Journal of Thrombosis and Circulation
Open Access

OPEN ACCESS Freely available online

Research Article

Switch To Heparin and Risk of Bleeding In Patients on Apixaban Undergoing Cardiac

Walid Amara[1]*, Rodrigue Garcia[2], Jerome Taieb[3], Estelle Gandjbackh[4], Antoine Dompnier[5], Saida Cheggour[6], Frederic Georger[7], Antoine Milhem[8], Jacques Mansourati[9]

[1]GHI Le Raincy-Montfermeil, France ; [2]CHU de Poitiers, Poitiers, France ; [3]CH du Pays d'Aix, Aix-en-Provence, France ; [4]CHU Pitie-Salpetriere, Paris, France ; [5]CH d'Annecy, Annecy, France ; [6]CH Avignon, Avignon, France ; [7]CH Beziers, Beziers, France ; [8]CH La Rochelle, La Rochelle, France ; [9]CHU de Brest, Brest, France

ABSTRACT

Aim: This study aimed to describe clinical characteristics and real-life management of patients undergoing cardiac rhythm procedures and therapies while receiving apixaban.

Methods: This observational, multicentre study prospectively collected data from patients with non valvular atrial fibrillation (AF) undergoing cardiac rhythm procedures (ablation, pacemaker/ cardioverter defibrillator (ICD) implantation, cardioversion) while receiving apixaban. Patients were followed for up to 30 (±5) days post-procedure.

Complications occurring within the 30 days after the procedure were collected. **Results:** A total of 959 patients were enrolled at 25 centres (September 2015–September 2017). Of these, 115 (12.0%) patients underwent a pacemaker or ICD implantation, 359 (37.4%) AF ablation, 265 (27.6%) flutter ablation and 220 (22.9%) electrical cardioversion. Management of apixaban in the per procedural period was left to investigators' preference. Early complications included 18 bleeding events (1 tamponade requiring drainage, 2 pericardial effusions without drainage, 11 non-major bleedings for catheter ablation, 4 for pacemaker/ICD implantation). The number of patients bridging from apixaban to heparin/low-molecular-weight heparin (LMWH) was higher for ablation than for the other procedures (51.2% for ablation *vs* 11.5% and 2.6% for patients undergoing pacemaker/ICD implantation and cardioversion, respectively; $P<0.001$); the median duration of bridging for all procedures was 24 hours. Comparing patients with and without bleeding events revealed a higher rate of heparin/LMWH bridging in patients with bleeding events (60% vs 35.9%; $P=0.03$). **Conclusion:** Periprocedural bridge from Apixaban to Heparin/LMWH during cardiac rhythm procedures is associated with an increased rate of bleeding events at 30 days.

Among 959 patients with nonvalvular atrial fibrillation undergoing cardiac rhythm procedures while receiving apixaban, bridging to heparin/low-molecular-weight heparin was more common with ablation than with pacemaker/ICD implantation or cardioversion (51.2% vs 11.5% and 2.6%, respectively; $P<0.001$), and was associated with a risk of bleeding events ($P=0.03$). This observational, multicentre study provides important real-life data regarding the management of anticoagulation therapy in patients with nonvalvular atrial fibrillation undergoing cardiac rhythm procedures while receiving apixaban.

- Among 959 patients treated at 25 French centres from September 2015 to September 2017 and followed for up to 30 (±5) days post-procedure, bridging to heparin/low-molecular-weight heparin was more common with ablation than with pacemaker/ICD implantation or cardioversion (51.2% vs 11.5% and 2.6%, respectively; $P<0.001$).
- The median duration of bridging was 24 hours for all procedures, and switching was associated with an increased risk of bleeding events ($P=0.03$).

Keywords: Apixaban; Anticoagulation; Bleeding complications; Cardiac rhythm procedures; Heparin bridging

***Correspondence to:** Walid Amara, GHI Le Raincy-Montfermeil, 93370 Montfermeil, France, Tel: 01 79 72 78 71, Fax: 01 79 72 78 71, Email: walamara@gmail.com

Received: July 20, 2020; **Accepted:** September 16, 2020; **Published:** September 23, 2020

Citation: Walid Amara, Rodrigue Garcia, Jerome Taieb, Estelle Gandjbackh, Antoine Dompnier, Saida Cheggour, et al. (2020) Switch To Heparin and Risk of Bleeding In Patients on Apixaban Undergoing Cardiac Rhythm Procedures: The Amper Af Study. J Thrombo Cir. 6:133. 10.35248/2572-9462-6.136.

Copyright: ©2020 Amara W, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia [1,2]. and its prevalence is expected to rise to approximately 14–17 million by 2030 in Europe[3,4]. Nonvalvular AF (NVAF) is associated with a 5-fold risk of stroke [5-8]. A great number of cardiac electrophysiology procedures and therapies (radiofrequency ablations, cryoablations, pacemaker, implantable cardioverter defibrillator (ICD) implantations, and cardioversions) are performed in patients receiving anticoagulants. Atrial arrhythmias represent the majority of indications of catheter ablation procedures in a great number of centres. European Heart Rhythm Association (EHRA) consensus guidelines recommend withdrawal of anticoagulation therapy before implantation of a pacemaker/ICD or AF ablation, but not before cardioversion [9].The usual strategy in patients undergoing a device replacement used to involvebridging oral anticoagulation with heparin; however this strategy was associated with an increased risk of perioperative bleeding complications (i.e. pocket haematoma) [10]. Therefore, European guidelines recommended oral anticoagulant withdrawal <7 days without heparin/low-molecular-weight heparin (LMWH) bridging, or even continued anticoagulation, in patients with a low thromboembolic risk [9-11].

Apixaban is a direct active site inhibitor of factor Xa, oral anticoagulant [12]. Indicated for the prevention of stroke and systemic embolism in adult patients with NVAF and ≥1risk factor (s) for stroke. Evaluation of apixaban during electrophysiology procedures is still necessary, especially in a real-life setting. Apixaban discontinuation modalities by physicians are particularly unknown as well as the measures taken in case of bleeding management. The aim of this study was to evaluate patient characteristics and treatment management, and to identify factors associated with bleeding complications in patients undergoing an electrophysiology procedure (i.e., ablation, pacemaker/ICD implantation or cardio version) while receiving apixaban for NVAF in a real-life setting. Patient management in relation to European guidelines was also explored.

METHODS

Study design

This prospective, observational, multicentre study enrolled consecutive patients undergoing electrophysiology procedures while receiving apixaban as anticoagulation therapy as indicated for NVAF. The study was conducted in public, university or general hospitals, as well as private clinics. Patients were separated into 3 groups: 1) those undergoing radiofrequency or cryotherapy ablation for AF, atrial flutter or atrial tachycardias; 2) those undergoing all types of electronic device (PM or ICD) implantations; and 3) those undergoing an electrical cardioversion.

The studywas conducted in accordance with Good Clinical Practice, as defined by the International Conference on Harmonization, and in accordance with the ethical principles underlying European Union Directive 2001/20/EC and the United States Code of Federal Regulations, Title 21, Part 50 (21CFR50). The study design was approved by the relevant ethics committees, independent review committees, regulatory authorities, and/or other local governance bodies, and all patients provided informed consent prior to enrolment into the study.

Patients

Eligible patients were males or females over the age of 18 undergoing an electrophysiology procedure (ablation or pacemaker/ICD implantation or cardio version). Patients had a history of NVAF and were receiving treatment with apixaban 5 or 2.5 mg twice daily for at least three weeks prior to the procedure. Patients with cognitive impairment or inability to understand and provide consent were excluded. Pregnant (or potentially pregnant) patients, and those participating in other clinical trials were also excluded.

OBJECTIVES

The primary objective of the study was to describe patient characteristics and the clinical management of patients undergoing one of the main electrophysiology procedures (ablation or pacemaker/ICD implantation or cardio version) while receiving apixaban for NVAF. The use of risk scores (e.g. CHADS2, CHA_2DS_2VASc, HASBLED, HEMORR2HAGES) was evaluated, and strategies used for prevention of bleeding or embolic complications (e.g. use of trans-esophageal echocardiography [TEE]) were evaluated. Secondary objectives included the determination of the number of major and minor bleeding events, the number of stroke and embolic events and the number of deaths. Exploratory objectives included the analysis of predictive factors of bleeding and embolic events. Factors explored included the type of procedure, patient demographics (i.e. patient age or gender), the use of TEE, bleeding scores, anti platelet treatments and the effect of apixaban dose (10 vs 5 mg/day) on outcomes.

Outcome measures

Patients were followed for 30 days. Follow-up visits were conducted at inclusion, on Day 2 and on Day 30 (±5). At each visit, patients were interviewed and physically examined, with the exception of Day 30 (±5), when a telephone interview was permitted. Investigators had access to electrocardiography and biological data of patients. Data were collected via an electronic case report form. Total, major, and non-major bleeding events, as well as the number of stroke and systemic embolic events, were evaluated at Day 1 and during the follow-up period between Day 2 until Day 30 (±5). Major bleeding events were defined according to International Society on Thrombosis and Haemostasis criteria; i.e. clinically overt bleeding accompanied by a decrease in the haemoglobin level of ≥2 g/dL or transfusion of ≥2 units of packed red cells, occurring at a critical site, or resulting in death. Life-threatening bleeding events, a subcategory of major bleeding were defined as fatal bleeding, symptomatic intracranial bleeding, bleeding with a decrease in the haemoglobin level of ≥50 g/L, or bleeding requiring transfusion of ≥4 units of blood or inotropic agents, or requiring surgery. Intracranial haemorrhage was defined as haemorrhagic stroke, and subdural or subarachnoid haemorrhage. Stroke was defined as the sudden onset of a focal neurological deficit in a location consistent with the territory of a major cerebral artery and categorized as is chaemic, haemorrhagic or unspecified. Systemic embolism was defined as an acute vascular occlusion of an extremity or organ, documented by means of imaging, surgery or autopsy. Non-major bleeding events were defined as clinically overt bleeding that did not satisfy the criteria for major bleeding, and that led to hospital admission, physician-guided medical or surgical treatment, or a change in anti-thrombotic therapy, and other non-major bleedings. Haematomas at the access-site for ablation procedures and the pocket of pacemakers/ICD implantations were also evaluated.

A significant haematoma was defined as one requiring re-operation, producing impending or wound breakdown/skin necrosis, requiring prolongation of hospitalization or rehospitalization, or requiring interruption of anticoagulation for >24 hours. All AEs

were collected from enrolment until 30 (±5) days and followed until resolution or stabilization. Severity and causal relationship with the treatment (apixaban and/or procedure) were recorded. AEs were defined as any new untoward medical occurrence or worsening of a pre-existing medical condition. Serious adverse events (SAEs) were defined as any untoward medical occurrence that was life threatening, or resulted in death, inpatient hospitalization or prolongation of existing hospitalization, or persistent or significant disability/incapacity.

Statistical analyses

The number of patients was calculated to allow an estimation of true proportion with an acceptable precision in each group of patients. As the number of criteria to be described according to the primary objective was relatively large, the number of needed patients was calculated for a wide range of observed percentages. A sample size of 300 patients per group was determined to be sufficient to minimally reach a precision of 5.5% for proportions. The targeted sample size of 200 patients undergoing a cardio version was determined to be sufficient to minimally reach a precision of 6.9% for proportions.

For the primary endpoint, patient baseline characteristics were reported as mean (± standard deviation [SD]) or median (inter quartile range [IQR]) for continuous variables and as numbers and percentages for categorical data. For binary endpoints, 95% confidence intervals (CI) were based on the normal approximation to the binomial distribution, and 95% CI for continuous endpoints were based on the normal distribution. Comparisons were made using the Student t-test, or chi-square analysis where appropriate, with $P<0.05$ denoting statistical significance. Multivariate analysis was used for the evaluation of predictive factors using a logistic regression (threshold of 5%) for bleeding events. We tested the effect of LMWH switch adjusted for the type of procedure and patient age. Age was included in the model as a continuous variable, and each type of procedure was a binary variable coded in 0 or 1.

RESULTS

Patients

A total of 1013patients were enrolled at 25 centres in France between September 2015 and September 2017; however, information regarding the procedure was missing in 54 patients resulting in a study population of 959 patients. Demographics and clinical characteristics of the overall population are shown in Table 1. Median patient age was 69.0 (IQR 61.0, 76.75) years, the majority of patients (70.8%) were male, and the mean (± SD) CHA_2DS_2-VASc score was 2.3 (± 1.5). The majority of patients (84.9%) received the higher dose of apixaban 10mg/day. The most prevalent concomitant disorders were hypertension (51% of patients), diabetes (15%) and vascular disease (10%), and 55 patients (5.7%) had a history of stroke. Mean (± SD) creatinine value was 93.0 (± 25.5) mmol/L, median bodyweight was 82.8 (± 17.8) kg and mean creatinine clearance (Cockroft-Gault) was 82.2(± 34.4) mL/min.

Primary endpoint

A total of 115 (12.0%) patients underwent a pacemaker or ICD implantation, 624 (65.1%) underwent an ablation procedure, and 220 (22.9%) underwent electrical cardio version. Among the 557 patients receiving catheter ablation only 322 patients (57.8%) had atrial fibrillation ablation and 235 (41.2%) had atrial flutter ablation.

Comparison of patient characteristics among the three groups of patients undergoing the various procedures revealed statistically significant differences (**Table 1**). Mean age differed significantly depending on the procedure, with patients receiving pacemaker/ICD implantation seemingly older than those undergoing cardioversion or ablation ($P<0.001$). Proportions of patients receiving the lower dose of apixaban 5 mg/day prior to the procedure, concomitant amiodarone,or pacemaker/ICD implantations as emergency procedures also varied significantly depending on the procedure (both $P<0.001$; **Table 1**). The number of patients switching from apixaban to heparin/LMWH was higher for catheter ablations than for the other procedures [Table 1]; TEE was significantly more often performed in these patients than for those undergoing cardio version ($P<0.001$). Median CHA_2DS_2-VASc and HAS-BLED scores were significantly higher in patients undergoing pacemaker/ICD implantation than in those undergoing other procedures (both $P<0.001$) [Table 1]. Among the 10 (11.5%) patients undergoing a pacemaker/ICD implantation who switched to heparin/LMWH, the median duration of switching was 24 hours (IQR 0.6-73.5). Of the patients undergoing ablation, 299 (51.2%) were switched to heparin/LMWH for a median duration of 24 hours (IQR 11.0,39.2). For patients undergoing cardio version, the number of patients who were switched to unfractionated heparin or enoxaparin was low (n=5; 2.6%).

Secondary endpoints

Complication rates at 30 days, summarized in Table 2, were low in all procedures. The mean prevalence of bleeding events was 2.1% (1.1–3.1%).There were 2 deaths (1 patient with heart failure associated with severe aortic stenosis and 1 patient with myocardial infarction after discharge).

Exploratory endpoints

Analysis of patients with versus without bleeding events revealed a higher rate of heparin or LMWH switching in patients with a bleeding event (60.0% *vs* 35.9%; $P=0.03$). The rate of heparin or LMWH switching was also significantly higher in patients undergoing AF versus atrial flutter ablation (77.3% *vs* 14.1%; $P<0.001$). Only one embolic event (non-disabling stroke) occurred. Multivariate logistic regression showed that heparin or LMWH switching remained significantly associated with bleeding events after adjustment for patient age and procedure type (QR:4.29;95%(1.39-13,25); p=0.01 [Table 3].

DISCUSSION

Due to the higher risk of bleeding complications, current clinical guidelines and expert consensus no longer recommend withdrawal of oral anticoagulants with heparin/LMWH bridging in patients with a trial fibrillation undergoing electrophysiology procedures [9,11]. Despite this, the use of heparin/LMWH bridging was common in our study, especially among patients undergoing ablation, of whom approximately half switched to heparin/LMWH. According to EHRA 2018 guidelines [9]. It is possible to withdraw anticoagulation therapy for 24 hours or more while undergoing AF a blation, or continuation of non-vitamin K antagonist oral anticoagulant (NOAC) therapy is also possible. In making this decision, several factors should be considered. While it may not be very clear whether patients should receive heparin/LMWH or not, the thromboembolic risk in these patients should be weighed.

Pooled data from these randomized studies showed that uninterrupted NOAC therapy was associated with a low incidence of major bleeding, cardiac tamponade and clinical cerebrovascular

Table 1: Comparison of patient demographics and clinical characteristics in patients with atrial fibrillation treated with apixaban undergoing rhythmology procedures.

	All patients (N=959)	Pacemaker/ICD implantation (N=115)	Ablation (N=624)	Cardioversion (N=220)	P-value
Median age (IQR), years	69 (61, 76.75)	80 (72, 85)	65 (59, 72)	69 (61, 76.75)	<0.001
Males, n (%)	679 (70.8)	72 (62.6)	457 (73.2)	150 (68.2)	0.04
Type of atrial fibrillation, n (%)	-	-	-	-	<0.001
Paroxysmal	435 (45.5)	53 (46.1)	362 (58.3)	20 (9.1)	-
Permanent	86 (9.0)	40 (34.8)	27 (4.3)	19 (8.7)	-
Persistent	434 (45.4)	22 (19.1)	232 (37.4)	180 (82.2)	
Apixaban dose prior to the procedure, n (%)	-	-	-	-	<0.001
5 mg/day	144 (15.1)	47 (40.9)	74 (11.9)	23 (10.5)	-
10 mg/day	811 (84.9)	68 (59.1)	547 (88.1)	196 (89.5)	-
Concomitant medications, n (%)	-	-	-	-	-
Aspirin	91 (11.9)	13 (15.1)	60 (12.5)	18 (9.1)	0.3
Clopidogrel	20 (2.6)	2 (2.3)	13 (2.7)	5 (2.5)	0.9
Amiodarone	357 (46.7)	29 (33.7)	202 (42.0)	126 (64.0)	<0.001
Verapamil	11 (1.4)	1 (1.2)	6 (1.2)	4 (2.0)	0.7
Diltiazem	7 (0.9)	0	6 (1.2)	1 (0.5)	0.4
Median CHA2DS2-VASc score (IQR)	3 (1, 3)	3 (3, 4)	2 (1 , 3)	3 (1, 3)	<0.001
Median HAS-BLED score (IQR)	2 (1, 2)	3 (2, 3)	1 (0 , 2)	2 (1, 2)	<0.001
Procedure circumstances, n (%)	-	-	-	-	<0.001
Emergency	26 (2.7)	13 (11.3)	9 (1.4)	4 (1.8)	-
Planned	933 (97.3)	102 (88.7)	615 (98.6)	216 (98.2)	-
Antiplatelet treatment stopped, n (%)	2 (0.2)	0	2 (0.3)	0 (0.0)	0.6
Heparin or LMWH use, n (%)	279 (29.1)	9 (7.8)	267 (42.8)	3 (1.4)	<0.001
TEE, n (%)	337 (35.1)	NA	300 (48.1)	37 (16.8)	<0.001
Spontaneous contrast, n (%)	65 (6.8)	NA	54 (8.7)	11 (5.0)	<0.001
Switch to heparin or LMWH, n (%)	314 (36.4)	10 (11.5)	299 (51.2)	5 (2.6)	<0.001
Median duration of heparin switch (IQR), hours	24 (11.5, 39.8)	24 (0.6, 73.5)	24 (11.0 , 39.2)	48 (18.0, 388.0)	0.3

HAS-BLED, Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile International Normalised Ratio, Elderly, Drugs or alcohol score; ICD, implantable cardioverter defibrillator; IQR, interquartile range; LMWH, low-molecular-weight heparin; NA, not applicable; TEE, trans-oesophageal echocardiogram; VKA, vitamin K antagonist.

Table 2: Complications within 30 days of procedure in patients with atrial fibrillation receiving Apixaban. [a]International Society on Thrombosis and Haemostasis (ISTH) major bleeding, [b]ISTH non-major, [c]Non-disabling stroke, [d]Not related to the procedure, ICD, implantable cardioverter defibrillator.

n (%)	Pacemaker/ICD implantation (N=115)	AF ablation (N=359)	Other ablation (N=265)	Electric cardioversion (N=220)
Pocket haematoma with infection	1 (0.7)	0	0	0
Major bleedinga	0	2 (0.6)	0	0
Minor bleedingb	2(1.7)	10 (2.8)	1 (0.4)	3 (1.4)
Tamponade needing drainage	0	1 (0.3)	0	0
Pericardial effusion without drainage	0	1 (0.3)	1 (0.4)	0
Embolic event	0	1 (0.2)c	0	0
Deathd	1 (0.9)	0	0	1 (0.5)

Table 3: Multivariate analysis. CI, confidence interval; ICD, implantable cardioverter defibrillator; LMWH, low-molecular-weight heparin; OR, odds ratio.

	OR (95% CI)	P-value
Switch to heparin or LMWH	4.29 (1.39, 13.25)	0.01
Patient age	1.01 (0.97, 1.06)	0.55
Procedure	-	-
Pacemaker/ICD implantation	3.21 (0.50, 20.67)	0.22
Ablation	0.99 (0.18, 5.50)	0.99
Electric cardioversion	2.01 (0.54, 7.52)	0.3

events, supporting the use of uninterrupted NOACs at the time of AF ablation [13-16]. Whereas, another study, which randomized patients in three groups continued versus interrupted a pixaban versus continued VKA showed similar outcomes between the uninterrupted and interrupted apixaban group [17]. The optimal duration of interruption of novel oral anticoagulants is also currently unknown in patients undergoing procedures. The ongoing Perioperative Anticoagulant Use for Surgery Evaluation (PAUSE; NCT02228798) study is prospectively evaluating a safe, standardized protocol for the perioperative management of patients with AF who are receiving a direct oral anticoagulant (dabigatran, rivaroxaban or apixaban) and require treatment interruption for an elective surgery/procedure [18]. In this study, apixaban will be interrupted for 2 days in patients at low risk of bleeding and for 4–5 days in those at high risk. Interruptions of the other direct oral anticoagulants are generally longer [18].

Guidelines also recommend that cardio version can be performed without TEE in patients receiving anticoagulants for >3 weeks, or with previous TEE in patients with <3 weeks of anticoagulation, in order to exclude the presence of a thrombus in the left atrium [9,11]. In our study, the use of TEE was significantly more common in patients undergoing ablation than in those undergoing the other procedures. TEE was used in approximately one quarter of patients undergoing cardio version and almost half of those undergoing ablation. Left atrial thrombus should be excluded by TEE or CT imaging in all cases of AF ablation. Otherwise, many centres perform TEE during the procedure in order to secure the trans-septal access. Although the design of our study (observational) may be a limitation by the possible of selection of patients, the large number of patients gives more strength to the results.

CONCLUSION

While guidelines no longer recommend heparin/LMWH bridging in patients with a low thromboembolic risk, 24-hour bridging was common in our patients with NVAF receiving a pixaban and undergoing cardiac rhythm therapies and particularly AF ablation over this study period and was associated with a risk of bleeding events. Further studies on the necessity and modalities of NOACs interruption in patients undergoing procedures are still needed.

ACKNOWLEDGEMENT

The Authors would like to thank Cecile Ricard Epidemiologist / Biostatistician in Annecy who provided statistical help for the study. Also, medical writing assistance with the preparation of this manuscript was provided by Galien Health Publishing, with funding provided by National College of Hospital Cardiologists (NCHC).

FUNDING

This work was supported by the National College of Hospital Cardiologists (NCHC) with a grant from Bristol Myers Squibb.

CONFLICT OF INTEREST

WA: This work was supported by the National College of Hospital Cardiologists (NCHC) with a grant from Bristol Myers Squibb R.G., J.T., A.D., E.G., S.C., F.G., A.M., J.M: None declared.

REFERENCES

1. Lloyd J, Wang Tj, leip Ep, Larson mg, Levy d. Lifetime risk for development of atrial fibrillation: the framingham heart study. circulation 2004;110: 1042-1046.
2. Chughss, Havmoeller R, Narayanan K, Singh D, Rienstra M. Worldwide epidemiology of atrial fibrillation: A global burden of disease 2010 study. Circulation. 2014;129:837-847.
3. Krijthebp, kunst A, Benjamin EJ, Lip GY, Franco oh. Projections on the number of individuals with atrial fibrillation in the european union, from 2000 to 2060. Eur Heart J. 2013;34:2746-2751.
4. Zoni-berisso M, Lercari F, Carazza T, Domenicucci S. Epidemiology of atrial fibrillation: European perspective. Clin epidemiol. 2014;6:213-220.
5. Wolfpa, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The framingham study. Stroke 1991;22: 983-988.
6. Glotzer TV, Daoud EG, Wyse DG, Singer DE, Ezekowitz MD. The relationship between daily atrial tachyarrhythmia burden from implantable device diagnostics and stroke risk: The trends study. Circ Arrhythm Electrophysiol 2009;2:474-480.
7. Zieglerpd, Glotzer TV, Daoud EG, Wyse DG, Singer DE. Incidence of newly detected atrial arrhythmias via implantable devices in patients with a history of thromboembolic events. Stroke 2010;41:256-260.
8. Zieglerpd, Glotzer TV, Daoud EG, Singer DE, Ezekowitz MD. Detection of previously undiagnosed atrial fibrillation in patients with stroke risk factors and usefulness of continuous monitoring in primary stroke prevention. Am J Cardiol 2012;110:1309-1314.
9. Steffelj, Verhamme P, Potpara TS, Albaladejo P, Antz M. The 2018 european heart rhythm association practical guide on the use of non-vitamin k antagonist oral anticoagulants in patients with atrial fibrillation. Eur Heart J 218;39:1330-1393.
10. European heart rhythmassociation (EHRA)., european society of cardiology (ESC), heart rhythm society, heart failure society of america (HFSA), american society of echocardiography (ASE), american heart association (AHA), european association of echocardiography (ESE) of esc, heart failure association of esc.
11. Daubert JC, Saxon L, Adamson PB, Auricchio A, Berger RD, Beshai JF, et al. EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: Implant and follow-up recommendations and management. Europace 2012;14:1236-1286.
12. Kirchhofp, Benussi S, Kotecha D, Ahlsson A, Atar D. ESC guidelines for the management of atrial fibrillation developed in collaboration with eacts. Eur J Cardiothorac Surg 2016;50:e1-e88.
13. https://www.ema.europa.eu/documents/product-information/eliquis-epar-product-information_en.pdf
14. Cappator, Marchlinski FE, Hohnloser SH, Naccarelli GV, Xiang J. Uninterrupted rivaroxaban vs. Uninterrupted vitamin k antagonists for catheter ablation in non-valvular atrial fibrillation. Eur Heart J 2015;36:1805-1811.
15. Calkinsh, Willems S, Gerstenfeld EP, Verma A, Schilling R. Uninterrupted dabigatran versus warfarin for ablation in atrial fibrillation. N Engl J Med 2017;376:1627-1636.
16. Kirchhofp, Haeuslerkg, Blank B, De bono J, Callans D. Apixaban in patients at risk of stroke undergoing atrial fibrillation ablation. Eur Heart J 2018;39:2942-2955.
17. Cardosor, Willems S, Gerstenfeld EP, Verma A, Schilling R. Uninterrupted anticoagulation with non-vitamin k antagonist oral anticoagulants in atrial fibrillation catheter ablation: lessons learned from randomized trials. Clin Cardiol 2019;42:198-205.
18. Reynoldsmr, Allison JS, Natale A, Weisberg IL, Ellenbogen KA. A prospective randomized trial of apixaban dosing during atrial fibrillation ablation: The aeiou trial. Jacc Clin Electrophysiol 2018;4:580-588.
19. Douketisjd, Spyropoulos AC, Anderson JM, Arnold DM, Bates SM. The perioperative anticoagulant use for surgery evaluation (pause) study for patients on a direct oral anticoagulant who need an elective surgery or procedure: Design and rationale. Thromb Haemost 2017;117:2415-2424.