Europace (2011) **13**, 640–645
doi:10.1093/europace/eur038

Catheter ablation of atrial fibrillation in patients with therapeutic oral anticoagulation treatment

Antti Hakalahti[1], Paavo Uusimaa[1], Kari Ylitalo[1], and M.J. Pekka Raatikainen[2]*

[1]Division of Cardiology, Department of Internal Medicine, University of Oulu, Oulu, Finland; and [2]Heart Center Co., Tampere University Hospital, PO Box 2000, FI-33521 Tampere, Finland

Received 11 November 2010; accepted after revision 19 January 2011; online publish-ahead-of-print 11 March 2011

Aims Current guidelines recommend discontinuation of oral anticoagulation treatment (OAT) and switch to heparin 2–5 days before catheter ablation of atrial fibrillation (AF). However, increasing evidence leans against the 'bridge therapy' and support continuation of OAT during the procedure.

Methods and results We evaluated the safety of AF ablation among patients with therapeutic OAT. The study population comprised 193 consecutive patients who underwent 228 AF ablation procedures guided by electroanatomical mapping. Periprocedural international normalized ratio was <2 (1.6 ± 0.3) in 103 cases (Group 1) and ≥ 2 (2.4 ± 0.4) in 125 cases (Group 2). Heparin (5000 IU bolus followed by continuous infusion through an open-irrigated ablation catheter) was used in both groups. No intracardiac echocardiographic guidance was used and activated clotting time (ACT) was not monitored. The incidence of major (intracranial bleeding, tamponade, bleeding that required surgical intervention, or blood transfusion) and minor bleeding complications and all thrombo-embolic events were registered during the 3-month follow-up. There was no statistical difference in major ($P = 1.0$) and minor complications ($P = 0.74$) between the groups. The bleeding complications included one surgically corrected groin haematoma in both groups (0.9%), 25 small haematomas at the puncture site (11 in Group 1 (10.7%) and 14 in Group 2 (11.2%), $P = 0.90$), and two minor pericardial effusions in Group 1. In Group 2, one patient had ischaemic stroke 16 days after the procedure.

Conclusion Transseptal puncture and AF ablation can be performed safely in patients with ongoing OAT without intracardiac echocardiographic guidance and ACT monitoring.

Keywords Atrial fibrillation • Radiofrequency catheter ablation • Anticoagulation

Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia with a cumulative lifetime incidence of about one per four.[1] Although AF is not recognized by some patients,[2] it increases morbidity,[3] mortality,[4] and impairs quality of life.[5] Radiofrequency catheter ablation therapy is an effective treatment option[6–8] for an increasing number of patients with AF.[9] Development of ablation techniques, procedural instruments, and mapping devices has improved the safety of this procedure. However, the procedure still carries a pronounced risk for severe complications.[10–12] Prevention and management of these adverse events is complicated. In particular, the balancing between thrombo-embolic and bleeding complications is difficult. The use of antithrombotic medication reduces the risk of stroke and other thrombo-embolic events but at the same time it increases the risk of bleeding (e.g. tamponade) and access site complications.

Current guidelines recommend pausing oral anticoagulation therapy (OAT) and switching to heparin infusion 2–5 days before AF ablation.[13,14] However, the strategies used in different centres vary a lot and increasing evidence leans against the bridge therapy and support continuing OAT at the time of cardiac procedures.[15–19] It has been shown that pacemaker implantation and percutaneous coronary interventions can be performed safely in patients with uninterrupted OAT.[18,19] Likewise, some data indicate that transseptal (TS) puncture and AF ablation can be performed safely under continuous intracardiac echocardiography (ICE) guidance and intensive monitoring of the activated

* Corresponding author. Tel: +358 504434200, Email: pekka.raatikainen@sydankeskus.fi

clotting time (ACT) in patients with uninterrupted OAT.[15–17] In our and many other centres, ICE and ACT monitoring are not used routinely during AF ablation. Therefore, we elected to investigate the safety of AF ablation with uninterrupted OAT and simplified periprocedural heparinization protocol.

Methods

Study population

The study population consisted of 193 consecutive patients with drug-refractory AF. They underwent 228 AF ablation procedures (30 patients underwent one or two reablations) in Oulu University Hospital. In order to evaluate the safety of TS puncture and AF ablation in patients with ongoing therapeutic OAT, the patients were divided into two groups according to the periprocedural international normalized ratio (INR) level (*Figure 1*). Group 1 comprised 103 cases with subtherapeutic INR (<2.0) and Group 2 included 125 cases with therapeutic INR (2.0–3.0) during the procedure. No patient was excluded from the study, but in those with left atrial thrombus in transoesophageal echocardiography (TOE) and in those with INR >3.5 the procedure was postponed. Transoesophageal echocardiography was performed either a day before or on the same day as the procedure.

Oral anticoagulation therapy

Warfarin was used in all patients except for seven patients with contraindication to OAT (i.e. history of major bleeding, severe inflammatory bowel disease, and skin reaction to warfarin) regardless of the type of AF (e.g. paroxysmal, persistent, long-lasting persistent) and the CHA_2DS_2VAScscore.[6,20] In all patients in Group 2, INR was on therapeutic level for at least 3 weeks before the operation, whereas in the Group 1 the preoperative INR was <2.0. Most of the patients in Group 1 had a short pause in OAT prior to the ablation procedure. After the ablation, warfarin was continued for at least 3 months in both groups. The INR values were measured and adjusted in general health care.

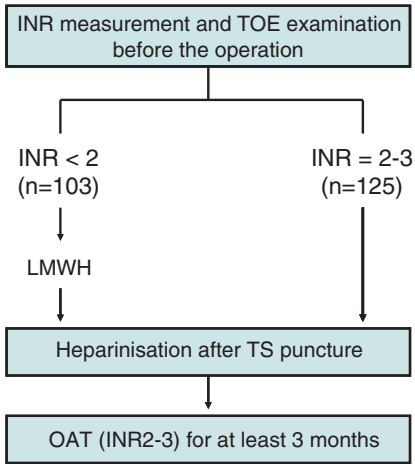

Figure 1 Anticoagulation protocol. Oral anticoagulation was used in all patients with no contraindication before ablation. In Group 1 ($n = 103$), the preoperative international normalized ratio was <2, whereas in the Group 2 ($n = 125$) international normalized ratio was on therapeutic level for at least 3 weeks before the operation. The patients in Group 1 were given low-molecular-weight heparin until the international normalized ratio was in therapeutic level. All patients were given heparin during the procedure but activated clotting time was not measured. After the ablation warfarin was continued for at least 3 months in both groups.

Perioperative use of heparin

Regardless of the preoperative INR value, all the patients were heparinized during the ablation procedure. A 5000 IU bolus of unfractionated heparin was given immediately after the first TS puncture. Thereafter, heparin was infused continuously through an open-irrigated ablation catheter. The infusion rate was 600 IU/h during electroanatomical mapping and 6000 IU/h during radiofrequency ablation. Activated clotting time was not monitored. At the end of the procedure, protamine was administered to partially reverse the heparinization if the total amount of heparin exceeded 14 000 IU. The catheters and introducers were removed immediately after the procedure and compression was applied to the insertion site to prevent bleeding for 10–20 min. Patients stayed supine for 4 h after the procedure. The patients with subtherapeutic INR were given low-molecular-weight heparin (LMWH, enoxaparine 1 mg/kg twice a day) until the INR was at therapeutic level, whereas in Group 2 no LMWH was used.

Transseptal puncture and radiofrequency ablation

The procedures were performed under conscious sedation with intravenous fentanyl and midazolam. After placing a quadripolar 5F catheter into the right ventricular apex and a steerable 10 pole 6F catheter into the coronary sinus via left femoral vein, left atrial access was obtained via right femoral vein. One or two TS punctures were performed with 8F or 8.5F TS sheath (Swartz SL 1, St Jude Medical, Inc., St Paul, MN, USA) and TS needle (BRK or BRK-1, St Jude Medical Inc.) under fluoroscopic and pressure control. No ICE or TOE monitoring was used to guide the TS puncture. The long sheaths were continuously flushed with heparinized saline.

A three-dimensional electroanatomical map of the left atrium and the pulmonary vein (PV) was constructed using a non-fluoroscopic navigation system (Carto™, Biosense Webster, Diamond Bar, CA, USA) as described previously.[21] The ostia of the PVs were identified by fluoroscopic visualization with the help of PV angiography or integration of a previous acquired computed tomography (CT) or magnetic resonance imaging (MRI) image. Pulmonary veins were isolated pairwisely by creating a wide circumferential line around the right- and left-side veins using an open-irrigated ablation catheter (Navistar Thermocool, Biosense Webster). The isolation of the veins was confirmed by careful remap of the lines and PV ostia or by using a circumferential diagnostic catheter. Additional left atrial line(s) (e.g. roof line, posterior line, mitral annulus line) were done in patients with long-lasting persistent AF. Right atrial isthmus line was done in all patients with pre- or perioperative documentation of typical isthmus-dependent atrial flutter.

Follow-up

The follow-up in this study focused on bleeding and thrombo-embolic complications. Major bleeding was defined as intracranial bleeding, cardiac tamponade, or bleeding that required surgical intervention or blood transfusion. Minor bleeding was defined as haematoma that required no intervention. After the procedure the patients stayed in the hospital for at least 24 h under continuous electrocardiogram

monitoring. Nurses examined patient repeatedly and if any major complication was suspected, the situation was evaluated by a doctor. All patients were examined by a physician before discharge and at the 3-month follow-up visit.

The patients were instructed to contact the hospital if any adverse events occurred. Transthoracic echocardiography and/or chest X-ray were performed if the patient had chest pain, dyspnoea, or other cardiac symptoms. If the patients had neurological symptoms, a head and brain CT or MRI was performed. At the 3-month follow-up visit, the patients were examined and all complications were registered and verified from patient records.

Statistical analysis

PASW statistics 17.0 (SPSS Inc.) was used for statistical analysis. Nominal variables are expressed as numbers and percentages and compared by Fisher's exact test or χ^2 test when appropriate. Ordinal variables are presented as mean ± standard deviation and compared with Wilcoxon rank sum test. Continuous variables are expressed as mean ± standard deviation and compared with independent variables *t*-test. All tests were two-sided and a *P*-value of <0.05 was considered statistically significant.

Results

The baseline characteristics of the patients are shown in *Table 1*. Most of the patients had paroxysmal or persistent AF. There were no difference in the age of the patients between the groups ($P = 0.56$). Patients in Group 2 had a higher prevalence of prior thrombo-embolic events (10 vs. 3%; $P = 0.04$), whereas vascular disease was more common in Group 1 (9 vs. 3%; $P = 0.03$). There was no difference in the overall CHA_2DS_2-VASc ($P = 0.66$) and HAS-BLED score[6,22] ($P = 0.12$) between the groups. Left ventricular ejection fraction (LVEF) and left atrial diameter were 63 ± 8% and 41 ± 5 mm in Group 1 and 62 ± 10% ($P = 0.34$) and 41 ± 6 mm ($P = 0.91$) in Group 2, respectively. Mean INR levels in Groups 1 and 2 were 1.6 ± 0.3 and 2.4 ± 0.4, respectively, ($P < 0.001$). The use of heparin was similar in both groups. The total dose of heparin was 10 552 ± 1506 IU in Group 1 and 10 486 ± 1750 IU in Group 2 ($P = 0.78$) (*Table 2*). There was no difference in the use of protamine between the groups.

Bleeding complications

There was no statistically significant difference in the major ($P = 1.00$) or minor bleeding complications ($P = 0.90$) between the groups (*Table 3*). The major bleeding complications included two femoral haematomas (0.9%) requiring surgery, one in each group. They were detected and operated right after the procedure. Both were due to damage of the femoral artery wall. No patient required blood transfusion and there were no tamponades. One procedure was postponed, because contrast media were observed in the pericardial space after problematic TS puncture. Transthoracic echocardiography showed no pericardial effusion, but the procedure was cancelled and performed later on by a more experienced operator with no complications. Minor bleeding complications in Group 1 included 11 groin haematomas and 1 mild

Table 1 Baseline characteristics

	Group 1 (*n* = 103)	Group 2 (*n* = 125)	Total (*n* = 228)	*P*- value
INR	1.6 ± 0.3	2.4 ± 0.4	2.1 ± 0.5	<0.001
Age	54 ± 9	54 ± 9	54 ± 9	0.56
Paroxysmal AF	69 (67%)	59 (47%)	128 (56%)	0.003
Persistent AF	23 (22%)	47 (38%)	70 (31%)	0.01
Long-lasting persistent AF	11 (11%)	19 (15%)	30 (13%)	0.32
Congestive heart failure	5 (5%)	4 (3%)	7 (4%)	0.74
Hypertension	42 (41%)	60 (48%)	102 (45%)	0.28
Age ≥75	0 (0%)	0 (0%)	0 (0%)	1.0
Diabetes mellitus	6 (6%)	5 (4%)	11 (5%)	0.55
Stroke/TIA/thrombo-embolism	3 (3%)	12 (10%)	15 (7%)	0.04
Vascular disease	9 (9%)	3 (2%)	12 (5%)	0.03
Age between 65 and 74	7 (7%)	6 (5%)	13 (6%)	0.52
Female	20 (19%)	25 (20%)	45 (20%)	0.91
$CHADS_2$ score	0.5 ± 0.7	0.7 ± 0.9	0.6 ± 0.8	0.15
CHA_2DS_2-VASc score	0.9 ± 0.9	1.0 ± 1.1	1.0 ± 1.0	0.66
Systolic blood pressure >160 mmHg	4 (4%)	3 (2%)	7 (3%)	0.70
History of bleeding	12 (12%)	10 (8%)	22 (10%)	0.35
Labile INRs	42 (41%)	38 (30%)	80 (35%)	0.10
Use of aspirin/NSAIDs/alcohol	20 (19%)	15 (12%)	35 (15%)	0.12
HAS-BLED score	0.9 ± 0.9	0.7 ± 0.8	0.8 ± 0.9	0.12
LVEF, %	63 ± 8	62 ± 10	62 ± 9	0.34
LA size, mm	41 ± 5	41 ± 6	41 ± 6	0.91

NSAIDs, non-steroidal anti-inflammatory drugs; LA, left atrial.

Table 2 Procedural data

	Group 1 ($n = 103$)	Group 2 ($n = 125$)	Total ($n = 228$)	*P*-value
Procedure time, min	145 ± 42	148 ± 49	147 ± 46	0.66
RF time, min	45 ± 13	44 ± 15	45 ± 14	0.59
Total heparin dose	10 552 ± 1506	10 486 ± 1750	10 515 ± 1645	0.78

RF, radiofrequency.

Table 3 Complications

	Group 1 ($n = 103$)	Group 2 ($n = 125$)	Total ($n = 228$)	*P*-value
Ischaemic stroke	0 (0%)	1 (0.8%)	1 (0.4%)	1.00
Major bleeding	1 (1.0%)	1 (0.8%)	2 (0.9%)	1.00
Minor bleeding	11 (10.7%)	14 (11.2%)	25 (11.0%)	0.90
Pericardial effusion	1 (1.0%)	0 (0%)	1 (0.4%)	0.45
Complicated TS puncture	1 (1.0%)	0 (0%)	1 (0.4%)	0.45

pericardial effusion (11.7%). In Group 2, there were 14 minor groin haematomas (11.2%). In 11 cases, ultrasound examination of the groin area was performed in order to exclude bleeding (three in Group 1 vs. eight in Group 2; $P = 0.35$).

Thrombo-embolic complications

There were no thrombo-embolic complications during the procedure and hospital stay in either group. During the follow-up, no thrombo-embolic complications were detected in Group 1 (*Table 3*). In Group 2, a 56-year-old man with $CHADS_2$ score of 1 ($CHA_2DS_2VASC = 1$) had dysphasia 16 days after the procedure. At that time, he had been in AF for 4 days and his INR was 1.6. Brain CT revealed an ischaemic stroke (0.4%). The stroke was treated rapidly with thrombolytic therapy and dysphasia disappeared during the following months.

Discussion

The results of this 'real-life' study indicate that it is safe to perform AF ablation in patients with uninterrupted OAT using a simplified heparinization protocol with no ACT monitoring. In our study, TS puncture and ablation were performed under fluoroscopic guidance without using ICE or TOE surveillance. Our protocol proved safe with a low rate of bleeding and thrombo-embolic events. Hence, uninterrupted OAT provided a feasible and safe alternative to the inconvenient and expensive 'bridge' therapy for patients undergoing AF ablation.

Oral anticoagulation therapy before and after ablation

Current guidelines recommend 'bridge' therapy, i.e. stopping OAT and switching to unfractionated heparin 2–5 days before AF ablation.[13,14] The rationale behind this common consensus has been the assumption that in order to reduce the risk of bleeding during the TS puncture and AF ablation, the procedure should be postponed until INR is <1.5. However, according to our data, continuation of warfarin throughout the procedure did not increase bleeding and there were no statistical differences in the thrombo-embolic events between the groups. In keeping with these findings, the results of two large retrospective trials recently demonstrated that uninterrupted OAT is safe and may even reduce the risk of thrombo-embolic and bleeding complications compared with the guideline approach.[16,17] Moreover, Wazni *et al.*[15] reported that spontaneous echo contrast, which is considered a risk for thrombus formation, is more common if OAT is paused prior to AF ablation.

Similar findings supporting the use of uninterrupted OAT have also been made in other cardiac procedures. Compared with uninterrupted OAT, bridging to heparin has been found to increase hospital stay[18] and bleeding complications[23] at pacemaker or implantable cardioverter-defibrillator implantation. In the study by Annala *et al.*,[24] uninterrupted warfarin treatment was found as safe and less costly during diagnostic coronary angiography. Karjalainen *et al.*[19] found that percutaneous coronary intervention was equally safe during uninterrupted OAT compared with stopping anticoagulation therapy for the average of 3 days before the procedure. Hence, it seems obvious that the 'bridge' therapy do not improve the safety of AF ablation and other cardiac procedures. In contrast, such a strategy may confer less protection against thrombo-embolic events during the post-ablation period while waiting to achieve therapeutic INR values after the preoperative pause.

Ablation in the left atrium creates a hypercoagulative milieu that increases the risk of thrombo-embolic events during the early post-operative period. To lower the risk of thrombo-embolic events after the ablation, we continued systemic anticoagulation for a minimum of 3 months as recommended.[13] Thereafter, the decision to stop or to continue OAT was made on the basis of the individual stroke risk factors. Recently, Bunch *et al.*[25] suggested that post-operative warfarin is not needed in low-risk patients following AF ablation. In our study, one patient with $CHADS_2$ score of 1 (CHA_2DS_2-VASc = 1) had ischaemic stroke 16 days after the ablation. During the ablation, his INR was at therapeutic level, but at the time of the stroke it had dropped to 1.6. Therefore, we recommend using OAT in the early post-ablation period.

Perioperative use of heparin and monitoring of the patients

There is no uniform recommendation for monitoring of the patients during the AF ablation procedure. Unlike the other investigators, who have evaluated the feasibility and safety of AF ablation in patients with uninterrupted OAT,[15–17] we did not use ICE monitoring to guide the TS puncture and the ablation procedure. Although ICE may be valuable in many cases,[26] it is not used routinely in our and many other centres during AF ablation. The main limitation for the routine use of ICE is that it increases the cost of the procedure markedly and it is also inconvenient to use by a single operator.

When the 'bridge' therapy is used, close attention to maintaining therapeutic heparin dosing during the procedure is important. It is well established that thrombi can form on the TS sheath almost immediately after crossing the septum. Therefore, most operators administer a loading dose of heparin prior to or immediately on TS puncture. After a loading dose, the lower level of anticoagulation is usually maintained at an ACT of at least 250–350 s throughout the procedure, because at lower ACT level thrombus formation may be increased.[27,28] However, it should be born in mind that in the studies by Ren *et al.*[27] and Wazni *et al.*[28] OAT was stopped before the procedure and open-irrigated catheters were not used. Therefore, it remains unclear whether intensive heparinization and monitoring of ACT every 15–30 min is needed in patients with uninterrupted OAT. We used a simplified protocol for perioperative heparinization. After the initial bolus, a small amount of heparin was infused continuously through the open-irrigated ablation catheter without monitoring the ACT. In addition, heparinized saline was used to reduce the risk of sheath-related thrombi. When comparing the results of our study with those of the previous studies,[10] it can be seen that the lack of ACT monitoring did not increase the risk of major thrombo-embolic and bleeding complications. Moreover, it is possible that by infusing heparin directly via the open-irrigated ablation catheter, the risk of catheter charring and local thrombus formation at the ablation site is reduced.

Study limitations

Our study carries all the inherent limitations of a non-randomized observational study. However, the strength of this study is that it offers 'real-life' information of the safety of our method in an unselected patient population. In our study, most of the procedures were performed by an operator with experience of >500 AF ablations. Although there were no differences in the operator experience between the groups, the experience of the operator should be taken into account when considering starting to use our approach. The prevalence of risk factors for thrombo-embolic events was low with only 11% of the patients having $CHADS_2$ score ≥2. The CHA_2DS_2VASc score was ≥2 in 25% and ≥3 in 7% of the patients. Therefore, the results should be extrapolated to high-risk patients with caution. In addition, because 'bridge' therapy, ACT-guided heparin dosing, or ICE-guided TS catheterization, was not used and there were no patients without periprocedural heparinization, several issues remain to be established.

Conclusions

According to our data, uninterrupted OAT provides a feasible and safe alternative to the inconvenient 'bridge' therapy for patients undergoing AF ablation. The therapeutic INR level at the time of the procedure did not increase bleeding complications although we did not use ICE to monitor TS puncture and the ablation procedure. Our strategy is likely to reduce the cost of the procedure and to improve post-operative anticoagulation therapy while causing no delay in achieving therapeutic INR values after the procedure.

Conflict of interest: M.J.P.R. has been consulting in clinical cases where the Carto™ system might be useful.

Funding

This study was supported by Finnish Foundation for Cardiovascular Research.

References

1. Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS *et al.* Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation* 2004;**110**:1042–6.
2. Flaker GC, Belew K, Beckman K, Vidaillet H, Kron J, Safford R *et al.* Asymptomatic atrial fibrillation: demographic features and prognostic information from the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. *Am Heart J* 2005;**149**:657–63.
3. Stewart S, Hart CL, Hole DJ, McMurray JJ. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. *Am J Med* 2002;**113**:359–64.
4. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998;**98**:946–52.
5. Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: a systematic review. *Am J Med* 2006;**119**:448e1–9.
6. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S *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). *Europace* **12**:1360–420.
7. Noheria A, Kumar A, Wylie JV Jr., Josephson ME. Catheter ablation vs antiarrhythmic drug therapy for atrial fibrillation: a systematic review. *Arch Intern Med* 2008;**168**:581–6.
8. Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi F Jr. *et al.* Circumferential pulmonary-vein ablation for chronic atrial fibrillation. *N Engl J Med* 2006;**354**:934–41.
9. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV *et al.* Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA* 2001;**285**:2370–5.
10. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J *et al.* Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation* 2005;**111**:1100–5.
11. Dagres N, Hindricks G, Kottkamp H, Sommer P, Gaspar T, Bode K *et al.* Complications of atrial fibrillation ablation in a high-volume center in 1000 procedures: still cause for concern? *J Cardiovasc Electrophysiol* 2009;**20**:1014–9.
12. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J *et al.* Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. *J Am Coll Cardiol* 2009;**53**:1798–803.
13. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ *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 developed in partnership with the European Heart Rhythm Association (EHRA) and the European Cardiac Arrhythmia Society (ECAS); in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), and the Society of Thoracic Surgeons (STS). Endorsed and approved by the governing bodies of the American College of Cardiology, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, and the Heart Rhythm Society. *Europace* 2007;9:335–79.

14. Natale A, Raviele A, Arentz T, Calkins H, Chen SA, Haissaguerre M *et al.* Venice Chart international consensus document on atrial fibrillation ablation. *J Cardiovasc Electrophysiol* 2007;**18**:560–80.
15. Wazni OM, Beheiry S, Fahmy T, Barrett C, Hao S, Patel D *et al.* Atrial fibrillation ablation in patients with therapeutic international normalized ratio: comparison of strategies of anticoagulation management in the periprocedural period. *Circulation* 2007;**116**:2531–4.
16. Hussein AA, Martin DO, Saliba W, Patel D, Karim S, Batal O *et al.* Radiofrequency ablation of atrial fibrillation under therapeutic international normalized ratio: a safe and efficacious periprocedural anticoagulation strategy. *Heart Rhythm* 2009; **6**:1425–9.
17. Di Biase L, Burkhardt JD, Mohanty P, Sanchez J, Horton R, Gallinghouse GJ *et al.* Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. *Circulation* **121**:2550–6.
18. Tolosana JM, Berne P, Mont L, Heras M, Berruezo A, Monteagudo J *et al.* Preparation for pacemaker or implantable cardiac defibrillator implants in patients with high risk of thrombo-embolic events: oral anticoagulation or bridging with intravenous heparin? A prospective randomized trial. *Eur Heart J* 2009;**30**:1880–4.
19. Karjalainen PP, Vikman S, Niemela M, Porela P, Ylitalo A, Vaittinen MA *et al.* Safety of percutaneous coronary intervention during uninterrupted oral anticoagulant treatment. *Eur Heart J* 2008;**29**:1001–10.
20. Lip GY, Frison L, Halperin JL, Lane DA. Identifying patients at high risk for stroke despite anticoagulation: a comparison of contemporary stroke risk stratification schemes in an anticoagulated atrial fibrillation cohort. *Stroke* 2010;**41**:2731–8.
21. Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G *et al.* Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. *Circulation* 2000;**102**:2619–28.
22. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro heart survey. *Chest* **138**:1093–100.
23. Tompkins C, Cheng A, Dalal D, Brinker JA, Leng CT, Marine JE *et al.* Dual antiplatelet therapy and heparin 'bridging' significantly increase the risk of bleeding complications after pacemaker or implantable cardioverter-defibrillator device implantation. *J Am Coll Cardiol* **55**:2376–82.
24. Annala AP, Karjalainen PP, Porela P, Nyman K, Ylitalo A, Airaksinen KE. Safety of diagnostic coronary angiography during uninterrupted therapeutic warfarin treatment. *Am J Cardiol* 2008;**102**:386–90.
25. Bunch TJ, Crandall BG, Weiss JP, May HT, Bair TL, Osborn JS *et al.* Warfarin is not needed in low-risk patients following atrial fibrillation ablation procedures. *J Cardiovasc Electrophysiol* 2009;**20**:988–93.
26. Saliba W, Thomas J. Intracardiac echocardiography during catheter ablation of atrial fibrillation. *Europace* 2008;(Suppl 3):iii42–iii47.
27. Ren JF, Marchlinski FE, Callans DJ, Gerstenfeld EP, Dixit S, Lin D *et al.* Increased intensity of anticoagulation may reduce risk of thrombus during atrial fibrillation ablation procedures in patients with spontaneous echo contrast. *J Cardiovasc Electrophysiol* 2005;**16**:474–7.
28. Wazni OM, Rossillo A, Marrouche NF, Saad EB, Martin DO, Bhargava M *et al.* Embolic events and char formation during pulmonary vein isolation in patients with atrial fibrillation: impact of different anticoagulation regimens and importance of intracardiac echo imaging. *J Cardiovasc Electrophysiol* 2005;**16**:576–81.