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Antithrombotic treatment in patients with atrial fibrillation and acute coronary syndromes: results of the European Heart Rhythm Association survey

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The management of an acute coronary syndrome (ACS) in a patient with existing atrial fibrillation (AF) often presents a management dilemma both in the acute phase and post-ACS, since the majority of AF patients will already be receiving oral anticoagulation (OAC) for stroke prevention and will require further antithrombotic treatment to reduce the risk of in-stent thrombosis or recurrent cardiac events. Current practice recommendations are based largely on consensus option as there is limited evidence from randomized controlled trials. Prior to the launch of the new European Heart Rhythm Association (EHRA) consensus document, a survey was undertaken to examine current clinical management of these patients across centres in Europe. Forty-seven centres submitted valid responses, with the majority (70.2%) being university hospitals. This EHRA survey demonstrated overall the management of ACS in AF patients is consistent with the available guidance. Most centres would use triple therapy for a short duration (4 weeks) and predominantly utilize a strategy of OAC (vitamin K antagonist, VKA or non-vitamin K antagonist oral anticoagulant, NOAC) plus aspirin and clopidogrel, followed by dual therapy [(N)OAC plus clopidogrel] until 12 months post-percutaneous coronary intervention, followed by (N)OAC monotherapy indefinitely. Where NOAC was used in combination with antiplatelet(s), the lower dose of the respective NOAC was preferred, in accordance with current recommendations.

Keywords Atrial fibrillation • Acute coronary syndrome • Anticoagulation • Dual antiplatelets • Non-vitamin antagonist oral anticoagulants • Triple therapy • Vitamin K antagonist • EHRA survey

Introduction

Acute coronary syndrome (ACS) commonly occurs in patients with atrial fibrillation (AF), which often requires percutaneous coronary intervention (PCI) typically including stenting. However, the occurrence of ST-segment elevation myocardial infarction (STEMI) or a non-ST-segment elevation acute coronary syndrome (NSTE-ACS) in a patient with existing AF often presents a management dilemma both in the acute phase and post-ACS, since the majority of AF patients will likely already be receiving oral anticoagulation

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(OAC) for stroke prevention and will require further antithrombotic treatment (ATT) to reduce the risk of in-stent thrombosis or recurrent cardiac events. This requires a delicate balancing of the risk of thromboembolic and atherothrombotic events against the increased chance of bleeding, and should be undertaken on an individual patient basis.[1,2]

In 2014, a joint consensus document was published to provide guidance on the management of ATT in AF patients presenting with ACS and/or undergoing PCI[3] in the setting of limited available evidence from randomized controlled trials (RCTs) about the optimal antithrombotic strategy post-ACS in patients with AF. Since 2014, further observational studies and RCT data has been published and non-vitamin K antagonist oral anticoagulants (NOACs) are more commonly used. In addition, there are more recent European guidelines on the management of AF[4] and management of STEMI,[5] focused updates on dual antiplatelet therapy in coronary artery disease[6] and the European Heart Rhythm Association (EHRA) NOAC practical guide[7] (which includes a chapter on the management of AF in patients with coronary artery disease). Therefore, the 2014 consensus guidance on the management of AF patients with ACS was updated in 2018[8] and EHRA conducted a survey to capture the current management of ACS in AF patients in Europe prior to the launch of the new consensus document.

Methods and results

The EHRA electrophysiology research network was utilized to distribute a 22-item questionnaire survey on-line between 26 July and 7 September 2018. Fifty-seven centres responded, and 47 unique responses were included in the analyses (three were duplicate responses and seven were blank). Where complete data was not available the number of responses is indicated and the proportion reported as a percentage of the available answers. Most of the 47 centres were university hospitals (70.2%), with 9 (19.2%) non-university hospitals and 5 (10.6%) private hospitals. Almost all centres (95.7%) had a 24-h, 365-day primary percutaneous coronary intervention (PCI) service, with the majority (66.0%) performing >1000 PCIs annually, 13 (27.7%) with between 501 and 1000 PCIs per year, 1 (2.1%) centre each with 101–500 or 1–100 PCIs annually, and only one centre where no such procedures were undertaken. Only one centre reported no experience of managing an AF patient on a NOAC with an ACS over the previous 12 months.

Acute management of atrial fibrillation patients on oral anticoagulation presenting with an acute coronary syndrome

ST-elevation myocardial infarction within an optimal timeframe for primary percutaneous coronary intervention

Among STEMI patients on a vitamin K antagonist (VKA), most (91.5%) centres would proceed with a primary PCI on uninterrupted VKA regardless of the international normalized ratio (INR) value, however, 4 (8.5%) centres would only proceed if the INR value was below a certain level, although there was no consensus among the respondents about the cut-off INR value (ranging from 2.5 to 3.5). Among STEMI patients on a NOAC, 31/46 (67.4%) centres would proceed with primary PCI without NOAC interruption, whereas 15/46 (32.6%) centres would temporarily discontinue NOAC therapy before the PCI.

Figure 1A presents the pre-procedural loading with antiplatelet drugs among STEMI patients with AF receiving VKA or NOAC therapy; respondents were able to choose multiple responses. A similar pattern of pre-procedural antithrombotic regimens were employed regardless of the presence of VKA or NOAC at presentation. Dual antiplatelet therapy was the most commonly selected option, added to VKA by 28/46 (60.9%) centres and to NOAC by 26/46 (56.5%) centres (*Figure 1A*). Aspirin plus clopidogrel was the most frequently used dual antiplatelet regimen in combination with VKA [19/46 (41.3%) centres], or a NOAC [24/46 (51.2%) centres]. Addition of aspirin only or clopidogrel only to VKA was employed in 6/46 (13.0%) and 10/46 (21.7%) centres, and to a NOAC in 4/46 (8/7%) and 10/46 (21.7%) centres, respectively. Pre-procedural use of either ticagrelor or prasugel alone or in combination with aspirin was less often preferred, particularly in addition to NOAC [prasugel or ticagrelor alone ($n = 1$); aspirin plus ticagrelor ($n = 2$)], while more centres would utilize the newer $P2Y_{12}$ inhibitors in addition to VKA [prasugel or ticagrelor alone ($n = 2$); aspirin plus prasugel ($n = 2$); aspirin plus ticagrelor ($n = 7$)]. Very few centres used parenteral anticoagulation peri-procedurally in addition to VKA or NOAC (*Figure 1B*). Unfractionated heparin was the most commonly selected option, added to VKA by 6/46 (13.0%) centres and to NOAC by 7/46 (15.2%), with 5 (10.9%) centres adding GPIIb/IIIa inhibitors to either VKA or NOAC only in selected patients.

Non-ST-segment elevation acute coronary syndrome

The management of a NSTE-ACS in AF patients was very similar regardless of the existing VKA or NOAC therapy (*Figure 2*). The majority of centres would proceed with the PCI within the first 24 h after admission; more specifically, 40/46 centres (87.0%) would carry out PCI within the first 24 h in patients taking a VKA, and 41/45 centres (91.1%) would do so in patient taking a NOAC, whereas 6/46 (13.0%) and 5/45 centres (11.1%) would postpone the PCI for as long as possible in patients taking VKA or NOAC, respectively. Bare-metal stents (BMS) were preferred over drug-eluting stents (DES) in only 8/46 (17.4%) and 7/45 centres (15.6%) among patients on VKA and NOAC, respectively. Risk of bleeding was taken into consideration when choosing alternative treatment strategies. Seven centres would consider angioplasty without stent implantation, and five centres would consider bypass surgery instead of PCI, in patients at high risk of bleeding.

Preferred pre-procedural and peri-procedural antithrombotic strategies are shown in *Figure 3A*. Almost half of the centres (21/46, 46.7%) would add dual antiplatelet therapy (aspirin plus clopidogrel) to OAC, while only a few centres would use aspirin in combination with either ticagrelor (one centre) or prasugel (two centres). Very few centres used parenteral anticoagulation peri-procedurally in addition to OAC (*Figure 3B*); three would use enoxaparin or other low molecular weight heparin and five would use unfractionated heparin, with four centres utilizing GPIIb/IIIa inhibitors only in selected patients.

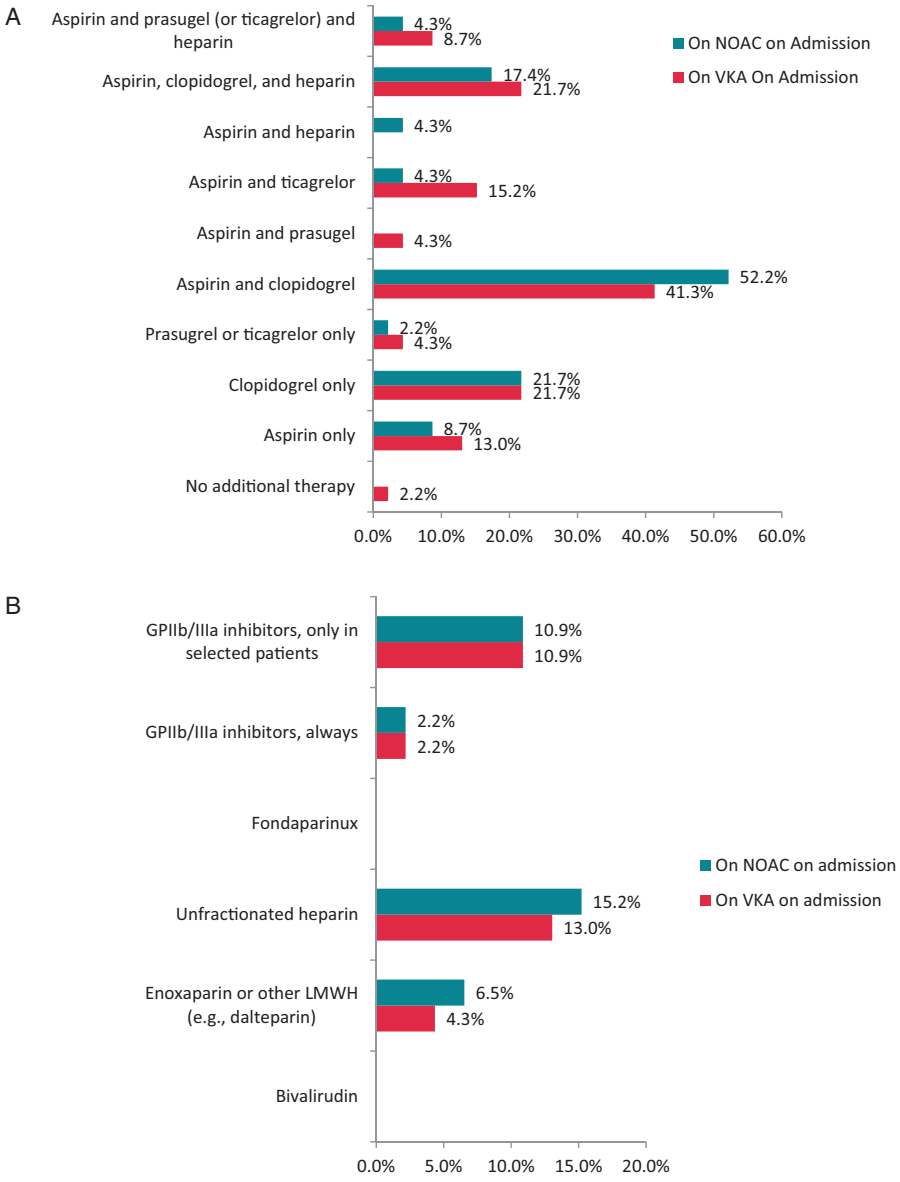

Figure 1 (*A*) Pre-procedural loading with antiplatelet therapy among STEMI patients with AF receiving VKA or NOAC therapy prior to admission. Three respondents indicated they did not perform PCI and therefore could not answer this question. (*B*) Peri-procedural parenteral anticoagulation among STEMI patients with AF receiving VKA or NOAC therapy prior to admission. Three respondents indicated they did not perform PCI and therefore could not answer this question. AF, atrial fibrillation; NOAC, non-vitamin K antagonist oral anticoagulant; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; VKA, vitamin K antagonist.

Post-procedural management of atrial fibrillation patients undergoing primary percutaneous coronary intervention for acute coronary syndrome

Patients with CHA_2DS_2-VASc score ≥2 and a HAS-BLED score of 1

In patients with AF who have undergone a primary PCI for ACS, initial post-intervention antithrombotic options differed depending on the patient's risk of stroke and risk of bleeding. Among those with a CHA_2DS_2-VASc score ≥2 and a HAS-BLED score of 1, triple therapy (OAC plus dual antiplatelet therapy with aspirin and clopidogrel) was preferred by the majority of centres (36/45, 80.0% for those on VKA at baseline and 34/45 centres, 75.6% for patients on NOAC at baseline) (see *Figure 4A*). Most centres would continue the OAC that was in place prior to the PCI (100% for NOAC and 27/36 centres, 75.0% for VKA).

However, centres differed in the duration of triple therapy, with 12/27 (44.4%) and 15/34 centres (44.1%) opting for 4 weeks of triple therapy in patients taking VKA and NOAC at baseline, respectively, whereas 15/27 (55.6%) and 19/34 centres (55.9%) would undertake

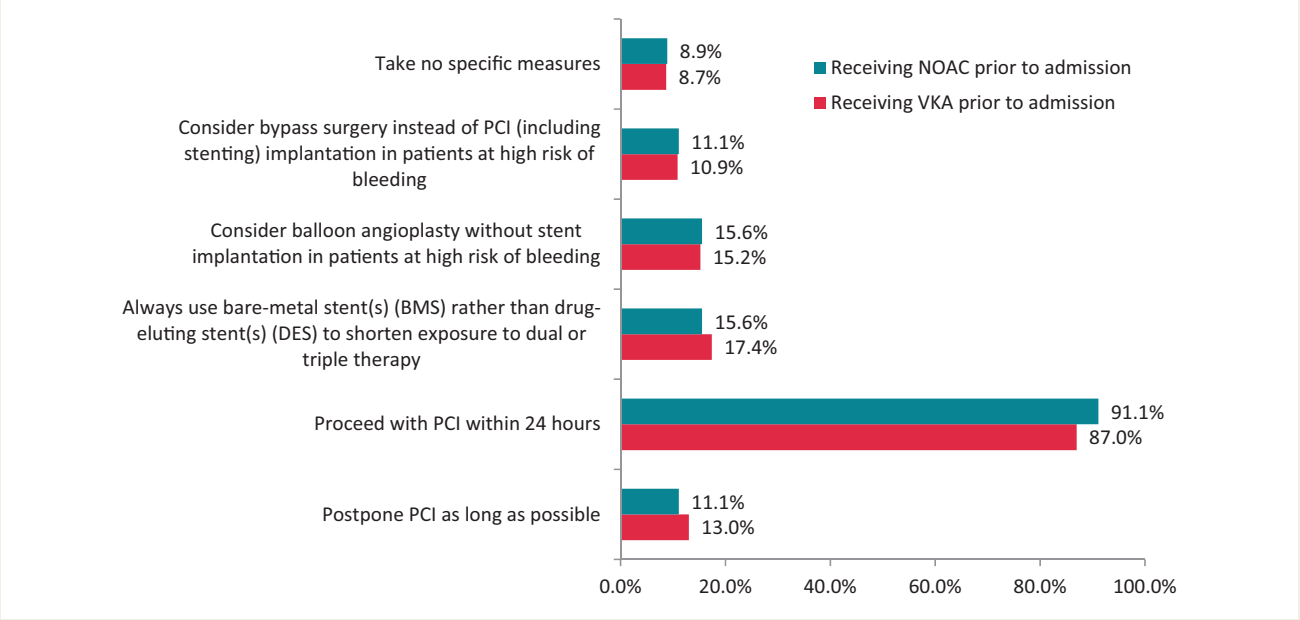

Figure 2 Acute management of non-ST-segment elevation ACS among patients with AF receiving VKA or NOAC therapy. ACS, acute coronary syndrome; AF, atrial fibrillation; NOAC, non-vitamin K antagonist oral anticoagulant; PCI, percutaneous coronary intervention; VKA, vitamin K antagonist.

6 months of triple therapy in patients taking VKA or NOAC at baseline, respectively. Two out of 45 (4.4%) and 6/45 centres (13.3%) would add clopidogrel alone to the pre-existing OAC (VKA and NOAC, respectively).

Among patients who were taking VKA prior to their PCI, one-third of centres would consider switching them to a NOAC post-PCI (in combination with either dual antiplatlet therapy or clopidogrel only), with a preference for a short duration of triple therapy (4 weeks), whereas only one centre would consider switching a patient from a NOAC to VKA plus clopidogrel (see *Figure 4A*). Aspirin alone in combination with VKA was not chosen by any centre as a treatment option; only one centre would give NOAC and aspirin. No centres would use ticagrelor or prasugel in combination with OAC (either VKA or NOAC) post-PCI.

After completing the initial period of either dual or triple therapy, most centres (34/45, 75.6%) would continue dual therapy (OAC plus one antiplatelet drug) for 12 months post-PCI and 6/45 (13.3%) centres would continue dual therapy indefinitely (see *Figure 4B*). There did not appear to be a clear preference for VKA or NOAC as the OAC of choice in this dual therapy regimen, although clopidogrel was the preferred antiplatelet agent in combination with OAC (either VKA or NOAC). No centre would continue triple therapy until 12 months post-PCI, however, 7/45 centres (15.6%) would choose OAC monotherapy (most with NOAC) after the initial period of either dual or triple therapy (see *Figure 4B*).

Patients with CHA_2DS_2-VASc score of 4 and a HAS-BLED score of 3

Among AF patients with a CHA_2DS_2-VASc score of 4 and a HAS-BLED score of 3 (higher risk of stroke and higher risk of bleeding) the preferred initial post-PCI antithrombotic regimen was more variable (see *Figure 4C*). Triple therapy for 4 weeks was preferred by most centres [26/45 (57.8%) with VKA and 28/45 (62.2%) with NOAC], with OAC in combination with aspirin and clopidogrel being most commonly chosen; the responses differed slightly depending on which OAC patients were receiving prior to PCI (see *Figure 4C*). Use of the newer $P2Y_{12}$ inhibitors (prasugel and ticagrelor) in combination with aspirin and OAC was selected as an option by very few centres (two centres in combination with VKA and one with NOAC). Longer-term use of triple therapy (for 6 months) was selected by 7 (15.6%) centres, with dual therapy (OAC plus antiplatelet) for 4 weeks chosen by several centres [16/45 (35.6%) with VKA and 18/45 (40.0%) with NOAC], with OAC in combination with clopidogrel preferred.

After completing the initial period of either dual or triple therapy, most centres would continue dual therapy until 12 months post-PCI in patients at high risk of stroke and high risk of bleeding, with the majority selecting OAC (VKA or NOAC) plus clopidogrel (see *Figure 4D*). One centre would continue dual therapy indefinitely. No centres would continue triple therapy until 12 months post-PCI. Six out of 45 (13.3%) and 8/45 (17.8%) centres, respectively would continue VKA or NOAC alone and 7/45 (15.6%) would switch patients from a VKA to NOAC.

If prescribing a NOAC in combination with either mono- or dual antiplatelet therapy following PCI in patients with normal renal function, most [32/45 (71.1%)] centres would choose dabigatran 110 mg bid, regardless of the CHA_2DS_2-VASc score and HAS-BLED score; the lower dose of each of the NOACs was preferred over the standard dose when given in combination with antiplatelet therapy (see *Figure 5*).

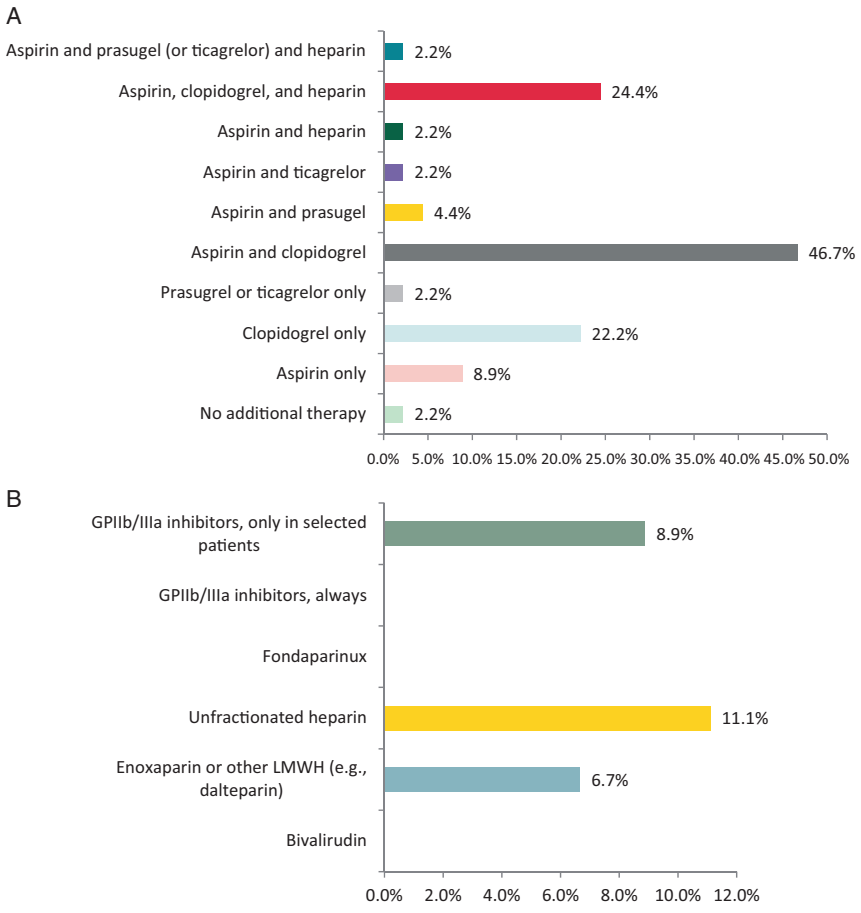

Figure 3 (*A*) Pre-procedural loading with antiplatelet therapy among non-ST-segment elevation ACS among patients with AF receiving OAC (either VKA or NOAC) prior to admission. Three respondents indicated they did not perform PCI and therefore could not answer this question. (*B*) Peri-procedural parenteral anticoagulation among non-ST-segment elevation ACS among patients with AF receiving OAC (either VKA or NOAC) prior to admission. Three respondents indicated they did not perform PCI and therefore could not answer this question. ACS, acute coronary syndrome; AF, atrial fibrillation; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulation; PCI, percutaneous coronary intervention; VKA, vitamin K antagonist.

Discussion

The main findings of this survey were that most centres would use triple therapy for a short duration (4 weeks) and predominantly utilize a strategy of OAC (VKA or NOAC) plus aspirin and clopidogrel, followed by dual therapy [(N)OAC plus clopidogrel] until 12 months post-PCI, followed by (N)OAC monotherapy indefinitely. Where NOAC was used, the lower dose of the respective NOAC was preferred, in accordance to current recommendations.

Acute management of a ST-elevation myocardial infarction within an optimal timeframe for primary percutaneous coronary intervention in atrial fibrillation patients on oral anticoagulation therapy

The majority (91.5%) of respondents would proceed to PCI without interruption of the baseline OAC which is in accordance with current clinical guidelines.[4,5,7–9] However, respondents were more likely to choose this approach when the patient was on VKA at the time of the ACS; approximately one-third (32.6%) of respondents would temporarily discontinue the NOAC before proceeding with PCI compared with only 8.5% discontinuing VKA. This practice of pre-procedural discontinuation of the NOAC reflects the guidance given in the 2018 NOAC practical guide[7] and is similar to clinical practice reported in the previous EHRA survey on this aspect of acute management of ACS in an AF patient.[10]

The choice of pre-procedural antithrombotic strategies was heterogeneous but the pattern was similar regardless of the presence of VKA or NOAC at presentation, with dual antiplatelet therapy consisting of aspirin and clopidogrel being the most preferred combination. The 2017 dual antiplatelet therapy focused update,[6] 2016 AF guidelines[4] and 2018 NOAC practical guide[7] and 2018 EHRA consensus[8] discourages use of prasugel or ticagrelor as components of a triple therapy regimen, yet a few centres would utilize them for triple

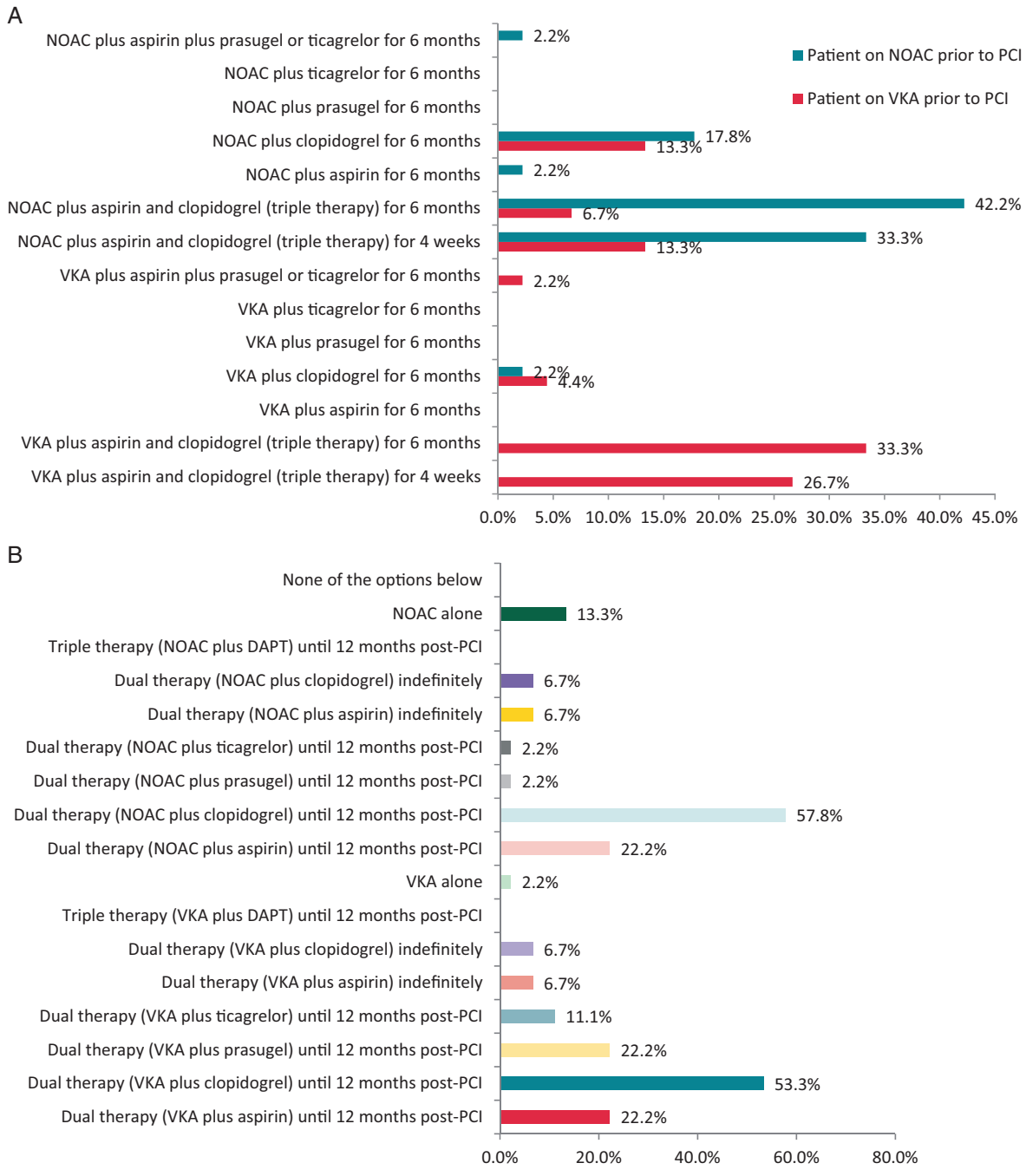

Figure 4 (*A*) Initial post-PCI antithrombotic therapy among patients with AF and a CHA_2DS_2-VASc score ≥2 and a HAS-BLED score of 1, receiving either VKA or NOAC therapy prior to PCI. (*B*) Longer-term antithrombotic therapy post-PCI (after the initial phase) among patients with AF and a CHA_2DS_2-VASc score ≥2 and a HAS-BLED score of 1, who received either VKA or NOAC therapy prior to PCI. (*C*) Initial post-PCI antithrombotic therapy among patients with AF and a CHA_2DS_2-VASc score of 4 and a HAS-BLED score of 3, receiving either VKA or NOAC therapy prior to PCI. (*D*) Longer-term antithrombotic therapy treatment post-PCI (after the initial phase) among patients with AF and a CHA_2DS_2-VASc score of 4 and a HAS-BLED score of 3, receiving either VKA or NOAC therapy prior to PCI. AF, atrial fibrillation; DAPT, dual antiplatelet therapy; NOAC, non-vitamin K antagonist oral anticoagulant; PCI, percutaneous coronary intervention; VKA, vitamin K antagonist.

therapy, more often in combination with VKA than NOAC. The current guidance[4,6–8] does not discount the use of one of the newer $P2Y_{12}$ inhibitor in combination with OAC (VKA or NOAC), in patients at higher risk of thrombotic complications, which may explain why a few centres would utilize prasugel or ticagrelor together with (N)OAC. In addition, parenteral anticoagulation with

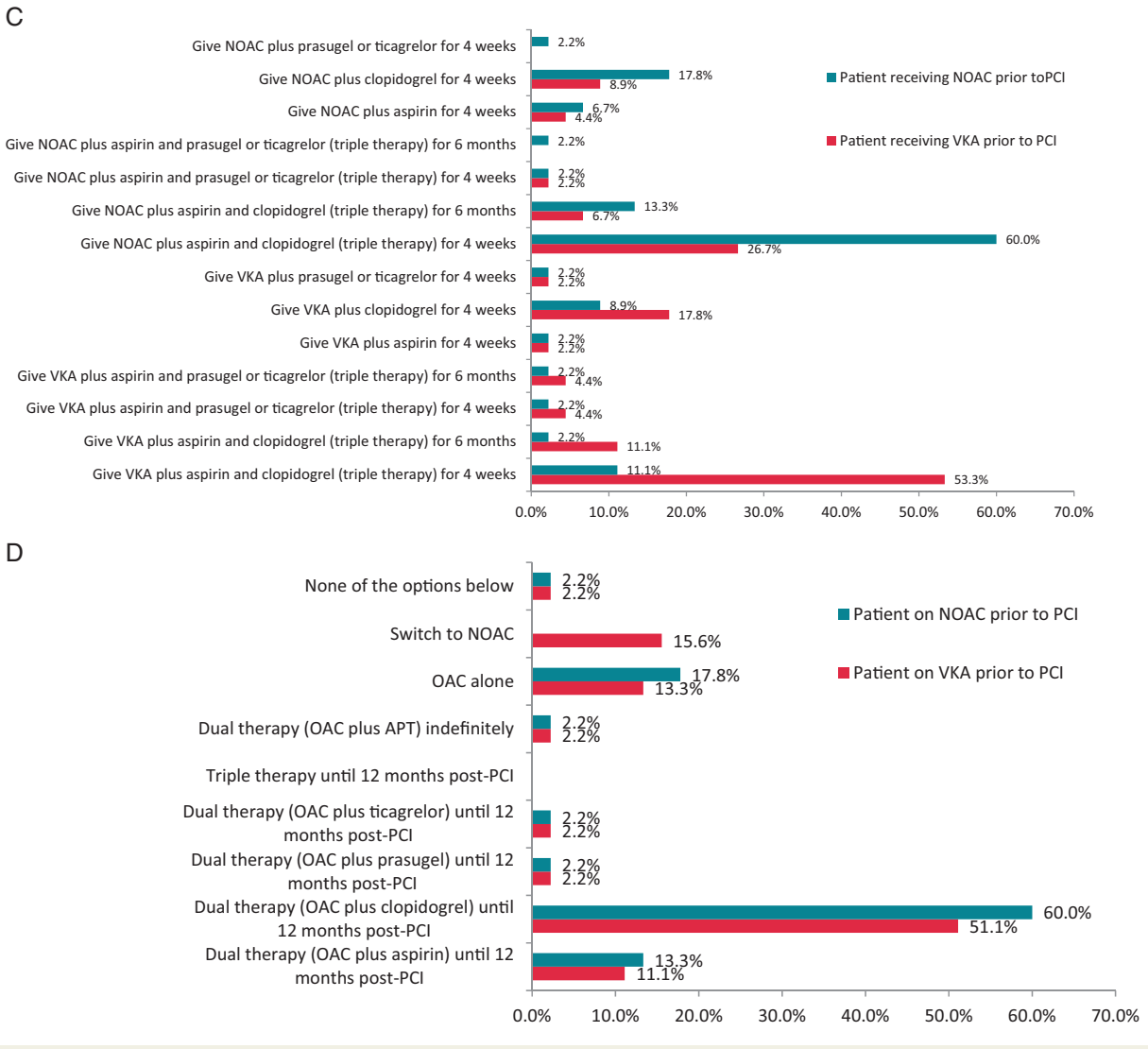

Figure 4 Continued.

unfractionated heparin, enoxaparin or bivalirudin (but not fondaparinux) is recommended in the management of acute STEMI[7–9] and is reflected in the responses of this survey. Use of GPIIb/IIIa inhibitors is only advocated in bail-out situations[7] and this recommendation appears to be adhered to as respondents would only use these drugs in selected patients.

Acute management of a non-ST-segment elevation acute coronary syndrome in atrial fibrillation patients on oral anticoagulation therapy

Guidance on the management of a NSTE-ACS is highly dependent on the individual risk profile of the patient.[11] This survey demonstrates similar management of a NSTE-ACS in AF patients regardless of the existing (N)OAC therapy, which is contrary to current recommendations.[4–7] The majority of centres would proceed with the PCI within 24 h, with only a few (11–13%) opting to postpone the PCI for as long as possible. However, current recommendations,[7] advocate stopping the NOAC at admission, delaying PCI, and starting fondaparinux (preferred) or low-molecular weight heparin (≥12 h after last NOAC dose) in non-urgent cases, whilst urgent cases should be treated as for STEMI.[7] Bare metal stents are no longer advocated to shorten the length of time on dual or triple therapy post-PCI, however, a few (16–17%) centres would always use BMS, rather than employing contemporary DES which are now preferred.[5,7,8] A few centres would employ angioplasty without stenting or bypass surgery in patients at high risk of bleeding but this approach is no longer advocated.

Dual antiplatelet therapy is recommended for all NSTE-ACS on presentation regardless of subsequent invasive procedure or not.[12] However, slightly less than half (46.7%) of the centres would add dual

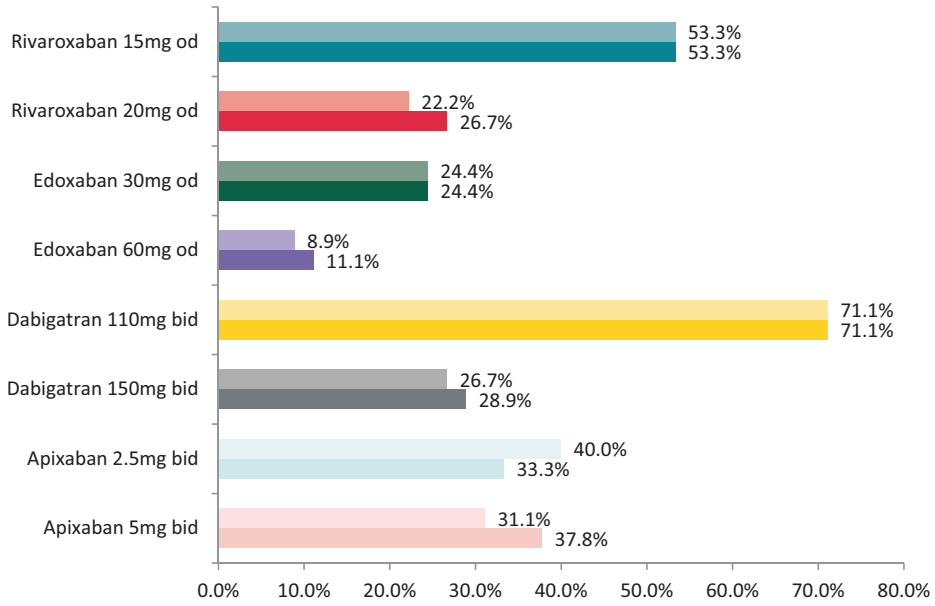

Figure 5 Preferred NOAC following a PCI when given in combination with mono- or dual antiplatelet therapy for AF patients with normal renal function (CrCl ≥75 mL/min) and a CHA_2DS_2-VASc score ≥2 and a HAS-BLED score of 1 (darker colour) or CHA_2DS_2-VASc score of 4 and a HAS-BLED score of 3 (lighter colour). AF, atrial fibrillation; NOAC, non-vitamin K antagonist oral anticoagulant; PCI, percutaneous coronary intervention.

antiplatelet therapy (aspirin and clopidogrel) to OAC pre-procedurally, with only one to two centres opting to use aspirin in combination with either ticagrelor or prasugel.

Antithrombotic strategies (dual or triple therapy) post-percutaneous coronary intervention in atrial fibrillation patients

Current recommendations on the duration of triple therapy and antithrombotic options differ depending on the patient's risk of stroke, atherothrombotic risk, risk of bleeding, and stent type (newer generation DES vs. other stent types).[7,11] Although the focused update of the European Society of Cardiology (ESC)[6] recommends triple therapy (OAC plus dual antiplatelet therapy) for all AF patients following ACS who undergo PCI with stenting, followed by dual therapy [ideally (N)OAC plus clopidogrel (or aspirin/prasugel/ticagrelor)], the data show no additional benefit over and above dual therapy but confer a higher bleeding risk,[13–15] and therefore, the duration should be kept as short as possible. Consequently, the 2018 EHRA practical guide on NOACs[7] mentions the option of using triple therapy (aspirin, ticagrelor, and OAC) for only 1–7 days (until discharge) and then dual therapy [ticagrelor (or clopidogrel, or aspirin) plus OAC] for 12 months. However, in this EHRA survey, triple therapy was preferred by most centres regardless of the stroke and bleeding risk, although a shorter duration (4 weeks) was favoured in those at higher risk of bleeding.

With regards to dual antithrombotic therapy, clopidogrel in combination with OAC was also a popular initial ATT strategy. Among patients with a CHA_2DS_2-VASc score ≥2 and a HAS-BLED score of 1, aspirin alone in combination with OAC was only selected by one centre (NOAC plus aspirin) and no centres would use ticagrelor or prasugel in combination with (N)OAC post-PCI, which is in line with current clinical recommendation (NOAC or VKA plus clopidogrel preferred).[7,8] Two RCTs, PIONEER AF-PCI[16] and RE-DUAL PCI[17] compared dual therapy [NOAC (two different doses) plus $P2Y_{12}$ inhibitor] with VKA-based triple therapy (VKA, $P2Y_{12}$ inhibitor and low-dose aspirin) and demonstrated a significant reduction in clinically significant bleeding[16] or major or clinically relevant non-major bleeding with the NOAC plus $P2Y_{12}$ inhibitor dual therapy options compared with triple therapy.

The results of this EHRA survey suggest that the practice of dual ATT with a NOAC and $P2Y_{12}$ inhibitor regimen is infrequently employed in clinical practice. There are currently two on-going RCTs, AUGUSTUS[18] and ENTRUST AF PCI,[19] which are examining the effect of apixaban or edoxaban, respectively, vs. warfarin in combination with either single or dual antiplatelet therapy in AF patients with ACS and/or PCI but again both are underpowered for efficacy. A recent systematic review and meta-analysis of four published RCTs of OAC and antiplatelet therapy in AF patients undergoing PCI (WOEST, ISAR-TRIPLE, PIONEER-A-PCI, and REDUAL-PCI)[20] demonstrated a significant reduction in TIMI major or minor bleeding with dual ATT compared with triple ATT [hazard ratio (HR) 0.53, 95% credible interval (CrI) 0.36–0.85)], with a similar risk of major adverse cardiovascular events with dual and triple ATT (HR 0.85, 95% CrI 0.48–1.29). There is still no definitive answer regarding the efficacy of triple therapy vs. dual ATT (OAC plus APT) or the optimal duration for triple therapy.

After completing the initial period of either dual or triple therapy, three-quarters of centres would continue dual therapy until 12 months post-PCI, with most selecting (N)OAC plus clopidogrel, in accordance with clinical guidance,[4–9] with seven (15.6%) centres continuing either VKA or NOAC alone 12 months post-PCI, while one centre would continue dual therapy indefinitely. This demonstrates that respondents' clinical practice reflects implementation of current recommendations.

There is currently no recommendation to switch patients from a NOAC to a VKA after PCI,[7] and only one centre reported this strategy, however, one-third of centres would consider switching a patient from VKA to NOAC post-PCI (in combination with either dual antiplatlet therapy or clopidogrel).

Choice of non-vitamin K antagonist oral anticoagulant

This survey also revealed that centres adhere to current recommendations[4–9] in prescribing the lower dose of each NOAC tested in the RCTs for stroke prevention in AF when a NOAC is utilized in combination with aspirin or clopidogrel, with dabigatran 110 mg bid favoured, which might reflect the availability of an antidote.

The past and the present

The present survey reflects changes in clinical practice since the previous EHRA survey in 2014.[10] The current survey demonstrates the growing confidence of cardiologists in performing a primary PCI without interrupting the NOAC in patients presenting with STEMI (39% vs. 67.4%), and a dramatic reduction in the use of BMS (from 54.1% in 2014 to 16–17% in 2018) in patients presenting with ACS and pre-procedural and peri-procedural dual antiplatelet therapy loading (75.6% in 2014 compared with 46.7% in 2018). There are also striking differences noted in the duration of triple and dual ATT in patients with AF after PCI. From the 2014 survey, most (83.8%) centres would continue triple therapy for 3–6 months for a drug-eluting stent, with 16.2% continuing triple therapy for 9–12 months. In contrast, currently the majority (57.8–62.2%) of centres would utilize triple therapy for a shorter duration (4 weeks) for patients at high risk of stroke and bleeding, with a smaller proportion continuing triple therapy for a maximum of 6 months. Among patients at lower risk of bleeding (and stroke), the current survey suggests that the majority (56%) would continue triple therapy for 6 months. Regarding the current preferred duration of dual therapy after PCI, around three-quarters of the centres would continue this for up to 12 months, with 13.3% and 2.2% continuing this indefinitely among those at low and high risk of bleeding, respectively. This demonstrates an inversion of the clinical preference and practice of 2014, where 21.6% of centres would continue dual therapy for up to 12 months and 62.2% continuing this indefinitely, perhaps reflecting a more individualized therapeutic approach based on bleeding risk currently.

Limitations

The overall response rate was low; only 33% participated. In addition, the majority (70.2%) of responders were from university hospitals and thus the results of this EHRA survey may not be representative of current clinical practice across Europe. Those who respond to online surveys may be more knowledgeable about current clinical recommendations (response bias). In addition, they may be reporting the 'correct' answer which may not reflect their actual clinical practice (social desirability bias) as knowledge is not always translated into action/practice.

Conclusions

This EHRA survey demonstrates that the management of ACS in AF patients is generally in line with the available guidelines. Antithrombotic management of ACS in AF patients is a highly debated topic and the optimal combination of OAC and antiplatelet(s) and the duration of therapy remain unanswered. Further research is needed to inform the management of such patients, and the ongoing trials will contribute to filling at least some of the knowledge gaps.

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References

1. Proietti M, Mujovic N, Potpara TS. Optimizing stroke and bleeding risk assessment in patients with atrial fibrillation: a balance of evidence, practicality and precision. *Thromb Haemost* 2018;**118**:2014–7.
2. Lip G, Freedman B, De Caterina R, Potpara TS. Stroke prevention in atrial fibrillation: past, present and future. Comparing the guidelines and practical decision-making. *Thromb Haemost* 2017;**117**:1230–9.
3. Lip GY, Windecker S, Huber K, Kirchhof P, Marin F, Ten Berg JM *et al.* Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of

Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). *Eur Heart J* 2014;**35**:3155–79.
4. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B *et al*. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 2016;**18**:1609–78.
5. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H *et al*. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;**39**:119–77.
6. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A *et al*. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the task force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2018;**39**:213–60.
7. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L *et al*. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Europace* 2018;**20**:1231–42.
8. Lip GYH, Collet JP, Haude M, Byrne R, Chung EH, Fauchier L *et al*. 2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: a 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). *Europace* 2019;**21**:192–3.
9. Lip GYH, Banerjee A, Boriani G, Chiang CE, Fargo R, Freedman B *et al*. Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report. *Chest* 2018;**154**:1121–201.
10. Potpara TS, Lip GY, Dagres N, Estner HL, Larsen TB, Blomström-Lundqvist C; Conducted by the Scientific Initiatives Committee, European Heart Rhythm Association. Management of acute coronary syndrome in patients with non-valvular atrial fibrillation: results of the European Heart Rhythm Association Survey. *Europace* 2014;**16**:293–8.
11. Sibbing D, Angiolillo DJ, Huber K. Antithrombotic therapy for acute coronary syndrome: past, present and future. *Thromb Haemost* 2017;**117**:1240–8.
12. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U *et al*. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2019;**40**:87–165.
13. Lamberts M, Gislason GH, Olesen JB, Kristensen SL, Schjerning Olsen AM, Mikkelsen A *et al*. Oral anticoagulation and antiplatelets in atrial fibrillation patients after myocardial infarction and coronary intervention. *J Am Coll Cardiol* 2013;**62**:981–9.
14. Kerneis M, Talib U, Nafee T, Daaboul Y, Pahlavani S, Pitliya A *et al*. Triple antithrombotic therapy for patients with atrial fibrillation undergoing percutaneous coronary intervention. *Prog Cardiovasc Dis* 2018;**60**:524–30.
15. Jacobs MS, Tieleman RG. Optimal antithrombotic treatment of patients with atrial fibrillation undergoing percutaneous coronary intervention: triple therapy is too much! *Neth Heart J* 2018;**26**:334–40.
16. Gibson CM, Mehran R, Bode C, Halperin J, Verheugt FW, Wildgoose P *et al*. Prevention of bleeding in patients with atrial fibrillation undergoing PCI. *N Engl J Med* 2016;**375**:2423–34.
17. Cannon CP, Bhatt DL, Oldgren J, Lip GYH, Ellis SG, Kimura T *et al*.; RE-DUAL PCI Steering Committee and Investigators. Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation. *N Engl J Med* 2017;**377**:1513–24.
18. Lopes RD, Vora AN, Liaw D, Granger CB, Darius H, Goodman SG *et al*. An open-label, 2 × 2 factorial, randomized controlled trial to evaluate the safety of apixaban vs. vitamin K antagonist and aspirin vs. placebo in patients with atrial fibrillation and acute coronary syndrome and/or percutaneous coronary intervention: rationale and design of the AUGUSTUS trial. *Am Heart J* 2018;**200**:17–23.
19. Vranckx P, Lewalter T, Valgimigli M, Tijssen JG, Reimitz PE, Eckardt L *et al*. Evaluation of the safety and efficacy of an edoxaban-based antithrombotic regimen in patients with atrial fibrillation following successful percutaneous coronary intervention (PCI) with stent placement: rationale and design of the ENTRUST-AF PCI trial. *Am Heart J* 2018;**196**:105–12.
20. Golwala HB, Cannon CP, Steg PG, Doros G, Qamar A, Ellis SG *et al*. Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials. *Eur Heart J* 2018;**39**:1726–35.