Heart and Vessels (2019) 34:632–640
https://doi.org/10.1007/s00380-018-1280-8

ORIGINAL ARTICLE

Radiofrequency catheter ablation prior to percutaneous coronary intervention in patients with atrial fibrillation coexisting with stable coronary artery disease: a single-center pilot study

Satoshi Kawada[1] · Atsuyuki Watanabe[1] · Yoshimasa Morimoto[1] · Koji Nakagawa[1] · Nobuhiro Nishii[2] · Kazufumi Nakamura[1] · Hiroshi Morita[2] · Hiroshi Ito[1]

Received: 13 May 2018 / Accepted: 5 October 2018 / Published online: 15 October 2018

Abstract
Atrial fibrillation (AF) frequently coexists with cardiovascular disease (CAD) in a clinical setting. However, the optimum therapy for AF patients who have concomitant CAD is unclear. We retrospectively examined the efficacy and safety of radiofrequency catheter ablation (RFCA) prior to percutaneous coronary intervention (PCI) in patients with AF who had concomitant stable CAD. Between January 2014 and December 2015, a total 264 patients (179 men; mean age, 65.5 ± 10.1 years) who were referred to undergo a first RFCA procedure were reviewed in this study. Of the 264 patients, 41 (15.5%) had stable CAD detected by multi-detector computed tomography before RFCA. Thirty-seven patients who had AF with stable CAD were divided into two treatment arms: (1) RFCA prior to PCI ($n = 13$) and (2) PCI prior to RFCA (n = 24) [four patients excluded because of left main coronary artery disease (LMCA) or triple vessel disease (TVD)]. The median follow-up was 14 (IQR 8–19) months. There was no significant difference in AF recurrence rate after the procedure between the RFCA first group and PCI first group ($P = 0.515$). No symptomatic cardiovascular events occurred the during follow-up period. The PCI first group had a significantly longer duration of triple therapy (188.5 ± 167 days vs 5.6 ± 24.5 days, $P = 0.01$) and all of the four bleeding events occurred during triple therapy ($P = 0.01$). The results of this single-center pilot study suggested that prior RFCA in patients with AF coexisting with CAD could have fewer serious bleeding events than prior PCI.

Keywords Atrial fibrillation · Pulmonary vein isolation · Coronary artery disease · Radiofrequency catheter ablation · Percutaneous coronary intervention

Introduction

Atrial fibrillation (AF) is one of the most common arrhythmias in the general population and it is associated with a 4–5-times increase in stroke risk [1] and a 1.5- to 1.9-fold increase mortality risk [2]. The prevalence in Japan is about 0.56%, about two-thirds of that in Western countries [1, 3]. In Japan, the incidence of AF increases with advancing age and the number of people with AF is estimated to be 1.034 million (prevalence of 1.09%) in 2050 [3].

According to the J-RHYTHM Registry, the prevalence of coronary artery disease (CAD) as an underlying heart disease in AF patients is about 10% in the Japanese population [4]. Triple therapy including an anticoagulant drug and additional dual antiplatelet therapy (DAPT) was recommended by the 2016 European guidelines for such patients who have to undergo percutaneous coronary intervention (PCI) [5]. However, the results of the WOEST trial showed that triple therapy is associated with a significantly higher rate of bleeding complications than is the use of clopidogrel plus warfarin (double therapy) even when used for a short time [6]. The optimum treatment for AF patients who have concomitant CAD remains unclear.

Recently, radiofrequency catheter ablation (RFCA) has become a common therapy for patients with symptomatic

✉ Satoshi Kawada
satoshikawada03@gmail.com; satoshikawada3@yahoo.co.jp

[1] Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kita-ku, Okayama, Japan

[2] Department of Cardiovascular Therapeutics, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kitaku, Okayama, Japan

AF and the outcome has improved [7]. In addition, a recent study suggested that a protocol of discontinuing oral anticoagulation (OAC) after successful RFCA of AF in patients who are maintained on single antiplatelet therapy is reasonable regardless of the patient's baseline risk [8]. In consideration of this issue, we tested the hypothesis that discontinuing OAC after successful RFCA prior to PCI in patients with AF coexisting with stable CAD will result in fewer serious bleeding events but without an additional cost of increased risk of recurrent coronary events or thromboembolism. In this study, we retrospectively examined the efficacy and safety of RFCA prior to PCI in patients with AF who have concomitant stable CAD.

Methods

Subjects

We retrospectively studied 264 consecutive patients with AF that was resistant to at least one antiarrhythmic drug who were referred to undergo pulmonary vein isolation (PVI) in our hospital between January 2014 and December 2015. Of the 264 patients, 41 (15.5%) had stable CAD detected by multi-detector computed tomography (MDCT) before RFCA. Written informed consent was obtained from all patients. All study protocols were approved by the institutional review board at Okayama University Hospital.

Study design

Prior to catheter ablation, all patients underwent MDCT to plan and guide the ablation procedure and detect significant coronary artery disease. Of the 264 patients, 41 had stable CAD detected by MDCT before admission. Left main coronary artery disease (LMCA) and triple vessel disease (TVD) had been detected in 4 patients. Two patients with LMCA and one vessel disease underwent coronary artery bypass graft (CABG) and Maze surgeries. The others with TVD underwent PCI following antiarrhythmic drugs, because they rejected surgery. Patients with LMCA and TVD were excluded from this study. Thirty-seven patients who had AF with stable CAD were divided into 2 treatment arms: (1) RFCA prior to PCI (2) PCI prior to RFCA. All patients had positive exercise testing for CAD. Then, the decision regarding treatment was left to the physician's clinical judgement. In the RFCA prior to PCI arm, RFCA was first performed with double therapy. Anticoagulation therapy was stopped if sinus rhythm had been maintained for 3–6 months. Then, PCI was performed with DAPT. In the PCI prior to RFCA arm, PCI was first performed with triple therapy. One antiplatelet drug was discontinued after 3–6 months, and then, RFCA was performed with double therapy. The trial schema is shown in Fig. 1.

Electrophysiological study and radiofrequency catheter ablation

All patients received oral anticoagulation for at least 1 month before the procedure. RFCA was principally performed with double therapy. Before admission, transesophageal echocardiography was performed in all patients to rule out atrial thrombi, and transthoracic echocardiography was performed to evaluate cardiac structure and function. Procedures were performed with administration of 70–100 units/kg of heparin to achieve a clotting time of > 300 s. In principle, the ablation procedure was based on electrical isolation of the pulmonary veins in all patients. PV isolation with confirmation of both entrance and exit blocks was required, and additional carvotricuspid isthmus ablation was performed when necessary. When sinus rhythm had not been restored after PVIs, the AF was terminated by cardioversion. Three-dimensional electroanatomical mapping was performed using the Carto 3 system (Biosense Webster, Inc). Radiofrequency (RF) was applied using an open irrigated-tip catheter (Navister Thermocool, Biosense Webster) with power output up to 30 W

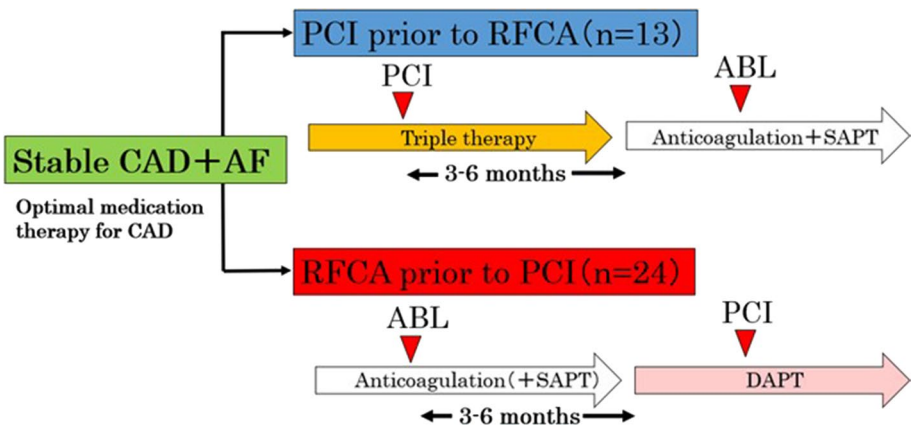

Fig. 1 Study design and patient flow. *CAD* coronary artery disease, *AF* atrial fibrillation, *RFCA* radiofrequency catheter ablation, *PCI* percutaneous coronary intervention, *DAPT* dual antiplatelet therapy, *SAPT* single antiplatelet therapy

close to the PV ostia using an irrigation rate of 20 ml/min (0.9% saline infused with the Cool Flow Pump, Biosense Webster) to maintain a tip temperature below 45 °C.

Percutaneous coronary intervention

All patients received 75 mg clopidogrel and 100 mg aspirin before the procedure. PCI was performed with triple therapy or with DAPT. We preferred the radial or brachial approach rather than the femoral approach, because femoral access was shown to be associated with increased bleeding risk [9]. Patients were treated in accordance with the European Society of Cardiology guidelines [10]. Procedures performed with administration of 70–100 units/kg of heparin to achieve a clotting time of > 300 s. Implantation of a new-generation drug-eluting stent (DES) for the target lesion was performed in all patients [10]. Acute device success was defined as successful delivery and deployment of the assigned device and withdrawal of the catheter with < 30% residual stenosis by angiography, regardless of whether bail out was required or not.

Follow-up and definitions of myocardial ischemia and bleeding

Patients were followed up at our institution for 1, 3, 6, and 12 months after the RFCA procedure including clinical interviews, ECG recording, and 24-h Holter registration. After a blanking period of 3 months, recurrence of AF was defined as any recording of AF on an ECG or an episode longer than 30 s on 24-h ECG Holter registration. Anticoagulation therapy was stopped if sinus rhythm had been maintained for 3–6 months. Patients were followed up at our institution for 1, 3, 6, and 12 months after the PCI procedure including clinical interviews and ECG recording. Routine follow-up angiography or MDCT was planned in all patients at 8–12 months.

Myocardial ischemia was defined as the occurrence of typical chest pain and new electrocardiogram changes. Stent thrombosis was considered to have occurred if the criteria for definite stent thrombosis of the Academic Research Consortium were met [11]. Bleeding was defined according to Bleeding Academic Research Consortium (BARC) criteria. Major bleeding was defined as the presence of intracranial or any overt, actionable sign of hemorrhage or clinically overt hemorrhage associated with a decrease in hemoglobin level of ≥ 3 g/dl or fatal bleeding (bleeding that directly results in death within 7 days) [12, 13].

Statistical analysis

Continuous variables are expressed as means ± standard deviation or medians and interquartile range (IQR). Categorical variables are expressed as numbers and proportions. Student's *t* test (Mann–Whitney *U* test if normality not satisfied) and the Chi square tests were used to compare groups. Each bleeding event was classified according to the BARC criteria (score of 1, 2, 3, 4, or 5, where 1 is minor and 5 is fatal) [12] AF recurrence-free survival and event-free survival were calculated using the Kaplan–Meier method. Differences between survival curves were compared using the log-rank test. All statistical analyses were performed using JMP 13.0 for Windows (SAS Institute, 2016, Cary, NC, USA). A value of $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics of the patients

Between January 2014 and December 2015, a total 264 patients (179 men (67.8%); mean age, 65.5 ± 10.1 years) who were referred to undergo a first RFCA procedure were reviewed in this study. The median follow-up period after the procedure was 14 (IQR 8–19) months. All of the patients had AF refractory to medical therapy, including 166 patients (62.9%) with paroxysmal AF, and 98 patients (37.1%) with persistent AF. The mean values for left atrial diameter (LAD) and left ventricular ejection fraction (LVEF) were 39.7 ± 5.9 mm and 62.0 ± 9.4%, respectively. Of the 264 patients, 41 had stable CAD detected by MDCT before admission. Mean age, creatinine (Cre) level, $CHADS_2$ score, and CHA_2DS_2VASc score were significantly higher for patients with CAD. Mean creatinine clearance (CCr) and left ventricular ejection fraction (LVEF) were lower for patients with CAD. The percentage of patients with CAD who were taking warfarin was higher than that of patients without CAD. Baseline characteristics of the participants in this study are shown in Table 1.

Thirty-seven patients who had AF with stable CAD detected by MDCT were divided into two treatment arms: (1) RFCA prior to PCI and (2) PCI prior to RFCA. Four patients excluded because of LMCA or TVD. Persistent AF rates in patients receiving RFCA prior to PCI and patients receiving PCI prior to RFCA were 29.4% and 41.7%, respectively. There was no significant difference between the RFCA prior to PCI group and PCI prior to RFCA group in lesion type according to the American College of Cardiology/American Heart Association lesion classification [RFCA first group: type A/B1, 17/24 (70.8%); PCI first group: type A/B1, 9/13 (69.2%), $P = 0.92$]. No significant differences in demographic and echocardiographic profiles were found between two groups. Baseline characteristics of the patients with CAD are shown in Table 2.

Table 1 Baseline patients characteristics

	Overall	Patients without CAD	Patients with CAD	*P* value[a]
Number of patients, *n*	264	223	41	
Clinical characteristics				
Age (years)	65.5 ± 10.1	65.6 ± 10.9	70.0 ± 6.1	0.01
Male gender, *n* (%)	179 (67.8)	98 (66.7)	27 (81.8)	0.14
Persistent AF, *n* (%)	98 (37.1)	63 (42.9)	11 (33.3)	0.33
Lesion type with ACC/AHA				
A/B1, *n* (%)	26 (9.8)	0 (0.0)	26 (70.3)	N/A
B1/C, *n* (%)	15 (5.7)	0 (0.0)	15 (29.7)	N/A
BNP (pg/ml) *	82.4 (159–39.4)	74.1 (36.9–140)	118 (47.7–217)	0.13
Cre (pg/m)	0.99 ± 0.82	0.87 ± 0.19	1.53 ± 1.99	0.01
CCr (ml/min)	62.2 ± 14.9	64.2 ± 13.2	56.3 ± 19.2	0.01
Left atrial diameter (mm)	39.7 ± 5.9	38.5 ± 5.3	41.1 ± 6.0	0.17
Left ventricular ejection fraction (%)	62.0 ± 9.4	62.5 ± 8.5	58.1 ± 11.2	0.01
$CHADS_2$ score	1.4 ± 1.0	1.3 ± 1.0	2.1 ± 1.1	0.01
CHA_2DS_2 VASc score	2.3 ± 1.5	2.1 ± 1.4	3.6 ± 1.4	0.01
Follow-up period (months)*	14 (8–19)	12 (8–19.2)	14 (8–19)	0.56
Anticoagulant				
Warfarin, *n* (%)	47 (17.8)	33 (18.2)	14 (37.8)	0.05
DOAC, *n* (%)	217 (82.2)	190 (81.8)	27 (62.2)	0.05

DOAC direct oral anticoagulant, *N/A* not available

*Median, 25th–75th percentiles

[a]*P* value (between patients with and those without coronary artery disease)

Table 2 Baseline characteristics of the patients with coronary artery disease

	Patients with RFCA prior to PCI	Patients with PCI prior to RFCA	*P* value
Number of patients, *n*	24	13	
Clinical characteristics			
Age (years)	69.4 ± 6.3	71.1 ± 6.1	0.48
Male gender, *n* (%)	14 (82.3)	10 (83.0)	0.37
Persistent AF, *n* (%)	5 (29.4)	5 (41.7)	0.69
Lesion type with ACC/AHA			
A/B1, *n* (%)	17 (70.8)	9 (69.2)	0.92
BNP (pg/ml) *	135 (47.6–271)	131 (56.5–256)	0.74
Cre (pg/m)	1.4 ± 1.9	1.9 ± 2.4	0.45
CCr (ml/min)	58.3 ± 17.3	50.7 ± 23.2	0.32
Left atrial diameter (mm)	43.0 ± 5.3	39.4 ± 6.7	0.12
Left ventricular ejection fraction (%)	59.0 ± 11.3	55.6 ± 11.1	0.42
$CHADS_2$ score	2.3 ± 1.2	1.8 ± 1.0	0.28
CHA_2DS_2 VASc score	3.8 ± 1.6	3.3 ± 1.2	0.30
Follow-up period (months)*	12 (5–17)	17.5 (13–19)	0.07
Anticoagulant			
Warfarin, *n* (%)	10 (41.6)	4 (30.7)	0.41
DOAC, *n* (%)	14 (58.4)	9 (59.3)	0.51

*Median, 25th-75th percentiles

DOAC direct oral anticoagulant

Catheter ablation and PCI procedure outcome

The rate of coronary stent device success was 100% and the incidence of target vessel revascularization (TLR) was 0% during the follow-up period. All patients were in sinus rhythm at the end of the first session and had evidence of complete pulmonary vein isolation. During the follow-up period, 49 patients (18.5%) had recurrent AF after a single ablation procedure. Figure 2a shows the Kaplan–Meier curves for AF recurrence after the procedure for patients with CAD and patients without CAD. Figure 2b shows the Kaplan–Meier curves for AF recurrence after the procedure in patients with PCI prior to RFCA and patients with RFCA prior to PCI. No significant difference was found in AF recurrence between two groups ($P=0.962$ and $P=0.515$, respectively). There was also no significant peri-procedural bleeding or in-hospital death.

Figure 3a, b show the Kaplan–Meier curves for AF recurrence in patients with PCI prior to RFCA and patients with RFCA prior to PCI who had paroxysmal AF and persistent AF, respectively. There was no recurrence AF during the follow-up period in patients with paroxysmal AF who received PCI prior to RFCA. No significant difference was also found in AF recurrence between the two groups ($P=0.508$ and $P=0.358$, respectively).

Safety

A total of 265 ablation procedures were performed. One episode of cardiac tamponade requiring pericardiocentesis occurred in a patient without CAD, but the outcome was good. No adverse events occurred in patients with CAD during RFCA. There were no symptomatic ischemic

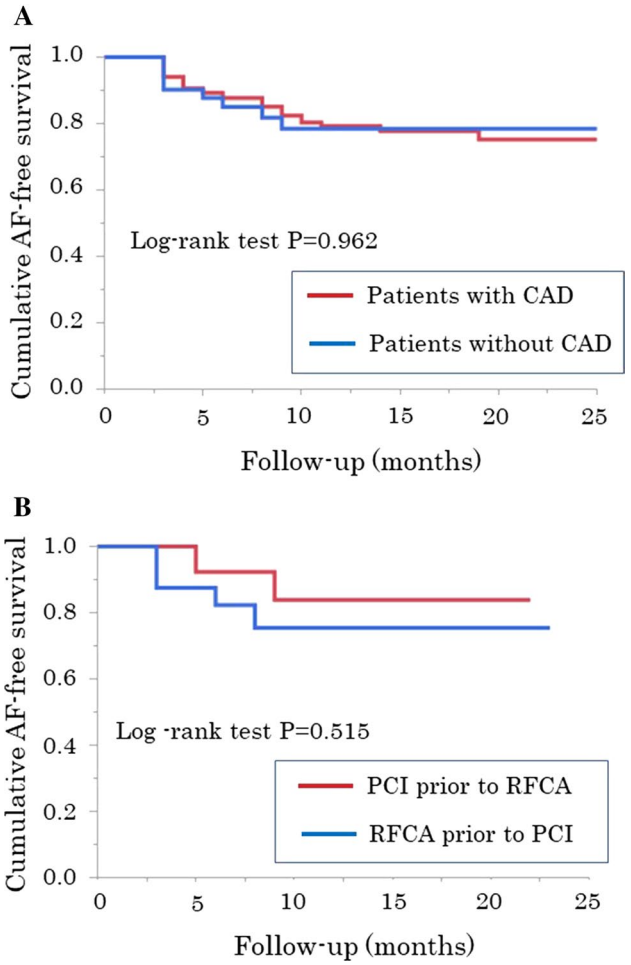

Fig. 2 Kaplan–Meier survival curves showing no significant difference in rates of freedom from AF between patients with CAD and those without CAD (Fig. 2a). Kaplan–Meier survival curves showing no significant difference in rates of freedom from AF between patients with PCI prior to RFCA and patients with RFCA prior to PCI (Fig. 2b)

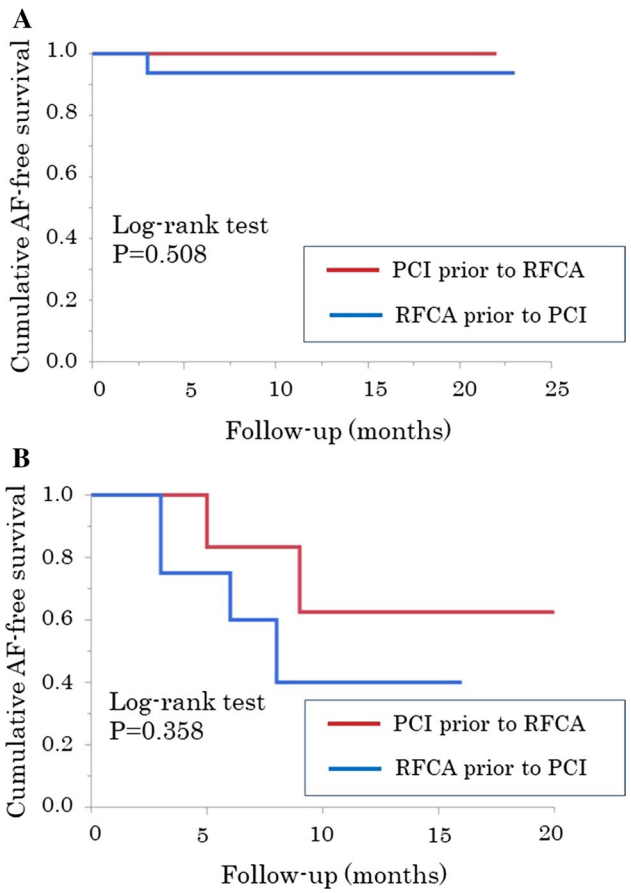

Fig. 3 Kaplan–Meier survival curves showing no significant difference in rates of freedom from AF between the patients with paroxysmal AF who received PCI prior to RFCA and patients who received RFCA prior to PCI (Fig. 3a). Kaplan–Meier survival curves showing no significant difference in rates of freedom from AF between patients with persistent AF who received PCI prior to RFCA and patients who received RFCA prior to PCI (Fig. 3b)

cerebrovascular events or cardiovascular events during the follow-up period. BARC minor bleeding occurred in one patient (7.7%) and BARC major bleeding occurred in three patients (23.1%) in the PCI first group; however, there was no BARC bleeding in the RFCA first group. Significant difference was found in the incidence of BARC bleeding between the RFCA first group and PCI first group ($P=0.01$) (Fig. 4a, Table 3). All of the patients in whom major or minor bleeding occurred had type A/B1 CAD lesions and were more frequently taking a direct oral anticoagulant (DOAC) than warfarin. The duration of triple therapy in the RFCA first group was significantly shorter than that in the PCI first group (5.6 ± 24.5 vs 188 ± 167 days, $P=0.01$) (Fig. 4b, Table 3). A noteworthy outcome is that most of the bleeding episodes occurred during triple therapy. Moreover, major bleeding occurred within 90 days after receiving triple therapy. Consequently, as expected, the rate of complications was higher in patients in the PCI first group than in patients in the RFCA first group. Details of the patients in whom bleeding occurred are given in Table 4.

Discussion

Main findings

Our study had three main findings. First, there was no significant difference in AF recurrence after the procedure between the RFCA prior to PCI group and PCI prior to RFCA group for patients with AF who have concomitant stable CAD. Second, RFCA prior to PCI strategy with double therapy could not increase risk of coronary events or thromboembolism. Finally, discontinuing of oral OAC after successful RFCA, and subsequent PCI with DAPT were found to minimize the risk of bleeding during the follow-up.

Optimum therapy for atrial fibrillation patients with stable coronary artery disease

Atrial fibrillation generally warrants anticoagulation, and DAPT is the established standard of care for patients with coronary stents [14, 15]. However, optimum therapy for AF patients who have concurrent CAD has remained unclear. Several options are now available for treating such patients.

The first approach is the use of triple therapy. Until recently, most guidelines recommended triple therapy [5, 16]. The 2016 European guidelines proposed a default time

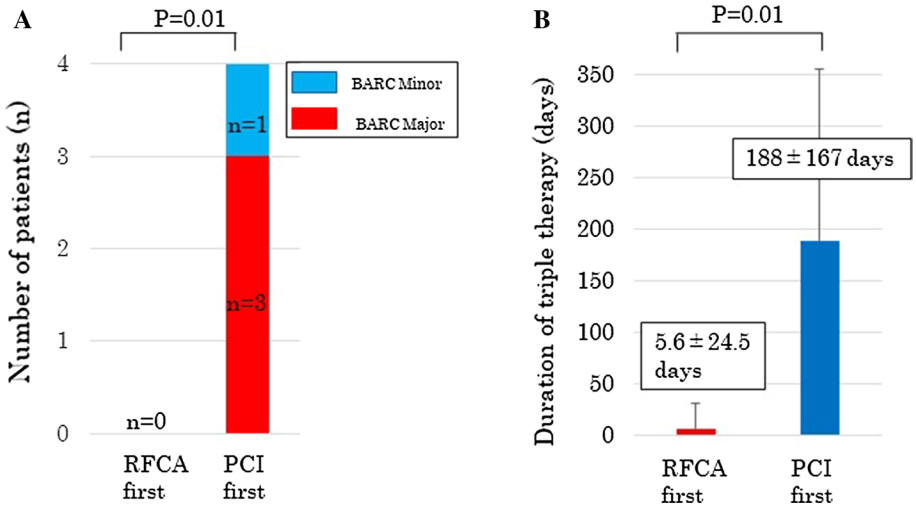

Fig. 4 The incidence of BARC bleeding and duration of triple therapy in RFCA first group and PCI first group (**a**, **b**)

Table 3 The incidence of bleeding and thromboembolic event

	Patients with RFCA prior to PCI	Patients with PCI prior to RFCA	*P* value
Duration of triple therapy (days)	5.6 ± 24.5	188.5 ± 167	0.01
Bleeding event (BARC minor)	0% (0/24)	7.7% (1/13)	0.05
Bleeding event (BARC major)	0% (0/24)	23.1% (3/13)	0.03
Systemic thromboembolic event	None	None	N/A
Cardiovascular event	None	None	N/A

Table 4 Details of the patients in whom bleeding occurred

Case	Age (years)	Sex	AF type	Lesion type with ACC/AHA	Type of bleeding	BARC score	BARC (Major/Minor)	Duration of triple therapy (days)	AF recurrence	Anticoagulant (mg/day)
1	59	Male	Persistent	B1	Melena (clinically overt bleeding, causing a decrease in hemoglobin 2 g/dl)	2	Major	90	Yes	Dabigatran 220
2	72	Male	Paroxysmal	A	Subcutaneous bleeding, hematoma leading to new hospitalization	3a	Major	21	None	Rivaroxaban 15
3	73	Male	Paroxysmal	A	Pseudoaneurysm (required surgical intervention)	3b	Major	30	None	Apixaban 10
4	65	Female	Persistent	B1	Bleeding of puncture site (bleeding that is not actionable but needs modification of the drug regimen)	1	Minor	390	None	Rivaroxaban 10

for triple therapy of 6 months for DES stent after elective PCI and thereafter stepping down to double therapy within 1 year [5]. The guideline also recommended that the period of triple therapy after PCI should be as short as possible because of the increasing bleeding risk. However, the results of the WOEST trial showed that triple therapy is associated with a significantly higher rate of bleeding complications than is the use of double therapy even if the period of triple therapy is short [6]. The second approach is the use of a double therapy. In the recent PIONEER AF-PCI trial [17], the rates of clinically significant bleeding were lower in two groups receiving rivaroxaban [low-dose rivaroxaban (15 mg od plus a P2Y12 inhibitor) and very low-dose rivaroxaban (2.5 mg bid plus DAPT)] than in the group receiving triple therapy, but there was no significant difference in major bleeding. Moreover, the rates of cardiovascular death were higher in the two groups receiving rivaroxaban than in the triple therapy group. Therefore, it is still too early to use single antiplatelet therapy plus rivaroxaban instead of conventional triple therapy. Recently, another trial showed that the risk of bleeding was significantly lower in patients with AF undergoing PCI who received double therapy with dabigatran (110 mg or 150 mg twice daily) and a P2Y12 inhibitor than in patients who received triple therapy [18]. The rates of major bleeding were significantly lower in both double therapy group than in the triple therapy group. The results of that trial showed that each of the two doses of dabigatran in the double therapy regimens led to a balance between the risk of bleeding and prevention of thromboembolic events, which offers clinicians reasonable options for the treatment of AF patients who have concurrent CAD. The third approach is the use of DAPT, which means discontinuing OAC after successful RFCA prior to PCI in patients with AF coexisting with stable CAD. The 2016 European guidelines recommended treatment with only DAPT and without anticoagulation for patients with a low stroke risk (CHA_2DS_2-VASc of 1 in males or 2 in females) [6]. For those patients receiving elective PCI, it is reasonable that DAPT should be used for 3–6 months and followed by OAC or antiplatelet monotherapy. However, long-term anticoagulation is recommended for patients at a high risk of stroke. Continuous ECG monitoring should be considered for detection of asymptomatic AF in patients in whom administration of systemic anticoagulants has been discontinued. However, RFCA has now become a common therapy for patients with symptomatic AF and has a better outcome than before [7]. In patients with drug-refractory paroxysmal AF, the results of multiple clinical trials have demonstrated the superiority of catheter ablation over AAD therapy for long-term maintenance of sinus rhythm [7]. In addition, results of recent studies have suggested that a protocol of discontinuing OAC after successful RFCA of AF in patients who are maintained on antiplatelet monotherapy is reasonable regardless of the

patient's baseline risk [8, 19]. It was shown that the most important factor influencing anticoagulation use was AF recurrence and not the CHADS2 risk score. According to present study, it might be more reasonable for patients with paroxysmal AF who had concomitant CAD than patients with persistent AF to discontinue OAC after RFCA followed by performing PCI with DAPT. Finally, surgical ablation with OAC or double therapy should be considered as a concomitant procedure during valve or CABG surgeries. According to the recent guidelines, surgical ablation at the time of concomitant closed atrial operation (isolated AVR, isolated CAGB, or AVR + CABG) is Class IIa [20]. In this study, we excluded patients who underwent CABG and Maze because of few numbers. The Maze procedure at the time of isolated CABG is excellent with 90% of patients free from AF with a 5 year follow-up without increasing complication, surgical ablation should recommend AF patients undergoing cardiac surgery [21].

Efficacy and safety of RFCA prior to PCI

It is not known which should come first, RFCA or PCI, for patients with AF coexisting with stable CAD. In a clinical setting, the physician's clinical judgment is usually used to decide which to perform first and to find the optimal balance between risks and benefits of treatment. Therefore, either can be used first, but the pros and cons should be weighed before making a decision. There would be both advantages and disadvantages whichever method is chosen.

Triple therapy is usually recommended for patients who will undergo PCI prior to RFCA. Regarding ischemic outcomes, a meta-analysis of non-randomized studies suggested that triple therapy is more efficacious than DAPT for the prevention of major adverse events and significantly reduces all-cause mortality [22]. However, another issue that needs to be addressed is that patients with AF in need of PCI represent a population that mainly consists of elderly patients with high rates of comorbidity. The role of non-major bleeding should not be underestimate since discontinuation of antiplatelet therapy in affected patients can lead to subsequent thrombotic complications. As a result, triple therapy would not only increase the risk of bleeding but also increase thrombotic complications such as stent thrombosis because of inappropriate discontinuation of antiplatelet therapy.

Less is known about the safety and efficacy of RFCA than the safety and efficacy of PCI prior to RFCA for AF patients with residual coronary ischemia. In addition, whether elimination of AF by RFCA results in a significant reduction in stroke risk is an important but yet unresolved issue [20]. Moreover, there have been no large, randomized prospective trials in which the safety of discontinuing anticoagulation in these high-risk patients after RFCA. In this study, ablation was considered to be successful if sinus rhythm was maintained with no symptomatic or documented episodes of AF. However, more intensive monitoring should be considered for detecting both symptomatic AF and asymptomatic AF. In our retrospective study, discontinuing OAC after successful RFCA prior to PCI in patients with AF coexisting with stable CAD resulted in fewer serious bleeding events without an increased risk of recurrent coronary events or thromboembolism. Therefore, we view the reduction in bleeding complications in this trial as being clinically meaningful.

Limitations

Several limitations must be considered in relation with this study. First, this study was a non-randomized retrospective analysis of a relatively small number of patients in a single center. In addition, the decision regarding treatment was left to the physician's clinical judgment. This may have led to selection bias with inclusion of patients who were likely to receive RFCA prior to PCI. Moreover, about 70% of the patients were having type A/B1 lesions, which might have been the reason for the low TLR, low bleeding rate, and low AF recurrence. Additional randomized studies are needed to establish treatment guidelines for patients with high risks for bleeding and thrombotic complications.

Conclusion

The results of this single-center pilot study suggested that prior RFCA in patients with AF coexisting with CAD could have fewer serious bleeding events than prior PCI. Further studies are warranted to confirm the advantage of prior RFCA in reducing bleeding events.

Compliance with ethical standards

Conflict of interest Dr. Ito reports grants and personal fees from Daiichi-Sankyo, grants from Sanofi, grants and personal fees from Berringer-Ingelheim, grants and personal fees from Bayer, grants from Pfizer, during the conduct of the study. Dr. Hiroshi Morita and Nobuhiro Nishii are affiliated with the endowed department by Japan Medtronic Inc.

References

1. Dewland TA, Olgin JE, Vittinghoff E, Marcus GM (2013) Incident atrial fibrillation among Asians, Hispanics, blacks, and whites. Circulation 128:2470–2477
2. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D (1998) Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 98:946–952
3. Inoue H, Fujiki A, Origasa H, Ogawa S, Okumura K, Kubota I (2009) Prevalence of atrial fibrillation in the general population

of Japan: an analysis based on periodic health examination. Int J Cardiol 137:102–107
4. Atarashi H, Inoue H, Okumura K, Yamashita T, Origasa H (2011) Investigation of optimal anticoagulation strategy for stroke prevention in Japanese patients with atrial fibrillation—the J-RHYTHM Registry study design. J Cardiol 57:95–99
5. Heidbuchel H, Verhamme P, Alings M, Antz M, Diener HC, Hacke W, Oldgren J, Sinnaeve P, Camm AJ, Kirchhof P, ESC Scientific Document Group (2017) Updated European Heart Rhythm Association practical guide on the use of non-vitamin-K antagonist anticoagulants in patients with non-valvular atrial fibrillation: Executive summary. Eur Heart J 38:2137–2149
6. Dewilde WJ, Oirbans T, Verheugt FW, Kelder JC, De Smet BJ, Herrman JP (2013) Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. Lancet (Lond, Engl) 381:1107–1115
7. Hakalahti A, Biancari F, Nielsen JC, Raatikainen MJ (2015) Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. Europace 17:370–378
8. Saad EB, d'Avila A, Costa IP, Aryana A, Slater C, Costa RE (2011) Very low risk of thromboembolic events in patients undergoing successful catheter ablation of atrial fibrillation with a CHADS2 score </=3: a long-term outcome study. Circ Arrhythm Electrophysiol 4:615–621
9. Pristipino C, Trani C, Nazzaro MS, Berni A, Patti G, Patrizi R (2009) Major improvement of percutaneous cardiovascular procedure outcomes with radial artery catheterisation: results from the PREVAIL study. Heart (Br Cardiac Soc) 95:476–482
10. Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V (2014) 2014 ESC/EACTS Guidelines on myocardial revascularization: the Task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 35:2541–2619
11. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA (2007) Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 115:2344–2351
12. Ndrepepa G, Schuster T, Hadamitzky M, Byrne RA, Mehilli J, Neumann FJ (2012) Validation of the Bleeding Academic Research Consortium definition of bleeding in patients with coronary artery disease undergoing percutaneous coronary intervention. Circulation 125:1424–1431
13. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J (2011) Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. Circulation 123:2736–2747
14. Schomig A, Neumann FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M (1996) A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. N Engl J Med 334:1084–1089
15. Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, Chrolavicius S (2006) Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. Lancet (Lond Engl 367:1903–1912
16. Lip GY, Windecker S, Huber K, Kirchhof P, Marin F, Ten Berg JM (2014) Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). Eur Heart J 35:3155–3179
17. Gibson CM, Mehran R, Bode C, Halperin J, Verheugt FW, Wildgoose P (2016) Prevention of bleeding in patients with atrial fibrillation undergoing PCI. N Engl J Med 375:2423–2434
18. Cannon CP, Bhatt DL, Oldgren J, Lip GYH, Ellis SG, Kimura T, Maeng M, Merkely B, Zeymer U, Gropper S, Nordaby M, Kleine E, Harper R, Manassie J, Januzzi JL, Ten Berg JM, Steg PG, Hohnloser SH, RE-DUAL PCI Steeering Committee and Investigators (2017) Dual antithrombotic therapy with dabigatran after PCI in atrial fibrillation. N Engl J Med 377:1513–1524
19. Bunch TJ, Crandall BG, Weiss JP, May HT, Bair TL, Osborn JS (2009) Warfarin is not needed in low-risk patients following atrial fibrillation ablation procedures. J Cardiovasc Electrophysiol 20:988–993
20. Calkins H, Hindricks G, Cappato R, Kim Y-H, Saad EB, Aguinaga L (2017) 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. Heart Rhythm 14:e275–e444
21. Prasad SM, Maniar HS, Camillo CJ, Schuessler RB, Boineau JP, Sundt TM (2003) The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. J Thoracic Cardiovasc Surg 126:1822–1828
22. Zhao HJ, Zheng ZT, Wang ZH, Li SH, Zhang Y, Zhong M (2011) "Triple therapy" rather than "triple threat": a meta-analysis of the two antithrombotic regimens after stent implantation in patients receiving long-term oral anticoagulant treatment. Chest 139:260–270