CLINICAL STUDY

Real-World Antithrombotic Therapy in Atrial Fibrillation Patients with a History of Percutaneous Coronary Intervention

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Summary

Optimal antithrombotic strategy for atrial fibrillation (AF) patients with a history of percutaneous coronary intervention (PCI) has been under debate. The actual prescription trend of antithrombotic therapy for these patients remains unclear, especially in chronic phase.

Patients with AF having at least a 1-year history of PCI were retrospectively evaluated in 2010, 2012, 2014, and 2016. A total of 266 patients were finally enrolled in this study. The proportion of patients prescribed with oral anticoagulants (OACs) gradually increased over the study period (56%, 67%, 73%, and 74% in 2010, 2012, 2014, and 2016, respectively). According to the type of OACs, the proportion of direct oral anticoagulant (DOAC), launched in 2011, increased compared with warfarin (DOAC versus warfarin = 3% versus 64% in 2012, 24% versus 49% in 2014, and 32% versus 42% in 2016). Single antiplatelet therapy (SAPT) with OAC was the most popular prescription every year, and its proportion increased over the study period (41%, 44%, 55%, and 59%, respectively). The proportion of OAC monotherapy gradually increased (2%, 3%, 8%, and 9%, respectively), whereas that of triple therapy, i.e., dual antiplatelet therapy with OAC, gradually decreased (14%, 22%, 8%, and 5% in 2010, 2012, 2014, and 2016, respectively).

Antithrombotic therapy trends for AF patients with a history of PCI were changing every year. The prescription rate of triple therapy gradually decreased, in contrast, that of OAC monotherapy gradually increased from 2010 to 2016. However, the evidence for OAC monotherapy in these patients remains insufficient.

Key words: Warfarin, Direct oral anticoagulant, Coronary artery disease

Anticoagulation for atrial fibrillation (AF) is recognized as an important therapy for the prevention of thromboembolic events. Although the prescription rate of oral anticoagulants (OACs) has been increasing, especially after the launch of direct OACs (DOACs), it remains unsatisfactory.1-5)

On the contrary, patients undergoing percutaneous coronary intervention (PCI) are prescribed dual antiplatelet therapy (DAPT), i.e., acetylsalicylic acid (ASA) and a P2Y12 receptor inhibitor, for a certain period to prevent stent thrombosis.6) Therefore, if those patients are diagnosed as having AF, they are often treated with DAPT and OAC, i.e., triple therapy, in acute phase. Recent European guidelines recommend shortening the period of triple therapy for AF patients with a history of PCI, as long as these patients do not have a higher risk of stent thrombosis.7) These guidelines also recommend anticoagulant monotherapy after 1 year of PCI to reduce the risk of bleeding complications.8) However, the actual prescription trend of antithrombotic therapy in chronic phase, i.e., after 1 year of PCI, for these patients remains unclear. In this study, we evaluated the actual prescription status of antithrombotic therapies and the change in its trend for AF patients with a history of PCI, in chronic phase.

Methods

Subjects: We retrieved patient data from the Cardiovascular Secondary Prevention Center of Kitasato University. Annual check-up, which included electrocardiography (ECG), chest x-ray, echocardiography, 24-hours Holter ECG, and laboratory tests, was performed in our center. Additional examinations, such as cardiac scintigraphy, were performed if necessary. Cardiologists evaluated these data and commented to general practitioners. The choice of treatment was at the discretion of general practitioners. A total of 5,959 patients were registered in this center by the end of 2017. We biennially evaluated the proportion of the antithrombotic prescription for these patients from January 2010 to December 2016.

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Figure 1. Study protocol. We evaluated patients with atrial fibrillation (AF) having a history of percutaneous coronary intervention (PCI) every other year from January 2010 to December 2016 in our secondary prevention center.

The number of patients who visited our hospital and could be evaluated was 3,645 in 2010; 2,318 in 2012; 2,223 in 2014; and 2,440 in 2016 (from January to December in each year). To focus on the prescription trends in the chronic phase of the disease, patients diagnosed as having AF with at least a 1-year history of PCI were enrolled in the study (Figure 1).

This study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by the ethics committee of Kitasato University Hospital.

Baseline characteristics and OAC status: All patients received basic physical examination, which included assessing the patient’s age, gender, comorbidities, type of AF, CHADS$_2$, and CHA$_2$DS$_2$-VASc score as the risk stratification of ischemic stroke, HAS-BLED score as the risk stratification of hemorrhagic events, and DAPT score as the stratification of cardiovascular and hemorrhagic events. The definitions of CHADS$_2$, CHA$_2$DS$_2$-VASc, HAS-BLED, and DAPT scores have been described previously. $^{8-11}$ Briefly, CHADS$_2$ score is the sum of points for the following conditions: congestive heart failure (CHF), hypertension, age $\geq$ 75 years, diabetes mellitus (1 point of each), and prior stroke or transient ischemic attack (2 points). CHA$_2$DS$_2$-VASc score is a revision of the CHADS$_2$ score and extends it by including additional risk factors of age ($\geq$ 75 years, 2 points; 65-74 years, 1 point; < 65 years, 0 point), current cigarette smoker, diabetes mellitus, myocardial infarction (MI) at presentation, prior PCI or prior MI, presence of paclitaxel-eluting stent, stent diameter of <$3\,\text{mm}$, CHF or left ventricular ejection fraction of <$30\%$ (2 points), and vein graft PCI (2 points).

The decision of antithrombotic therapy depends on the type of the stent implanted in patients. Types of stents include bare metal stent (BMS); first-generation drug-eluting stents (DESs) such as sirolimus-eluting stent (Cypher$^{\text{a}}$) and paclitaxel-eluting stent (Taxus$^{\text{a}}$); and second-generation DESs. We classified the enrolled patients into 3 groups by the type of stent: group A, use of first DES; group B, use of DESs, excluding first-generation DESs; and group C, use of only BMS.

In this study, antiplatelet drugs included aspirin, clopidogrel, ticlopidine, and prasugrel. OACs included warfarin and the 4 currently available DOACs dabigatran, rivaroxaban, apixaban, and edoxaban.

Clinical complications: We also evaluated stroke and major bleeding complications following antithrombotic therapy. Stroke was defined as the sudden onset of a focal neurologic deficit in a location consistent with the territory of a major cerebral artery, including both ischemic and hemorrhagic strokes. It was confirmed by computed tomography (CT) or magnetic resonance imaging. Major bleeding was defined as following the ISTH definition. $^{12}$

Study analysis: Continuous variables were described as mean value $\pm$ standard deviation. Categorical variables were described as absolute numbers and percentages. Categorical variables were compared using the Chi-squared test when appropriate; else, Fisher exact test was used. Continuous variables were compared using one-way
The trend of oral anticoa (49% in 2010, 42% in 2012, 34% in 2014, and 32% in 2016) received only BMS significantly decreased year on year for trend). In contrast, the proportion of those who received full-dose DOAC (16% in 2012, 21% in 2014, and 35% in 2016; P < 0.001 for trend) increased over the study period (2%, 2%, 8%, and 9% in 2010, 2012, 2014, and 2016, respectively; P = 0.012 for trend). Proportion of patients prescribed with triple therapy clearly decreased after 2012 (14%, 22%, 8%, and 5% in 2010, 2012, 2014, and 2016, respectively; P = 0.010 for trend). Although the proportion of patients receiving OAC monotherapy each year was small, it gradually increased over the study period (2%, 2%, 8%, and 9% in 2010, 2012, 2014, and 2016, respectively; P = 0.041 for trend).

The relationship of OAC and antiplatelet therapy: We classified patients into 5 groups by the type of antithrombotic therapy: group 1, single antiplatelet therapy (SAPT); group 2, DAPT; group 3, SAPT with OAC; group 4, DAPT with OAC (i.e., triple therapy); and group 5, OAC monotherapy. As shown in Figure 3, SAPT with OAC group was the most common prescription among the 5 groups each year studied, and the rate of this prescription increased over the years (41%, 44%, 55%, and 59% in 2010, 2012, 2014, and 2016, respectively; P = 0.012 for trend). Proportion of patients prescribed with triple therapy clearly decreased after 2012 (14%, 22%, 8%, and 5% in 2010, 2012, 2014, and 2016, respectively; P = 0.010 for trend). Although the proportion of patients receiving OAC monotherapy each year was small, it gradually increased over the study period (2%, 2%, 8%, and 9% in 2010, 2012, 2014, and 2016, respectively; P = 0.041 for trend).

Clinical complications: Details of patients who experienced thromboembolic or bleeding events are provided in Table II. Nine patients had major bleeding complications, and 1 patient had stroke. Importantly, 5 of these patients died of bleeding complications. All patients who had complications had been prescribed multiple antithrombotic therapy: 3 were prescribed triple therapy, 4 DAPT, and 3 ASA with OAC.

Table I. Baseline Characteristics

<table>
<thead>
<tr>
<th>Clinical background</th>
<th>2010 (n = 45)</th>
<th>2012 (n = 55)</th>
<th>2014 (n = 79)</th>
<th>2016 (n = 87)</th>
<th>P value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>40 (89)</td>
<td>50 (91)</td>
<td>68 (86)</td>
<td>75 (86)</td>
<td>0.469</td>
</tr>
<tr>
<td>Age (years)</td>
<td>72.0 ± 7.7</td>
<td>73.8 ± 6.8</td>
<td>74.5 ± 7.0</td>
<td>75.1 ± 7.6</td>
<td>0.804</td>
</tr>
<tr>
<td>Abnormal renal or liver function, n (%)</td>
<td>5 (11)</td>
<td>2 (4)</td>
<td>9 (11)</td>
<td>7 (8)</td>
<td>0.998</td>
</tr>
<tr>
<td>CHF, n (%)</td>
<td>12 (27)</td>
<td>10 (18)</td>
<td>19 (24)</td>
<td>21 (24)</td>
<td>0.944</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>37 (82)</td>
<td>46 (84)</td>
<td>70 (89)</td>
<td>77 (89)</td>
<td>0.235</td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>24 (53)</td>
<td>33 (60)</td>
<td>52 (66)</td>
<td>62 (71)</td>
<td>0.041</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>22 (49)</td>
<td>20 (36)</td>
<td>33 (42)</td>
<td>36 (41)</td>
<td>0.662</td>
</tr>
<tr>
<td>Prior stroke or TIA, n (%)</td>
<td>2 (4)</td>
<td>4 (7)</td>
<td>8 (10)</td>
<td>6 (7)</td>
<td>0.611</td>
</tr>
</tbody>
</table>

Data associated with AF

- PAF, n (%) 28 (62) 31 (56) 49 (62) 56 (64) 0.578
- CHADS2 score 2.0 ± 1.2 1.9 ± 1.1 2.3 ± 1.2 2.2 ± 1.1 0.253
- CHA2DS2-VASC score 3.5 ± 1.4 3.4 ± 1.2 3.7 ± 1.3 3.7 ± 1.3 0.121
- HAS-BLED score 2.8 ± 0.8 2.9 ± 0.7 3.0 ± 0.9 3.0 ± 0.8 0.093

Data associated with PCI

- History of ACS, n (%) 25 (56) 26 (47) 31 (39) 46 (53) 0.812
- DAPT score 1.8 ± 1.4 1.3 ± 1.2 1.4 ± 1.4 1.7 ± 1.4 0.182
- Use of first-gen DES, n (%) 21 (51) 23 (42) 34 (45) 28 (33) 0.074
- Use of DES excluding first-gen DES, n (%) - 9 (16) 16 (21) 30 (35) 0.009
- Use of only BMS, n (%) 20 (49) 23 (42) 26 (34) 27 (32) 0.046

Data are presented as mean ± SD or n (%). For descriptions of HAS-BLED, CHADS2, and CHA2DS2-VASC scores, please see text. PAF indicates paroxysmal atrial fibrillation; CHF, congestive heart failure; CKD, chronic kidney disease; TIA, transient ischemic attack; ACS, acute coronary syndrome; DES, drug-eluting stent; First-gen DES, e.g., Cypher® and Taxus®, first-generation DES; Second-gen DES, e.g., Nobori®, Endeavor®, Promus®, Xience®, Resolute®, SYNERGY®, and Ultimaster®, second-generation DES; BMS, bare metal stent.

ANOVA on the basis of the distribution. The prescription trend among the groups was tested using Cochran-Armitage test for categorical variables or Jonckheere-Terpstra test for continuous variables. A P value of < 0.05 was considered statistically significant. All statistical analyses were performed using the EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan).19

Results

Enrolled patients and baseline characteristics: Of the 266 patients enrolled in the study, 45 in 2010, 55 in 2012, 79 in 2014, and 87 patients in 2016 were diagnosed as having AF with at least a 1-year history of PCI (Figure 1).

Baseline characteristics are detailed in Table I. The proportion of male-to-female ratio, age, comorbidities, type of AF, CHADS2 score, CHA2DS2-VASC score, and HAS-BLED score did not show any difference in each year.

Regarding the type of stent, the proportion patients receiving newer DESs significantly increased every year (16% in 2012, 21% in 2014, and 35% in 2016; P = 0.009 for trend). In contrast, the proportion of those who received only BMS significantly decreased year on year (49% in 2010, 42% in 2012, 34% in 2014, and 32% in 2016; P = 0.046 for trend).

The trend of oral anticoagulant therapy: Figure 2 shows the trend of OAC therapy for AF patients with a history of PCI. The OAC prescription rate was only 56% in 2010, although they had basically an indication for OAC. However, the OAC prescription gradually increased yearly (56%, 67%, 73%, and 74% in 2010, 2012, 2014, and 2016, respectively, represented by a thick black bar; P = 0.041 for trend). Regarding OAC specification, all prescriptions of OAC in 2010 were of warfarin. After the launch of DOAC in 2011, the proportion of DOAC as an OAC increased from 3% in 2012 to 42% in 2016 (24%, 2014; P < 0.0001 for trend).

The relationship of OAC and antiplatelet therapy: We classified patients into 5 groups by the type of antithrombotic therapy: group 1, single antiplatelet therapy (SAPT); group 2, DAPT; group 3, SAPT with OAC; group 4, DAPT with OAC (i.e., triple therapy); and group 5, OAC monotherapy. As shown in Figure 3, SAPT with OAC group was the most common prescription among the 5 groups each year studied, and the rate of this prescription increased over the years (41%, 44%, 55%, and 59% in 2010, 2012, 2014, and 2016, respectively; P = 0.012 for trend). Proportion of patients prescribed with triple therapy clearly decreased after 2012 (14%, 22%, 8%, and 5% in 2010, 2012, 2014, and 2016, respectively; P = 0.010 for trend). Although the proportion of patients receiving OAC monotherapy each year was small, it gradually increased over the study period (2%, 2%, 8%, and 9% in 2010, 2012, 2014, and 2016, respectively; P = 0.041 for trend).

Clinical complications: Details of patients who experienced thromboembolic or bleeding events are provided in Table II. Nine patients had major bleeding complications, and 1 patient had stroke. Importantly, 5 of these patients died of bleeding complications. All patients who had complications had been prescribed multiple antithrombotic therapy: 3 were prescribed triple therapy, 4 DAPT, and 3 ASA with OAC.
Figure 2. The trend of anticoagulant therapy in atrial fibrillation (AF) patients with a history of percutaneous coronary intervention (PCI). Change in oral anticoagulant (OAC) status from 2010 to 2016 is shown. Only 56% of patients were prescribed OAC in 2010, although this rate (thick black bar) gradually increased over the study period (Cochran-Armitage test: \( P = 0.041 \)). After the launch of DOAC, the proportion of direct OAC (DOAC) increased from 2012 to 2016 (Cochran-Armitage; \( P < 0.0001 \)), similar to the proportion of OAC.

Figure 3. The trend of antithrombotic therapy. The proportion of single antiplatelet therapy (SAPT) with oral anticoagulant (OAC) and OAC monotherapy significantly increased, whereas those of dual antiplatelet therapy (DAPT) and triple therapy (DAPT with OAC) decreased from 2010 to 2016 (Cochran-Armitage test; \( P = 0.003 \) in the DAPT, \( P = 0.010 \) in the DAPT with OAC for trend, respectively). See the text for more details.

Discussion

We demonstrated the recent trend of antithrombotic therapy in chronic phase for AF patients with a history of PCI. The main findings of this study were as follows: 1) the proportion of OAC prescription gradually increased over the study period; 2) regarding the type of OAC, the proportion of DOAC, rather than warfarin, increased; 3) SAPT with OAC was the most common prescription, whose rate of prescription increased over the study period; 4) the proportion of OAC monotherapy gradually increased, although this increase was small; and 5) the pro-
portion of triple therapy, i.e., DAPT with OAC, gradually decreased over the study period.

**Transition of the recommended antithrombotic strategy for patients with AF undergoing PCI:** Antithrombotic therapy is crucial in preventing both stent thrombosis after PCI and AF-related thromboembolic events. Previous studies have shown that warfarin alone was not sufficient to avoid stent thrombosis, and DAPT alone was not adequate to prevent AF-related thromboembolic events; therefore, patients with AF undergoing PCI are typically prescribed multiple thromboembolic drugs, i.e., triple therapy, especially in the acute phase of the disease. However, a higher risk of bleeding complication associated with multiple antithrombotic drugs has been recently recognized. Several studies were, therefore, focused on how to reduce multiple antithrombotic medications while preventing thromboembolic complications. Recent guidelines post these studies recommend reducing the number or administration period of multiple antithrombotic drugs. In this study, we focused on the trend change in patients with AF after PCI in the chronic phase. Overall, OAC prescription rate gradually increased, whereas the prescription rates of DAPT (P = 0.003) and triple therapy decreased (P = 0.010). In addition, SAPT with OAC was the most common prescription in the entire study, the rate of which gradually increased (P = 0.012 for trend; Figure 3). Moreover, OAC monotherapy, which is not at common strategy in our clinical practice, also gradually increased in the study period between 2010 and 2016 (P = 0.041 for trend). General practitioners sometimes change the antithrombotic regimen by themselves without our advice. For example, there were some patients for whom general practitioners chose OAC monotherapy to avoid the risk of major/minor bleeding events or a concern of high bleeding risk such as a frailty (data not shown), suggesting that general practitioners also consider the risk of bleeding complications while prescribing multiple antithrombotic drugs. Therefore, this study represents the change in trend of antithrombotic therapy prescription for patients with AF receiving PCI in the real-world settings.

**Recent evidence of antithrombotic therapy for patients with AF undergoing PCI:** New evidence has recognized the safety of DOAC instead of warfarin for patients with AF receiving PCI, although these data are not for the chronic phase of the disease. For example, in the RE-DUAL PCI study, the risk of bleeding in AF patients with at least a 1-year history of PCI was lower among those who received dual therapy with dabigatran and a P2 Y12 inhibitor than among those who received triple therapy with warfarin (non-inferiority P < 0.001, superiority P < 0.001). In the recently published AUGUSTUS study, the dual therapy of P2Y12 with apixaban demonstrated a lower incidence of bleeding events than P2Y12 with warfarin. In this study, although we focused on the chronic phase, the rate of DOAC, rather than warfarin, prescription was significantly increased (Figure 2, P < 0.0001 for trend). These data would additionally accentuate these trends in future.

In terms of OAC monotherapy, there is no robust evidence for the actual safety and benefit for patients in the chronic phase of the disease, although the current European/North American guidelines recommend the recently published OAC-ALONE study, a randomized controlled trial that compared OAC monotherapy with SAPT with OAC, demonstrated non-inferiority of OAC monotherapy to SAPT with OAC in the secondary end-point defined as a composite of primary endpoint or major bleeding (non-inferiority P = 0.016, superiority P = 0.96). This result may support the strategy of OAC monotherapy for patients with AF receiving PCI. However, it should be emphasized that 75.2% of the prescribed OACs was warfarin in the OAC-ALONE study. As shown in Figure 2 in this study, the proportion of DOAC as OAC increased year on year after the launch of DOAC, in line with the results of Fushimi-AF study and GARFIELD AF registry. The safety profile of DOAC may have contributed to the increase in the proportion of OAC prescription for patients AF receiving PCI. However, in terms of the efficacy and safety of DOAC monotherapy for such patients in the chronic phase of the disease remain unknown.

**Table II.** Bleeding and Ischemic Events

<table>
<thead>
<tr>
<th>Age at event (years)</th>
<th>Gender (M/F)</th>
<th>Antiplatelet and anticoagulant therapy</th>
<th>Duration of anticoagulant therapy (months)</th>
<th>Duration of antiplatelet therapy (months)</th>
<th>Event (Bleeding or Cerebrovascular event)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>Male</td>
<td>DAPT + warfarin</td>
<td>132</td>
<td>29</td>
<td>Cerebral hemorrhage</td>
<td>Survive</td>
</tr>
<tr>
<td>85</td>
<td>Male</td>
<td>DAPT + warfarin</td>
<td>25</td>
<td>48</td>
<td>Hematuria (bladder cancer)</td>
<td>Survive</td>
</tr>
<tr>
<td>82</td>
<td>Male</td>
<td>DAPT + warfarin</td>
<td>145</td>
<td>117</td>
<td>Hemothorax due to cancer pleurisy (primary is renal cancer)</td>
<td>Survive</td>
</tr>
<tr>
<td>64</td>
<td>Male</td>
<td>DAPT (ticlopidine)</td>
<td>-</td>
<td>5</td>
<td>Discharge blood</td>
<td>Survive</td>
</tr>
<tr>
<td>70</td>
<td>Male</td>
<td>DAPT</td>
<td>-</td>
<td>60</td>
<td>Left putamen hemorrhage, subarachnoid hemorrhage</td>
<td>Death</td>
</tr>
<tr>
<td>77</td>
<td>Male</td>
<td>DAPT</td>
<td>-</td>
<td>73</td>
<td>Cerebral hemorrhage</td>
<td>Death</td>
</tr>
<tr>
<td>76</td>
<td>Male</td>
<td>DAPT</td>
<td>-</td>
<td>71</td>
<td>Brainstem and cerebellar hemorrhage</td>
<td>Death</td>
</tr>
<tr>
<td>72</td>
<td>Male</td>
<td>ASA + DOAC (dabigatran)</td>
<td>52</td>
<td>Left putamen hemorrhage, subarachnoid hemorrhage</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>85</td>
<td>Female</td>
<td>ASA + warfarin</td>
<td>89</td>
<td>82</td>
<td>Diverticular bleeding, intratumor bleeding (HCC)</td>
<td>Death</td>
</tr>
<tr>
<td>74</td>
<td>Male</td>
<td>ASA + warfarin</td>
<td>98</td>
<td>157</td>
<td>Cardiogenic embolic stroke</td>
<td>Death</td>
</tr>
</tbody>
</table>

DAPT indicates dual antiplatelet therapy; ASA, acetalsalicylic acid; DOAC, direct oral anticoagulant; and HCC, hepatocellular carcinoma.
aim to address this concern. This study was designed to compare rivaroxaban monotherapy and rivaroxaban with SAPT for AF patients with at least a 1-year history of PCI or coronary bypass graft. It is expected to provide the new evidence of DOAC monotherapy for the AF patients with stable CAD in chronic phase.

The bleeding risk for AF patients beyond 1 year after PCI under multiple antithrombotic therapy: The concern of bleeding complications is always raised with multiple antithrombotic therapy. A Danish registry, which enrolled a total of 12,165 patients with AF hospitalized for MI and/or undergoing PCI, showed that triple therapy increased bleeding complications compared with OAC plus aspirin or DAPT. It is not difficult to expect that multiple antithrombotic therapy is prone to bleeding complications, although data for such patients in chronic phase are scarce. The Tokyo Woman’s Medical University registry, which enrolled patients implanted with DES, demonstrated that the bleeding risk with triple therapy was about 3 times higher than that with DAPT during the median follow-up of 459 days. Recently, Matsumura-Nakano et al. evaluated bleeding complications in patients with AF from 3 Japanese PCI-related studies. They reported that the cumulative 3-year incidence of major bleeding was 12.8% in AF patients who underwent PCI. Although the strategies of antithrombotic therapy were based on the physician’s judgment in this study, the bleeding complications were not ignorable in the chronic phase of the disease. In this study, all patients with major bleeding complications were taking multiple antithrombotic therapies: 2 patients were taking SAPT and OAC therapy; 4 patients were taking DAPT; and 3 patients were taking triple therapy (Table II). The ESC guidelines in 2010 state that warfarin monotherapy may be considered in patients with stable CAD after one year of PCI (class IIb recommendation). These Japanese reports also suggested the existence of bleeding risks even with multiple antithrombotic therapy in chronic phase after PCI. Our results on the decrease in the prescription rate of triple therapy was in line with the questionnaire survey about the antithrombotic strategy for these patients among the fellows of the Japanese College of Cardiology, which showed a decrease in the prescription rate of triple therapy from 15% in 2014 to 5% in 2016. Maintaining a balance between bleeding and thromboembolic risk is always a concern in patients receiving antithrombotic therapy. Recent evidence, along with further studies, may change the real-world prescription trend of antithrombotic strategies for patients with AF undergoing PCI in chronic phase.

Study limitations: The present study has several limitations. First, the sample size of the study was limited because our center performs annual check-ups, each group partially included the same patients. Second, this study was a single-center retrospective observational cross-sectional study, posing a risk for possible bias. Third, the data in this study were only extracted from annual check-up data from the Cardiovascular Secondary Prevention Center of Kitasato University; therefore, a detailed ordinary treatment by general practitioners cannot be evaluated such as an INR control of warfarin. Fourth, the regular prescription for the study patients was at the discretion of general practitioners. However, our suggestion would affect their prescription. Therefore, these results in this study should be interpreted with caution.

Conclusions

The prescription trend of antithrombotic therapy in chronic phase for AF patients with a history of PCI has noticeably changed in recent years. The prescription rate of triple therapy has gradually decreased compared to that of OAC monotherapy, which has increased gradually. All patients with major bleeding complications were taking multiple antithrombotic therapies. Although OAC monotherapy might be associated with lower bleeding risk, the evidence of OAC monotherapy for this patient population remains insufficient. Therefore, further studies are warranted to elucidate the optimal antithrombotic therapy for patients with AF receiving PCI, in chronic phase.

Disclosure

Conflicts of interest: A.H., J.O., Y.S., S.K., Y.A, R.N., N. H, N.I, G.I., A.S., J.K., and S.N. have no conflict of interest. H.F received lecture fees from Boehringer Ingelheim and Daiichi-Sankyo. J.A. received research funding from Bristol-Meyers, Pfizer, Boehringer Ingelheim, Bayer, Daiichi-Sankyo, and lecture fees from Sanofi, Bristol-Meyers, Pfizer, Boehringer Ingelheim, Bayer, and Daichi-Sankyo.

References


