# Warfarin-resistant left ventricular thrombus completely dissolved by rivaroxaban

## Introduction

Left ventricular thrombus is a critical complication of acute myocardial infarction and has a relatively high incidence and mortality rate. Although its incidence has declined as a result of early revascularization and potent dual antiplatelet therapy (van Dantzig et al, 1996; Osherov et al, 2009; Solheim et al, 2010), left ventricular thrombus is still a challenging problem in patients with acute myocardial infarction. Currently, oral vitamin K antagonists are a standard treatment for left ventricular thrombus (O'Gara et al, 2013). Direct oral anticoagulants have been proposed as an alternative therapy to oral vitamin K antagonists for preventing strokes, as well as for treating deep vein thrombosis and pulmonary embolism. Direct oral anticoagulants provide a comparable anticoagulation effect to oral vitamin K antagonists, and have fewer drug and food interactions (Harder, 2014). This article reports a case of late left ventricular thrombus after acute myocardial infarction, which was successfully dissolved by rivaroxaban (a direct oral anticoagulant) after treatment with warfarin failed.

**Dr Li-Yen Huang**, Attending Physician, Division of Cardiology, Department of Internal Medicine, Armed Forces Taoyuan General Hospital, Taoyuan, Taiwan and Division of Cardiology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

**Dr Tsun-Hou Chang**, Attending Physician, Department of Radiology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

**Dr Chun-Hsien Wu**, Attending Physician, Division of Cardiology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

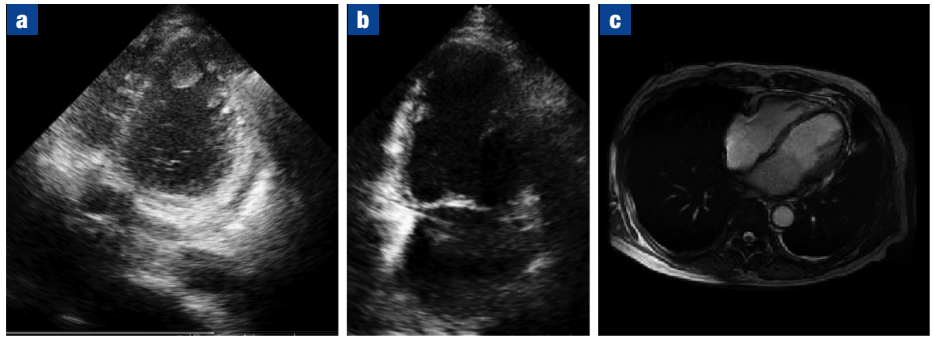
**Dr Tsung-Neng Tsai**, Attending Physician, Division of Cardiology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Correspondence to: Dr T-N Tsai (vinecristine@yahoo.com.tw)

## Discussion

Left ventricular thrombus is a serious complication in patients with acute myocardial infarction and systolic heart failure. Prevention, recognition and adequate treatment of left ventricular thrombus is important because of the increased risk of stroke and systemic embolization (Srichai et al, 2006). Previously, oral vitamin K antagonists were the first choice to prevent and treat left ventricular thrombus (Steg et al, 2012). The disadvantages of oral vitamin K antagonists, such as increased bleeding risks, multiple food and drug interactions, individualized dosing adjustments and need for frequent monitoring, have been well described (Harder, 2014). Surgical thrombectomy should be considered in the event of a recurrent, large and mobile left ventricular thrombus despite adequate anticoagulation therapy (Cousin et al, 2014).

Figure 1. **a.** Echocardiography upon admission revealed a thrombus over the left ventricular apex. After failure with optimal warfarin treatment for 3 months, rivaroxaban was prescribed for 1 month. Subsequent **(b)** echocardiograph and **(c)** magnetic resonance imaging showed complete dissolution of the thrombus.




## CASE REPORT

A 64-year-old man had coronary artery disease with acute anterior wall myocardial infarction, and underwent percutaneous coronary intervention with drug-eluting stent implantation in the middle portion of the left anterior descending artery, 3 years before this admission. He was diagnosed with adenocarcinoma of the colon stage IIIB on admission for acute myocardial infarction. He received chemotherapy and radiotherapy with partial remission, and was followed up as an outpatient. After coronary intervention, dual antiplatelet therapy (aspirin 100 mg/day and clopidogrel 75 mg/day) was administered for 12 months, followed by single antiplatelet therapy (clopidogrel 75 mg/day).

The patient was well until he visited the outpatient department with dyspnoea and bilateral lower extremity oedema, which he had been experiencing over the course of the preceding week. An echocardiogram revealed akinesia of the anterior wall and apex, with a 2.2×1.7 $cm^2$ thrombus over the left ventricular apex (*Figure 1a*).

Warfarin was prescribed and maintained at the optimal therapeutic range (international normalized ratio between 2.0 and 3.0) for 3 months. Transthoracic echocardiography revealed no significant reduction in the size of the left ventricular thrombus. Owing to the paradoxical atrial fibrillation found on his electrocardiogram upon admission, rivaroxaban (15 mg/day) was used instead of warfarin.

After 1 month's treatment, an echocardiogram showed that the thrombus had dissolved completely (*Figure 1b*); this was further confirmed on magnetic resonance imaging (*Figure 1c*). The patient was free of symptoms, and had no other complications such as gastrointestinal bleeding at outpatient follow up 6 months later.

© 2018 MA Healthcare Ltd

Rivaroxaban, a direct oral anticoagulant, is a direct factor Xa inhibitor that blocks thrombin formation, and has been approved for the treatment of deep venous thrombosis and pulmonary embolism, and for the prevention of thromboembolism in patients with atrial fibrillation (Camm et al, 2012; Harder, 2014). It has a high oral bioavailability and rapid onset of action (Harder, 2014). Compared to warfarin in stroke prevention, rivaroxaban has a similar antithrombotic effect with less risk of major bleeding (Patel et al, 2011). Moreover, rivaroxaban has a similar efficacy in preventing recurrent venous thromboembolism and produces fewer major bleeding events, in contrast with treatment with a vitamin K antagonist in patients with cancer (Prins et al, 2014).

In the current case, active colon cancer was diagnosed at the time of acute myocardial infarction, and a large left ventricular thrombus was subsequently detected on regular echocardiography follow up. The thrombus did not dissolve despite optimal oral vitamin K antagonist therapy, but was successfully treated with rivaroxaban with complete dissolution, possibly because rivaroxaban reduces thrombin production and loosens the structure of the clot formation, which ultimately makes the thrombus more susceptible to fibrinolytic enzymes (Varin et al, 2013). The authors suggest that rivaroxaban could be used as an alternative treatment for left ventricular thrombus post-myocardial infarction, particularly in patients with active cancer who are at risk of thromboembolism and/or bleeding during anticoagulant therapy.

## Conclusions

To the best of the authors' knowledge, this is the first report of the successful resolution of left ventricular thrombus by rivaroxaban treatment in a patient with colon cancer. This suggests that rivaroxaban has potent fibrinolytic effects, and may provide an alternative therapeutic option both in patients with left ventricular thrombus who are resistant to oral vitamin K antagonists treatment and in patients who have cancer. **BJHM**

### LEARNING POINTS

- Left ventricular thrombus is a well-recognized complication of acute myocardial infarction.
- Patients with cancer have a higher risk of developing intracardiac thrombus.
- Oral vitamin K antagonists were considered the first choice to prevent and treat left ventricular thrombus.
- Rivaroxaban is an alternative treatment for post-myocardial infarction left ventricular thrombus, particularly in patients with active cancer who are at risk of thromboembolism.


Camm AJ, Lip GYH, De Caterina R et al; ESC Committee for Practice Guidelines (CPG). 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J. 2012 Nov 01;33(21):2719–2747. https://doi.org/10.1093/eurheartj/ehs253

Cousin E, Scholfield M, Faber C, Caldeira C, Guglin M. Treatment options for patients with mobile left ventricular thrombus and ventricular dysfunction: a case series. Heart Lung Vessel. 2014;6(2):88–91.

Harder S. Pharmacokinetic and pharmacodynamic evaluation of rivaroxaban: considerations for the treatment of venous thromboembolism. Thromb J. 2014;12(1):22. https://doi.org/10.1186/1477-9560-12-22

O'Gara PT, Kushner FG, Ascheim DD et al; CF/AHA Task Force. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013 Jan 29;127(4):529–555. https://doi.org/10.1161/CIR.0b013e3182742c84

Osherov AB, Borovik-Raz M, Aronson D et al. Incidence of early left ventricular thrombus after acute anterior wall myocardial infarction in the primary coronary intervention era. Am Heart J. 2009 Jun;157(6):1074–1080. https://doi.org/10.1016/j.ahj.2009.03.020

Patel MR, Mahaffey KW, Garg J et al; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011 Sep 08;365(10):883–891. https://doi.org/10.1056/NEJMoa1009638

Prins MH, Lensing AW, Brighton TA et al. Oral rivaroxaban versus enoxaparin with vitamin K antagonist for the treatment of symptomatic venous thromboembolism in patients with cancer (EINSTEIN-DVT and EINSTEIN-PE): a pooled subgroup analysis of two randomised controlled trials. Lancet Haematol. 2014 Oct;1(1):e37–e46. https://doi.org/10.1016/S2352-3026(14)70018-3

Solheim S, Seljeflot I, Lunde K, Bjørnerheim R, Aakhus S, Forfang K, Arnesen H. Frequency of left ventricular thrombus in patients with anterior wall acute myocardial infarction treated with percutaneous coronary intervention and dual antiplatelet therapy. Am J Cardiol. 2010 Nov;106(9):1197–1200. https://doi.org/10.1016/j.amjcard.2010.06.043

Srichai MB, Junor C, Rodriguez LL et al. Clinical, imaging, and pathological characteristics of left ventricular thrombus: A comparison of contrast-enhanced magnetic resonance imaging, transthoracic echocardiography, and transesophageal echocardiography with surgical or pathological validation. Am Heart J. 2006 Jul;152(1):75–84. https://doi.org/10.1016/j.ahj.2005.08.021

Steg PG, James SK, Atar D et al; Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012 Oct 01;33(20):2569–2619. https://doi.org/10.1093/eurheartj/ehs215

van Dantzig JM, Delemarre BJ, Bot H, Visser CA. Left ventricular thrombus in acute myocardial infarction. Eur Heart J. 1996 Nov 01;17(11):1640–1645. https://doi.org/10.1093/oxfordjournals.eurheartj.a014746

Varin R, Mirshahi S, Mirshahi P et al. Whole blood clots are more resistant to lysis than plasma clots - greater efficacy of rivaroxaban. Thromb Res. 2013 Mar;131(3):e100–e109. https://doi.org/10.1016/j.thromres.2012.11.029



Correspondence

If you would like to comment on any of the articles in *British Journal of Hospital Medicine*, please write in no more than 250 words to:

Professor Rob Miller, Editor-in-Chief, BJHM
c/o Rebecca Linssen, MA Healthcare
St Jude's Church, Dulwich Road, London SE24 0PB

Email: rebecca.linssen@markallengroup.com

BRITISH JOURNAL OF HOSPITAL MEDICINE

© 2018 MA Healthcare Ltd