Neth Heart J (2012) 20:12–15
DOI 10.1007/s12471-011-0223-0

ORIGINAL ARTICLE

Continuation of vitamin K antagonists as acceptable anticoagulation regimen in patients undergoing pulmonary vein isolation

B. Oude Velthuis · J. Stevenhagen · J. M. van Opstal · M. F. Scholten

Published online: 8 December 2011

Abstract
Background Recent studies have demonstrated that radiofrequency isolation of the pulmonary veins (PVI) is an effective treatment for symptomatic atrial fibrillation. Based on these positive results, non- pharmacological therapy has been incorporated in the guidelines for drug refractory atrial fibrillation, resulting in an increased popularity. The prevention of thromboembolic complications remains an important issue.
Methods In January 2010, we adopted an anticoagulation strategy based on continuation of vitamin K antagonists (VKAs) and selective use of transoesophageal echocardiogram (TEE). We retrospectively analysed the results of this strategy in all patients referred for PVI treatment. VKAs were started for all patients 2 months prior to treatment. Discontinuation of oral anticoagulation was considered 3 months after treatment based on thromboembolic and bleeding risk profile. Bleeding and thromboembolic complications were registered during outpatient clinic follow-up up until 3 months.
Results We performed 151 PVI procedures from January 2010 to March 2011. All patients were seen 6 weeks after discharge. No transient ischaemic accidents or ischaemic cerebrovascular incidents occurred pre-, peri- or postprocedure. Four (2.7%) procedures were complicated by tamponade requiring pericardiocentesis.
Conclusions Our data support the increasing evidence for continuation of periprocedural administration of VKAs complemented by a selective TEE approach as a safe therapy for thromboembolic complications.

Keywords Anticoagulation · Atrial fibrillation · Catheter ablation · Stroke · Transesophageal echocardiography

B. Oude Velthuis · J. Stevenhagen · J. M. van Opstal · M. F. Scholten (✉)
Department of Cardiology, Thoraxcentrum Twente,
Medisch Spectrum Twente,
P.O. Box 50000, 7500 KA Enschede, the Netherlands
e-mail: marcoen.scholten@mst.nl

Introduction

Atrial fibrillation (AF) is the most common and sometimes highly symptomatic abnormality of the heart rhythm, which is characterised by chaotic and uncoordinated activation of the atria. With the advent of advanced electrophysiological studies, significant progress in understanding the mechanism of this arrhythmia has been made. Several possible mechanisms have been identified which may also be interrelated. Haissaguere identified focal triggers within the pulmonary veins as potential targets of non-pharmacological therapy [1]. This extended the therapeutic regimen and interest in the procedure resulted in further refinement of the pulmonary vein isolation (PVI) technique. Current studies report success rates of up to 89% for paroxysmal AF [2]. Based on these results PVI is more frequently applied in patients with more comorbidity [3]. Management of pre-, peri-, and postprocedural thromboembolic complications remain an important issue requiring special attention to anticoagulation strategies [3, 4]. Risk stratification in all patients with AF is based on the CHA_2DS_2-VASc score guiding prescription of VKAs or

antiplatelet therapy. In PVI, additional mechanisms increase the risk of thromboembolic complications. Formation of emboli due to introduction and application of RF energy, even in a continuous bloodstream, can introduce periprocedural complications. Char development caused by overheating can occur at the tip of the catheter or at the site of ablation [5]. Soft thrombus formation due to heat-induced denaturation and aggregation of proteins can occur independently of heparin concentration and also in serum [6]. To minimise thromboembolic risk, an aggressive anticoagulant regimen is employed during pulmonary vein isolation. The downside is an increased risk of haemorrhagic complications still outweighing the prevention of thromboembolic complications. Postprocedural complications can occur since extensive ablation in the left atrium creates a thrombotic environment due to endothelial damage [7]. According to the ESC guideline, a strategy consisting of VKA therapy complemented by a periprocedural low-molecular-weight heparin (LMWH) bridging and routine TEE screening is recommended [8]. We present the analysis of a different anticoagulation regimen around PVI procedures.

Methods

Pre-ablation management is divided into three phases: screening, patient counselling and anticoagulation therapy, which start in the outpatient clinic. Postprocedural care consists of antiarrhythmic drug management, anticoagulation and symptom management possibly requiring a redo procedure.

Screening

Screening for non-pharmacological AF therapy is performed at the atrial fibrillation outpatient clinic. We register bleeding and thromboembolic risk at baseline using the CHA_2DS_2-VASc and HASBLED risk score [8]. Eligible patients are started on VKAs, if not already initiated, at least 2 months prior to the intervention. The international normalised ratio (INR) is kept at a therapeutic level of 2.5–3.5. Checkups are performed weekly at local anticoagulation clinics prior to the intervention. To support the clinical management of atrial fibrillation, initial laboratory tests and transthoracic echocardiography (TTE) are performed to provide essential information during the procedure.

Periprocedural management

Patients are admitted at least 4 h preceding intervention after an INR check has been performed. VKAs are continued, regardless of the AF subtype or CHA_2DS_2-VASc score risk stratification. In cooperation with local anticoagulation clinics, the aim is to obtain an INR between 2 and 3 on the day of the procedure. A bridging strategy using LMWHs is not employed at our centre. The guideline recommends routine exclusion of a thrombus by TEE, which is employed by most centres [8]. However, this is largely based on literature using TEE in a setting prior to cardioversion. In practice, we employ two clinical variables for identification of high-risk patients requiring TEE screening: patients with previous valve surgery or a $CHADS_2$ >2 and persistent AF. After the introduction of the updated ESC AF guidelines, we adopted the CHA_2DS_2-VASc score with a cut-off value of >3.

Blood typing is already performed during screening at the outpatient clinic. In addition, packed red blood cells and fresh frozen plasma for treatment of acute blood loss are readily available. A cardiothoracic surgical team is ready 24 h a day for emergency interventions.

The catheter ablation is performed in patients in a fasting state and under general anaesthesia. Vascular access is obtained using the Seldinger technique for both femoral veins. We use the right femoral vein for introduction of one SL0 8.5 Fr sheath and one archiles steerable sheath (St. Jude Medical, USA), continuously flushed with heparinised saline. Transseptal access is obtained by two separate punctures of the atrial septum. Transseptal punctures are performed using intracardiac echocardiography (ICE) and fluoroscopy. After transseptal access, ICE monitoring is discontinued and this sheath is used to place the coronary sinus catheter. Systemic heparinisation is started and titrated to an activated clotting time above 350 s. For catheter ablation, we use an irrigated 4 mm RF-ablation catheter at a maximum power of 30–35 W and an irrigation rate of 20 ml/min. PV isolation is performed by wide circumferential ablation, encircling all ipsilateral PVs. Isolation of a PV is defined as complete disappearance of PV potentials demonstrated by a multipolar circular diagnostic catheter. After completion of the procedure, a TTE is performed to check for pericardial effusion. Femoral sheets are left in place to reduce immediate bleeding complications.

Follow-up

Following the procedure, patients are observed at the cathlab post anaesthesia care unit (PACU). Prior to transfer to the cardiology ward, the sheets are pulled when the activated clotting time is ≤250 s. If the postprocedural echo shows an increase in pericardial effusion, further observation is performed on the coronary care unit. Patients known for tamponade will routinely undergo a TTE after transfer from the PACU. Patients are kept for an overnight stay and are under continuous rhythm registration. Prior to discharge, puncture sites are routinely checked for complications. Unless indicated, patients are not examined for

neurological symptoms. Our standard follow-up strategy consists of four visits. The initial check-up is scheduled within 6 weeks after discharge. The following visits are planned with a 3-month interval. Depending on the distance to our hospital, some patients continue follow-up at the referring centre. In addition, we document symptoms of atrial fibrillation, post-procedural complications and progress of recovery in an electronic patient file. Patients with recurrent symptoms after a treatment stabilisation period of 90 days receive a 7-day event recorder capable of auto-detecting AF (Vitaphone GmbH, Mannheim, Germany) to guide further therapy [9]. All patients are kept on VKAs regardless of symptoms for 3 months, after which discontinuation is permitted in patients with a CHA_2DS_2-VASc score <1.

Statistical analysis

Categorical variables are represented by frequencies and percentages. Continuous variables are summarised by mean±SD. Data were analysed using SPSS 15.0 software (SPSS Inc., Chicago, IL).

Results

At discharge, three patients demonstrated a small haematoma in the groin, which was treated conservatively. On auscultation, seven patients had a murmur over the femoral artery in which echography showed an aneurysm spurium. Five cases were treated conservatively; thrombin injection was required in two. In one patient, a major vascular complication occurred after laborious introduction of a guide wire. Fluoroscopy evaluation and abdominal echography showed free abdominal fluid based on perforation of the left common iliac vein, which was treated using emergency endovascular surgery. Three (2%) patients required pericardiocentesis during or within 48 h after PVI, and conservative management was possible in one patient (Table 1). One (0.7%) patient developed clinical symptoms of tamponade without any signs of a complicated procedure. After drainage, patients were stable without the need for emergency surgery, vasoconstrictors, blood or fluid resuscitation. All patients presented for follow-up 6 weeks after discharge, and 131 patients (86.8%) completed follow-up up to 3 months in our centre. We registered no thrombotic events or haemorrhagic strokes during the follow-up period.

Table 1 Complications and risk score

Interventions	151
Lone/Paroxysmal/Persistent	6 (4.0%)/117 (77.5%)/28 (18.5%)
Subtherapeutic INR on admission	20 (13.2%)
TEEs performed	3 (2.0%)
Persistent AF and CHA_2DS_2-VASc >3	3 (2.0%)
HASBLED ≥3	10
CHA_2DS_2-VASc ≥2	50
Minor vascular complications[1]	10 (6.6%)
Major vascular complications[2]	1 (0.7%)
History TIA/CVA	12 (8.0%)
TIA/CVA	0 (0%)/0 (0%)
Aborted procedure due to contrast extravasation/ PE requiring pericardiocentesis <48 h/PE requiring pericardiocentesis >48 h[3]	1 (0.7%)/3 (2.0%)/1 (0.7%)

INR international normalised ratio, *AF* atrial fibrillation, *TEE* transoesophageal echocardiogram, *TIA* transient ischaemic attack, *CVA* cerebrovascular accident, *PE* pericardial effusion

1=Small haematoma treated conservatively or aneurysm spurium treated with direct thrombin injection

2=Perforation of the left common iliac vein requiring endovascular stent surgery

3=Three patients developed tamponade within 48 h. One patient demonstrated some pericardial effusion initially treated conservatively although requiring pericardiocentesis 7 days post PVI

Continuous variables given as mean±standard deviation; other data are number of patients (% of the group)

Discussion

The ESC guideline on atrial fibrillation recommends a twofold strategy for the prevention of thromboembolic complications in patients treated with a PVI, incorporating routine TEE screening and a LMWH bridging strategy as an adequate anticoagulation regimen. The HRS/EHRA/ECAS consensus statement is less strict for routine TEE in patients with paroxysmal AF in sinus rhythm prior to the intervention [10]. A recent study reporting a low incidence of LAA thrombus (0%) in patients with paroxysmal AF and a structurally normal heart supports a less stringent approach [11]. This questions the use of routine TEE screening. Optimal identification of high-risk patients remains a challenge, although several factors have been identified which can guide decision making. Thrombus was associated with persistent AF, female sex, structural heart disease and LA diameter >48.5 mm, allowing for a more discriminating approach. Puwanant et al. evaluated the $CHADS_2$ score as a useful risk stratification model, and the new CHA_2DS_2-VASc may further refine prediction since female sex as reported by Calvo et al. is also incorporated in this new model [11, 12]. Sudden discontinuation of VKAs introduces a potential risk. In some studies, abrupt cessation of VKAs resulted in a sudden increase in thrombotic events, giving rise to the rebound hypothesis posed by Grip et al. [13]. Evidence supporting this theory remains inconclusive. However, several studies suggest that

the risk of thromboembolic events might be increased in high-risk patients. We therefore present the results of an alternative strategy with a selective approach for TEE imaging and without interruption of VKAs. In our population, no (transient) ischaemic stroke occurred while a low number of haemorrhagic complications was maintained. Continuation of VKAs without a bridging strategy using LMWHs might be considered a safe and simpler approach in clinical practice. The resulting strategy might further optimise patient burden in the work-up for PVI treatment. Our finding should be viewed in light of some study limitations. The incidence of early thrombotic events following a PVI procedure proved highest in the first 2 weeks [7]. The low mean CHA_2DS_2-VASc score in our population indicates a low thromboembolic risk and may partly explain the complication rate. A large global survey of electrophysiology laboratories shows increasing comorbidity in patients treated with PVI [3]. However, the added risk for stroke caused by the PVI procedure results from a different aetiology not reflected by the CHA2DS2-VASc score. In light of the low incidence rates, this study analyses a small population and therefore requires validation in a large cohort. A recent study by Gaita et al. showed silent ischaemic lesions on magnetic resonance imaging, possibly related to a decline in cognitive function [14]. The impact of the presented anticoagulation strategy on silent ischaemic lesions should be evaluated in future studies.

References

1. Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998;339:659–66.
2. Jais P, Cauchemez B, Macle L, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. Circulation. 2008;118:2498–505.
3. Cappato R, Calkins H, Chen SA, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circ Arrhythm Electrophysiol. 2010;3:32–8.
4. Gopinath D, Lewis WR, Biase LD. Pulmonary vein antrum isolation for atrial fibrillation on therapeutic Coumadin: special considerations. J Cardiovasc Electrophysiol. 2011;22:236–9.
5. Nazeri A, Rasekh A, Massumi A, et al. Coalescence of splines on a basket mapping catheter during ablation using a closed-loop irrigation catheter. Europace. 2009;11:258–9.
6. Demolin JM, Eick OJ, Munch K, et al. Soft thrombus formation in radiofrequency catheter ablation. Pacing Clin Electrophysiol. 2002;25:1219–22.
7. Oral H, Chugh A, Ozaydin M, et al. Risk of thromboembolic events after percutaneous left atrial radiofrequency ablation of atrial fibrillation. Circulation. 2006;114:759–65.
8. Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010;31:2369–429.
9. Muller A, Scharner W, Borchardt T, et al. Reliability of an external loop recorder for automatic recognition and transtelephonic ECG transmission of atrial fibrillation. J Telemed Telecare. 2009;15:391–6.
10. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) task force on catheter and surgical ablation of atrial fibrillation. Hear Rhythm. 2007;4:816–61.
11. Calvo N, Mont L, Vidal B, et al. Usefulness of transoesophageal echocardiography before circumferential pulmonary vein ablation in patients with atrial fibrillation: is it really mandatory? Europace. 2011;13:486–91.
12. Puwanant S, Varr BC, Shrestha K, et al. Role of the CHADS2 score in the evaluation of thromboembolic risk in patients with atrial fibrillation undergoing transesophageal echocardiography before pulmonary vein isolation. J Am Coll Cardiol. 2009;54:2032–9.
13. Grip L, Blomback M, Schulman S. Hypercoagulable state and thromboembolism following warfarin withdrawal in post-myocardial-infarction patients. Eur Heart J. 1991;12:1225–33.
14. Gaita F, Caponi D, Pianelli M, et al. Radiofrequency catheter ablation of atrial fibrillation: a cause of silent thromboembolism? Magnetic resonance imaging assessment of cerebral thromboembolism in patients undergoing ablation of atrial fibrillation. Circulation. 2010;122:1667–73.