

Preference for oral anticoagulation therapy for patients with atrial fibrillation in Europe in different clinical situations: results of the European Heart Rhythm Association Survey

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The purpose of this European Heart Rhythm Association Survey was to assess the clinical practice in relation to the use of oral anticoagulation therapy for patients with atrial fibrillation (AF) in Europe. Of special interest were patients undergoing percutaneous coronary intervention (PCI), cardioversion procedures, catheter ablation, surgery, and those suffering from anticoagulation-related bleeding. Of 38 responding centres, non-vitamin K antagonist oral anticoagulants (NOACs) were used for stroke prophylaxis and were preferred (33.3%) or considered equal (48.5%) to vitamin K antagonists (VKAs). Only 3% did not use NOACs at all. There were some practice differences regarding the use of NOACs in combination with dual antiplatelet therapy in AF patients undergoing PCI, and only 12% preferred using NOACs in this setting. Bare metal stents were preferred rather than drug-eluting stents in AF patients at high bleeding risk. There were clear practice differences between centres regarding the use of triple therapy. Most of the major bleeding events would be handled using symptomatic and supportive measures (e.g. mechanical compression, fluid replacement, blood transfusion, prothrombin complex concentrate, or recombinant Factor VIIIa). More than 80% of the centres offer either VKA or NOAC for at least 3 weeks before and after cardioversion and 70% offer either VKA or NOAC before and after AF catheter ablation. Patients treated with an NOAC were routinely re-assessed in most centres.

Keywords

Anticoagulation • New oral anticoagulants • Warfarin • Stroke • Bleeding • CHA₂DS₂VASc • HAS-BLED • EHRA survey • EP Wire • Guidelines

Introduction

Non-vitamin K antagonist oral anticoagulants (NOACs) are increasingly used for stroke prevention in patients with non-valvular atrial fibrillation (AF) in clinical practice. As NOACs become widely used, it is relevant to gain some insights into preferences among European physicians for particular oral anticoagulation (OAC) therapy in AF patients in different clinical situations.¹ Addressing these issues, we conducted a European Heart Rhythm Association (EHRA) survey in order to assess the clinical practice in relation to the use of OAC therapy for patients with AF in Europe, in different clinical situations. Of special interest were AF patients undergoing percutaneous

coronary intervention (PCI) or cardioversion procedures (electrical or pharmacological), AF ablation, as well as issues regarding the peri-operative management of anticoagulants and handling of NOAC-related bleeding.

Methods and results

Participating centres

This survey is based on an electronic questionnaire sent out to the EHRA Electrophysiology (EP) Research Network participating centres. Of 38 responding centres, 65.8% were university hospitals,

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21.0% were private hospitals, and 13.2% were other centres. The survey was conducted in February 2015.

Preferred oral anticoagulants for stroke prevention

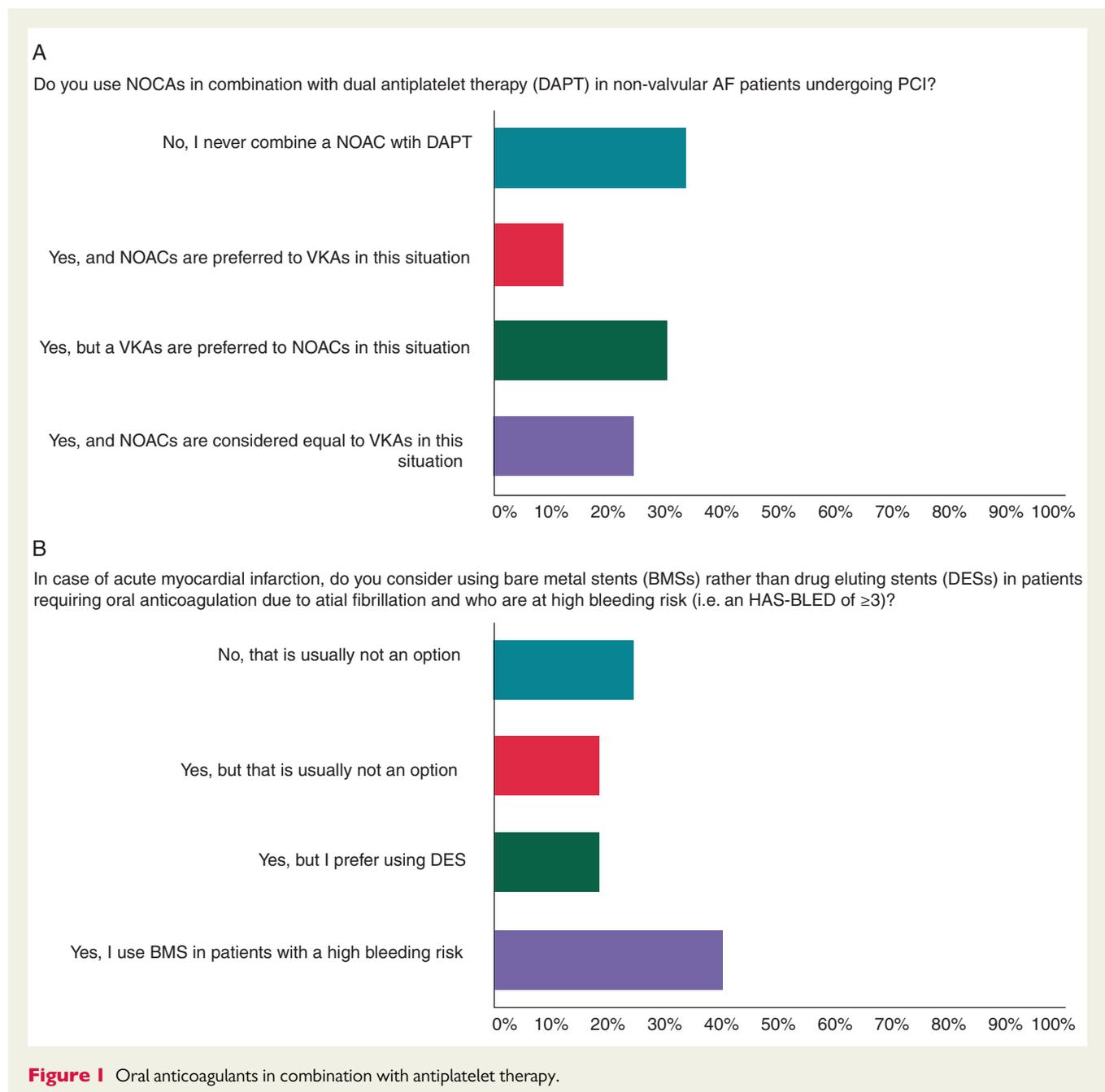
Most of the responding centres used NOACs for stroke prophylaxis in AF patients, either as the preferred option (33.3%) or equal to vitamin K antagonists (VKAs, 48.5% of centres). Only 3% of centres did not use NOACs at all.

Patients treated with NOACs were routinely re-assessed in 26.6% of the centres, while in 50% of the centres re-assessment was performed depending on the patient's risk profile (i.e. frailty, bleeding,

cancer, or co-medication). In patients with moderate renal impairment (i.e. creatinine clearance 30–49 mL/min), 76.7% of the centres used either VKA or NOAC. Only five and two centres used only VKA or NOAC, respectively.

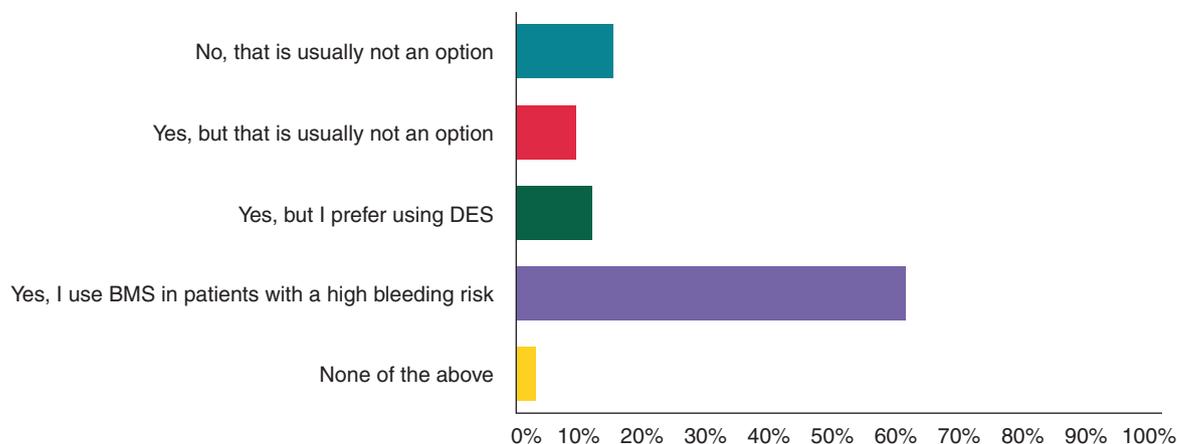
Oral anticoagulants in combination with antiplatelet therapy in patients requiring a coronary stent

Regarding the use of OAC in combination with dual antiplatelet therapy (DAPT), only 12% of centres preferably used NOACs in non-valvular AF patients undergoing PCI. Bare metal stents (BMSs) were preferred over drug-eluting stents (DESs) in case of acute myocardial



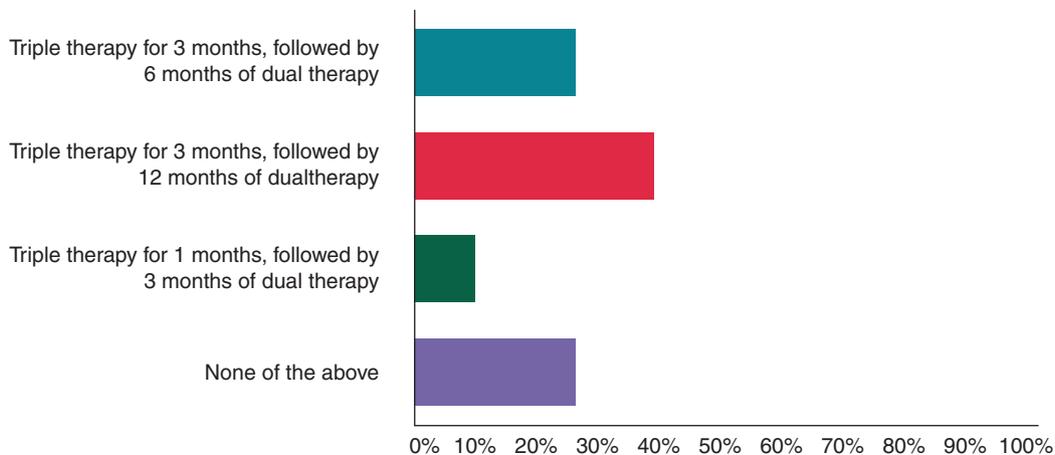
C

In case of elective PCI, do you consider using bare metal stents (BMSs) rather than drug eluting stents (DESs) in patients requiring oral anticoagulation who are at high bleeding risk (i.e., an HAS-BLED of ≥ 3)?



D

In patients with a DES who need the triple therapy with an OAC plus aspirin (75–100 mg/day) and clopidogrel (75 mg/day), I treat the patient as follows:



NOAC = non-vitamin K antagonist oral anticoagulant; VKA = vitamin K antagonist; OAC = oral anticoagulant

Figure 1 continued

infarction and in elective PCI in AF patients at high bleeding risk (i.e. an HAS-BLED of ≥ 3) (Figure 1).

Perioperative management of anticoagulation and antiplatelet therapy in patients with a recently implanted stent

There were clear differences between centres regarding the perioperative management of anticoagulation and antiplatelet therapy. Nearly half of the centres considered continuation of aspirin in the perioperative period, based on an individual decision weighing

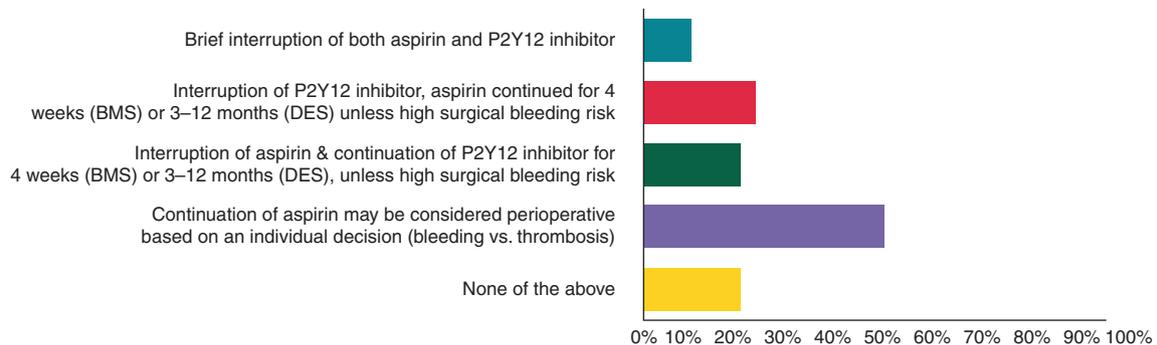
thrombosis risk against bleeding risk. A little <10% considered a brief interruption of both aspirin and P2Y12 inhibitor, and under 10% would continue treatment with any OAC (Figure 2).

Management of bleeding in patients taking a non-vitamin K antagonist

In case of minor or moderate bleeding episodes, most centres would continue treatment or delay next NOAC dose, whereas most of major bleedings would be handled using symptomatic therapy and supportive measures (e.g. mechanical compression of the bleeding site, fluid replacement, blood transfusion, etc.). In case of a major

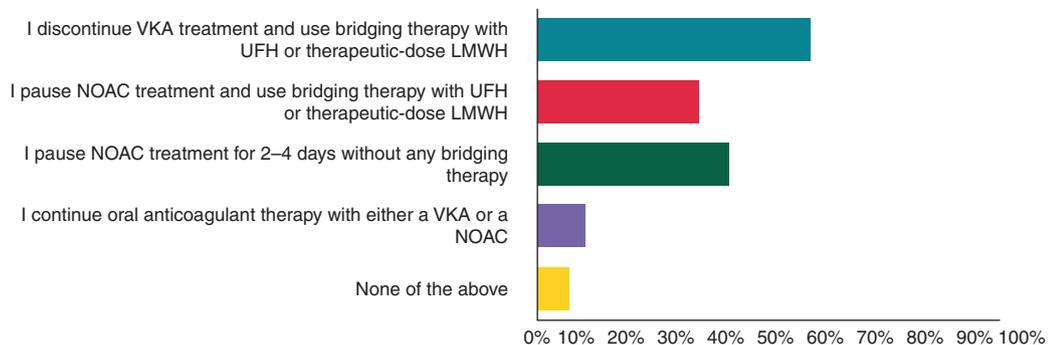
A

How do you handle the anti-platelet therapy in an AF patient with a newly implanted stent during noncardiac surgery such as a hip replacement (please, tick all that apply)?



B

How do you handle the anticoagulation therapy in an AF patient with a newly implanted stent and a high thromboembolic risk (CHA₂DS₂-VASc score >3) during non-cardiac surgery such as hip replacement (multiple answers possible)



P2Y12 inhibitor = clopidogrel, prasugrel, ticagrelor; UFH = unfractionated heparin; LMWH = low molecular weight heparin; NOAC = non-vitamin K antagonist oral anticoagulant; BMS = bare metal stent; DES = drug eluting stent

Figure 2 Perioperative handling of anticoagulation and antiplatelet therapy in patients with a newly implanted stent.

bleeding, 77.4% of centres would use a prothrombin complex concentrate (PCC) or activated recombinant factor VII (rFVIIa). Please, see Figure 3 for details.

Preferred oral anticoagulants in patients undergoing cardioversion or ablation

More than 80% of 30 responding centres used either VKA or NOAC for at least 3 weeks before and after cardioversion (electrical or pharmacological) and more than 70% used either VKA or NOAC before and after AF catheter ablation. One centre never used OAC before pharmacological cardioversion. More than 80% used either VKA or NOAC for ≥ 4 weeks after electrical or pharmacological conversions. One centre always used VKA and three centres always used NOACs.

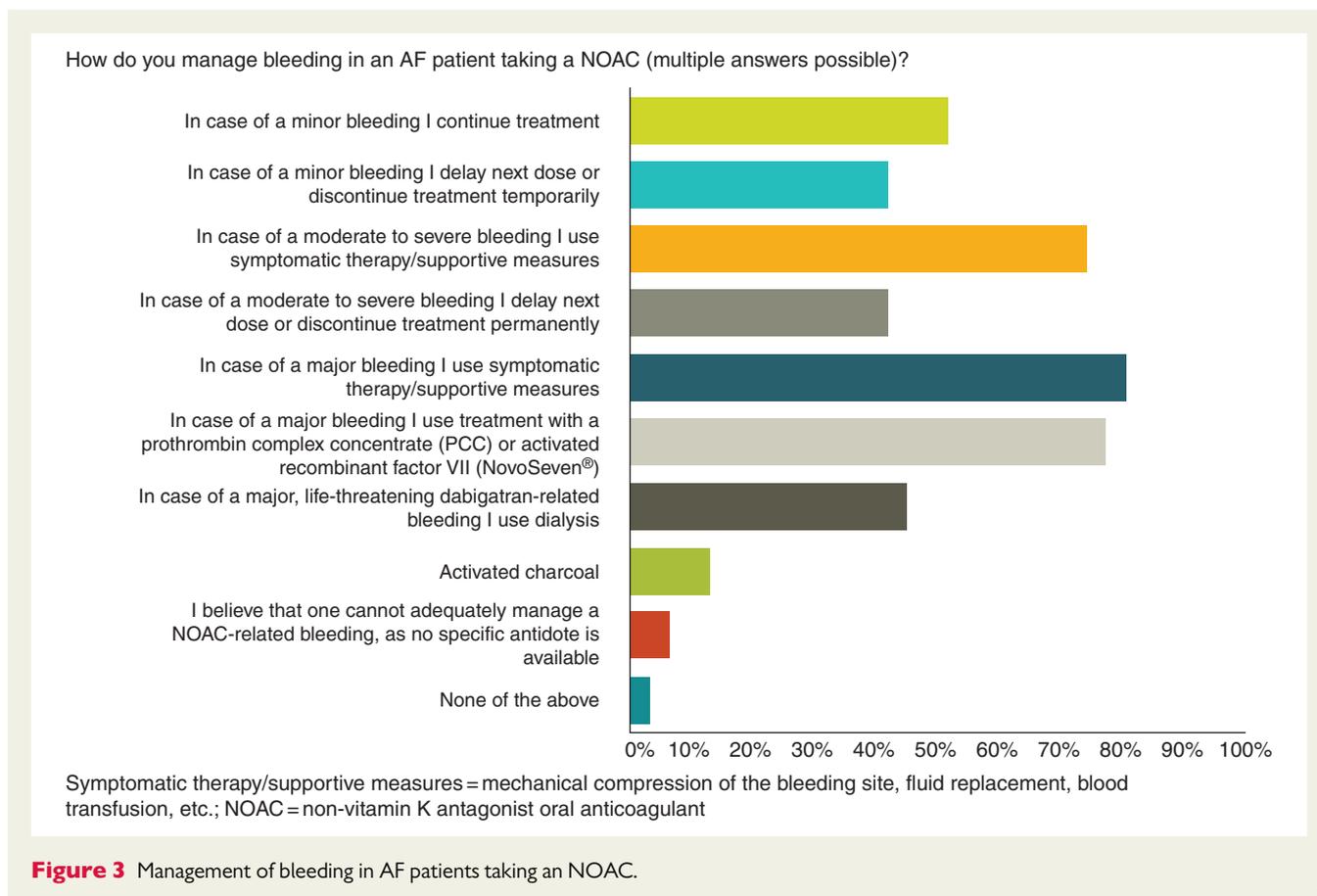
More than 70% of the centres used either VKA or NOAC before AF catheter ablation, six centres always used VKA and two centres always used NOAC. In patients with a CHA₂DS₂-VASc score ≥ 2 , more than 80% of the centres used either VKA or NOAC after the ablation. Only two and three centres use exclusively VKA or NOAC, respectively.

Discussion

This EP Wire survey provides some insights into current European clinical practice and preferred options regarding the use of OAC therapy for stroke prevention in AF patients in different clinical situations, including patients undergoing PCI, cardioversion or AF ablation, or non-cardiac surgery. This survey also provided information about the management of NOAC-related bleeding in clinical practice in European centres.

The latest ESC Guidelines on AF management generally favour the evidence-based use of NOACs over VKAs in most patients with non-valvular AF.² Indeed, most European centres which participated in this EP Wire Survey were using both NOACs and VKAs, and considered the two alternatives as equal or preferred the use of NOACs rather than VKAs.

Practical considerations about NOAC use were addressed by the EHRA Practical Guide for NOAC use,³ which recommended a mandatory monitoring of renal function in AF patients taking a NOAC, suggesting that renal function should be assessed annually in patients with normal or mild renal impairment, and perhaps two to three times per year in patients with moderate renal impairment



(i.e. creatinine clearance 30–49 mL/min). Our findings suggest that most centres participating in this survey comply with this recommendation. The guideline also stated that management of NOAC-related bleeding should be largely supportive, given that these drugs have a relatively short (5–17 h) half-life and do not have clinically available specific antidotes at present.⁴ This also appears to be acknowledged in clinical practice in the European centres which participated in this survey.

Efficacy and safety of dabigatran, rivaroxaban, and apixaban in patients undergoing AF cardioversion or AF ablation has been addressed in the *post hoc* analyses of the respective clinical randomized trials (i.e. the RE-LY, ROCKET AF, and ARISTOTLE trials)^{5–7} and further validated in the prospective randomized trials (e.g. X-VERT⁸) some of which are presently ongoing (i.e. RE-CIRCUIT with dabigatran; NCT02348723 and AXAFA with apixaban; NCT02227550). Accumulating data are reassuring regarding the use of NOACs vs. VKAs in patients undergoing cardioversion or ablation. Our survey has demonstrated that all three NOACs were used in the majority of participating centres.

There were some differences regarding the use of NOACs in combination with DAPT in AF patients undergoing PCI, and only 12% of centres preferred using NOACs in this setting. The 2014 ESC/EACTS Guidelines on myocardial revascularization⁹ recommend that patients with a definite indication for OAC (e.g. AF patients with a CHA₂DS₂VASc score of ≥ 2), OAC should be used in addition to antiplatelet therapy. Furthermore, these guidelines recommended that new-generation DESs are preferred over BMSs among patients requiring OAC if bleeding risk is low (i.e. an HAS-BLED of ≤ 2).

They also stated that in patients with acute coronary syndrome and AF at low bleeding risk, initial triple therapy with NOAC/VKA, aspirin (75–100 mg/day) and clopidogrel (75 mg/day) should be considered for a period of 6 months irrespective of stent type, followed by NOAC/VKA and aspirin (75–100 mg/day) or clopidogrel (75 mg/day) continued for up to 12 months in patients with DES. In our survey, there were differences between centres, but very few data exist and no clear recommendation is available (Class of recommendation IIa and Level of evidence C). One open-label randomized study in patients requiring PCI and taking OAC,¹⁰ investigated if double vs. triple therapy (clopidogrel alone compared with clopidogrel and aspirin) increased the risk of serious bleeding. This study showed that the use of clopidogrel without aspirin was associated with a significant reduction in bleeding complications and no increase in the rate of thrombotic events.

Conclusions

This EPWire survey reaffirms that the ESC guidelines have to a significant degree been implemented in centres responding to this survey. Reassuring information on current practice in Europe for the use of NOACs for stroke prophylaxis in AF is evident, especially regarding safety issues as renal function and handling of bleeding complications. This has also been confirmed in a previous survey showing that the principal aspects of the ESC guidelines on the management of AF, and those on acute coronary syndrome, have been adopted.^{11,12} In the present survey, some differences in clinical practice were

evident, in particular regarding the use of NOACs in combination with one or two antiplatelet drugs, reflecting the need for clearer recommendations. Large randomized studies regarding these anticoagulation strategies are ongoing and will hopefully provide more sound evidence.

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