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Diagnosis and management of left atrial appendage thrombus in patients with atrial fibrillation undergoing cardioversion or percutaneous left atrial procedures: results of the European Heart Rhythm Association survey

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Practices regarding indications and timing for transoesophageal echocardiography (TOE) before cardioversion (CV) of atrial fibrillation (AF) or left atrial (LA) interventional procedures, and preferred imaging techniques and pharmacotherapy, in cases of thrombus resistant to chronic oral anticoagulation (OAC) treatment, are largely unknown. The European Heart Rhythm Association (EHRA) conducted a survey to capture contemporary clinical practice in those areas of AF care. A 22-item online questionnaire was developed and distributed among the EHRA electrophysiology research network centres. The survey contained questions regarding indications, type and timing of imaging before CV or LA procedures and management of LA appendage (LAA) thrombus with special emphasis on thrombus resistant to OAC. Of 54 responding centres 63% were university hospitals. Most commonly, TOE would be performed in cases of inadequate or unclear pre-procedural anticoagulation, even in AF lasting <48 h (52% and 50%, respectively), and 15% of centres would perform TOE before AF ablation in all patients. If thrombus was diagnosed despite chronic OAC, the prevalent strategy was to change current OAC to another with different mechanism of action; 51% of centres would wait 3–4 weeks after changing the OAC before using another imaging test, and 60% of centres reported two attempts to dissolve the thrombus. Our survey showed a significant utilization of TOE before CV or AF ablation in European centres, extending beyond AF guidelines-suggested indications. When thrombus was diagnosed despite chronic pre-procedural OAC, most centres would use another anticoagulant drug with different mode of action.

Keywords Atrial fibrillation • Left atrial appendage • Thrombus • Stroke • Anticoagulation • Cardioversion • Ablation • Guidelines • EHRA survey

Introduction

Left atrial (LA) thrombosis is a contraindication to electrical or pharmacological cardioversion (CV) or catheter ablation (CA) in patients with atrial fibrillation (AF).[1] A ≥3-week course of effective oral anticoagulant (OAC) therapy is recommended to prevent periprocedural thromboembolism in AF patients scheduled for elective CV or CA or, alternatively, transoesophageal echocardiography (TOE) may be used to exclude LA thrombus before the procedure.[1,2] However, despite continuous OAC therapy, LA appendage (LAA) thrombus,

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or sludge formation are sometimes detected on preprocedural TOE (up to 5% absolute risk); therefore, some centres routinely perform TOE in all patients undergoing CV or CA.[2–6]

Thrombus resolution in previously non-anticoagulated patients can be achieved with either a vitamin K antagonist (VKA) or non-vitamin K antagonist oral anticoagulant (NOAC),[2,7,8] whereas treatment options for patients with LAA thrombus who are already on OAC are less clear.[9–11] To capture the contemporary routine clinical practice regarding pre-procedural diagnostic work-up in AF patients scheduled for CV or CA of AF and subsequent management of AF patients with LA thrombosis, the European Heart Rhythm Association (EHRA) Scientific Initiatives Committee (SIC) conducted a centre-based survey.

Methods and results

This centre-based survey was conducted among the EHRA Electrophysiology Research Network centres, between 14 February 2019 and 7 March 2019, using a 22-item internet-based questionnaire; 54 centres responded (46% response rate), mostly University hospitals ($n = 34$, 63%), followed by non-University hospitals ($n = 11$, 20%), and private centres ($n = 9$, 17%). In case of incomplete data, results were reported as a percentage of the available responses.

Most of the responding centres routinely performed pharmacological ($n = 51$, 94%) or electrical CV ($n = 53$, 98%) and AF ablations ($n = 51$, 94%), whereas percutaneous interventional procedures were performed in fewer centres (LAA closure $n = 37$, 68.5%; mitral valve edge-to-edge repairs $n = 26$, 48%). The LAA thrombus prevalence was estimated to be 1–2% by 21 respondents (42%), 3–5% by 14 (28%), <1% by 13 (26%), and 6–10% by 2 respondents (4%).

Periprocedural imaging

Local practice indications for a cardiac imaging before CV or CA in patients with AF lasting <48 h and ≥48 h are presented in *Figure 1*. Unsurprisingly, the history of LA thrombus was a common indication for TOE regardless of the duration of AF episode.

In addition, many centres would also perform TOE in patients with AF lasting <48 h in case of lacking or incomplete information about prior anticoagulation ($n = 26$, 52% and $n = 25$, 52%, respectively), and 6 centres (12%) would routinely perform TOE before any LA procedure, regardless of the type, or duration of AF.

In most centres ($n = 48$, 94%), TOE was the first-line imaging test, followed by contrast TOE, computed tomography (CT), or the combination of TOE and CT (each reported by a single centre, 2%). In case of inconclusive or unclear result of the first imaging test: 25 centres (52%) would proceed with another imaging test before treatment decision, the procedure would be postponed, and patients re-scheduled for imaging after a change in OAC in 15 centres (31%), whereas in 7 centres (14.5%) OAC would not be changed. Only one centre would continue with the procedure as scheduled if no clear thrombus was identified (2%). When first-line imaging was unclear, 34 respondents (71%) considered CT confirmatory, followed by contrast TOE ($n = 11$, 23%) and intracardiac echocardiography ($n = 3$, 6%). When CT was the first-line test, TOE with or without contrast was utilized as the second test.

Thrombus management

If LAA thrombus was diagnosed in previously non-anticoagulated patients, the most prevalent first-line treatment among the participating centres would be the initiation of a NOAC ($n = 30$, 64%), whereas a VKA would be prescribed in 14 centres (30%).

In case of thrombus persistence after a course of treatment with a VKA, NOAC-eligible patients would be switched to a NOAC in 20 centres (42.5%), while thorough assessment of adherence to, and quality of, VKA therapy would be the first step in 11 centres (23.4%) and 8 centres (17.0%) would increase the target INR to 2.5–3.5. Low-molecular weight heparin (LMWH) instead of VKA would be used in 3 centres (6.4%). When NOACs were contraindicated, 21 centres (45%) would increase target INR to 2.5–3.5; 12 (25.5%) would reassess prior INRs and calculate the time in therapeutic range (TTR) before making a decision about further treatment, and 7 centres (15%) would switch from VKA to LMWH (or unfractionated heparin, $n = 1$, 2%). In both clinical situations, antiplatelets were utilized infrequently: only 2 centres (4.3%) would add a single antiplatelet to VKA and none would prescribe dual antiplatelet therapy.

When thrombus was diagnosed despite chronic NOAC treatment, the most often reported strategy was to switch from NOAC to VKA with target INR 2.5–3.5, followed by target INR 2–3: together they accounted for about half of the responses across all NOACs (*Figure 2*). When NOAC to NOAC change was considered, there was a slight preference for using apixaban or dabigatran as the next choice (*Figure 3*). Other strategies comprised change of treatment to LMWH or remaining on the same drug and dose, with subsequent repeated imaging. Seven centres (15%) reported lack of experience with edoxaban at the time of the survey.

Repeat imaging

Imaging would be repeated 3–4 weeks after the change of OAC in 24 centres (51%), 14 centres (30%) would postpone repeat imaging for 5–6 weeks, and in 5 centres (11%) the time to repeated imaging would exceed 2 months.

In cases of LAA thrombus diagnosis on repeat imaging, proposed strategies varied significantly and comprised substitution of current OAC for another drug not administered previously, additional antiplatelet or LMWH on top of the current OAC or no change of treatment followed by another imaging test (*Figure 4*), whereas in 6 centres (13%) the planned procedure would be cancelled.

Most centres ($n = 20$, 42.5%) would repeat imaging 3–4 weeks after a second change of treatment for LAA thrombus, while the rest would wait 5–6 weeks ($n = 13$, 27.7%) or longer than 2 months ($n = 14$, 29.8%). The majority of centres reported two treatment changes ($n = 28$, 59.6%) before the final decision to proceed with or abandon the procedure, while 12 centres (25.6%) would not change the treatment more than once and 6 (12.8%) would accept three changes of treatment or more than four ($n = 1$, 2%).

Discussion

This survey provided an insight into current clinical practice related to periprocedural diagnosis and management of the LAA thrombus in patients with AF undergoing AF CV or CA. The main findings of our survey are as follows:

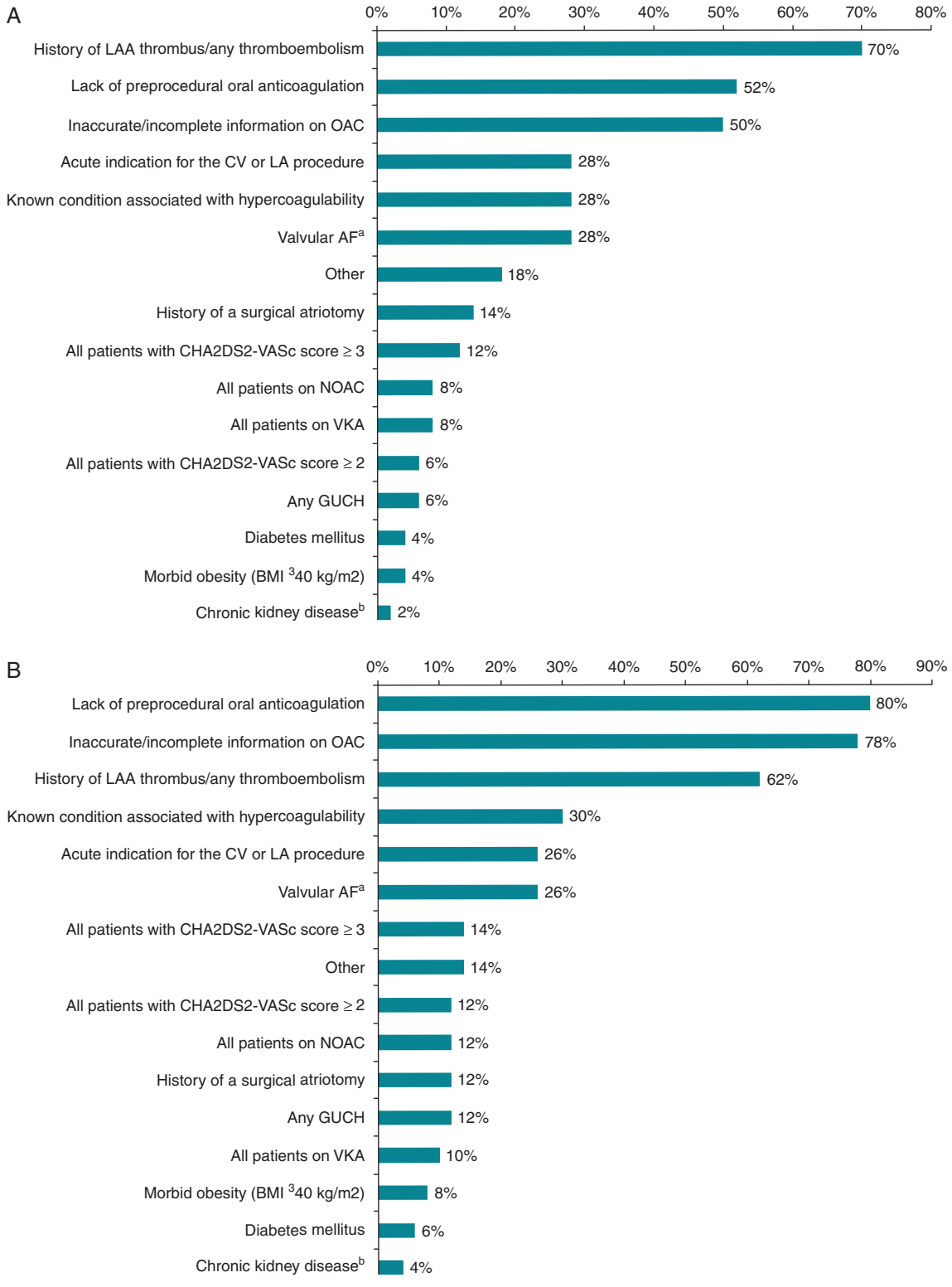

Figure 1 Indications for cardiac imaging before a cardioversion or left atrial interventional procedure in patients with atrial fibrillation lasting <48 h (*A*) and ≥48 h (*B*). AF, atrial fibrillation; BMI, body mass index; CV, cardioversion; GUCH, Grown Up Congenital Heart; LA, left atrium; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulant; VKA, vitamin K antagonist. [a]Valvular AF defined as mitral valve stenosis or a prosthetic valve. [b]Chronic kidney disease defined as a glomerular filtration rate of <60 mL/min/1.73 m^2 for >3 months.

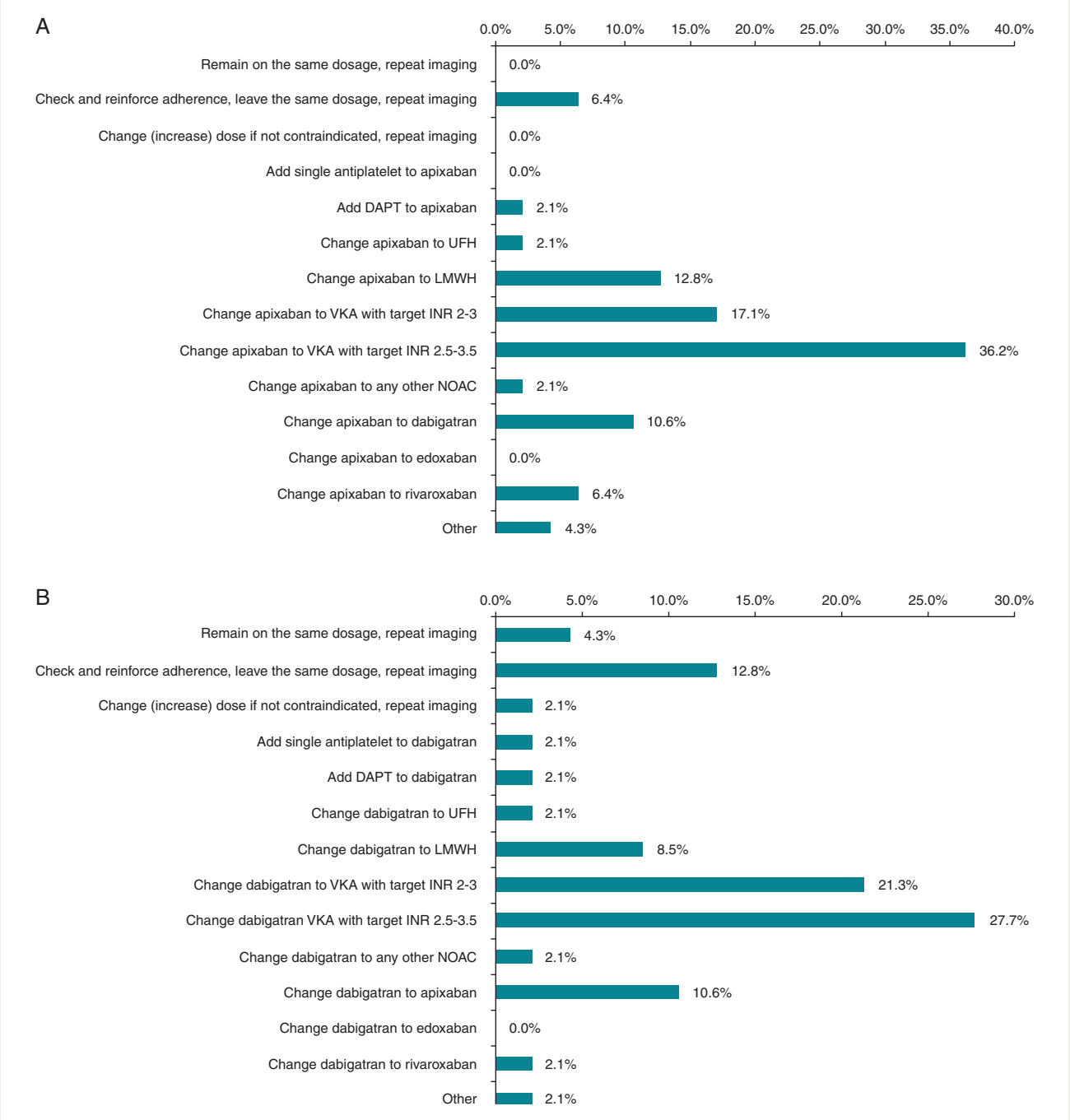

Figure 2 Clinical decisions in patients with left atrial appendage thrombus despite chronic use of: apixaban (*A*), dabigatran (*B*), edoxaban (*C*), and rivaroxaban (*D*). DAPT, dual antiplatelet therapy; LMWH, low-molecular weight heparin; NOAC, non-vitamin K antagonist oral anticoagulant; UFH, unfractionated heparin; VKA, vitamin K antagonist.

i. The most common indication for pre-procedural imaging of the LA/LAA (apart from a history of the LAA thrombosis or any prior thromboembolic event) was an unreliable information about pre-procedural OAC, irrespective of AF duration before CV/CA (i.e. <48 h or ≥48 h). Also, one in four patients with an acute indication for CV would undergo pre-procedural LA/LAA imaging irrespective of pre-procedural duration of AF,
ii. Transoesophageal echocardiography was the most commonly used first-line imaging to exclude the LA/LAA thrombus,
iii. When LA/LAA thrombosis was diagnosed in non-anticoagulated AF patients, a NOAC was the most common first-choice treatment (64%),
iv. When LA/LAA thrombus was diagnosed in patients already taking OAC, the current drug would be switched for another OAC in 50% of responding centres, and most centres (81%) would postpone the procedure and repeat imaging in up to 6 weeks, and
v. Most of the centres would proceed with two OAC switches and repeated imaging before performing or giving up the procedure.

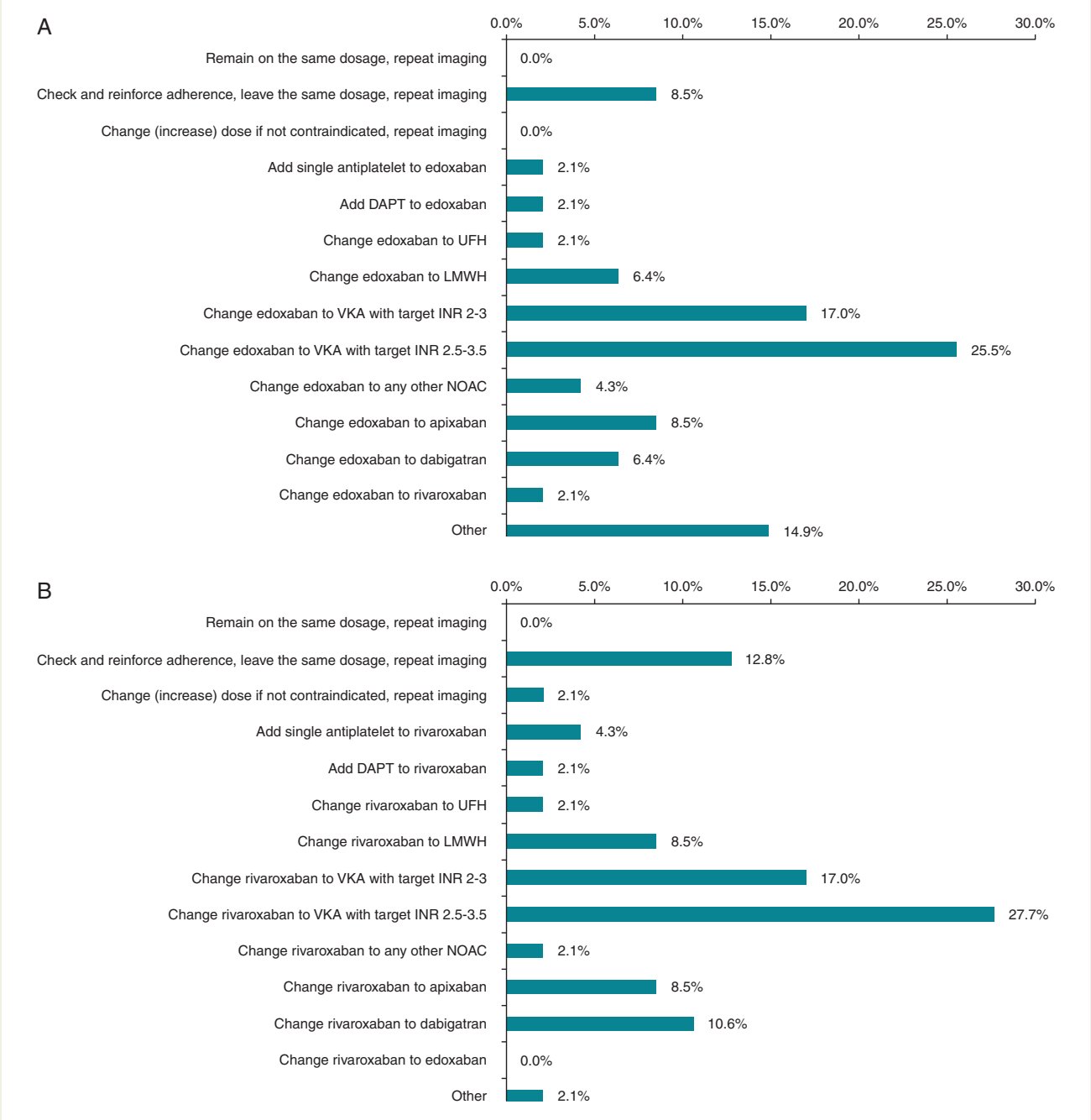

Figure 2 Continued.

Pre-procedural imaging—indications and techniques

International Guidelines for AF management recommend imaging to exclude the LAA thrombosis in patients with AF lasting for ≥48 h who were not taking OAC before CV/CA or have not completed a minimum 3-week course of therapeutic OAC before the procedure. Pre-procedural LAA thrombosis exclusion before CV/CA is also reasonable when the information about pre-procedural OAC (especially NOACs) is uncertain or incomplete. However, non-anticoagulated patients with AF <48 h can be cardioverted without previous long-term OAC (but anticoagulation should be started as soon as possible).[1,2,12–14]

Our survey showed that the history of LAA thrombosis or thromboembolic events, inadequate/incomplete information about pre-procedural OAC therapy, questionable adherence to OAC in the pre-procedural period, or an acute indication for CV/CA were the most common indications for pre-procedural LAA imaging irrespective of pre-procedural AF duration. A variety of other reasons for

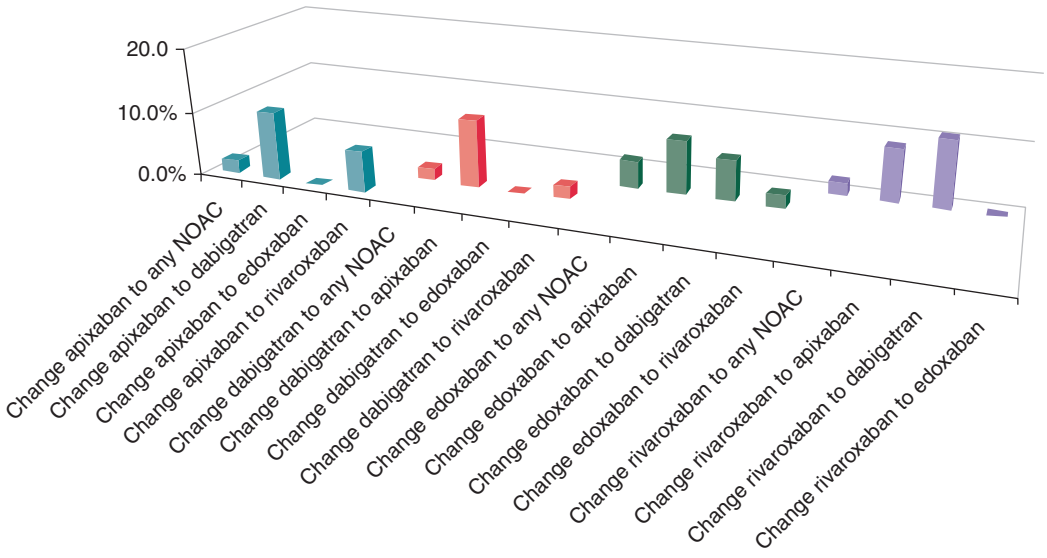

Figure 3 Preferred substitution of one NOAC for another in cases of left atrial appendage thrombus resistant to anticoagulation. NOAC, non-vitamin K antagonist oral anticoagulant.

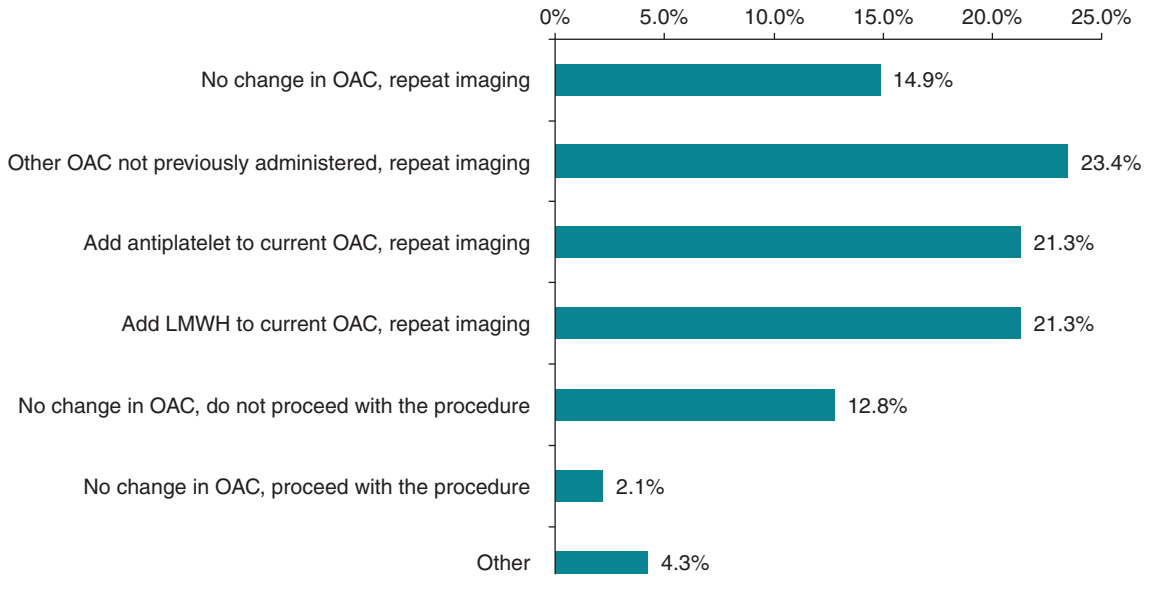

Figure 4 Strategy adopted in case of thrombus persistence in left atrial appendage after the first change of oral anticoagulation regimen. LMWH, low-molecular weight heparin; OAC, oral anticoagulant.

pre-procedural LAA imaging were also stated by some centres, but the decision to rule out the LAA thrombosis using pre-procedural imaging was rarely driven by individual patient stroke risk (i.e. the CHA_2DS_2 VASc score value) and apparently was not influenced by the pre-procedural AF duration.

In concordance with international AF guidelines, TOE was the pre-procedural imaging modality of choice. High utilization of TOE was evident, regardless of pre-procedural duration of AF, and may reflect a high accessibility to this imaging test in participating centres but also a conservative approach to the safety of the procedure. Of note, about 15% of centres used pre-procedural TOE in all patients scheduled for AF ablation, irrespective of the type of AF or OAC status at admission.

In case of equivocal result of the first test, approximately half the responding centres would perform another imaging test (mainly cardiac CT), and half would postpone the procedure. A recent meta-

analysis comparing TOE to CT (22 studies) or cardiac magnetic resonance imaging (4 studies) indicated a very high sensitivity and specificity of CT for identifying LAA thrombi (sensitivity 0.99 and specificity 0.94 vs. TOE).[15]

Management of patients diagnosed with the left atrial appendage thrombosis

Recent studies showed low rates of thromboembolic events in patients treated with NOACs for ≥3 weeks before CV.[2,7,16,17] However, a documented LAA thrombosis is a contraindication for CV/CA.[1,2] Reportedly, the risk of thrombus formation despite continuous OAC can be as high as 5%, and probably is similar between patients taking VKA and NOAC.[5,18] Although imaging was not mandatory in the randomized clinical trials comparing NOACs vs. warfarin for stroke prevention in AF patients undergoing CV, if LA/LAA thrombus was diagnosed before CV[19], the procedure was postponed for at least three weeks of continuous anticoagulation.[7,16,17]

In this survey, when LAA thrombus was diagnosed in a non-anticoagulated patient, the most prevalent first-line treatment was the use of a NOAC, whereas LMWH was rarely chosen. This is in accordance with AF guidelines, where NOACs are generally recommended as the first-line OAC therapy for stroke prevention in AF patients, including those undergoing CV or CA for AF.[1,2]

However, optimal management of patients diagnosed with LAA thrombosis while taking an OAC is less well established.[1,2] Evidence-based data on the effectiveness of NOAC for the LAA thrombus resolution in patients previously taking a VKA is scarce, but switching from VKA to a NOAC was the most prevalent strategy reported in our survey.[8,20,21] In case of contraindication to NOACs, some participating centres opted for increasing the target TTR of INR values and meticulous assessment of VKA adherence. Importantly, the guidelines recommended careful assessment of the history of VKA treatment with time in TTR calculation the preferred management strategy in only 23.0–25.5% of centres regardless of indication or contraindication to NOACs. Overall, unfractionated heparin or antiplatelet drugs were used rarely.

Even less is known about optimal treatment of the LAA thrombus in patients already on NOACs, and suggested strategies comprised a change from one NOAC to another or no change of the treatment.[9–11,22] Our survey showed that, regardless of the index NOAC, the most prevalent strategy was to change NOAC to VKA, with either higher (2.5–3.5) or standard target INR (2.0–3.0) (~50% of the respondent). When NOAC to NOAC substitution was considered, apixaban or dabigatran were most commonly chosen as the replacement.

After changing the OAC drug, about half of the centres would perform another imaging test after 3–4 weeks of new OAC treatment, in line with the anticipated time frame needed for LAA thrombus resolution.[1,2] Data are lacking to inform the optimal management of AF patients with persistent LAA thrombus despite optimized OAC therapy. A single publication described resolution of warfarin- and dabigatran-resistant thrombus by apixaban.[10] If the thrombus was still present after a course of OAC, the adopted strategy was another change of NOAC, or addition of either antiplatelet agent or LMWH to the current treatment (*Figure 4*).

Study limitations

In addition to the limitations inherent to observational cross-sectional studies, our survey mostly reflects the management of AF in University Hospitals, whereas current practice in non-academic (or medium-to low volume) centres across Europe may be different, depending of the knowledge about guideline-recommended AF management, availability of diagnostic assessment tools and local policies in AF management.

Conclusions

Our study revealed a significant utilization of TOE before AF CV or ablation regardless of the type or duration of AF, which represented a more conservative strategy than suggested by current AF guidelines. When thrombus was diagnosed despite chronic pre-procedural OAC, most respondents opted for a change of OAC drug, using a drug with different mode of action. More data are needed to inform optimal management of AF patients with persistent LAA thrombosis despite optimized OAC therapy.

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