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Peri-interventional combined anticoagulation and antithrombotic therapy in atrial fibrillation ablation: A retrospective safety analysis

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Abstract

Background: *Catheter ablation (CA) of atrial fibrillation (AF) requires an intensified peri-interventional anticoagulation scheme to avoid thromboembolic complications. In patients with cardiac or extracardiac artery disease, an additional antiplatelet treatment (AAT) is at least temporally necessary especially after a percutaneous intervention with stent implantation. This raises the question whether these patients have a higher peri-interventional bleeding risk during CA of AF.*

Methods: *The data of 1235 patients with CA of AF were retrospectively analyzed in terms of bleeding events, ablation type, antithrombotic medication and comorbidities such as coronary artery disease and components of the HAS- BLED score. Peri-interventional bleeding events were classified in accordance with the BARC classification. Differentiations were made between slight femoral bleeding (based on type 1), severe femoral bleeding and pericardial effusion without pericardiocentesis (based on type 2) with the need of further hospitalization, the need of transfusion (based on type 3a) and pericardial tamponades requiring pericardiocentesis (based on type 3b).*

Results: *1131/1235 (91.6%) patients were exclusively under anticoagulation and 187 (15.3%) patients were also on AAT. There were no statistically significant differences in type 1 and 3b bleeding complications or the occurrence of femoral pseudoaneurysms between both groups. However, type 2/3a bleeding complications, mostly femoral bleedings, were significantly more frequent in the patient group with AAT (3.2% vs. 7.5%, $p = 0.006$).*

Conclusions: *An additional antiplatelet therapy increases the risk of severe femoral bleeding events during CA of AF. It appears reasonable to perform the elective procedure of AF ablation after the discontinuation of AAT.* (Cardiol J 2018; 25, 2: 213–220)

Key words: atrial fibrillation ablation, antiplatelet medication, anticoagulation, femoral bleedings, percardial tamponades, pseudoaneurysms

Introduction

Atrial fibrillation (AF) is the most common sustained heart rhythm disorder in humans, especially at an increased age. In addition to rate control, rhythm control is an optional strategy for patients with symptomatic AF [1]. The efficacy of currently available antiarrhythmic drugs for rhythm control of AF patients is poor and AF relapses are common [2]. In patients with drug-refractory

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paroxysmal AF, the results of multiple clinical trials have demonstrated that catheter ablation (CA) is superior to antiarrhythmic drugs therapy in long-term maintenance of sinus rhythm [3]. The intervention is highly elective and subject to stringent safety requirements. Even minor complications are undesirable. Patients undergoing CA of AF have a transient increased risk of thromboembolism during, immediately after and for several weeks to months after the procedure [4]. This is because transseptal sheath placement, insertion of electrode catheters and radiofrequency energy application can precipitate thrombus formation. Substantial areas of damaged left atrial endothelium become a nidus for thrombus formation. This thrombus is at high risk of causing peri- and post-interventional strokes. Therefore, a peri- and post-interventional anticoagulation is mandatory. Depending on the CHA_2DS_2VASc score (C = congestive heart failure, H = hypertension, A = age > 75 years, D = diabetes, S = stroke, V = vascular disease, A = age > 65 years, S = sex category woman) and the HAS-BLED score (H = hypertension, A = abnormal kidney or liver function, S = stroke, B = history of bleeding, L = labile international normalized ratio [INR], E = elderly > 65 years, D = drugs), life-long anticoagulation may be necessary [1]. But it may cause an increased risk of bleeding [5]. Comorbidities such as coronary artery disease and peripheral artery disease require an additional antiplatelet treatment (AAT), especially after a percutaneous intervention and stent implantation. Therefore, it raises the question whether patients with a combined antithrombotic therapy and anticoagulation have a higher peri-interventional risk of bleeding. Under examination herein were the various bleeding complications in CA of AF and clarified if they occurred more often under combined anticoagulation and AAT compared to anticoagulation alone.

Methods

Retrospectively, the data of 1235 patients with CA of AF, during the period of 2005–2015, at the Heart Center of University Hospital Tuebingen, were analyzed using electronical datasets of patient charts. The study got approval by the local ethics committee. All adult patients (> 18 years) who underwent CA of AF during this period were included in the analysis. Patient data were analyzed in terms of patient characteristics and in terms of bleeding complications. The following data were retrospectively assessed: age, sex, type of antiplatelet medication (acetylsalicylic acid [ASA], clopidogrel, ticagrelor, prasugrel) and anticoagulation before ablation (type of non-vitamin K oral anticoagulant [NOAC], vitamin K antagonists [VKA], heparin, none), the usage of one or two antiplatelet medications, ablation type and the presence of coronary artery disease. Additionally, the components of HAS-BLED score were collected for risk stratification: history of hypertension, age > 65 years, history of stroke, medication predisposing to bleeding (antiplatelet agents, non-steroidal anti-inflammatory drugs), history of prior bleeding events, labile INR (time in therapeutic range < 60%), hepatic impairment (cirrhosis or serum bilirubin > 2 × normal or aspartate aminotransferase [AST]/alanine aminotransferase [ALT]/alkaline phosphatase [AP] > 3 × normal, renal insufficiency (on dialysis, after kidney transplantation or with creatinine concentration > 2.26 mg/dL or > 200 μmol/L) and alcohol or drug abuse [6]. Patients were separated into two groups: one group of patients with only anticoagulation and a second group with AAT plus anticoagulation. The bleeding events as endpoints were classified according to Bleeding Academic Research Consortium (BARC) [7]. Modified, the bleeding types 1-3b were used here and are defined as follows: slight bleedings (type 1) defined as slight femoral bleeding at the puncture site. Type 2 bleedings constituted severe femoral bleeding events, which required re-installation of a pressure bandage and re-sonographic control. In casesof abnormal findings in the examination of the inguinal region for example one-sided flow noise, pulsating swelling or large hematoma, the patient underwent vascular ultrasound. In this way, pseudoaneurysms could be determined. Type 2 also included patients with a pericardial effusion without the need for a pericardiocentesis. Type 3a bleedings required a transfusion. A pericardial tamponade with the need for pericardiocentesis was assigned to type 3b. These events prolonged hospitalization. Normally, the patients were hospitalized for 2 days after CA but if there was a bleeding complication the hospitalization was prolonged until the patients were stable in terms of hemoglobin or the aneurysm was no longer perfused, or no pericardial effusion could be detected after repeated echocardiographic control.

Ablation procedure

Preprocedural transoesophageal echocardiography was performed to exclude intracardiac thrombi in all patients. Vascular ultrasound was only used in difficult femoral conditions. The abla-

tion procedure was performed under sedation with a continuous infusion of propofol. For CA of AF, circumferential pulmonary vein isolation (PVI) and the cryoballoon PVI were used. During the ablation a 6-F decapolar catheter (Bard, Electrophysiology Division, Lowell, MA, USA) was positioned within the coronary sinus via the left femoral vein. A puncture of the radial artery with a 4-F sheath was performed for invasive control of blood pressure. In the cryoablation group a 14 F sheath was placed in the left atrium via the right femoral vein after a single transseptal puncture. In the radiofrequency (RF) ablation group a single transseptal puncture was performed and two sheaths, 8 F nonsteerable and 11 F steerable, were placed into the left atrium through one puncture site via the right femoral vein. A temperature probe in the esophagus (Sensitherm, St. Jude Medical) at the level of the left atrium was used with a cut off value of 39.0°C. A geometry of the left atrium was created using the NAVX- or the CARTO-system and a circumferential pulmonary vein ablation controlled by simultaneous mapping with a circular catheter placed in the pulmonary vein and with ipsilateral pulmonary vein ablation using irrigated RF energy application. In addition, a circular mapping catheter was placed in the left superior or left inferior pulmonary vein. After completing the circumferential ablation lines PVI was reevaluated using the circular mapping catheter. After the procedure patients got a compression bandage for 12 h.

Anticoagulation strategies

The antiplatelet medication was not interrupted during ablation. VKA were continued. In cases of INR < 1.8 low-molecular-weight heparin, or in cases of glomelural filtration rate (GFR) < 30 mL/min intravenous heparin was given before and after ablation. However, NOACs were interrupted 24–48 h prior to ablation. During ablation, intravenous heparin was continuously administered to keep activated clotting time in the range of 300–400 s. After ablation heparin was not antagonized with protamine, but was continuously used until INR exceeded 2.0, or NOACs were continued. In patients with NOAC treatment before ablation and GFR > 50 mL/min an accelerated loading dose scheme of dabigatran was used [8], otherwise the preceding NOAC was continued. Therapeutic anticoagulation was continued for at least 3 months.

Statistical analysis

The results of patient characteristics were expressed as mean ± standard deviation. The differences in percentage were analyzed using the χ^2 test. The associations of risk variables with the significant endpoints were tested by univariate and multivariate logistic analyses. Only the variables, that were univariate significant, were included in multivariate analysis. The significance level was set at $p < 0.05$.

Table 1. Patients' characteristics.

Number of patients	1235
Age [years]	61.0 ± 10.4
Females	432 (35.0%)
Coronary artery disease	223 (18.1%)
Method of ablation:	
Radiofrequency energy	937 (75.9%)
Cryoenergy	298 (24.1%)
Platelet inhibitor before ablation:	
Acetylsalicylic acid	176 (14.3%)
Clopidogrel	21 (1.7%)
Prasugrel	1 (0.1%)
Ticagrelor	4 (0.3%)
One platelet inhibitor	172 (13.9%)
Two platelet inhibitors	15 (1.2%)
Anticoagulation before ablation:	
Vitamin K antagonists	599 (48.5%)
Rivaroxaban	198 (16%)
Dabigatran	119 (9.6%)
Apixaban	30 (2.4%)
Heparin	185 (15,1%)
None	229 (18.4%)
HAS-BLED score	1.28 ± 0.9
Age > 65 years	458 (37.1%)
Hypertension	795 (64.4%)
Renal insufficiency	5 (0.4%)
Hepatic impairment	28 (2.3%)
Stroke history	76 (6.2%)
Prior major bleeding or predisposition to bleeding	18 (1.5%)
Labile international normalized ratio setting	3 (0.2%)
Medication predisposing to bleeding (platelet inhibitor)	187 (15.1%)
History of alcohol or drug usage	10 (0.8%)

Results

Table 1 shows the patient characteristics. Among the 1235 patients were 432 (35%) women. The average age was 61.0 ± 10.4 years. 937 (75.9%)

Table 2. Effect of additional platelet inhibitors on bleeding complications.

	Platelet inhibitor	No platelet inhibitor	P
Slight femoral bleeding (BARC 1)	12 (6.4%)	43 (4.1%)	0.157
Severe femoral bleeding (BARC 2/3a)	14 (7.5%)	34 (3.2%)	0.006
Pseudoaneurysms	6 (3.2%)	38 (3.6%)	0.778
Pericardial effusion (puncture not required) (BARC 2)	6 (3.2%)	49 (4.7%)	0.372
Pericardial effusion (puncture required) (BARC 3b)	0 (0.0%)	13 (1.2%)	0.126

patients were treated with circumferential PVI with RF energy and 298 (24.1%) with cryoballoon PVI. 223 (18.1%) patients had coronary artery disease. 204 patients had any type of antiplatelet medication. ASA was used in 176 (14.3%) patients, clopidogrel in 21 (1.7%), prasugrel in 1 (0.1%) and ticagrelor in 4 (0.3%). 1131/1235 (91.6%) patients had anticoagulation before the procedure. 599 (48.5%) patients were on VKA, 198 (16%) on rivaroxaban, 119 (9.6%) on dabigatran, 30 (2.4%) on apixaban and 185 (15.1%) only on low molecular weight heparin. However, there was only 1 patient with IV heparins prior to ablation, which was therefore assigned to the low molecular weight heparin group. 229 (18.5%) of the patients had no anticoagulation prior to CA. 124 (10%) patients were only on antiplatelet medication. In addition to anticoagulation, 15 (1.2%) patients had an additional dual antiplatelet therapy, which means they had a triple therapy (TT). Patients with TT had a percutaneous intervention within the prior 1–6 months (depending on the type of stent). In 172 (13.9%) of the patients only 1 antiplatelet drug was taken additionally, so they had a dual therapy (DT), or the antiplatelet was singularly used. Patients under DT mainly took this due to a 1 to 12-month previous percutaneous intervention (depending on the type of stent), a small number due to a high cardiovascular risk profile potentially compromising the progress of coronary or peripheral artery disease.

The investigation of the components of the HAS-BLED score revealed the following results: 458 (37.1%) patients were > 65 years old, 795 (64.4%) had hypertension, 76 (6.2%) had a history of stroke, 3 (0.2%) had a labile INR, 5 (0.4%) suffered from renal insufficiency and 28 (2.3%) from hepatic impairment, 18 (1.5%) had a prior major bleeding or a predisposition to bleeding and 10 (0.8%) had a history of alcohol or drug usage.

Further research with regard to bleeding complications depending on AAT presented the following (Table 2). According to BARC 1 (slight femoral bleedings) there was no statistically significant difference between the groups of sole anticoagulation and AAT (43 (4.1%) vs. 12 (6.4%), $p = 0.157$). The same could be detected for pericardial effusions without the need for pericardial puncture (BARC 2) (49 [4.7%] vs. 6 [3.2%], $p = 0.372$). Regarding pericardial tamponades requiring puncture (BARC 3b) a significant result could not be achieved (13 [1.2%] vs. 0 [0%], $p = 0.126$). No statistical difference was shown in the formation of femoral pseudoaneurysms between both groups (38 [3.6%] vs. 6 [3.2%], $p = 0.778$). Only in severe femoral bleedings that were assigned to both BARC 2 and 3a, a significant difference could be detected ($p = 0.006$). 34 (3.2%) patients were revealed with anticoagulation monotherapy and 14 (7.5%) in patients with AAT.

In the group with severe femoral bleeding, HAS-BLED score was significantly higher than in the group with light femoral bleeding (1.8 ± 1.0 vs. 1.2 ± 0.9, $p < 0.001$).

Table 3 shows a subgroup analysis of the risk of bleeding based on the various parameters of the HAS-BLED score separately for patients receiving only a single oral anticoagulant versus those receiving additional antiplatelet therapy. Patients without AAT had more frequently had a stroke in the past. On the other hand, patients under AAT had a significantly higher HAS-BLED score. There are no differences in terms of other components such as age, hypertension, renal insufficiency, hepatic impairment, history of prior major bleeding, labile INR setting or history of alcohol and/or drug use ($p > 0.05$ for all).

In a binary regression analysis (Table 4), older age ($p = 0.001$) and the presence of an AAT ($p = 0.031$) were independent predictors for the endpoint "severe femoral bleeding". In contrast, the use of interrupted NOACs ($p = 0.007$) independently decreased the risk. Other components of the HAS-BLED score such as renal and hepatic impairment, hypertension, prior major bleeding, history of stroke, history of alcohol or drug usage,

Table 3. Effect of additional platelet inhibitors on bleeding complications depending on HAS-BLED score components.

	Platelet inhibitor (n = 187)	No platelet inhibitor (n = 1048)	P
HAS-BLED score	2.1 ± 0.8	1.1 ± 0.8	< 0.001
Age > 65 years	66 (35.3%)	392 (37.4%)	0.321
Hypertension	121 (64.7%)	674 (64.3%)	0.494
Renal insufficiency	1 (0.5%)	4 (0.4%)	0.561
Hepatic impairment	4 (2.1%)	24 (2.3%)	0.578
Stroke history	2 (1.1%)	74 (7.1%)	0.001
Prior major bleeding or predisposition to bleeding	5 (2.7%)	13 (1.2%)	0.123
Labile international normalized ratio setting	0 (0.0%)	3 (0.3%)	0.611
History of alcohol or drug usage	0 (0.0%)	10 (1.0%)	0.375

Table 4. Univariate and multivariate binary logistic regression analysis for prediction of severe femoral bleeding events (BARC type 2/3a).

Variable	Univariate analysis			Multivariate analysis		
	OR (95% CI)	z	p	OR (95% CI)	z	p
Age > 65 years	2.46 (1.37–4.42)	9.10	0.003	2.60 (1.44–4.70)	10.1	0.001
Hypertension	1.69 (0.87–3.29)	2.40	0.121			
Renal insufficiency	6.29 (0.69–57.49)	2.66	0.103			
Hepatic impairment	3.01 (0.90–10.64)	3.22	0.072			
History of stroke	0.65 (0.15–2.75)	0.33	0.562			
Prior major bleeding or predisposition to bleeding	3.18 (0.71–14.25)	2.29	0.130			
Labile international normalized ratio*						
Medication usage predisposing to bleeding (platelet inhibitor)	2.41 (1.27–4.59)	7.21	0.007	2.05 (1.07– 3.95)	4.64	0.031
History of alcohol or drug usage*						
NOAC	0.22 (0.08– 0.63)	8.15	0.004	0.24 (0.85–0.68)	7.22	0.007
Ablation type	0.72 (0.34–1.5)	0.78	0.38			

*No events for these properties; CI — confidence interval; NOAC — non-vitamin K oral anticoagulant; OR — odds ratio

labile INR and ablation type did not independently predict the endpoint ($p > 0.05$ for all).

The statistical relationship between severe bleeding events and risk variables was determined by the odds ratio as shown in Figure 1.

Patients under VKA therapy had the highest risk of severe femoral bleeding (5.7%), followed by patients without anticoagulation (4.8%). These patients, however, had a higher HAS-BLED score (1.4 ± 1.0 vs. 1.2 ± 0.9, $p = 0.012$) compared to the other patients. Because of this, no anticoagulation was often performed before the procedure in this group. Patients with NOAC therapy had the lowest risk of severe femoral bleeding (0.9%). Patients under heparin therapy had a severe femoral bleeding risk of 1.6%.

Discussion

Atrial fibrillation is the most common sustained heart rhythm disorder. In drug refractory therapy, an ablation can be performed. The procedure is usually highly elective. In addition to thrombembolism, bleeding events are the most common complications. These should be kept as low as possible. In this context, it is important to determine

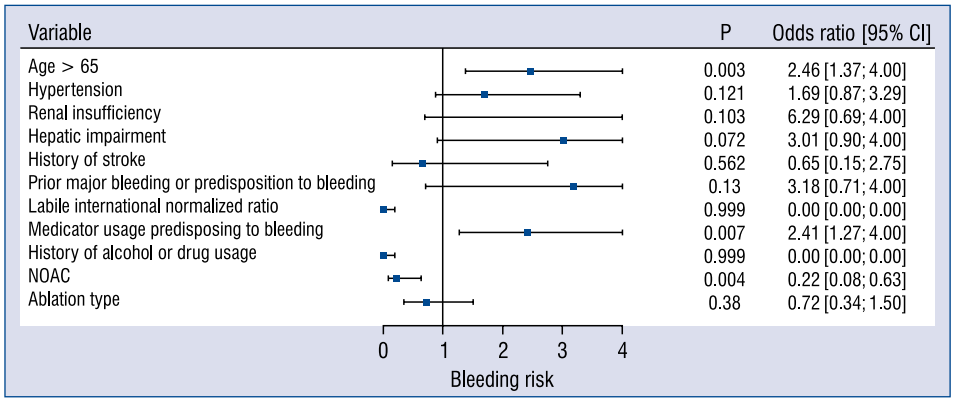

Figure 1. Forest plot of univariate logistic regression analysis for different risk variables; CI — confidence interval; NOAC — non-vitamin K oral anticoagulant.

the predictors of bleeding complications. Some patients suffer from AF as well as from cardiac or extracardiac atherosclerosis, which makes it often necessary to take an additional platelet inhibition, especially after stent implantation. It is important to investigate whether these patients are more likely to have bleeding complications and derive strategies for prevention. Previous studies were limited to the effects of solely anticoagulants on peri-interventional bleeding risks, vascular damage and pericardial tamponades associated with CA of AF [5, 9–16]. Data on the risk of AAT in patients undergoing CA of AF does not seem to be well studied.

In this study patients with AAT had a significantly higher risk of severe femoral bleeding. This risk was more than double in the retrospective study. However, there were no significant differences in terms of slight femoral bleedings, pericardial effusions and femoral pseudoaneurysms. The formation of pseudoaneurysms might be dependent on the interventionists, the type of puncture, the patient's anatomy and the compression bandage. Nevertheless, the slight bleeding complications are probably underestimated because of the nature of a retrospective study design, which were also reported in other studies [17].

The use of DT or TT in patients with AF undergoing percutaneous coronary intervention (PCI) have a much broader database. Patients with TT and subsequent re-PCI have a higher risk of major bleedings than patients with DT or dual antiplatelet therapy alone [18, 19]. On the other hand, patients under TT have a significantly lower risk of thromboembolism [18, 20], so it is associated with lower all-cause mortality [18] due to a reduced risk of stent thrombosis [21] by an adequate antiplatelet therapy.

On the other hand, the HAS-BLED score was significantly increased in patients with severe femoral bleedings and in patients with platelet inhibitor. The latter is to be expected since the fact of a platelet inhibitor is thus included in this score. Basically, the oral anticoagulation (OAC) should be given carefully in patients with a HAS-BLED score ≥ 3. But, the HAS-BLED score alone should not exclude patients from a possible OAC [21].

At the same time, patients with a higher HAS-BLED score usually have a high risk of stroke as well (CHA_2DS_2VASc), so they benefit from an OAC disproportionately. The present data shows that patients without platelet inhibitor had significantly more strokes in prehistory. This is because most of the patients were already under OAC due to an AF associated stroke in the past.

229 patients had no anticoagulation prior to the procedure. 124 of these had only antiplatelet medication. These were young patients with CHA_2DS_2VASc score 0 or 1 or high HAS-BLED score and thus high bleeding risk.

The singular use of ASA or no use of antithrombocytic therapy in patients with CHA_2DS_2-VASc score 0 or 1 and lack of risk factors was consistent with the former European Society of Cardiology (ESC) guidelines [22]. It is now recommended to perform oral anticoagulation in patients with CHA_2DS_2VASc score 1. In case of CHA_2DS_2-VASc score 0 or in women under 65 years no permanent anticoagulation is recommended [23].

In the context of a regression analysis, age and antiplatelet medication as components of the HAS-BLED score were responsible for the severe femoral bleeding events as independent risk factors. The fact that increased age has a meaningful influence on bleeding complications is well known

[24]. Despite the small number of patients with AAT, it can be identified as an independent predictor for bleeding events in CA of AF. The variables of unstable INR, alcohol and drug abuse seem to be associated with a small risk, but cannot be exploited due to the low drop rate. Limited liver and renal function are associated with increased risk of bleeding. Here too, the case numbers are very small. In addition, the liver and renal insufficiencies are very strict and highly defined in the HAS-BLED score, namely cirrhosis or serum bilirubin > 2 × normal or AST/ALT/AP > 3 × normal for hepatic impairment and dialysis, transplant, creatinine > 2.26 mg/dL or > 200 μmol/L for renal insufficiency [6]. Patients, who meet these criteria, are rarely subjected to a CA of AF. Due to the retrospective design, the cases for previous severe bleeding could be underestimated.

Here, the use of NOAC is associated with a lower risk of bleedings. But here NOACs were interrupted 24–48 h before ablation, so a lower dose level has to be assumed and this result is inaccurate. It could also be shown that there is a significantly lower risk of bleeding under NOAC than under VKA. Other studies proved the same [12, 17]. The use of NOAC became more attractive the later years due to both more experience and resulting better controllability and demonstrated lower bleeding risk in general [9–17].

However, this study is mainly concerned with the question of bleeding probability under AAT.

To minimize the risk of bleeding events, the selection of patients is important. There are different criteria that should be considered before CA of AF such as duration and symptoms of AF, age, predisposing medication and comorbidities. Also, obesity might be a risk factor due to a difficult punctuation situation. Further, in order to reduce the bleeding complications, the pre-, peri- and post-interventional femoral monitoring could be extended as well as the duration of the compression bandage, but the latest was only under consideration of the respective risk of the development of thrombosis.

Limitations of the study

A limitation of this study there need to be mention of the retrospective and oberservational nature of the study design. Furthermore, this observation study was carried out over a long period of time. During this time, various anticoagulation and antiplatelet regimes were used. Especially with the introduction of NOACs and their lower risk of bleeding need to be mentioned here.

Conclusions

When determining ablation, both the risk of bleeding by calculating the HAS-BLED score and the risk of thromboembolism by calculating the CHA_2DS_2VASc score should be assessed. If an elective CA of AF is desired in patients with DT or TT the data supports a waiting strategy until the AAT can be discontinued to minimize the risk of peri-interventional bleedings. On the other hand, an earlier termination of AAT should be avoided due to the potential increased risk of mortality, for example, due to stent thrombosis. However, larger controlled studies are necessary for definite conclusions.

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Conflict of interest: None declared

References

1. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2014; 64(21): e1–76.
2. Lafuente-Lafuente C, Longas-Tejero M, Bergmann JF, et al. Antiarrhythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. Cochrane Database Syst Rev. 2012, doi: 10.1002/14651858.cd005049.pub3.
3. Bonanno C, Paccanaro M, La Vecchia L, et al. Efficacy and safety of catheter ablation versus antiarrhythmic drugs for atrial fibrillation: a meta-analysis of randomized trials. J Cardiovasc Med (Hagerstown). 2010; 11(6): 408–418, doi: 10.2459/JCM.0b013e328332e926, indexed in Pubmed:19834326.
4. Vazquez SR, Johnson SA, Rondina MT. Peri-procedural anticoagulation in patients undergoing ablation for atrial fibrillation. Thromb Res. 2010; 126(2): e69–e77, doi: 10.1016/j.thromres.2009.11.031, indexed in Pubmed: 20053426.
5. 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(1): 32–38, doi: 10.1161/CIRCEP.109.859116, indexed in Pubmed: 19995881.
6. Pisters R, Lane DA, Nieuwlaat R, et al. 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. 2010; 138(5): 1093–1100, doi: 10.1378/chest.10-0134, indexed in Pubmed: 20299623.
7. Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. Circulation. 2011; 123(23): 2736–2747, doi: 10.1161/CIRCULATIONAHA.110.009449, indexed in Pubmed: 21670242.

8. Seizer P, Gramlich M, Frische C, et al. Postinterventional use of dabigatran in patients undergoing ablation therapy using an accelerated loading dose scheme - a single center experience. Thromb Res. 2015; 136(2): 486–487, doi: 10.1016/j.thromres.2015.06.006, indexed in Pubmed: 26092430.
9. Arshad A, Johnson CK, Mittal S, et al. Comparative safety of periablation anticoagulation strategies for atrial fibrillation: data from a large multicenter study. Pacing Clin Electrophysiol. 2014; 37(6): 665–673, doi: 10.1111/pace.12401, indexed in Pubmed: 24797604.
10. Duytschaever M, Berte B, Acena M, et al. Catheter ablation of atrial fibrillation in patients at low thrombo-embolic risk: efficacy and safety of a simplified periprocedural anticoagulation strategy. J Cardiovasc Electrophysiol. 2013; 24(8): 855–860, doi: 10.1111/jce.12148, indexed in Pubmed:23600918.
11. Nairooz R, Ayoub K, Sardar P, et al. Uninterrupted New Oral Anticoagulants Compared With Uninterrupted Vitamin K Antagonists in Ablation of Atrial Fibrillation: A Meta-analysis. Can J Cardiol. 2016; 32(6): 814–823, doi: 10.1016/j.cjca.2015.09.012, indexed in Pubmed: 26810476.
12. Wu S, Yang Ym, Zhu J, et al. Meta-Analysis of efficacy and safety of new oral anticoagulants compared with uninterrupted vitamin k antagonists in patients undergoing catheter ablation for atrial fibrillation. Am J Cardiol. 2016; 117(6): 926–934, doi: 10.1016/j.amjcard.2015.12.027, indexed in Pubmed: 26803384.
13. Vamos M, Cappato R, Marchlinski FE, et al. Efficacy and safety of rivaroxaban compared with vitamin K antagonists for periprocedural anticoagulation in catheter ablation of atrial fibrillation: a systematic review and meta-analysis. Europace. 2016; 18(12): 1787–1794, doi:10.1093/europace/euv408, indexed in Pubmed: 26797248.
14. Rillig A, Lin T, Plesman J, et al. Apixaban, rivaroxaban, and dabigatran in patients undergoing atrial fibrillation ablation. J Cardiovasc Electrophysiol. 2016; 27(2): 147–153, doi: 10.1111/jce.12856, indexed in Pubmed: 26464027.
15. Kuwahara T, Abe M, Yamaki M, et al. Apixaban versus warfarin for the prevention of periprocedural cerebral thromboembolism in atrial fibrillation ablation: multicenter prospective randomized study. J Cardiovasc Electrophysiol. 2016; 27(5): 549–554, doi: 10.1111/jce.12928, indexed in Pubmed:26766541.
16. Santarpia G, De Rosa S, Polimeni A, et al. Efficacy and safety of non-vitamin k antagonist oral anticoagulants versus vitamin K antagonist oral anticoagulants in patients undergoing radiofrequency catheter ablation of atrial fibrillation: a meta-analysis. PLoS One. 2015; 10(5): e0126512, doi:10.1371/journal.pone.0126512, indexed in Pubmed: 25974377.
17. Winkle RA, Mead RH, Engel G, et al. Peri-procedural interrupted oral anticoagulation for atrial fibrillation ablation: comparison of aspirin, warfarin, dabigatran, and rivaroxaban. Europace. 2014; 16(10): 1443–1449, doi: 10.1093/europace/euu196, indexed in Pubmed: 25115168.
18. Sambola A, Mutuberría M, García Del Blanco B, et al. Impact of triple therapy in elderly patients with atrial fibrillation undergoing percutaneous coronary intervention. PLoS One. 2016; 11(1): e0147245, doi: 10.1371/journal.pone.0147245, indexed in Pubmed: 26808678.
19. Sambola A, Mutuberría M, García Del Blanco B, et al. Effects of triple therapy in patients with non-valvular atrial fibrillation undergoing percutaneous coronary intervention regarding thromboembolic risk stratification. Circ J. 2016; 80(2): 354–362, doi: 10.1253/circj.CJ-15-0923, indexed in Pubmed:26725763.
20. Bavishi C, Koulova A, Bangalore S, et al. Evaluation of the efficacy and safety of dual antiplatelet therapy with or without warfarin in patients with a clinical indication for DAPT and chronic anticoagulation: a meta-analysis of observational studies. Catheter Cardiovasc Interv. 2016; 88(1): E12–E22, doi: 10.1002/ccd.26234, indexed in Pubmed: 26354765.
21. Thompson PL, Morton AC. Antithrombotic therapy in patients with combined coronary heart disease and atrial fibrillation. Panminerva Med. 2016; 58(1): 23–33, indexed in Pubmed: 26658287.
22. Camm AJ, Lip GY, De Ca, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation--developed with the special contribution of the European Heart Rhythm Association. Europace. 2012; 14(10): 1385–413.
23. Kirchhof P, Benussi S, Kotecha D, et al. Wytyczne ESC dotyczące leczenia migotania przedsionków w 2016 roku, opracowane we współpracy z EACTS. Kardiol Pol. 2016; 74(12): 1359–469.
24. Bo M, Li Puma F, Badinella Martini M, et al. Effects of oral anticoagulant therapy in older medical in-patients with atrial fibrillation: a prospective cohort observational study. Aging Clin Exp Res. 2017; 29(3): 491–497, doi: 10.1007/s40520-016-0569-7, indexed in Pubmed: 27100358.