

## A Complex PCI Case with AF Suffering from VLST with NOAC Treatment

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### Abstract

According to World Health Organization (WHO), ischemic heart disease is the highest cause of death in the world. As current guidelines recommend, Dual-Antiplatelet Therapy (DAPT) of aspirin and P2Y12 receptor inhibitor should be used at least 1 year in Acute Coronary Syndrome (ACS) patients with or without Percutaneous Coronary Intervention (PCI). We here present a complex PCI case who had complicated with atrial fibrillation (AF) after more than 1 year's DAPT. Then, he took new oral anticoagulants (NOAC) only. Unfortunately, we found total thrombotic occlusion in his right coronary artery (RCA) stents. Finally, he was accepted coronary artery bypass grafting surgery (CABG).

**Keywords:** Stent thrombosis; Atrial fibrillation; Antithrombotic therapy

### Introduction

Antithrombotic therapy is important in the ACS patients whether they undergo PCI or are managed medically [1-3]. However, it is a difficult problem in ACS patients with AF to choose antithrombotic drugs. We present a challenging case who had accepted stents implantation due to acute myocardial infarction (AMI) complicating with AF after more than 1 year's DAPT. After that, he took anticoagulant drugs (warfarin or dabigatran etexilate) only. Unluckily, he still had very late stent thrombosis (VLST) in his RCA stents. We here discuss how to choose antithrombotic drugs in such patients.

### Case Report

A 73-year-old man was admitted to our hospital emergency department because of frequent chest tightness and palpitation for two years in Nov 9, 2015. The electrocardiogram (ECG) showed atrial tachycardia (AT) (Figure 1). The patient had accepted percutaneous coronary intervention (PCI) in other hospital implanting three stents due to acute myocardial infarction (AMI) in June 2013: one in the Left Anterior Descending (LAD)(2.75\*30 mm RESOLUTE) and two in the right coronary artery (RCA)(5.0\*28 mm and 5.0\*20 mm TAXUS liberte). After fifteen months of regular dual-antiplatelet therapy (DAPT) of aspirin and clopidogrel, coronary angiography (CAG) showed the stents in his RCA were totally occluded and another two stents (2.5\*33 mm FIREBIRD and 3.5\*38 mm FIREHAWK) were implanted inside the original stents in September 2014. Then, after 1 year of regular DAPT, he was diagnosed as atrial fibrillation (AF) and he began to take warfarin instead of aspirin and clopidogrel. In October 12, 2015, he was operated with AF radiofrequency catheter ablation (RFCA) in our hospital. His dual-source CT coronary angiography

(DSCT-CA) in October 2015 revealed that 60% stenosis of proximal segment and mild stenosis in RCA stents. However, he felt chest tightness and palpitation again and checked ECG still showed AT and brain natriuretic peptide (BNP) was 9927 ng/L in Oct 23, 2015. Four days later, he received electroversion and temporary pacemaker implantation. Before that, doctors changed warfarin with new oral anticoagulants (NOAC), dabigatran etexilate. The patient denied the history of high blood pressure and diabetes mellitus.

After admission, his ECG showed QTc was 470 ms and T-wave had slight inversion in II, III, aVF. His hs-cTnT was 21.58 ng/L, D-Dimer was 0.84 mg/L and international normalized ratio (INR) was 1.25. 24-hour Holter indicated that sinus bradycardia and sinus arrest. In Nov 24, 2015, he re-examined DSCT-CA which indicated 75% stenosis of proximal and middle segment in RCA, but the stents in RCA might be occluded. Then at that night, his CAG showed total thrombotic occlusion in the RCA stents. Then, we decided to operate percutaneous trans luminal coronary angioplasty (PTCA) repeatedly by using balloons of 1.5 × 15 mm Maverick, 2.0 × 20 mm Sprinter and 2.5 × 12 mm Quantum (Figures 2 and 3). We changed NOAC with DAPT of aspirin and clopidogrel immediately after operation. In Nov 27, 2015, he examined emission computed tomography (ECT) which showed his left ventricular ejection fraction (LVEF) was 45%. Finally, he was operated with coronary artery bypass grafting surgery (CABG) and mitral valve replacement and RFCA in Dec 2, 2015.

### Discussion

Atherosclerotic cardiovascular disease (ASCVD) is the world's number one cause of death and disability, and disproportionately affects individuals living in low-income and middle-income countries [4,5]. In China, the prevalence of cardiovascular disease is in a rising phase, and the mortality is high [6]. With the development of PCI and antithrombotic drugs, the mortality of ASCVD has greatly decreased. AHA/ACC [2] recommends that in patients receiving a stent (bare-metal stent (BMS) or drug-eluting stent (DES)) during PCI, aspirin

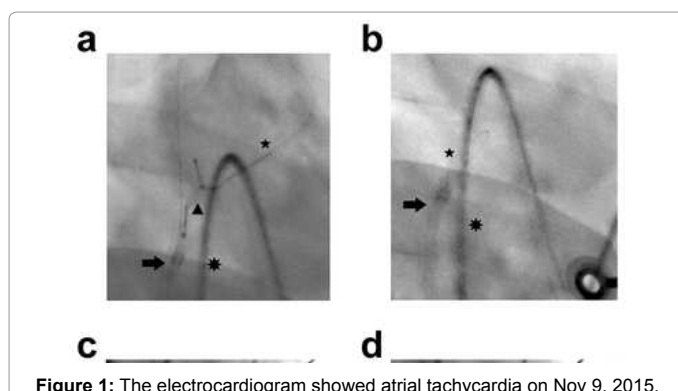


Figure 1: The electrocardiogram showed atrial tachycardia on Nov 9, 2015.

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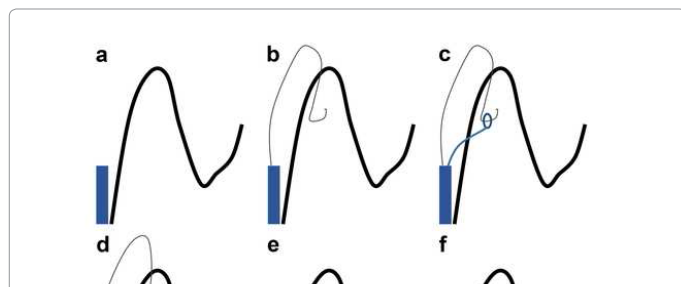


Figure 2: Coronary angiography showed total thrombotic occlusion in the RCA stents.



Figure 3: We operated percutaneous transluminal coronary angioplasty (PTCA) repeatedly by using balloons of 1.5 × 15 mm Maverick, 2.0 × 20 mm Sprinter and 2.5 × 12 mm Quantum. The blood flow in the RCA stents occlusion was slightly improved and the thrombolysis in myocardial infarction (TIMI) was 0-1 level.

should be continued daily (Class I, Level A) and P2Y12 inhibitor should be given for at least 12 months (Class I, Level B). ESC [1] also advocates that in patients with NSTEMI-ACS, DAPT with aspirin and clopidogrel has been recommended for 1 year over aspirin alone, irrespective of revascularization strategy and stent type (Class I, Level A). However, evidence to support the extension of DAPT after DES implantation beyond 1 year is limited. P2Y12 inhibitor administration in addition to aspirin beyond 1 year may be considered after careful assessment of the ischemic and bleeding risks of the patient (Class IIb, Level A) [1]. Our patient above has stuck to the guidelines taking DAPT regularly for more than 1 year. Theoretically, he could take aspirin alone. After 1 year of DAPT, he was diagnosed as AF.

Then, how to choose antithrombotic drugs in acute coronary syndrome (ACS) patients with AF? As current guidelines recommend, triple-antiplatelet therapy (TAPT), including DAPT and oral anticoagulant (OAC), often applies to patients with non-valvular AF undergoing PCI to avoid thromboembolism as well as stent thrombosis and restenosis [7,8]. However, TAPT increases the risk for bleeding events compared to either DAPT or OAC alone and therefore might be associated with adverse outcomes, such as bleeding complications [9]. Careful consideration is required to balance the benefit and the risk of bleeding in each individual patient. So, we should evaluate carefully patients' CHA2DS2-VASc (Congestive heart failure, Hypertension, Age  $\geq$  75 years [doubled], Diabetes mellitus, Prior Stroke or TIA or thromboembolism [doubled], Cardiovascular disease, Age 65 to 74 years, Sex category) and HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly) score. In 2014, AHA/ACC/HRS [10] recommends that in patients with AF following coronary revascularization (percutaneous or surgical), it may be reasonable to use clopidogrel concurrently with OAC but without aspirin (Class II, Level B). Considering his CHA2DS2-VASc  $>2$  and HAS-BLED  $\geq 2$ , and his DAPT  $>1$  year, we decided to give warfarin alone after diagnosing AF. Past researches had confirmed that NOAC offered significant

reductions in stroke, intracranial haemorrhage and mortality, compared with warfarin, with a similar risk of major bleeding [11]. Dabigatran was the first NOAC approved by the US Food and Drug Administration (FDA) for prevention of stroke in patients with AF and was a direct thrombin inhibitor. Considering its advantages, our patient took dabigatran only before electroversion and temporary pacemaker implantation in Oct 24, 2015. However, he had AF again in Nov 9, 2015. Before RFCA, he re-examined DSCT-CA which showed that the stents in his RCA might be occluded. So, we decided to carry out CAG, which revealed total thrombotic occlusion in the RCA stents. Due to his two PCI experiences in the RCA, we advised him to accept CABG surgery.

Through this case, we can be sure that anticoagulation is not a substitute for antiplatelet drugs, not even NOAC, due to their different mechanisms of action. AF thrombus is a vein thrombus or "red thrombus", which is rich in fibrin and red blood cells. Anticoagulant therapy is mainly used for the prevention and treatment of venous thrombosis. OAC includes vitamin K antagonist agent (VKA) (warfarin) and NOAC (factor Xa inhibitors and the direct thrombin inhibitor). Conversely, thrombus in ACS patients is artery thrombus or "white thrombus", which is rich in platelets and relatively less in fibrin. Antiplatelet therapy is for the prevention and treatment of artery thrombotic diseases. So, in ACS patients with AF, we still need to combine anticoagulation with antiplatelet drugs. The current guidelines [1,2,10] are discussing more about the choice of antithrombotic drugs before and after PCI in patients who have already developed AF before ACS attacks them. In spite of this, these guidelines and consensus are limited in leading such patients to choose appropriate antiplatelet and anticoagulation drugs to balance ischemia and bleeding. Even worse, guidelines for antithrombotic therapy in patients with AF who undergo PCI and stents implantation are still poorly followed in clinical practice [12]. Unfortunately, current guidelines rarely mention the choice of antithrombotic agents in ACS patients who have accepted PCI operation complicating with AF after 1 year of DAPT. Such patients are in an embarrassing position: OAC alone or dual therapy or triple therapy. In 2014, an European consensus [13] just mentioned that in an ACS patient who develops new onset AF, and is at high stroke risk (CHA2DS2-VASc  $>2$ ), OAC should be started, whether with a VKA or NOAC. Limited data suggest that use of the new P2Y12 inhibitors would increase the risk of major bleeding, and thus, clopidogrel would be the preferred P2Y12 inhibitor. Such recommendations are ambiguous and guidelines do not point out clearly how to choose antithrombotic drugs in patients with ACS after PCI complicating with AF. Guidelines need to be improved in this area. This is indeed a complex problem, because we have to take into account the risks from two aspects. One is the risk of stroke and major cardiovascular events (such as recurrent MI, stent restenosis and stent thrombosis) the other is the risk of bleeding (Cerebral or gastrointestinal bleeding). It is a challenge for cardiologist to weigh the advantages and disadvantages in clinical application.

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