Abstract
Atrial fibrillation (AF) remains the most common arrhythmia. The sinus rhythm restoration procedure without adequate anticoagulant preparation may lead to a thromboembolic event in approximately 5–7% of patients. The initiation of oral anticoagulation significantly reduces this risk by inhibiting formation of embolic material in the heart cavities, especially in the left atrial appendage (LAA). However, there is a group of patients who develop embolic material in the LAA despite oral anticoagulation treatment. The best treatment method to dissolve thrombus in the LAA is not clear, due to the lack of studies with adequate power and endpoints that can determine the best management strategy. We present clinical trials comparing the efficacy and safety of oral anticoagulants in patients undergoing AF cardioversion. We evaluate the frequency of LAA thrombus formation in patients with AF on treatment with oral anticoagulants. Furthermore, we discuss the effectiveness of various treatment strategies on LAA thrombus resolution.

Keywords: electric cardioversion, atrial fibrillation, left atrial appendage thrombus, transoesophageal echocardiography, non-vitamin K antagonist oral anticoagulants

Electric cardioversion among patients treated with NOACs
In recent years, the results of three prospective, randomised trials comparing the efficacy and safety of NOAC versus heparin/VKA in patients undergoing electrical cardioversion were published, the X-VeRT trial with rivaroxaban, the ENSURE-AF trial with edoxaban, and the EMANATE trial with apixaban. In the X-VeRT trial, 1 504 patients with AF of unknown duration or lasting more than 48 hours were randomised into two groups, those receiving rivaroxaban once daily (20 or 15 mg depending on creatinine clearance) or those receiving VKAs in a 2:1 ratio. The incidence of stroke, systemic embolism, myocardial infarction and cardiovascular death was low (between 0.5 and 1%), which was comparable for NOAC and VKA in the 30-day
Table 1. Effectiveness and safety of oral anticoagulants among non-valvular AF patients who underwent ECV (data from randomised, controlled trials)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Trial design</th>
<th>NOAC</th>
<th>No of patients</th>
<th>Sample size, n</th>
<th>Observation period after randomisation</th>
<th>Efficacy, n (%)</th>
<th>Safety, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-VeRT</td>
<td>RCT to determine events after CV</td>
<td>Rivaroxaban</td>
<td>1504</td>
<td>1167 cardioverted</td>
<td>1002</td>
<td>502</td>
<td>30 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke 2 (0.20)</td>
<td>HS 0</td>
<td>IS 0</td>
</tr>
<tr>
<td>ENSURE-AF</td>
<td>RCT to determine events after CV</td>
<td>Edoxaban</td>
<td>2199</td>
<td>2149 received study drug</td>
<td>1095</td>
<td>1104</td>
<td>28 days to assess efficacy and 28 + 30 days to assess safety</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke 0</td>
<td>HS 0</td>
<td>IS 2 (0.18)</td>
</tr>
<tr>
<td>EMANATE</td>
<td>RCT to determine events after CV</td>
<td>Apixaban</td>
<td>1500</td>
<td>1338 cardioverted</td>
<td>753</td>
<td>747</td>
<td>30 days cardioverted</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke 0</td>
<td>HS 0</td>
<td>IS 2 (0.18)</td>
</tr>
<tr>
<td>RELY subgroup</td>
<td>Post hoc analysis of an open-label RCT</td>
<td>Dabigatran</td>
<td>1270 from 18 113</td>
<td>413 – D110 436</td>
<td>413 – D110 436</td>
<td>30 days</td>
<td>Stroke and SEa</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke and SEa 5 (0.77)</td>
<td>D110 2 (0.30)</td>
<td>Stroke and SEa 2 (0.48)</td>
</tr>
<tr>
<td>ROCET AF subgroup</td>
<td>Post hoc analysis of an open-label RCT</td>
<td>Rivaroxaban</td>
<td>321 from 14 264 underwent ECV, PCV, catheter ablation</td>
<td>160</td>
<td>161</td>
<td>During studyb</td>
<td>Stroke and SE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke and SE 2 (1.25)</td>
<td>D110 2 (0.48)</td>
<td>Stroke and SE 0</td>
</tr>
<tr>
<td>ARISTOTLE subgroup</td>
<td>Post hoc analysis of an open-label RCT</td>
<td>Apixaban</td>
<td>540 from 18 201</td>
<td>265</td>
<td>275</td>
<td>30 days</td>
<td>Stroke and SE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke and SE 2 (0.48)</td>
<td>D110 2 (0.48)</td>
<td>Stroke and SE 0</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48</td>
<td>Post hoc analysis of an open-label RCT</td>
<td>Edoxaban</td>
<td>365 from 21 105</td>
<td>140 – E60/30 114</td>
<td>140 – E60/30 114</td>
<td>30 days</td>
<td>Stroke and SE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke and SE 2 (0.48)</td>
<td>D110 2 (0.48)</td>
<td>Stroke and SE 0</td>
</tr>
</tbody>
</table>

*For all cardioversions, †for first-time cardioversions (n = 1 270), median follow up of 2.1 years.

RCT, randomised controlled trial; NOAC, novel oral anticoagulant; VKA, vitamin K antagonist; CV, cardioversion; All-cD, all-cause death; CRNMB, clinically relevant non-major bleeding; CVD, cardiovascular death; D110, dabigatran 110 mg; D150, dabigatran 150 mg; E30, endoxaban 30 mg; E60, endoxaban 60 mg; ECV, electrical cardioversion; FB, fatal bleeding; HS, hemorrhagic stroke; IS, ischaemic stroke; MB, major bleeding; PCV, pharmacological cardioversion; SE, systemic embolism.
of more than 48 hours and less than one year (Table 1). The third study was the apixaban study, EMANATE, which enrolled 1,500 patients. Apixaban was randomly administered to 753, while 747 patients received warfarin with heparin bridging therapy. In the apixaban group, no patients developed stroke at 30 days, compared to six in the heparin/VKA group. Systolic embolism events were not observed in either group. There were two deaths in the apixaban group (0.27%, 95% CI: 0.03–0.96%) and one in the heparin/VKA group. Finally, there were fewer major bleeding events in the apixaban group than in the heparin/VKA group (3/735 and 6/722 patients, respectively) (Table 1).

A meta-analysis of the above trials (n = 5,203 patients) revealed that the composite primary outcome (stroke/systemic embolism, myocardial infarction or cardiovascular death) was significantly reduced with NOAC treatment compared with VKA. This outcome occurred in 12 (0.42%) of 2,850 patients randomised to receive a NOAC versus 23 (0.98%) of 2,353 patients randomised to receive a VKA, with a pooled risk ratio of 0.42 (95% CI: 0.21–0.86; p = 0.017). Differences between NOAC and VKA in all-cause mortality and major bleeding were not observed.

Additional information confirming the above conclusions was provided by sub-analyses of the main registry studies concerning dabigatran (RELY study), rivaroxaban (ROCKET AF study), apixaban (ARISTOTLE study) and edoxaban (ENGAGE AF-TIMI 48 study). Sub-analyses included patients who underwent electrical cardioversion during the course of the study (Table 1).

The results of the above randomised trials have been confirmed by retrospective observational studies. Geurink et al. showed no differences in the incidence of stroke or TIA within the first year after ECV among 1,613 AF patients treated with NOAC or VKA. These results are comparable to results of another study based on a group of 2,150 patients undergoing ECV. Moreover, the use of NOAC has been shown to significantly reduce the time to ECV, eliminating the risk of unplanned postponement of the procedure due to non-therapeutic INR results.

In the Kalejs et al. study involving 525 patients, the average time for treatment before cardioversion was significantly lower for dabigatran (25 days) versus warfarin (35 days; p < 0.01). These results are in accordance with results from another study including 570 patients. The median time from the initiation of dabigatran to the first cardioversion was 32 versus 74 days with warfarin.

**Table 2. The frequency of LAA thrombus formation in patients treated with oral anticoagulants (data from RCTs)**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>NOAC</th>
<th>No of patients</th>
<th>Sample size, n</th>
<th>Patients with TEE performed, n</th>
<th>Patients with thrombus in LAA, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-VeRT</td>
<td>RCT to determine</td>
<td>Rivaroxaban</td>
<td>1,504</td>
<td>1,002</td>
<td>502</td>
<td>NOAC 1.0% VKA 1.1%</td>
</tr>
<tr>
<td>ENSURE-AF</td>
<td>RCT to determine</td>
<td>Edoxaban</td>
<td>2,199</td>
<td>1,095</td>
<td>1104</td>
<td>NOAC 7.1% VKA 7.2%</td>
</tr>
<tr>
<td>EMANATE</td>
<td>RCT to determine</td>
<td>Apixaban</td>
<td>1,500</td>
<td>753</td>
<td>747</td>
<td>NOAC 0% VKA 0%</td>
</tr>
<tr>
<td>RELY subgroup</td>
<td>Post hoc analysis of</td>
<td>Dabigatran</td>
<td>1,270 from 18,113</td>
<td>413 (D110)</td>
<td>436</td>
<td>NOAC 1.8% VKA 1.1%</td>
</tr>
<tr>
<td>ROCET AF subgroup</td>
<td>Post hoc analysis of an open-label RCT</td>
<td>Rivaroxaban</td>
<td>321 from 14,264</td>
<td>421 (D150)</td>
<td>436</td>
<td>NOAC 1% VKA 1%</td>
</tr>
<tr>
<td>ARISTOTLE subgroup</td>
<td>Post hoc analysis of</td>
<td>Apixaban</td>
<td>540 from 18,201</td>
<td>160</td>
<td>161</td>
<td>NOAC 1.2% VKA 1.1%</td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 subgroup</td>
<td>Post hoc analysis of an open-label RCT</td>
<td>Edoxaban</td>
<td>365 from 21,105</td>
<td>140 (E60/30)</td>
<td>114</td>
<td>NOAC 0% VKA 0%</td>
</tr>
</tbody>
</table>

†EMANATE trial – 14 patients from 855 underwent only computed tomography.

NOAC: novel oral anticoagulant; VKA: vitamin K antagonist; TEE: transoesophageal echocardiography; LAA: left atrial appendage; CV: cardioversion; D110, dabigatran 110 mg; D150, dabigatran 150 mg; E30, edoxaban 30 mg; E60, edoxaban 60 mg; ECV, electrical cardioversion; PCV, pharmacological cardioversion; RCT, randomised controlled trial.

**Thrombi in the left atrial appendage in patients treated with oral anticoagulants**

The main source of embolic material (approximately 90%) in non-valvular AF is the left atrial appendage (LAA). Thrombi in the LAA occur in 5–27% of patients with AF naïve to oral anticoagulation. This rate is comparable in patients treated with subtherapeutic doses of VKA. More intensive treatment with vitamin K derivatives while maintaining the INR within the therapeutic range between 2 and 3 led to a lower incidence of embolic material, with a frequency of LAA occurring in approximately 0.6–8.3% of cases. Based on the current knowledge, it seems that the incidence of embolic material in the LAA is similar among patients treated with VKA and NOACs.

In the ARISTOTLE study, 743 cardioversions were performed in 540 patients. The procedure was preceded by TEE in 171 patients, 86 of whom were treated with apixaban and 85 who were treated with warfarin; no LAA thrombus was detected in any of the groups. In the RELY study, 1,983 cardioversions were performed in 1,270 patients; TEE was performed more often before the procedure in patients treated with dabigatran than those treated with warfarin (25.5 vs 24.1 vs 13.3% of cases for dabigatran 2 × 110 mg, dabigatran 2 × 150 mg, and warfarin, respectively). A thrombus was found in 1.8% of patients treated with dabigatran 2 × 110 mg, 1.2% treated with dabigatran 2 × 150 mg, and 1.1% treated with warfarin. Unfortunately, no data on the rate of echocardiographic examinations and their results have been published in the ROCKET-AF (rivaroxaban) and ENGAGE AF-TIMI 48 (edoxaban) study populations.

An analysis of the studies comparing NOAC and VKA in patients undergoing electrical cardioversion obtained the following results regarding the incidence of thrombus in the LAA: ENSURE-AF study, 8.0% in the edoxaban group and 7.1% in the warfarin group; XVeRT study, 5.1% in the rivaroxaban group.
group and 4.6% in the VKA group; and EMANATE study, 7.2% of patients in the apixaban group and 7.1% in the VKA group. It is worth noting that in these studies, TEE was not performed routinely.

In the meta-analysis of the above studies (excluding the EMANATE study), the incidence of thrombus in the LAA was estimated to be approximately 5% in both the VKA and NOAC groups. A similar rate of thrombus occurrence was demonstrated by Frenkel et al., who analysed the results of TEE performed in 388 patients prior to AF/flutter ablation. A thrombus was detected in 4.4% of 183 patients treated with NOACs and in 2.9% of 205 patients treated with warfarin. In the NOAC group, a thrombus was found in 3.4% of 93 dabigatran users and 4.8% of 62 rivaroxaban users. Interestingly, no thrombi were recorded in the group of 28 patients treated with apixaban.

In another study in which the results of TEE performed before electrical cardioversion of persistent AF (lasting at least seven days) were analysed among 127 patients treated with apixaban, the incidence of LAA thrombus was 5.9%. Furthermore, in a retrospective study of 559 patients in the Asian population, thrombi in the LAA were detected in 2.6 and 2.8% of patients treated with NOAC and VKA, respectively, despite prior anticoagulation treatment for a minimum of three weeks.

### Predictive factors of embolic material in the heart cavities

It should be remembered that the thrombotic process in the LAA may take place despite adequate and long-term anticoagulation with the use of both vitamin K-derivative and non-vitamin K-derivative drugs. It is challenging to extract patients at high risk of LAA by thrombus appearance. Scales for the clinical risk of thromboembolic events in AF (CHADS, and CHA2DS2-VASc) can be helpful; both scales have the potential to predict LAA thrombus occurrence. Most studies showed a positive correlation with the scores 0.62 and 0.75 for the CHADS, and CHA2DS2-VASc scores, respectively.

In studies by Uz et al. and Tang et al., which enrolled a total of 1 100 patients, no thrombus was detected in patients in the studies with a score of 0–2 and 0, respectively, on the CHA2DS2-VASc scale. However, a low CHADS score cannot reliably rule out embolic material in the LAA. In the ACUTE study, a thrombus was detected by TEE among 14 out of 138 patients without anticoagulant treatment, despite a CHADS score of 0.

Various biomarkers have been shown to increase the diagnostic utility of these scales in detecting thromboembolic material in the LAA. B-type natriuretic peptide concentration, mean red blood cell volume (MCV), mean platelet volume (MPV), uric acid concentration, eosinophil count and D-dimer levels provide additional prognostic information for the occurrence of embolic material. Among patients treated with anticoagulants, separate clinical factors such as chronic heart failure, age, female gender, structural heart disease, other cardiomyopathy, use of anti-arrhythmic drugs, duration of arrhythmia, and higher CHADS, or CHA2DS2-VASc scores may be helpful in identifying patients with a high probability of thrombus in the LAA.

Echocardiographic predictors of thrombosis in the LAA include features and parameters assessing the structure and function of the heart as a whole, as well as the atrium or its appendage separately. It has been shown that a reduced ejection fraction (EF) (EF < 50%), hypertrophy, increased left ventricular end-diastolic pressure, left atrial enlargement [left atrium (LA) > 50 mm, LA area > 30 cm², LA volume index > 28 ml/m²], or degree of spontaneous blood contrasting in the LA cavity may indicate patients with a higher risk of LAA thrombus.

The LAAVs differ in shape, size and orientation with regard to the surrounding structures. Based on pathomorphological studies, it is known that the LAA most often has two lobes (54%), and less frequently three lobes (23%), one lobe (20%) and four lobes (3%). The number of lobes has been shown to be an independent risk factor for thrombus occurrence, as is the higher position of the appendage and its increased volume.

Based on computed tomography images, Di Base et al. divided the morphology of the LAA into four types: chicken wing (48%), cactus (30%), sleeve (19%) and cauliflower (1%). They demonstrated that cerebrovascular events were significantly more frequent in the group of patients with LAA morphologies other than the chicken wing. The reason for this dependence may be the lower flow velocity in non-chicken-wing-shaped appendices. Low LAA flow velocity is correlated with thrombus formation and ischaemic stroke.

### Should patients using NOACs for three weeks or more undergo TEE prior to electrical cardioversion?

Based on the published results of the European Heart Rhythm Association (EHRA) survey containing knowledge about everyday clinical practice in 54 European clinical centres, it is known that TEE remains the most frequently performed imaging test before electrical cardioversion and AF ablation (94% of centres). But it has been shown that only 12% of centres perform this examination routinely before restoring sinus rhythm, regardless of the type and duration of the arrhythmia. There are currently discussions about the routine performance of TEE prior to electrical cardioversion.

The latest 2021 EHRA guidelines for the use of NOACs in patients with AF recommend ruling out LA/LAA thrombus with TEE in case of doubt about treatment adherence or if deemed high risk for LA thrombus. However, the authors do not specify in which patients the risk of the incidence of embolic materials in heart cavities is elevated. Experts leave the decision to perform a TEE to the physician.

It is difficult to compare results of VKA-based study with treatment with NOAC, but the findings of Siedl et al. are very interesting. In that study, the authors included patients with persistent AF and effective anticoagulation (receiving warfarin for three or more weeks, with INR 2–3) and divided the population into two groups; 719 patients in which cardioversion was performed after TEE (TEE-guided approach) and 357 patients undergoing cardioversion without TEE. In the TEE-guided approach the thrombus in the LAA was observed in 7.7% of the patients. During the first four weeks after ECV, the rate of thromboembolic complications were 0.8 in both groups. These results suggest that TEE-guided ECV does not reduce the risk of embolism, and the thrombus, even if present, may not necessarily be dislocated to cause thromboembolic complications.

Furthermore, thromboembolic complications may be caused by embolic material formed after ECV. New development of
thrombus may be associated with the transient LA and LAA dysfunction ('stunning') caused by electric shock.\textsuperscript{44} Berger \textit{et al.} analysed data from 32 studies with a total number of 4,621 patients. They showed thromboembolic events among 92 patients; 82\% of embolic episodes occurred in the first three days and 98\% within 10 days of cardioversion.\textsuperscript{66}

The most recent meta-analysis of studies in patients undergoing pharmacological and electrical cardioversion showed a peri-procedural stroke or systemic embolism rate of 0.41\% in the NOAC group versus 0.61\% in the VKA group.\textsuperscript{70} Considering that the mean incidence of thrombus in the LAA despite NOAC treatment is 5\%, the conclusion emphasises the fact that not every thrombus in the LAA will cause a stroke during cardioversion of the arrhythmia.

According to current knowledge, it is not easy to answer the question whether to perform TEE or not before cardioversion in AF patients using NOACs. According to the authors, a practical decision-making algorithm proposed by Gorczyca \textit{et al.} is very interesting.\textsuperscript{43} The authors analysed commonly known risk factors of LAA thrombus based on results from previous studies and they merged them in a simple screening path.

Gorczyca \textit{et al.} recommend pre-procedural TEE in patients who had left atrial appendage thrombus (LAAT) in the past, regardless of treatment strategy, and also in those with any suspicion of unsystematic NOAC use. In the remaining patients, the necessity for TEE should be decided upon after considering individual thromboembolic risk. The authors suggest TEE in patients with any strong LAAT risk factors, such as previous intracardiac thrombus, irregular use of NOAC, inappropriate dose reduction of NOAC, previous stroke/TIA/systemic embolism, CHA\textsubscript{2}DS\textsubscript{2}-VASc score ≥ three points, glomerular filtration rate < 60 ml/min/1.73 m\textsuperscript{2}, reduced left ventricular EF, or moderate or severe left atrial enlargement.

Management of patients with a thrombus in the LAA

Embolic material in the LAA is associated with a high risk of cerebrovascular events. Leung \textit{et al.} demonstrated a high (10.4\%) annual incidence of stroke and systemic embolism, and a 15.8\% rate of annual mortality in patients with embolic material in the LAA, despite treatment with vitamin K derivatives.\textsuperscript{45} In another study of 317 patients with recent stroke, a thrombus in the LA was detected in 20\% of patients, all of which were located in the LAA.\textsuperscript{67} If such a material is detected, electrical cardioversion should be abandoned.

Unfortunately, the 2021 EHRA practical guidelines do not specify the exact treatment method to dissolve the embolic material in the LAA, which has arisen despite chronic anticoagulant treatment.\textsuperscript{43} This is due to the lack of studies with adequate power and endpoints that can determine the best management strategy.

Before the widespread use of NOACs, strategies for managing embolic material in the LAA, despite the use of oral anticoagulation, included stricter INR control, adding or changing treatment to low-molecular weight heparin, or increasing the VKA dose to achieve an INR in the range of 3–4.\textsuperscript{40} The use of NOACs creates new therapeutic possibilities in the presence of embolic material in the LA and/or its appendage; however, available data are limited to a small number of studies and case reports.

A prospective study has been published assessing the effect of rivaroxaban on a newly detected thrombus in the LAA, the X-TRA study.\textsuperscript{71} Sixty patients were enrolled in the study, of which full data were available for 53 patients, and the mean CHA\textsubscript{2}DS\textsubscript{2}-VASc score was two points. Three-quarters of the patients (76.7\%) had not been treated with anticoagulants before, and the remainder were treated with suboptimal or ineffective doses of VKA. Follow-up TEE showed that after six weeks, there was resolution in 41.5\% of patients, reduction in thrombus size in 19\%, no change in 17\%, and an increase in size in 22.5\% of patients.

The authors of this study simultaneously performed a retrospective, observational study (CLOT-AF). Finally, complete data, with control echocardiography, were obtained for 96 patients, most of whom were treated with VKA. Resolution (total resolution or reduction) of thrombotic material in the LA/LAA was demonstrated in 62.5\% of the patients.

A prospective, randomised trial, RE-LATED AF-AFNET 7 is currently underway to compare the efficacy of dabigatran 2 × 150 mg with phenprocoumon (INR 2–3) in the treatment of LAA thrombus; 110 patients are planned to be included in the study.\textsuperscript{72} Moreover, the publication by Marisco \textit{et al.}, which reviews the literature on the effects of NOACs on LA/LAA thrombus, is interesting.\textsuperscript{73}

It is worth mentioning the retrospective study by Mitamura \textit{et al.}, which included 198 patients treated with dabigatran anticoagulation due to AF (98 patients received a dose of 2 × 150 mg), who underwent TEE before electrical cardioversion.\textsuperscript{74} Dabigatran was used for up to three weeks in 21\% of patients, and up to six weeks in 55\% of patients. LA thrombi were found in 4\% of the studied population: one patient who was treated with 2 × 150 mg dabigatran and seven patients treated with 2 × 110 mg dabigatran. Echocardiography was repeated in six patients, at the earliest after 23 days in one patient, and among the others after a minimum of six weeks. Complete resolution of the thrombotic material was observed in five patients. One patient was treated with a dose of 2 × 150 mg, two patients had an increased dose from 2 × 110 mg to 2 × 150 mg, and one patient was switched to warfarin.

In the EMANATE study, a thrombus was detected in 30 apixaban-treated patients and in 31 heparin/VKA-treated patients. Another follow-up TEE was performed, after an average of 37 days, among 23 patients (77\%) in the apixaban group and 18 (58\%) in the heparin/VKA group. The resolution of thrombotic material was found in 12/23 (52\%) patients treated with apixaban and in 10/18 (56\%) patients treated with VKA.\textsuperscript{75} In the RIVA-TWICE study, Piotrowski \textit{et al.} showed that a strategy with rivaroxaban 15 mg twice daily seemed to be safe and may have dissolved LAA thrombus in seven of 15 included patients (46.7\%) who had been treated before with rivaroxaban 20 mg once a day.\textsuperscript{76}

Kołakowski \textit{et al.} analysed data of 129 patients with LAA thrombus despite adequate anticoagulation treatment and compared the effectiveness of four different strategies of thrombus resolution (all 181 cycles): switch to different mechanism, switch to similar mechanism, implementation of combination therapy (i.e. adding antiplatelet therapy), and deliberate no change in treatment.\textsuperscript{77} They showed that any change in treatment was three times more effective than deliberate no change in treatment, but no particular strategy seemed to be more effective than another.
The overall effectiveness was 51.9% regardless of the number of cycles, and 42.6% for the first cycle of treatment.

Conclusion

Based on previously published randomised and observational studies, NOACs appear to be an effective and safe alternative to VKA in patients undergoing cardioversion for AF. However, we must remember that there is a group of patients (about 5%) who will develop a LAA thrombus despite oral anticoagulation treatment, which is comparable in the NOAC and VKA groups. The presence of thrombi in this location is associated with an increased risk of peripheral embolism, mainly stroke. However, performing cardioversion in these patients can be particularly dangerous. There are known predictors of LAA thrombus occurrence; however, it is still difficult to identify patients with LAA thrombus without imaging. Therefore, there is an ongoing discussion about the routine performance of TTE, particularly in the NOAC-treated population. The 2021 EHRA practical guidelines do not specify which patients treated with NOACs should undergo TEE prior to cardioversion to exclude LA/LAA thrombi. In addition, they do not specify the methods of management with thrombotic material in this location, mainly because of limited data on this subject. Because of the available anticoagulants with different mechanisms of action, many treatment strategies can be used, but only some of them have been assessed in a prospective study focused on this issue. Therefore, further research is needed on this subject.

References

26. Wallace TW, Atwater BD, Daubert JP, et al. Prevalence and clinical characteristics associated with left atrial appendage thrombosis in fully anticoagulated patients undergoing catheter-directed atrial fibrillation...


