospective data are urgently required.

Clearly, a very careful balance is needed between stroke prevention (especially in a ‘high risk’ AF patient requiring OAC), recurrent cardiac ischemia (eg, post-ACS and/or stent use) and bleeding risk attributed to adding antiplatelet therapy to OAC use.

Disclosures

None.

Timothy Watson, MRCP
Gregory Y.H. Lip, MD, FRCP
University Department of Medicine
City Hospital
Birmingham, UK

Table. Suggested Management Strategy for Patients With Nonvalvular Atrial Fibrillation Requiring Anticoagulation, and Percutaneous Coronary Intervention With Stenting*

<table>
<thead>
<tr>
<th>Stroke Risk Category</th>
<th>‘Usual’ Strategy Recommended</th>
<th>Perceived Potential Bleeding Risk</th>
<th>ACS Presentation</th>
<th>Post PCI Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Aspirin</td>
<td>...</td>
<td>...</td>
<td>Bare metal stent— aspirin plus clopidogrel for 4 weeks, then aspirin DES—aspirin plus clopidogrel for 6–12 months, then aspirin</td>
</tr>
<tr>
<td>High</td>
<td>Warfarin</td>
<td>Low</td>
<td>No</td>
<td>Use bare metal stent if possible Bare metal stent—triple therapy with warfarin, aspirin plus clopidogrel for 2–4 weeks; then change to warfarin plus clopidogrel for up to month 12, then warfarin alone DES—triple therapy with warfarin, aspirin and clopidogrel for 3–6 (or more) months, then warfarin plus clopidogrel for up to month 12, then warfarin alone</td>
</tr>
<tr>
<td>High†</td>
<td>Warfarin</td>
<td>High†</td>
<td>No</td>
<td>Use bare metal stent if possible Bare metal stent or DES—triple therapy with warfarin, aspirin and clopidogrel for 3–6 (or more) months, then warfarin plus clopidogrel for up to month 12, then warfarin alone</td>
</tr>
<tr>
<td>High†</td>
<td>Warfarin</td>
<td>High†</td>
<td>Yes</td>
<td>Bare metal stent or DES—triple therapy with warfarin, aspirin and clopidogrel for 4 weeks; then change to warfarin alone DES—triple therapy with warfarin, aspirin and clopidogrel for 4 weeks, then warfarin plus clopidogrel for up to month 12, then warfarin alone</td>
</tr>
</tbody>
</table>

Doses: aspirin 75 mg/day; clopidogrel 75 mg/day. Warfarin dose adjusted to target INR 2.0–2.5.

DES indicates drug eluting stent; PCI, percutaneous coronary intervention; ACS, acute coronary syndrome.

*From Lip and Karpha,7 with permission.

†Particular attention paid to the following risk factors: (1) patients who are over 75 years of age; (2) those who were taking antiplatelet drugs or nonsteroidal anti-inflammatory drugs; (3) those who were on multiple other drug treatments (polypharmacy); (4) those with uncontrolled hypertension; (5) those who gave a history of bleeding (for example, peptic ulcer or cerebral haemorrhage); and (6) those with a history of poorly controlled anticoagulation therapy.
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Timothy Watson and Gregory Y.H. Lip

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