ESC European Society of Cardiology

European Heart Journal - Case Reports (2022) **6**(2), 1–6
https://doi.org/10.1093/ehjcr/ytac044

CASE REPORT
Heart failure

Amphetamine-induced cardiomyopathy complicated by embolic stroke: a case report

Lucy Chapman *†, **Ismail Khalifa**†, **Neha Sheriff**, and **Niall Colwell**

South Tipperary General Hospital, Clonmel, Ireland

Received 7 April 2021; first decision 26 July 2021; accepted 26 January 2022; online publish-ahead-of-print 9 February 2022

Background Amphetamine use causes cardiomyopathy via catecholamine-mediated effects such as tachycardia, hypertension, vasoconstriction, and direct cardio-toxic effects. Traditionally, an increased risk of haemorrhagic stroke is associated with amphetamine use. However, up to one-third of stimulant-associated cardiomyopathy patients have left ventricular (LV) thrombus formation leading to an increased risk of systemic embolization. We report a case of amphetamine-induced cardiomyopathy complicated by embolic stroke secondary to LV thrombus.

Case summary A 38-year-old man with 6-month history of sustained amphetamine use presented to the emergency department with left-sided weakness, facial droop, and dysarthria. Angiography confirmed right middle cerebral artery thrombus. Prompt mechanical thrombectomy yielded full neurological recovery. Dyspnoea prompted transthoracic echocardiography showing dilated cardiomyopathy with an ejection fraction of 5% and LV thrombus. Anticoagulation was initiated with warfarin as well as pharmacological therapy for heart failure with reduced ejection fraction including bisoprolol, spironolactone, loop diuretic, and sacubitril/valsartan. He was discharged successfully following resolution of ventricular thrombus and medical management of heart failure. Clinical recovery was hampered by psychosocial factors resulting in non-adherence to medical therapy and continued amphetamine use.

Conclusion Sustained amphetamine use can result in severe dilated cardiomyopathy with LV thrombus formation and embolic complications such as ischaemic stroke. Avoidance of amphetamines in conjunction with guideline-directed pharmacological management are key components of therapy. However, psychosocial factors can exert significant influence on recovery.

Keywords Case report • Amphetamine-induced cardiomyopathy • Cardioembolic stroke

ESC Curriculum 6.2 Heart failure with reduced ejection fraction • 2.2 Echocardiography

* Corresponding author. Tel: 01410300, Email: chapmale@tcd.ie
† The first two authors shared first authorship and contributed equally to the study.
Handling Editor: Elizabeth Paratz
Peer-reviewers: Nikos Papageorgiou and Lucrecia Maria Burgos
Compliance Editor: Lavanya Athithan
Supplementary Material Editor: Gonçalo Costa

Learning points

- Stimulant use such as amphetamines and methamphetamines results in serious complications such as cardiomyopathy, left ventricular (LV) thrombus formation, and stroke.
- Stimulant use is increasing and the contribution of drugs to the pathophysiology of cardiomyopathy and stroke in a younger patient population must not be overlooked.
- Cessation of stimulant use is the main stay of treatment for amphetamine-induced cardiomyopathy.
- Pharmacological therapy for heart failure including the use of combination valsartan/sacubitril can also be employed in the management of associated cardiomyopathy.
- Warfarin remains the anticoagulant of choice in LV thrombus formation. Further research is required to assess the efficacy of direct oral anticoagulants therapy in this clinical context.

Introduction

The European Monitoring Centre for Drugs and Drug Addiction noted rising rates of stimulant use such as amphetamine and methamphetamines between 2006 and 2014.[1] Stimulant use causes dilated cardiomyopathy via catecholamine-mediated effects such as tachycardia, hypertension, vasoconstriction, and direct cardio-toxic effects.[2,3] Up to one-third of patients with methamphetamine-induced cardiomyopathy have evidence of left ventricular (LV) thrombus formation.[4] However, the use of amphetamine and methamphetamines is associated with a preponderance of haemorrhagic rather than ischaemic stroke.[5] We report a case of amphetamine-induced cardiomyopathy with LV thrombus formation and subsequent cardioembolic stroke.

Timeline

6 months before presentation	Sustained amphetamine use
2 h before presentation	Wake-up stroke symptoms
Initial presentation (IP)	Left-sided weakness, facial droop, and dysarthria
1 h after IP	Right middle cerebral artery thrombus identified on angiography
3 h after IP	Mechanical clot retrieval at thrombectomy centre
12 h after IP	Paroxysmal nocturnal dyspnoea and desaturation
28 h after IP	Transthoracic echocardiogram (TTE) identified cardiomyopathy with ejection fraction of 5% and left ventricular (LV) thrombus
29 h after IP	Intravenous diuresis and anticoagulation started
8 days after IP	Weaned off supplemental oxygen
17 days after IP	Resolution of LV thrombus
27 days after IP	TTE shows interval improvement of ejection fraction to 27% from 5%
28 days after IP	Discharged from hospital
2 months after IP	Did not attend outpatient follow-up appointments
3 months after IP	Readmitted with decompensated heart failure and recurrent LV thrombus
4 months after IP	Discharged from hospital
6 months after IP	Readmitted with decompensated heart failure and recurrent LV thrombus

Continued

Case presentation

A 38-year-old man presented as a wake-up stroke to the emergency department with left arm weakness, left facial droop, and slurred speech. Initial NIH Stroke Scale (NIHSS) score was eight. Computed tomography brain excluded haemorrhagic stroke with cerebral angiography revealing occlusive thrombus in the right middle cerebral artery. On arrival to a thrombectomy centre, NIHSS score had progressed to fourteen. Successful clot retrieval was achieved and post-thrombectomy NIHSS score was zero.

He had no prior medical or surgical history and no contributory family history. Increasing amphetamine use over the previous 6 months was noted with daily use for the preceding 3 months. The mode of amphetamine administration was intranasal inhalation. He denied alcohol or other illicit drug use. Urine toxicology was positive for amphetamines alone.

On transfer back to referring hospital, telemetry confirmed sinus tachycardia ranging from 110 to 120 beats per minute. Admission electrocardiogram (ECG) was abnormal with low limb lead voltages, anterior Q waves, lateral T-wave inversion, and prolonged QT interval (*Figure 1*). These ECG findings have been associated with methamphetamine-induced cardiac pathology.[6] Baseline laboratory investigations were normal aside from mildly elevated liver transaminases (alanine transaminase of 118 IU/L; reference range 5–41 IU/L and aspartate aminotransferase of 75 IU/L; reference range 5–40 IU/L). Troponin was normal as per local reference range.

Paroxysmal nocturnal dyspnoea with desaturation to 70% was noted on the first night of admission. Crepitations were appreciated on lung auscultation with findings suggestive of pulmonary oedema on chest X-ray. Saturations of 96% were achieved using supplementary oxygen at 2 L/min.

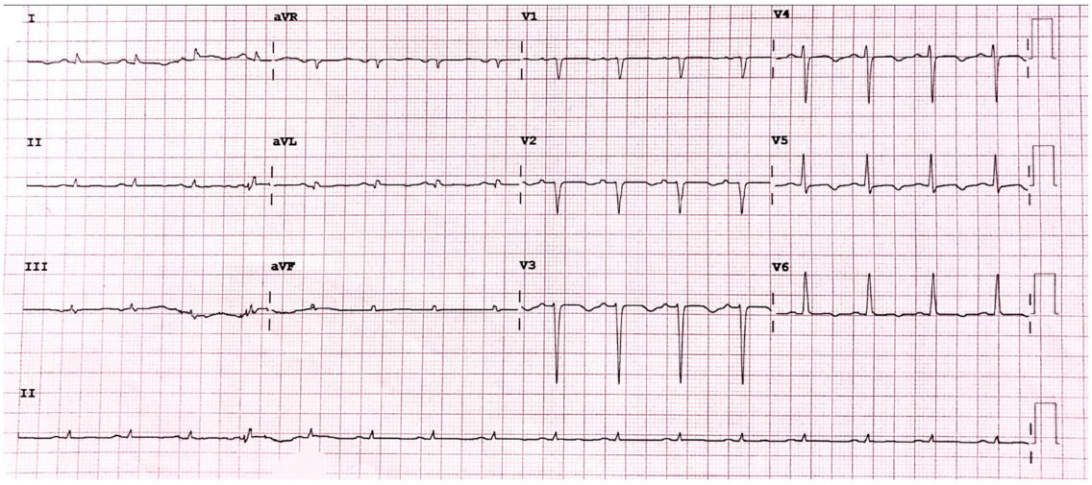


Figure 1 Admission electrocardiogram with sinus tachycardia, anterior Q waves, lateral T-wave inversion, and prolonged QT.

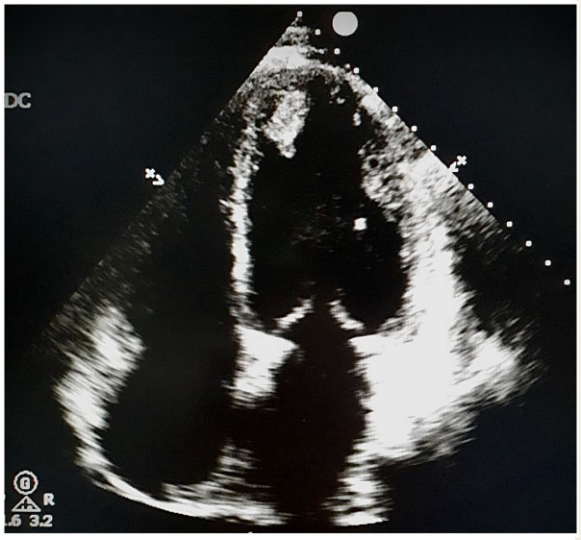


Figure 2 Apical four-chamber view echocardiogram showing echogenic density seen in left ventricular apex consistent with thrombus. Severe global reduction in left ventricular function (left ventricular ejection fraction estimated at 5%).

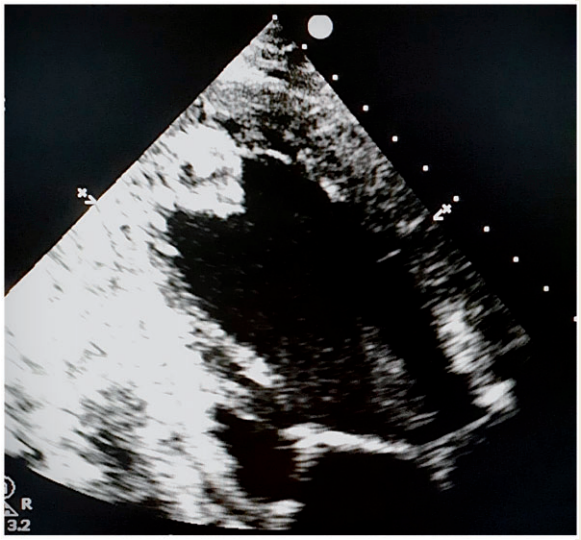


Figure 3 Apical five-chamber view echocardiogram showing left ventricular thrombus and severe global reduction in left ventricular function.

Transthoracic echocardiogram (TTE) demonstrated LV global hypokinesis with left ventricular ejection fraction (LVEF) of 5% and dilatation of all cardiac chambers. A 3 cm apical LV thrombus was visualized (*Figures 2* and *3*, *Videos 1* and *2*). Subsequent coronary angiogram revealed normal coronary arteries. Magnetic resonance imaging (MRI) brain confirmed acute infarction in the right basal ganglia with no infarction in other vascular territories (*Figure 4*). Interestingly, virology screening was positive for Epstein-Barr virus (EBV) Immunoglobulin M consistent with acute infection.

Anticoagulation was initiated with low-molecular-weight heparin (LMWH) bridging therapy until warfarin achieved therapeutic international normalized ratio (INR). Pharmacological therapy for heart failure was commenced and up-titrated according to tolerability including angiotensin II receptor blocker (ARB), beta-blockade,

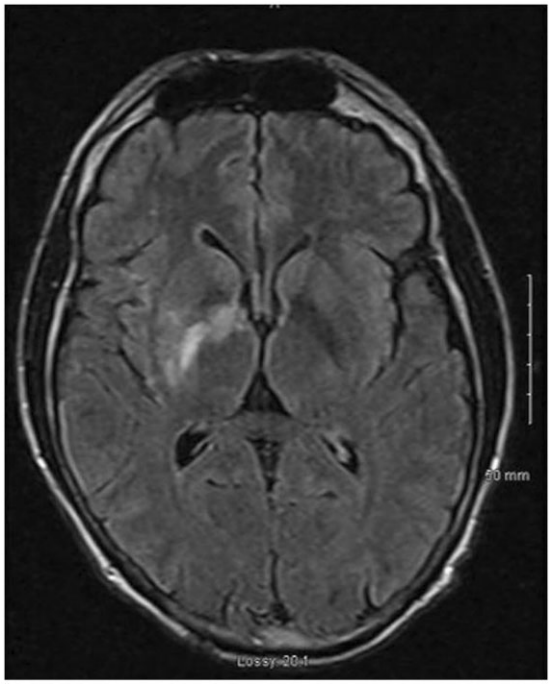


Figure 4 Magnetic resonance imaging brain depicting increased signal on FLAIR in the right basal ganglia involving the lentiform nucleus as well as the genu and anterior limb of the internal capsule.

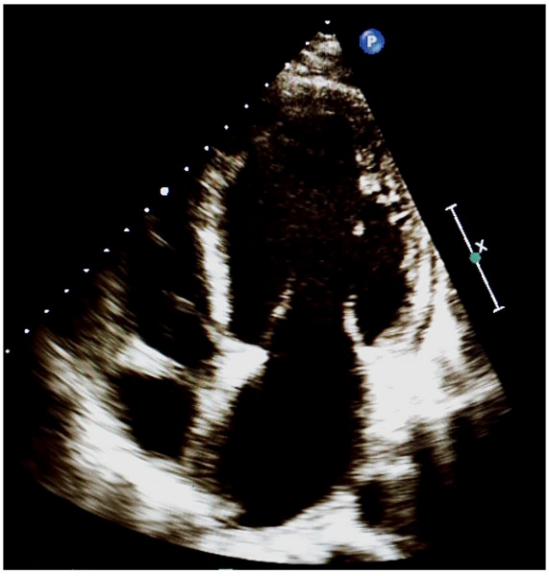
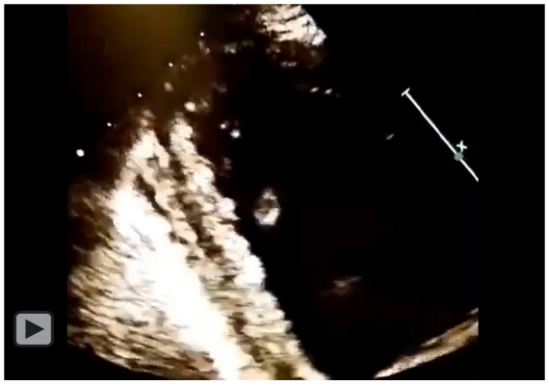


Figure 5 Apical four-chamber view echocardiogram demonstrating resolution of left ventricular thrombus.



Video 1 Mobile echogenic density in the apical region of the left ventricle consistent with thrombus. Marked reduction in left ventricular systolic function.

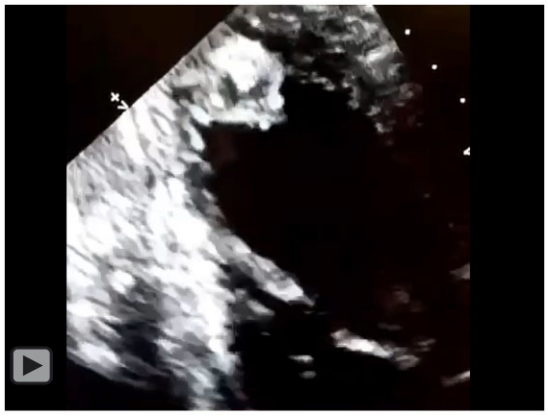
mineralocorticoid receptor antagonist (spironolactone), and intravenous loop diuretic. By the 8th day of admission, supplemental oxygen was no longer required and 5.8 kg weight reduction was achieved. Valsartan/sacubitril was subsequently instituted following tolerability to initial ARB therapy. By Day 17 of admission, thrombus was no longer demonstrated on echocardiogram (*Figure 5*, *Video 3*). Twenty-seven days following initial presentation, interval TTE demonstrated LVEF improvement to 27%.

Medications at discharge included warfarin, bisoprolol 5 mg, spironolactone 12.5 mg, valsartan/sacubitril 24/26 mg twice daily, and furosemide 40 mg once daily. Inpatient medication education was provided. Outpatient follow-up as well as enrolment with a general practitioner was arranged.

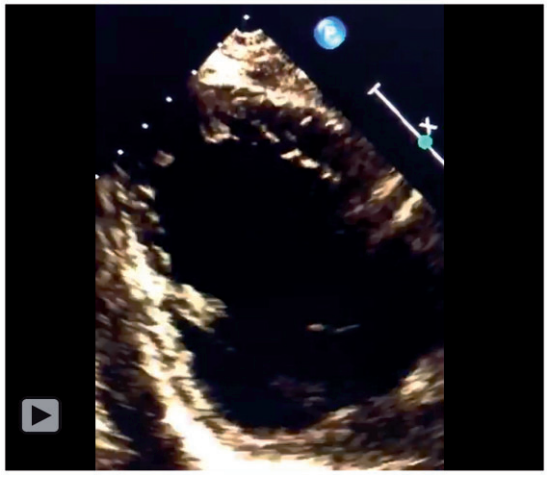
During the next 6 months, the patient did not attend follow-up and was readmitted twice with decompensated heart failure and recurrent thrombus formation due to medication non-adherence and sporadic amphetamine use. On first readmission, TTE demonstrated severe dilated cardiomyopathy with an LVEF of 5–10% and reformation of two distinct LV thrombi. Interval TTE, 37 days later, revealed resolution of thrombi and some improvement in LVEF to 10–15%. Subsequently, on second readmission, TTE showed thrombus had recurred for a third time and LVEF remained at 10%. On this occasion, urine toxicology was positive for amphetamines. The patient stated that psychosocial factors including unemployment and homelessness triggered amphetamine relapse.

Discussion

Our case highlights the consequences of amphetamine use namely cardiomyopathy, LV thrombus formation and cardioembolic stroke which is important given rising European rates of stimulant use.[1] A male predominance (83%) has been previously observed in amphetamine-associated cardiomyopathy.[7] As mentioned, haemorrhagic stroke is more commonly seen with stimulant use[5] rather than the cardioembolic mechanism observed in our case. However, with up to one-third of methamphetamine-induced cardiomyopathy patients demonstrating LV thrombus formation,[4] the risk of ischaemic stroke remains an important concern.



Video 2 Echogenic density in the apex of the left ventricle consistent with left ventricular thrombus.



Video 3 Near total resolution of left ventricular thrombus on day seventeen of admission.

Stimulants such as amphetamines exert negative effects through catecholamine signalling resulting in tachycardia, hypertension, vasoconstriction, and vasospasm.[3,8] Persistent catecholamine exposure can result in cardio-toxic effects,[2,3] including changes in myocardial contractility and myocardial fibrosis.[9] Structural changes may include a dilated cardiomyopathy with or without reduction in ejection fraction or a hypertrophic cardiomyopathy.[10]

Cessation of stimulant use and pharmacologic therapy for heart failure have been employed in the management of stimulant-induced cardiomyopathy.[11,12] Rapid echocardiographic recovery has been observed in amphetamine-induced cardiomyopathy with an improvement in LVEF of 7% in seven days.[11] To our knowledge, the use of combination valsartan and sacubitril (a neprilysin inhibitor) in amphetamine-induced cardiomyopathy has not been previously published in the literature.

Other factors which may have contributed to our patient's cardiomyopathy were explored. The history of drug use prompted virology screening revealing acute EBV infection. This suggested a viral cause for cardiomyopathy which compounded the cardio-toxic effects of amphetamines. Notably, our patient denied alcohol abuse which also leads to dilated cardiomyopathy. The normal coronary angiogram ruled out an ischaemic cardiomyopathy. A limitation of our case is the lack of cardiac MRI. However, over serial admissions, we have observed clinical and echocardiographic improvement following admission, cessation of amphetamine use and initiation of heart failure pharmacological management suggesting that amphetamine use is the main driver of his recurrent cardiomyopathy.

Studies have emerged suggesting that direct oral anticoagulants (DOACs) may be equivalent to warfarin therapy in preventing stroke and systemic emboli associated with LV thrombi.[13] However, given the paucity of high-level evidence for DOACs in LV thrombi, we opted for anticoagulation with warfarin with target INR of 2.5.[14] Warfarin remains challenging given our patient's non-adherence and poor engagement with follow-up, however, long-term use of LMWH was considered less favourable given the burden of daily injections.

Conclusion

Stimulant use is increasing and results in serious complications such as cardiomyopathy, LV thrombus formation, and stroke. The contribution of substance abuse to the pathophysiology of stroke and cardiomyopathy in a younger patient population must not be overlooked. Cessation of stimulant use is the main stay of treatment for amphetamine-induced cardiomyopathy but pharmacological therapy for heart failure can be additionally employed. Psychosocial factors related to substance abuse present challenges to the traditional chronic disease management paradigm.

Lead author biography

Dr Lucy Chapman graduated from Trinity College Dublin in 2013. Currently, she is specializing in Geriatric Medicine and is in her third year of specialist registrar training in Ireland. She has a sub-specialty interest in stroke medicine particularly cardioembolic stroke.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

References

1. European Monitoring Centre for Drugs and Drug Addiction. *European Drug Report 2017: Trends and Developments*. https://www.emcdda.europa.eu/system/files/publications/4541/TDAT17001ENN.pdf_el (5 July 2020).
2. Kaye S, McKetin R, Duflou J, Darke S. Methamphetamine and cardiovascular pathology: a review of the evidence. *Addiction* 2007;**102**:1204–1211.
3. Kevil C, Goeders N, Woolard M, Bhuiyan M, Dominic P, Kolluru G *et al.* Methamphetamine use and cardiovascular disease. *Arterioscler Thromb Vasc Biol* 2019;**39**:1739–1746.
4. Schürer S, Klingel K, Sandri M, Majunke N, Besler C, Kandolf R *et al.* Clinical characteristics, histopathological features, and clinical outcome of methamphetamine-associated cardiomyopathy. *JACC Heart Fail* 2017;**5**:435–445.
5. Lappin J, Darke S, Farrell M. Stroke and methamphetamine use in young adults: a review. *J Neurol Neurosurg Psychiatry* 2017;**88**:1079–1091.
6. Paratz E, Zhao J, Sherwen AK, Scarlato R, MacIsaac AI. Is an abnormal ECG just the tip of the ICE-berg? Examining the utility of electrocardiography in detecting methamphetamine-induced cardiac pathology. *Heart Lung Circ* 2017;**26**:684–689.
7. Kueh S-HA, Gabriel RS, Lund M, Sutton T, Bradley J, Kerr AJ *et al.* Clinical characteristics and outcomes of patients with amphetamine-associated cardiomyopathy in South Auckland, New Zealand. *Heart Lung Circ* 2016;**25**:1087–1093.
8. Mladěnka P, Applová L, Patočka J, Costa VM, Remiao F, Pourová J *et al.*; TOXOER and CARDIOTOX Hradec Králové Researchers and Collaborators. Comprehensive review of cardiovascular toxicity of drugs and related agents. *Med Res Rev* 2018;**38**:1332–1403.
9. Jellis C, Martin J, Narula J, Marwick TH. Assessment of nonischemic myocardial fibrosis. *J Am Coll Cardiol* 2010;**56**:89–97.
10. Richards JR, Harms BN, Kelly A, Turnipseed SD. Methamphetamine use and heart failure: prevalence, risk factors, and predictors. *Am J Emerg Med* 2018;**36**:1423–1428.
11. Crean AM, Pohl JEF. 'Ally McBeal heart?'—drug induced cardiomyopathy in a young woman. *Br J Clin Pharmacol* 2004;**58**:558–559.
12. Qutrio Baloch Z, Ayyaz M, Hussain M, Abbas SA, Samreen FNU. Methamphetamine-induced cardiomyopathy (MACM) in a middle-aged man; a case report. *Emerg (Tehran)* 2018;**2018**:e9–e3.
13. Tomasoni D, Sciatti E, Bonelli A, Vizzardi E, Metra M. Direct oral anticoagulants for the treatment of left ventricular thrombus—a new indication? A meta-summary of case reports. *J Cardiovasc Pharmacol* 2020;**75**:530–534.
14. Habash F, Vallurupalli S. Challenges in management of left ventricular thrombus. *Ther Adv Cardiovasc Dis* 2017;**11**:203–213.