Safety of novel oral anticoagulants in catheter ablation of atrial fibrillation

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ABSTRACT

INTRODUCTION: Limited data are available regarding safety of catheter ablation of atrial fibrillation (AF) in patients using novel oral anticoagulants (NOAC) before and after pulmonary vein isolation. We aimed to assess the safety of a simple anticoagulation protocol in consecutive patients presenting for catheter ablation of AF.

METHODS: From November 2011 to December 2014, we prospectively included 234 patients referred for catheter ablation of AF who had already received NOAC treatment. NOAC was continued for a minimum of three months after ablation. We assessed procedure-related bleeding or thromboembolic complications, bleeding or thromboembolic complications during a three-month follow-up period and patient-reported adherence to NOAC therapy. The study has not received financial support from external resources. The study was registered with ClinTrials.gov as NCT02569255.

RESULTS: A total of 171 patients were treated with dabigatran (94% 150 mg twice daily), 38 with rivaroxaban (100% 20 mg daily) and 25 with apixaban (100% 5 mg twice daily). NOACs were interrupted for 24 hours before and re-administered two hours after the ablation procedure, without bridging with low molecular weight heparin (LMWH). No periprocedural thromboembolic complications and no bleeding complications were registered except for one pericardial effusion which was percutaneously drained without further complications. No thromboembolic or bleeding complications during follow-up were registered. All patients continued the same NOAC during follow-up as before ablation.

CONCLUSIONS: Anticoagulation with NOAC with a short period of periprocedural interruption without bridging with LMWH seems safe and well-tolerated.

FUNDING: none.

TRIAL REGISTRATION: The trial is registered as ClinTrials.gov no. NCT01569255.

In recent years, an increasing number of patients with non-valvular atrial fibrillation have been anticoagulated with novel oral anticoagulation (NOAC) drugs as an alternative to vitamin K antagonists (VKA). International guidelines recommend ablation for atrial fibrillation during uninterrupted VKA treatment and international normalised ratio (INR) levels between 2 and 3 [1]. Many centres therefore still recommend a shift from NOAC to VKA before ablation of atrial fibrillation in order to minimise both the risk of bleeding to which there is no specific antidote, and to reduce the risk of thromboembolic complications. A shift from NOAC to VKA potentially increases the risk of thromboembolic complications prior to AF ablation due to periods of unstable INR [2]. It also represents a logistic problem that complicates patient handling prior to AF ablation and it may unnecessarily increase the waiting time for AF ablation. In a setting in which three different NOACs have been approved for anticoagulation in non-valvular atrial fibrillation, the aim of this prospective study was to assess the safety and acceptability of NOACs both regarding the ablation procedure and during a three-month follow-up period.

METHODS

Patients

From November 2011 to December 2014, we prospectively included 234 consecutive patients with a mean age of 60 ± 8.6 years and 187 males with paroxysmal or persistent atrial fibrillation and referred for catheter ablation. In the same period, a total of 1,258 atrial fibrillation ablations were performed by one of the operators (PSH or HW).

Periprocedural management and anticoagulation

NOACs were paused 24 hours before the ablation procedure. No bridging with low-molecular weight heparin (LMWH) or unfractionated heparin was given. All patients underwent transoesophageal echocardiography immediately before the ablation procedure to exclude left atrial thrombi.

Immediately after trans-septal puncture, 100 IU/kg of unfractionated heparin was given and adjusted through the procedure to an intended target activated clotting time (ACT) above 300 s. Transseptal sheaths were continuously flushed with heparinised saline. At the end of the procedure, heparin was not reversed with protamine sulphate. The sheaths were removed and the vein punctures manually compressed until haemostasis.

NOACs were restarted with the same dose as before ablation two hours after the procedure.

A total of 171 patients were treated with dabigatran (162 with 150 mg twice daily), 38 patients with rivaroxaban (all 20 mg daily) and 25 with apixaban (all 5

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mg twice daily) before the ablation procedure. All patients continued with unchanged drug and dose after ablation.

Ablation

Transoesophageal echocardiography was performed in general anaesthesia with propofol and remifentanil. Mapping and ablation were performed with the patients in conscious sedation with low-dose propofol and remifentanil. One 6-F sheath was introduced into the right femoral vein for a catheter to reach the coronary sinus. Two 8.5-F trans-septal, non-steerable sheaths were introduced into the right femoral vein, and access to the left atrium was achieved using single or double trans-septal puncture at the operator's discretion.

A three-dimensional map of the left atrium and pulmonary vein ostia was obtained using the Carto system (Biosense Webster, Diamond Bar, CA) (**Figure 1**). A circular mapping catheter was used to map the left atrium as well as to ensure pulmonary vein isolation (PVI). An irrigated mapping and ablation catheter, Thermocool ST or Thermocool SF (Biosense-Webster, Diamond Bar, CA), was used for radiofrequency ablation (RFA) with a maximum power of 35 W, except for the posterior wall where a maximum power of 25 W was routinely used to avoid collateral tissue damage. PVI was ensured by elimination of pulmonary vein potentials from the circular mapping catheter in an ostial position (entrance block) as well as loss of conduction of locally captured pacing impulses from the circular mapping catheter (exit block).

At the discretion of the treating electrophysiologist, additional substrate modification was performed in some patients with persistent atrial fibrillation.

Complications

Periprocedural data on major bleeding complications and thromboembolic events were collected systematically in the patients' file. Major bleeding complications were defined as any bleeding requiring transfusion or surgical intervention and pericardial effusions requiring drainage. The patients were discharged the day after the procedure.

Follow-up

The authors (PSH) contacted all patients by mail and/or telephone and invited them to complete a standard questionnaire regarding late bleeding complications, thromboembolic events and adherence to medication three months after the ablation. A total of five patients (2.1%) neither answered the questionnaire nor responded to the phone calls. No particular characteristics in these five patients differed from the 98% of patients for whom follow-up was achieved.

Statistics

Data on patient characteristics are presented as means with standard deviations or as number and percentage of patients.

Trial registration: The trial is registered as ClinTrials.gov no. NCT01569255.

RESULTS

Patient characteristics

A total of 234 patients with symptomatic atrial fibrillation underwent AF ablation during a short pause of otherwise continuous NOAC treatment. The majority (n = 171; 73%) were treated with dabigatran before and after ablation, whereas 38 (16%) and 25 (11%) were treated with rivaroxaban or apixaban, respectively.

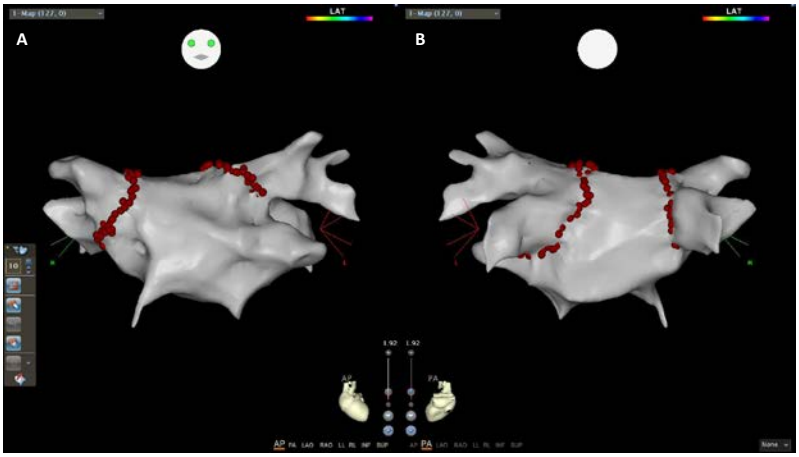
A few were treated with the lower recommended dose of dabigatran 110 mg × 2 (n = 10; 6%) due to age or concomitant amiodarone or verapamil treatment. The mean thromboembolic risk, as assessed using the CHA_2DS_2-VASc score, was 1 (range: 0-5), i.e. intermediate. The mean bleeding risk, as assessed using the HAS-BLED score, was 0.7 (range: 0-2), i.e. low.

Procedural data and periprocedural complications

Acute PVI was achieved in all patients. In 44 patients with persistent (n = 37) or long-standing persistent (n = 7) atrial fibrillation, additional left atrial substrate modification was performed (**Table 1**). The duration of the procedure was 107 ± 18 minutes, the fluoroscopy lasted

FIGURE 1

Anatomical reconstruction of the left atrium using the three-dimensional electro-anatomical mapping system Carto. **A**. The left atrium is seen in an antero-posterior projection together with the proximal part of the upper right and left pulmonary veins. **B**. The left atrium is seen from the posterior together with the upper as well as the two lower pulmonary veins.



●: Points of ablation by which the right- and left-sided pulmonary vein ostia have been isolated pairwise electrically from the body of the left atrium.

14 ± 8 minutes, and the radiofrequency application time was 28 ± 10 minutes.

Only one periprocedural complication, a pericardial tamponade, was observed. It was drained percutaneously without complications. Restart of NOAC was postponed until the morning of the first post-procedural day; and the patient went through a new and uncomplicated ablation procedure three weeks later. The rest of the patients resumed their previous NOAC treatment two hours after the ablation procedure. No late bleeding or thromboembolic complications were reported during the three-month follow-up period. All patients continued their pre-procedural NOAC treatment, both regarding the pharmacological agent and dose, for a minimum of three months. Recommendations on continuation of anticoagulation therapy beyond three months after AF-ablation followed international standards based on individual risk assessment.

DISCUSSION

The present prospective study involved patients with atrial fibrillation who were referred for AF ablation, all of whom were treated prior to and at least three months after ablation with either dabigatran, rivaroxaban or apixaban. We found no complications (either periprocedurally or during a three-month follow-up period) that could be attributed to the use of NOAC for anticoagulation therapy. A single periprocedural bleeding complication with tamponade, possibly related to the transseptal puncture, was treated with percutaneous drainage without complications. NOAC therapy was well-tolerated during the three months of follow-up.

A wide number of institutions that currently perform AF ablation recommend that the ablation procedure be performed during uninterrupted VKA treatment with an INR level of 2-3 [3]. In addition to VKA treatment, unfractionated heparin is administered during the ablation procedure with recommended ACT levels between 300 and 400 [3]. Post-procedural VKA treatment is generally recommended in all patients for a minimum period of three months after ablation [3]. However, in clinical practice, patients often have problems achieving stable INR intervals before planned ablation, and it can be challenging to achieve a stable INR interval after ablation due to e.g. supplementary amiodarone treatment. Furthermore, in line with the increasing use of NOAC in non-valvular atrial fibrillation, more patients need to be shifted from NOAC to VKA before AF ablation. This shift may give rise to potentially unstable levels of anticoagulation and an increased risk for both bleeding and thromboembolic events.

A number of smaller studies, most of which have a retrospective design, have concluded that the use of NOAC before and after left atrial ablation procedures can be done without increasing the risk of bleeding or thromboembolic complications [3-9]. However, several of these studies have paused NOAC for more than 24 hours before ablation with subsequent LMWH bridging until NOAC is restarted 1-2 days after ablation. This strategy is logistically challenging unless patients are kept in hospital for several days, and evidence to support the strategy is poor. Only a limited number of reports have been published on AF ablation strategy during uninterrupted NOAC therapy or initiation of NOAC therapy after left atrial ablation procedures in patients otherwise naïve to anticoagulation therapy [4, 10]. One of our concerns regarding the use of uninterrupted NOAC therapy is that currently we do not have access to a specific antidote to any of the present NOACs, which may aggravate a bleeding complication [11, 12]. Serious bleeding complications to AF ablation can be kept very low, as seen in the present study, and e.g. drainage of a pericardial effusion can often be performed despite on-

TABLE 1

Patient characteristics, procedural data and periprocedural complications.

Age, mean ± SD, yrs	60 ± 8.6
AF type, n (%)	
Paroxysmal	172 (74)
Persistent	55 (24)
Long-standing persistent	7 (3)
Hypertension, n (%)	82 (35)
Diabetes, n (%)	11 (5)
Previous stroke/TCI, n (%)	9 (4)
Cardiomyopati, n (%)	4 (2)
Ischaemic heart disease, n (%)	22 (9)
CHA_2DS_2-VASc score, mean (range)	1 (0-5)
HAS-BLED score, mean (range)	0.7 (0-3)
Dabigatran, n (%)	171 (73)
Rivaroxaban, n (%)	38 (16)
Apixaban, n (%)	25 (11)
Procedure mean ± SD, min.	107 ± 18
RFA-time, mean ± SD, min.	27.8 ± 10.3
X-ray-time, mean ± SD, min.	14.2 ± 7.7
Right atrial isthmus block, n (%)	69 (29)
Left atrial linear lesions, n (%)	44 (19)
Pericardial effusion, n (%)	1 (0.4)
Haematoma, n (%)	0
Pseudoaneurysm, n (%)	0
Stroke/TCI, n (%)	0
Gastrointestinal or urinary tract bleeding, n (%)	0

AF = atrial fibrillation; CHA_2DS_2-VASc = Congestive heart failure, Hypertension, Age ≥ 75 yrs (score 2), Diabetes, Stroke/transient ischaemic attack/ thromboembolic event (score 2), Vascular disease, Age 65-74 yrs, Sex category (female sex) (all scores 1 except otherwise stated); HAS-BLED = uncontrolled Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalised ratio, Elderly, concomitant Drugs/alcohol excess (1 point each); SD = standard deviation; RFA = radiofrequency ablation; TCI = transient cerebral ischaemia.

going NOAC treatment. Even so, however, we still find that the evidence for practicing AF ablation during uninterrupted NOAC treatment is scarce [10]. However, ongoing randomised prospective studies of uninterrupted NOAC versus uninterrupted VKA treatment may change this view. Our strategy did not include administration of protamine sulphate at the end of the procedure in order to neutralise the effect of unfractionated heparin provided during the AF ablation. This may increase the risk of bleeding during the immediate hours after ablation. However, we did not observe a single incidence of major haematoma formation in the groin or late tamponade in our present study including 234 patients. On the other hand, the strategy may reduce the risk of thromboembolic events during the first few hours after ablation, until the NOAC is reinitiated.

Study limitations

This was a single-centre, non-randomised, prospective observational study. Although prospectively included, the patients had a relatively low risk regarding both thromboembolic events (CHA_2DS_2-VASc score 1 (range: 0-5)) and bleeding (HAS-BLED score 0.7 (range: 0-2)). We did not include a control group in the present study and the follow-up was done by telephone and mail. We cannot rule out that this design may lead to under-reporting of complications. Extension of our results to a higher-risk population should therefore be done with caution.

CONCLUSIONS

A strategy including short-term pausing of NOAC in patients undergoing AF ablation seemed safe in our setting without bridging with LMWH. Only one procedural complication was seen, a pericardial tamponade. This complication was treated with percutaneous drainage without additional complications. No complications were observed. An even more simple logistic set-up with left atrial ablation during uninterrupted NOAC treatment still needs to be proven safe, especially since a specific antidote to the different NOAC is not yet clinically available. Routine use of NOAC in the setting of catheter ablation for atrial fibrillation needs further support from ongoing randomised controlled trials comparing NOAC with the currently recommended uninterrupted VKA treatment.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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