

Successful Resolution of Left Ventricular Thrombus after ST-Elevation Myocardial Infarction by Edoxaban in a Patient with High Bleeding Risk

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INTRODUCTION

Left ventricular (LV) thrombus is a relatively rare complication of myocardial infarction, with incidence ranged from 2.9% to 15% in different population.¹ It is potentially catastrophic since it may lead to embolic cerebrovascular accident. Patients with LV thrombus may have worse prognosis and quality of life. Risk factors include anterior ST elevation myocardial infarction (STEMI), large infarct size, LV aneurysm, suboptimal revascularization [those with Thrombolysis In Myocardial Infarction (TIMI) 0-1 flow], and cardiac arrest.

Anticoagulant therapy with a vitamin K antagonist in patients with STEMI is suggested, with class IIa recommendation for asymptomatic LV mural thrombi and class IIb recommendation for LV anterior apical akinesis or dyskinesia at a level of evidence of C, in the American College of Cardiology/American Heart Association (ACC/AHA) guidelines on the management of STEMI.²

However, warfarin is prone to multiple adverse drug effects, multiple drug and food interaction, and difficulties in maintaining time-in-the-therapeutic-range (TTR) of INR, especially in the Asian with atrial fibrillation.³ In one study, embolic events related to LV thrombus can be reduced when TTR \geq 50%, however, it is difficult to maintain in many patients, therefore they are exposed to complications related to suboptimal TTR control.⁴

Dual antiplatelet therapy is at risk of bleeding and its management is mentioned specifically.⁵ Moreover, triple therapy with warfarin have an unacceptable higher bleeding risk. In the WOEST trial, even though bleeding risk can be lowered by combination using clopidogrel and warfarin only, the risk is still high (19.4% vs. 44.4%).

In the current era, non-vitamin K antagonist oral anticoagulants (NOAC) appear to have similar efficacy, better safety, and fewer drug and food interactions than warfarin for those with non-valvular atrial fibrillation and with venous thromboembolism. Here, we demonstrate a case with successful resolution of LV thrombus by edoxaban.

CASE

A 70-year-old Taiwanese man, with history of hypertension and heavy smokers, was sent to emergency department with presentation of chest pain for three hours. An electrocardiography (ECG) showed QS pattern and ST elevation in V1-6 (Figure 1A). As STEMI was impressed, he received emergency cardiac catheterization, which showed triple vessel disease with proximal left anterior descending artery total occlusion, left circumflex artery 50% stenosis, and proximal right coronary artery 50% stenosis (Figure 1B). Thrombosuction and stenting with bare metal stent were performed (Figure 1C). Dual antiplatelet agents (DAPT) with aspirin and ticagrelor were kept, with addition of enoxaparin 1 mg/kg twice daily for two days, statin and beta-blocker.

ECG revealed V1-V6 QS pattern with T wave inversion and decreased ST elevation on the next day. Transthoracic echocardiography (TTE) revealed normal chambers size, Left ventricular hypertrophy with ejection frac-

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tion of 54% by 2D echocardiography (Simpson's method), and akinesia at mid to apical septal, anteroseptal and anterior walls with one 1.7*0.8 cm apical thrombus were disclosed. Warfarin was recommended for apical LV thrombus. However, gradual decrement in hemoglobin concentration from 11.3 g/dl to 9.8 g/dl in three days during hospitalization, with presence of tarry stool, was observed. For LV thrombus but recent gastrointestinal bleeding, dual antiplatelet agents were shifted to clopidogrel 75 mg daily, accompanied with fondaparinux 2.5 mg daily in order to lower the risk. Esophagogastroduodenoscopy revealed reflux esophagitis and hemorrhagic gastropathy. Sucralfate was thus added. No decrement in hemoglobin concentration and normal stool color were noted. Due to high bleeding risk in this patient, and relatively lower bleeding rate for edoxaban 30 mg daily is observed in ENGAGE-AF TIMI 48 while compared with studies for other NOAC,^{6,8,9} Fondaparinux was then shifted to edoxaban 30 mg daily directly without overlap.

One month later, repeated TTE was arranged for follow-up, which revealed left ventricle ejection fraction of 45% by Simpson's method, akinesia at apical septal to anterior walls and apex with complete resolution of LV

apical thrombus (Figure 2). The patient also remained uneventful thereafter.

DISCUSSION

Our case is a 70 year-old man with anterior STEMI and triple vessel disease, complicated with LV thrombus and gastrointestinal bleeding. Under concomitant use of clopidogrel 75 mg daily and edoxaban 30 mg daily, LV thrombus is resolved successfully without cardiovascular or gastrointestinal complications.

Several studies have been exploring the efficacy and safety of combination of NOAC and antiplatelet in patients with acute coronary syndrome. While its use in STEMI patient is promising, but increased bleeding risk was still present. Lower NOAC dosage is a way to minimize the bleeding risk, but is controversial and may still higher than dual antiplatelet alone. This includes rivaroxaban 2.5 mg twice daily with DAPT (ATLAS ACS 2 TIMI 51 study, PIONEER AF-PCI), rivaroxaban 2.5 mg twice daily with clopidogrel (GEMINI-ACS-1). In one study, combination of NOAC with clopidogrel has shown a better safety outcomes and similar efficacy compared to triple therapy. Another meta-analysis showed only a modest reduction in major cardiovascular events but an increased bleeding risk while adding NOAC to dual antiplatelet therapy for acute coronary syndrome. No de-

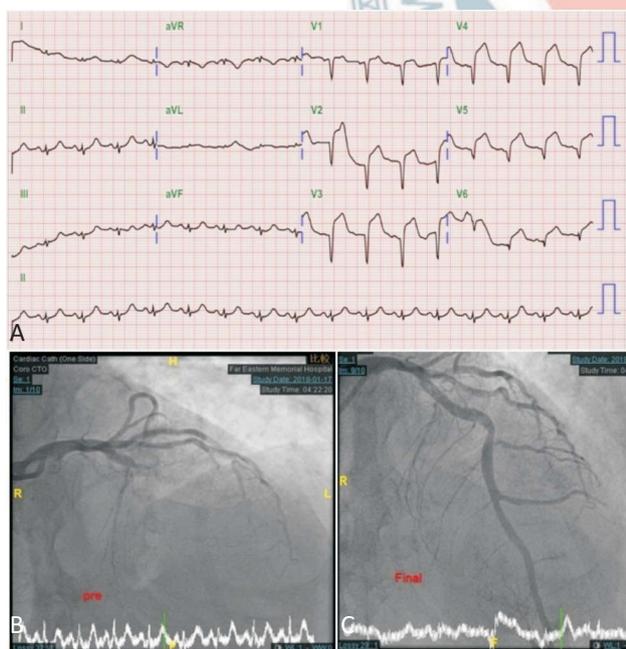


Figure 1. Electrocardiography at the day of admission (A), which showed QS pattern and V1-V6 ST elevation. Coronary angiography of left anterior descending artery before (B) and after stenting (C).

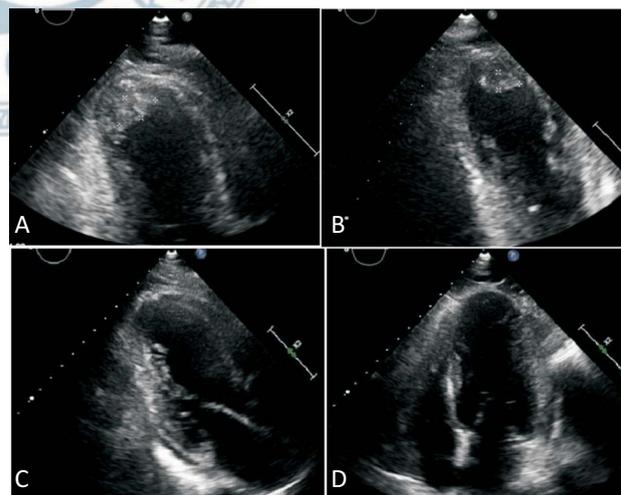


Figure 2. Echocardiogram during hospitalization. A 1.88 × 1.11 cm echogenic mass (*) at the apex of left ventricle was observed (A, B). Echocardiogram one month later showed complete resolution of left ventricular apical thrombus (C, D).

creased efficacy or increased bleeding risk is found while using NOAC to single antiplatelet therapy for acute coronary syndrome.

Dabigatran, a direct thrombin inhibitor, is also available for non-valvular atrial fibrillation, with dose-dependent bleeding risk increment, which can be minimized by using dabigatran 110 mg. In RE-DUAL trial, replacement of warfarin by dabigatran with clopidogrel has shown a similar thrombotic risk, with a reduction in major bleeding.⁶

However, the use of NOACs for LV thrombus is limited. In a meta-summary of case reports,⁷ apixaban, rivaroxaban and dabigatran have been reported for treating LV thrombus. LV thrombus resolution was met by 87.9% of the studied population by a median duration of 30 days. Even NOAC for LV thrombus is still under controversy and currently no known predictors for successful thrombus resolution, it showed non-inferiority in resolution rate with no difference in major bleeding events. Besides, edoxaban has not been reported for LV thrombus, but edoxaban 30 mg daily demonstrated the least bleeding rate of all anticoagulants.^{6,8,9}

Edoxaban, a factor Xa inhibitor, is non-inferior to warfarin in the prevention of stroke or systemic embolism for patient with nonvalvular atrial fibrillation. Besides, edoxaban has significantly lower rates of bleeding and death from cardiovascular causes, which is consistent even with addition of aspirin. In the subgroup analysis of ENGAGE trial,⁸ while compared with warfarin, edoxaban showed lesser stroke or systemic embolic events under 60 mg daily, and lesser bleeding events by either 60 mg daily or 30 mg daily, with concurrent aspirin use. On the other hand, the rate of myocardial infarction is not changed in the ENGAGE trial, but no more data for stent thrombosis is mentioned. These results may show that edoxaban is a safer and non-inferior medication with either aspirin or clopidogrel use, for those with myocardial infarction. Within other NOAC therapies, edoxaban demonstrated fewer drug interaction, potentially better safety profile, and better adherence due to daily dosing.⁹

In our knowledge, this case is the first successful case with the use of edoxaban for LV thrombus. In our patient, bleeding tendency was noted during dual antiplatelet therapy, but no recurrence of bleeding and in-stent restenosis were observed under clopidogrel and edoxaban therapy.

In conclusion, this is the first case report for successful resolution of LV thrombus in edoxaban therapy. Further investigation for the use, the combination strategies with antiplatelet therapy, and the duration of NOAC for LV thrombus is necessary in the future.

LEARNING POINTS

- LV thrombus is a complication of STEMI, with incidence ranged from 2.9% to 15% in different population.
- Vitamin K antagonist is suggested for asymptomatic LV mural thrombi and LV anterior apical akinesis or dyskinesis, in the current ACC/AHA guidelines.
- However, evidence in warfarin use for LV thrombus is limited, and warfarin contains multiple adverse drug effects.
- Use of NOAC is growing in patient with acute coronary syndrome, especially those with atrial fibrillation. But NOAC for LV thrombus is still under active exploration.

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DECLARATION OF AUTHOR(S) COMPETING INTERESTS

None.

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