

AHA SCIENTIFIC STATEMENT

Management of Patients at Risk for and With Left Ventricular Thrombus: A Scientific Statement From the American Heart Association

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ABSTRACT: Despite the many advances in cardiovascular medicine, decisions concerning the diagnosis, prevention, and treatment of left ventricular (LV) thrombus often remain challenging. There are only limited organizational guideline recommendations with regard to LV thrombus. Furthermore, management issues in current practice are increasingly complex, including concerns about adding oral anticoagulant therapy to dual antiplatelet therapy, the availability of direct oral anticoagulants as a potential alternative option to traditional vitamin K antagonists, and the use of diagnostic modalities such as cardiac magnetic resonance imaging, which has greater sensitivity for LV thrombus detection than echocardiography. Therefore, this American Heart Association scientific statement was commissioned with the goals of addressing 8 key clinical management questions related to LV thrombus, including the prevention and treatment after myocardial infarction, prevention and treatment in dilated cardiomyopathy, management of mural (laminated) thrombus, imaging of LV thrombus, direct oral anticoagulants as an alternative to warfarin, treatments other than oral anticoagulants for LV thrombus (eg, dual antiplatelet therapy, fibrinolysis, surgical excision), and the approach to persistent LV thrombus despite anticoagulation therapy. Practical management suggestions in the form of text, tables, and flow diagrams based on careful and critical review of actual study data as formulated by this multidisciplinary writing committee are given.

Key Words: AHA Scientific Statements ■ anticoagulants ■ thrombosis

Despite the many advances in cardiovascular medicine, decisions concerning the diagnosis, prevention, and treatment of left ventricular (LV) thrombus often remain challenging. There are only limited American Heart Association (AHA), American Stroke Association (ASA), and American College of Cardiology (ACC) guideline recommendations with regard to LV thrombus^{1,2} and limited recommendations in other organizational guidelines and expert consensus documents.^{3–8} Management issues in current practice are increasingly complex, including concerns about adding oral anticoagulant (OAC) therapy to dual antiplatelet therapy (DAPT), the availability of direct OACs (DOACs) as a potential alternative option to traditional vitamin K antagonists (VKA; predominantly warfarin), and the use of diagnostic modalities such as cardiac magnetic resonance (CMR)

imaging, which has greater sensitivity for LV thrombus detection than echocardiography.

There are on the order of 1 million myocardial infarctions (MIs) each year in the United States alone.⁹ The incidence of LV thrombus after anterior ST-segment elevation MI (STEMI) varies widely in different reports, from 4% to 39%, likely reflecting the patient population studied, timing and frequency of screening, and era of observation,^{10,11} and would probably be higher than reported in most series if CMR had been used routinely.^{12–15} Although the temporal incidence of LV thrombus after MI may be decreasing,^{10,11,16} likely related to improved reperfusion interventions, the risk of LV thrombus in such patients remains significant.^{16,17} Furthermore, it is estimated that there are many millions of patients in the United States alone with dilated (nonischemic)

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Table 1. Eight Key Clinical Management Issues Related to the Management of Patients at Risk for and With LV Thrombus

1. Is echocardiography adequate for detection of suspected LV thrombus, or is CMR (or cardiac CT) indicated when there is concern for LV thrombus?
2. In the era of DAPT after ACS and PCI, which patients should be considered for OAC therapy after anterior/apical MI and akinesis, particularly given the increased bleeding rates with combined OAC therapy and antiplatelet therapy?
3. In those patients with acute MI with visualized LV thrombus, when (if ever) can anticoagulation be stopped? Is a single echocardiogram after 3–6 mo of therapy not demonstrating LV thrombus enough to confidently discontinue?
4. Which, if any, patients with DCM or HFrEF (not related to acute MI) should be treated with preventive (prophylactic) OAC?
5. In those with DCM or HFrEF who form LV thrombus and thus may have a predilection to do this, can OAC ever be stopped (even if a follow-up echocardiogram demonstrates LV thrombus resolution)?
6. Is anticoagulation really indicated for laminated thrombus (not a more mobile, round, mural thrombus)?
7. Is DOAC a reasonable alternative to warfarin for the prevention and treatment of LV thrombus?
8. What management options are there in patients with persistent LV thrombus despite therapy?

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; CMR, cardiac magnetic resonance; CT, computed tomography; DAPT, dual antiplatelet therapy; DCM, dilated cardiomyopathy; DOAC, direct oral anticoagulant; HFrEF, heart failure with reduced ejection fraction; LV, left ventricular; MI, myocardial infarction; OAC, oral anticoagulant; and PCI, percutaneous coronary intervention.

cardiomyopathy (DCM),^{18,19} and to our knowledge there are no study data showing that the risk of LV thrombus in those with DCM has decreased substantially over the past decades. The incidence of LV thrombus in DCM may be anywhere between 20% and 36%.^{17,20–22} Thus, a large number of patients are potentially at risk for developing or do develop LV thrombus. Furthermore, depending on thrombus morphology and the time of follow-up, LV thrombus has in the past been associated with up to a 22% risk of embolization^{20–23} and a 37% risk of major adverse cardiovascular events (MACEs).¹⁷

Therefore, this AHA scientific statement was commissioned with the goals of addressing 8 key clinical management issues (Table 1) related to the management of patients at risk for and with LV thrombus.

METHODOLOGY

To develop this scientific statement, writing committee members were identified and selected from a broad array of relevant areas of expertise related specifically to addressing the aforementioned clinical questions on LV thrombus, including heart failure, coronary artery disease, preventive cardiology, stroke, anticoagulation, pharmacotherapy, echocardiography, CMR, and guideline/scientific statement methodology. The writing group searched for studies on LV thrombus on PubMed, Google Scholar, and other sources using such search terms as thrombus, anticoagulation, warfarin, DOAC, echocardiography, CMR,

cardiomyopathy, heart failure, and MI. Relevant studies were identified and reviewed.

In general, OAC was considered to be treatment with a VKA with a target international normalized ratio (INR) of 2 to 3 or full-dose DOAC (at doses used in contemporary trials for the prevention of cardioembolic event in patients with atrial fibrillation and in trials comparing VKA with DOAC for the treatment of LV thrombus). Except for 1 trial that specifically studied the effect of low-dose DOAC on LV thrombus, all studies in this scientific statement address full-dose anticoagulation, and suggested management strategies given should not be extrapolated to low-dose DOAC.

Consistent with recent AHA guidance on scientific statements, we have striven to keep this document as concise and readable as possible while seeking to address the many questions that caregivers may have on this topic. For this scientific statement, we have constructed a [Study Summary Tables Supplement](#), which summarizes in greater detail the specifics of studies discussed in this document and reviewed by the writing committee in formulating the text and conclusions.

For all sections, a primary author without relevant relationships with industry and ≥1 secondary authors drafted the initial text and conclusions. All sections, suggested management, tables, and the key flow diagram were then presented, reviewed, and discussed by all writing group members, and the manuscript was then revised according to those reviews and discussions. Consensus was reached for all conclusions and suggested management after 2 further conference calls and additional vetting through group emails. The manuscript was then reviewed by 3 external reviewers and revised accordingly. The finalized manuscript was approved by all writing group members.

PATHOPHYSIOLOGY

A commonly accepted paradigm (based on Virchow's triad of thrombogenesis) posits the pathogenesis of LV thrombus as occurring as a result of the interplay of 3 factors: (1) stasis attributable to reduced ventricular function, (2) endocardial injury, and (3) inflammation/hypercoagulability (Figure 1). The relative contributions of each of these factors to LV thrombus formation depend on the cause of the myocardial dysfunction and its duration. Although regional endocardial injury and inflammation may be the dominant factors after an acute MI, stasis attributable to globally reduced LV function may be the key factor in DCM.

Traditionally, LV thrombus is considered to form in the milieu of significant myocardial dysfunction with low LV ejection fraction (LVEF). After anterior wall MI, reduced LVEF is a significant risk factor for thrombus formation, and most thrombi occur in the area of apical wall motion abnormalities in hypokinetic, akinetic, or

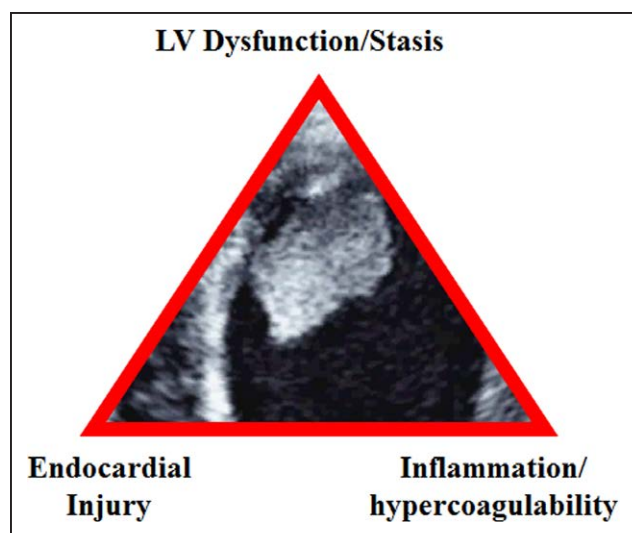


Figure 1. LV dysfunction, endocardial injury, and inflammation/hypercoagulability (Virchow's triad) contribute to the formation of LV thrombus in different cardiac conditions.

LV indicates left ventricular.

dyskinetic (aneurysm) segments. Regional LV dysfunction and reduced and abnormal kinetic energy flow patterns within the LV can predispose to LV thrombus even in the setting of only mild to moderate LV systolic dysfunction.^{24,25}

In the acute MI setting, the severity and extent of cardiac injury increase the risk of developing an LV thrombus. LV thrombus is more common in STEMI compared with non-STEMI. Larger injury (higher peak troponins), delayed reperfusion attributable to late presentation, and faint or no antegrade coronary flow (TIMI [Thrombolysis in Myocardial Infarction] grade 0 or 1) after reperfusion are other risk factors.²⁶ Monocytes and macrophages play an important role in healing after acute MI, and preliminary studies suggest that altered monocyte expression through compromised extracellular remodeling (eg, abnormal collagen I production) and prolonged loss of integrity of endocardium predispose to LV thrombus formation.²⁷ After an anterior wall MI, higher mean platelet volume, C-reactive protein, and fibrinogen levels also are associated with LV thrombus formation.^{28,29}

Lower LVEF and the presence of scar (indicated by the presence and extent of delayed gadolinium enhancement by CMR) are risk factors for LV thrombus formation in DCM.³⁰ Inflammation, hypercoagulability, and endocardial involvement by specific disease processes (eg, amyloidosis, eosinophilic myocarditis) are also important pathophysiological mediators in DCM that may increase the risk of LV thrombus formation.^{31–36} However, data in relation to specific DCM causes are sparse on both LV thrombus risk and the impact on clinically relevant thrombus/thromboembolism.

The key relevant studies on LV thrombus pathophysiology are summarized in the [Study Summary Tables Supplement](#).

IMAGING OF LV THROMBUS

The accurate detection of LV thrombus directly affects treatment and clinical outcomes. Transthoracic echocardiography is the standard imaging technique for the detection of LV thrombus. The use of ultrasound-enhancing-agent during echocardiography may up to double the sensitivity of LV thrombus detection.¹⁵ Thus, it would seem advisable to administer an echocardiography-enhancing agent to increase sensitivity in patients in whom there is concern for LV thrombus such as those with acute MI with anteroapical akinesis (or dyskinesis) and in those with suspected cardioembolic stroke. Transesophageal echocardiography does not generally improve visualization of the LV apex¹⁶ and is not regarded as a useful secondary imaging modality for the assessment of LV thrombus.

Data on the use of cardiac computerized tomography for the detection of LV thrombus are limited to case reports and small series.³⁷ No studies have validated cardiac computerized tomography-detected LV thrombus by pathology or clinical outcomes. Nevertheless, it is recognized that computerized tomography, whether done specifically as a cardiac study or for extracardiac indications, may incidentally identify LV thrombus.

Late gadolinium enhancement (LGE) imaging on CMR has been validated as a technique to detect LV thrombus through verification by pathology,³⁸ and the finding of CMR-detected LV thrombus is associated with increased short-term (6 months)³⁸ and long-term (median, 3.3 years)¹³ embolic events. Studies using LGE CMR as the reference standard have demonstrated that echocardiography has a low sensitivity for the detection of LV thrombus. One meta-analysis of 3 studies comprising a total of 431 patients with STEMI found a sensitivity of 29% for echocardiography with LGE CMR as the reference standard.¹² Although the use of an ultrasound-enhancing agent improves the sensitivity of echocardiography, it is still substantially lower compared with LGE CMR.^{13–15} LV thrombi detected by LGE CMR but not by echocardiography tend to be small in volume and mural in morphology.^{13,15}

The superiority of LGE CMR to detect LV thrombus is not simply related to the higher-resolution anatomic imaging; it is also related to tissue characterization of LV thrombus by LGE CMR, which, because of the lack of vascularity of LV thrombus and thus lack of LGE, easily distinguishes it from the surrounding myocardium (Figure 2).^{13–15,38}

CMR factors associated with increased risk for LV thrombus include severe LV systolic dysfunction,^{13,38} high myocardial scar burden,^{13,38} apical wall motion abnormalities after an acute MI,²⁴ history of acute cardioembolic event,³⁹ and LV aneurysm.⁴⁰

There are limited data on whether detection by CMR of LV thrombi not diagnosed by echocardiography actually leads to improved outcome. In 1 nonrandomized analysis

Patient A



Patient B

Figure 2. Examples of LV thrombus (red arrows) visualized by both CMR and echocardiography (patient A) and by only CMR (patient B).

CMR indicates cardiac magnetic resonance; and LV, left ventricular. Adapted with permission from Velangi et al.¹³ Copyright © 2019 American Heart Association, Inc.

of 110 patients found to have LV thrombus on CMR (89% of whom were started or continued on an anticoagulant), in those who had CMR- but not echocardiography-detected LV thrombi, there was no statistically significant difference in the incidence of the composite embolic end point compared with those in whom LV thrombus was detected by both echocardiography and CMR.¹³ It is unknown whether the patients with LV thrombus detected by CMR but not by echocardiography were treated with anticoagulation and, if not, whether they would have had a higher risk of embolism than patients with LV thrombus confirmed by both CMR and echocardiography who were treated.

CMR may be most appropriate (1) when there is the suggestion of a possible LV thrombus on echocardiogram but echocardiography imaging (even with an ultrasound enhancing agent) is not diagnostic and (2) when echocardiography does not demonstrate LV thrombus but a clinical concern (eg, cardioembolic stroke) remains.

The key relevant studies on imaging of LV thrombus are summarized in the [Study Summary Tables Supplement](#).

PREVENTION OF LV THROMBUS AFTER ACUTE MI

LV thrombus is a well-established complication of MI, particularly for STEMI involving the anteroapical wall with associated wall motion abnormalities, and is a potential precursor to embolic events. The incorporation of prompt reperfusion strategies, initially with thrombolysis and subsequently with percutaneous coronary interven-

tion (PCI), into standard treatment algorithms for STEMI seems to have reduced, but not eliminated, the risk of LV thrombus formation.

Evidence for anticoagulation strategies to prevent LV thrombus is limited and dated. In a meta-analysis of 307 patients with anterior MI from 4 small trials in the prereperfusion era (1980s), therapeutic anticoagulation with intravenous heparin, VKA, or both, agents reduced the incidence LV thrombus (odds ratio [OR], 0.32 [95% CI, 0.20–0.52]), but no data on safety events were reported, and these trials were underpowered to determine whether there was a beneficial reduction in MACEs or systemic embolism.⁴¹ Notably, these trials were undertaken among patients who did not receive reperfusion (PCI or thrombolysis), a P2Y₁₂ inhibitor, and rarely received aspirin. Furthermore, the duration of anticoagulation in these trials was short (predominantly in-hospital treatment only). A subsequent 1997 randomized trial of dalteparin therapy in 776 patients with anterior MI treated with thrombolytic therapy reported a reduced incidence of a composite end point of LV thrombus formation or systemic embolism but with increased rates of major bleeding and without a reduction in arterial embolism alone or death.⁴² Participants in this trial received aspirin (but not a P2Y₁₂ inhibitor), and the duration of dalteparin treatment was again brief (mean follow-up, 9 days).

No published randomized trials specifically address full-dose anticoagulation for the prevention of LV thrombus among patients with MI in the PCI era. Several contemporary observational studies have suggested that the addition of anticoagulation to DAPT to prevent LV thrombus among patients with anterior MI is not

associated with a reduction in MACEs^{43–45} and may in fact increase major bleeding.^{46–48} However, these observational studies are limited by significant biases, including indication bias. Nonetheless, studies of combination antiplatelet and anticoagulant therapy in patients with other indications for OAC (most commonly atrial fibrillation) have clearly demonstrated a several-fold increased risk of bleeding.^{49,50}

Collectively, historical clinical trials suggest that short-term prophylactic anticoagulation may reduce the risk of LV thrombus formation among patients with anterior MI, although these trials were underpowered to determine whether such prophylactic anticoagulation led to a clinically relevant reduction in systemic embolism or MACEs. The 2013 ACC/AHA STEMI guideline, based on Level of Evidence C, gives a Class IIb indication (may be considered) for prophylactic anticoagulation among patients with STEMI and anterior apical akinesis or dyskinesis at risk for LV thrombus, with a duration that can be limited to 3 months.¹ In our more current review of the literature, we found few data that clearly support routine anticoagulation in the current reperfusion/coronary stenting/DAPT era, nor did we find data supporting this specific duration of 3 months. Thus, factors such as perceived risk of thrombus formation, bleeding risk with combined antiplatelet and anticoagulant therapy, and patient preference should be taken into account when deciding on whether to initiate prophylactic anticoagulation.

Recently, 1 modest-sized single-center, open-labeled randomized trial of 279 patients specifically examined whether low-dose anticoagulation (rivaroxaban 2.5 mg twice daily for 30 days) in addition to DAPT could decrease the risk of LV thrombus compared with DAPT alone.⁵¹ The addition of low-dose rivaroxaban compared with no such therapy lowered the risk of LV thrombus formation (0.7% versus 8.6%; hazard ratio, 0.08 [95% CI, 0.01–0.62]), as well as net adverse clinical events, without increased bleeding. In addition to other limitations of the trial (eg, single center, open label), there was a high rate of patient dropout (16.5%), and >75% of patients had an LVEF>45%.^{51,52}

Although a practice of routine prophylactic anticoagulation in all patients does not appear to be supported by data, consideration of the pros and cons of prophylactic anticoagulant therapy to prevent LV thrombus in this setting on a patient-by-patient basis seems prudent. If prophylactic anticoagulation is initiated after MI, we suggest a 1- to 3-month duration because the risk of LV thrombus formation is highest within the first month after MI before declining.^{53–55}

The risk of LV thrombus formation after MI may be greatest in the first 2 weeks, and several studies have found increased incidence of LV thrombus detection by transthoracic echocardiography (or CMR) when performed 1 to 2 weeks after MI (compared with when performed in the first several days after MI).^{16,53–58} Therefore,

in patients after MI with anteroapical akinesis or dyskinesis in whom no LV thrombus is visualized in the first or several days after MI and anticoagulation initiation is not planned, a focused follow-up echocardiogram with an intravenous ultrasound-enhancing agent (or CMR if the echocardiography image quality is poor) might be considered. The timing of such a limited follow-up echocardiogram could be just before discharge in those with prolonged (eg, >3–7 days) hospital stays or within several weeks after MI (as has been suggested in a recent review¹⁶) for those discharged within ≈3 days of presentation. At present, however, it should be noted that there are no good study data that such a strategy of repeat imaging actually leads to a reduction in embolic events.

The key relevant studies on prevention of LV thrombus after acute MI are summarized in the [Study Summary Tables Supplement](#).

TREATMENT OF LV THROMBUS AFTER ACUTE MI

The formation of LV thrombus after acute MI is associated with a 5.5-fold increased risk of embolic events compared with no thrombus.⁴¹ Untreated, the annual stroke or systemic embolization rate is ≈10% to 15%. Protruding and mobile thrombi are perceived to be more likely to embolize than immobile, calcified, and laminated thrombi.^{23,59–61}

Limited evidence suggests that anticoagulation therapy is more likely to resolve LV thrombus and to lower embolic risk compared with no or subtherapeutic anticoagulation. One small double-blind randomized controlled trial found that complete thrombus resolution occurred more frequently among those who received warfarin compared with those who received no warfarin or antiplatelet therapy (60% versus 10%; $P<0.01$). LV thrombus resolution was also more common in individuals who received aspirin at a higher dose than used in contemporary practice (600 mg daily) compared with no warfarin or antiplatelet therapy (45% versus 10%; $P<0.01$).⁶² In a meta-analysis of 7 observational studies including 270 patients with LV anterior wall MI and LV thrombus, systemic anticoagulation was associated with a lower risk of embolic events (OR, 0.14 [95% CI, 0.04–0.52]).⁴¹ In a more recent study, among patients treated with warfarin, greater time in therapeutic range (TTR) was associated with less systemic thromboembolism (TTR ≥50%, 2.9%; TTR <50%, 19%; $P=0.036$).⁶³ The magnitude of benefit with good anticoagulation control (commonly defined when warfarin is used with a TTR ≥70%) likely outweighs the potential increased risk for bleeding among patients with LV thrombus, even in the presence of antiplatelet therapy.

The optimal duration of anticoagulation for the treatment of LV thrombus after MI is uncertain, with no randomized controlled trials examining alternative durations of therapy to date. The 2013 ACC/AHA STEMI guideline

states that the duration of therapy can be limited to 3 months, although this appears to be more expert opinion than based on clinical trial data. In contrast, in the AHA/ASA “2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack,” anticoagulation is recommended for ≥ 3 months, seemingly on the basis primarily of 1 small 1987 study of patients not treated with reperfusion therapy.⁶⁴

Until further data emerge, we favor repeat imaging at 3 months with the same modality of imaging (or better) that was used to initially diagnose the LV thrombus. If there is thrombus resolution, it seems reasonable to discontinue OAC at that time. Because the risk of recurrent LV thrombus is reasonably high in the first 3 months after MI,⁶⁴ earlier discontinuation of anticoagulation on the basis of imaging resolution of the initial thrombus alone could be falsely reassuring if the LV function remains significantly impaired or the initial wall motion abnormalities that predisposed to LV thrombus formation persist. However, if cardiac imaging is performed before 3 months for another indication (eg, when considering placement of an implantable cardioverter defibrillator), earlier discontinuation of anticoagulation might be reasonable if the thrombus has resolved and the LV function and wall motion abnormalities have improved (ie, no longer akinetic or dyskinetic).

LV thrombi may also develop in patients with a nonrecent (eg, >3 months) MI (or ischemic cardiomyopathy). No clinical trial data exist to inform the duration of anticoagulation in this setting. It is the consensus of this writing group that anticoagulation (VKA or DOAC) should be initiated for patients with LV thrombus in this setting for at least 3 to 6 months. A shared decision-making approach should be applied as to whether anticoagulation should be continued indefinitely, factoring in a given demonstrated milieu to form thrombus, improvement or lack of improvement in LV systolic function, bleeding risk, tolerability of OAC, and the patient's risk tolerances of possible stroke or bleeding complications.

In summary, therapeutic anticoagulation generally should be initiated for the treatment of LV thrombus after acute MI, typically for a duration of 3 months, with follow-up imaging at this time point. For patients with a history of more distant MI (or ischemic cardiomyopathy) who develop LV thrombus, we suggest initiation of OAC for at least 3 to 6 months, with a shared decision-making approach for indefinite therapy. The issue of persistent LV thrombus despite OAC is addressed in a subsequent section. The key relevant studies on treatment of LV thrombus after acute MI are summarized in the [Study Summary Tables Supplement](#).

PREVENTION OF LV THROMBOSIS IN DCM

For the purposes of this document, the term DCM is used to encompass those cardiomyopathies with depressed LV systolic function not attributable to myocardial ischemia/MI. LV thrombus is reportedly less common in

DCM compared with ischemic cardiomyopathy, possibly because of underdetection as the incidences of thromboembolic events have been found to be similar.^{30,38} No randomized controlled trials have addressed the primary prevention of LV thrombus per se in patients with DCM. Several randomized controlled trials have been conducted to evaluate the optimal antithrombotic regimen for the prevention of major adverse events in patients with heart failure in sinus rhythm.

HELAS (Heart Failure Long-Term Antithrombotic Study) randomized 197 patients with heart failure with reduced ejection fraction to warfarin, aspirin, or placebo.⁶⁵ The study results showed no significant difference in the incidence of thromboembolism between groups. The WASH pilot trial (Warfarin/Aspirin Study in Heart Failure) randomized 279 patients with heart failure with reduced ejection fraction (55% with nonischemic causes of the cardiomyopathy) to warfarin, aspirin, or placebo and found no significant difference between the groups in the composite end point of death, stroke, or MI.⁶⁶ The WATCH trial (Warfarin and Antiplatelet Therapy in Chronic Heart Failure) randomized 1587 patients with heart failure with reduced ejection fraction (27% with DCM) to warfarin, aspirin, or clopidogrel but was terminated early as a result of failure to reach target enrollment. No significant difference among groups in the composite end point of death, nonfatal MI, or nonfatal stroke was observed in those who had been enrolled.⁶⁷ The WARCEF trial (Warfarin versus Aspirin in Reduced Cardiac Ejection Fraction) randomized 2860 patients with heart failure with reduced ejection fraction ($\approx 57\%$ with DCM) to warfarin or aspirin. The study results showed a benefit with warfarin in terms of decreased risk of ischemic stroke (0.72 events per 100 patient-years versus 1.36 events per 100 patient-years; hazard ratio, 0.52 [95% CI, 0.33–0.82]; $P=0.005$). However, the warfarin group had increased major bleeding compared with the aspirin group (1.78 events per 100 patient-years versus 0.87 events per 100-patient years; $P<0.001$).⁶⁸

A recent Cochrane systematic review, which included 3 randomized trials, concluded that the available evidence does not support the routine use of anticoagulation in people with heart failure who remain in sinus rhythm.⁶⁹ The 2012 American College of Chest Physicians guidelines on antithrombotic therapy and prevention of thrombosis recommend against the use of antiplatelet therapy or warfarin for patients with systolic dysfunction without established coronary artery disease and no LV thrombus (Grade 2C).⁴

There are limited data on several specific types of DCM and associated risk factors for LV thrombus formation. These are discussed here and summarized in Table 2.

Takotsubo syndrome (stress cardiomyopathy) has been associated with a modest incidence of LV thrombus. A meta-analysis of 21 observational studies comprising

Table 2. Specific DCMs (Nonischemic) and Associated Risk Factors for Which Anticoagulation for the Prevention of LV Thrombus Might Be Considered

DCM	Risk factors associated with LV thrombus formation
Takotsubo syndrome	LV dysfunction with LVEF $\leq 30\%$ and/or apical ballooning ^{5,70,71}
Left ventricular noncompaction	History of stroke or TIA ² and/or LV dysfunction ^{6,72,73}
Peripartum cardiomyopathy*	Bromocriptine administration and/or LVEF $\leq 35\%$ ^{7,8,36,74,75}
Hypertrophic cardiomyopathy	Apical aneurysm ^{31,76,77}
Chemotherapy-related cardiomyopathy	LV restrictive filling pattern and/or LVEF $\leq 30\%$ ³²
Cardiac amyloidosis	AL type and/or LV restrictive filling pattern ⁹³
Cardiomyopathy attributable to Chagas disease	Apical aneurysm ³⁴
Eosinophilic myocarditis	Prior embolic episode ³⁵

DCM indicates dilated cardiomyopathy; LV, left ventricular; LVEF, left ventricular ejection fraction; and TIA, transient ischemic attack.

*Low-molecular-weight heparin is preferred antepartum when vitamin K antagonists are generally avoided because of the risk of teratogenicity and fetal bleeding. Both low-molecular-weight heparin and vitamin K antagonists are reasonable choices postpartum.⁷⁸

29410 patients with takotsubo syndrome revealed a pooled estimated LV thrombus rate of 1.8%.⁷⁰ Similarly, multicenter international registry data of 541 patients reported LV thrombus in 2.2%, with apical ballooning pattern and troponin I levels >10 ng/mL associated with an increased risk of LV thrombus formation.⁷¹ The European Society of Cardiology international expert consensus document on takotsubo syndrome states that in patients with LV dysfunction and apical ballooning, “although evidence is lacking, anticoagulation with intravenous/subcutaneous heparin would appear to be appropriate in such patients.”⁷⁵

LV noncompaction is characterized by excessive trabeculations and deep intertrabecular recesses. Studies suggest an increased risk of thromboembolism in patients with LV noncompaction related to LV thrombus formation in the deep intertrabecular recesses.⁷² A Heart Rhythm Society expert consensus statement recommends that anticoagulation may be reasonable with LV noncompaction and LV dysfunction (Class of Recommendation IIb; Level of Evidence B-NR).⁶ However, the literature supporting this recommendation is based on 1 small case series without control subjects.⁷⁹ The AHA/ASA “2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack” gives a Class IIa recommendation that in patients with ischemic stroke or transient ischemic attack (TIA) in the setting of LV noncompaction, treatment with warfarin can be beneficial to reduce the risk of recurrent stroke or TIA, although this is based strictly on expert opinion.² Note, however, that this is not really a recommendation for the primary prevention of LV thrombus, nor is it based on the systematic detection of LV thrombus.

Several observational studies report a higher incidence of LV thrombus and thromboembolism in patients with peripartum cardiomyopathy.^{36,74,75} The hypercoagulable state associated with pregnancy likely increases the risk of LV thrombus formation. A 2016 AHA scientific statement on DCMs states that “anticoagulation is reasonable in patients with peripartum cardiomyopathy and severe LV dysfunction to prevent thrombus formation given the risk of hypercoagulable state during pregnancy” (which is based on Level of Evidence C data).⁷ The European Society of Cardiology Heart Failure Association recommends heparin-based anticoagulation in acute peripartum cardiomyopathy with LVEF $\leq 35\%$ to decrease the risk of thromboembolism.⁸ Low-molecular-weight heparins are preferred antepartum when VKAs are generally avoided because of the risk of teratogenicity and fetal bleeding. Both low-molecular-weight heparins and VKAs are reasonable choices postpartum.^{8,78}

A small number of case reports and case series of LV thrombus have been reported in patients with other forms of DCM, including hypertrophic cardiomyopathy, chemotherapy-related cardiomyopathy, cardiac amyloidosis, cardiomyopathy attributable to Chagas disease, and eosinophilic myocarditis.^{31–35} No prospective observational studies or randomized clinical trials have evaluated the impact of anticoagulation in these patients for the primary prevention of LV thrombus.

In summary, no prospective trials support the routine use of OAC for the primary prevention of LV thrombus in patients with DCM in sinus rhythm. On a case-by-case basis, OAC could be considered in patients with specific types of DCM at increased risk for LV thrombus formation such as those with takotsubo syndrome, LV noncompaction, eosinophilic myocarditis, peripartum cardiomyopathy, and cardiac amyloidosis. In such cases in which OAC is implemented, the recommended duration of preventive OAC for these DCM subtypes is not established; indefinite OAC might be considered unless the LVEF improves or bleeding contraindication occurs.

The key relevant studies on the prevention of LV thrombus in nonischemic cardiomyopathy are summarized in the [Study Summary Tables Supplement](#).

TREATMENT OF LV THROMBUS IN DCM

As noted, LV thrombus is observed less frequently in DCM compared with ischemic cardiomyopathy. Consequently, there are few data on the incidence of LV thrombus and subsequent thromboembolic events in patients with DCM or on the treatment of LV thrombus once identified.

In a retrospective analysis of 159 patients with LV thrombus, only 21.5% had a nonischemic cause.¹⁷ Mean LVEF was 32%, and the vast majority of LV thrombi occurred in the LV apex. Most patients were treated

with OAC, with either a VKA or a DOAC, and 67% were also treated with an antiplatelet agent. A total of 62.3% achieved total LV thrombus regression over a median of 103 days. Thrombus recurrence or an increase in the size of the LV thrombus occurred in patients with poor medical adherence and in those with prothrombotic conditions such as active cancer, inflammatory or hematological diseases, or chronic renal failure. It is important to note that successful treatment of LV thrombus was associated with improved survival and fewer MACEs. Patients on anticoagulation for >3 months and with LVEF $\geq$ 35% had fewer MACEs.¹⁷

Clinical practice guidelines offer little discussion on anticoagulation for the treatment of LV thrombus in the setting of DCM and the duration of treatment. Furthermore, there is a paucity of study data on this. The most recent AHA statement⁷ on DCM suggests that VKA therapy is probably indicated for patients with image-proven intracardiac thrombus in the setting of cardiac amyloidosis, although treatment duration was unspecified. The 2012 American College of Chest Physicians guidelines on antithrombotic therapy and prevention of thrombosis suggest at least 3 months of OAC therapy for LV thrombus in DCM (Grade 2C).⁴

The consensus of this writing group, which is based on retrospective registry data and small, prospective observational studies, is for anticoagulation (VKA or DOAC) in patients with LV thrombus in the setting of DCM for at least 3 to 6 months, with discontinuation if LVEF improves to >35% (assuming resolution of the LV thrombus) or if major bleeding occurs.^{20,80,81} Whether anticoagulation should be continued indefinitely, given the proven milieu or predisposition to thrombus formation, even if follow-up imaging demonstrates resolution of the LV thrombus, cannot be determined but might be prudent in those in whom LV systolic function does not improve with guideline-directed therapies, in those who have persistent apical akinesis or dyskinesis, and in patients with patients with proinflammatory or hypercoagulable states such as malignancy or renal failure, assuming that such patients are able to tolerate OAC. This setting may be a particularly important case of shared decision-making in which the risks of indefinite anticoagulation (and increased pill burden plus additional anticoagulation monitoring and drug-drug and drug-food interactions in the case of warfarin) are balanced by the patient and health care professional against a possible (although theoretical) reduction in the risk of stroke.

The key relevant studies on treatment of LV thrombus in DCM are summarized in the [Study Summary Tables Supplement](#).

MURAL (LAMINATED) THROMBUS

An LV thrombus is categorized as mural (laminated) if its borders are mostly contiguous with the adjacent endocardium, as opposed to protuberant if its borders are distinct

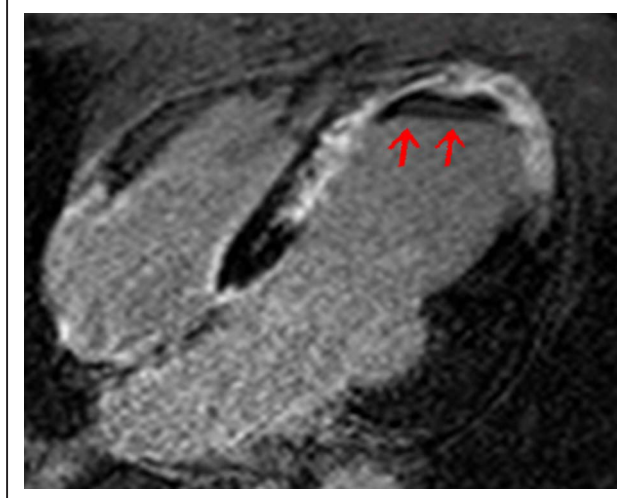


Figure 3. Example of an LV apical mural (laminar) thrombus (red arrows) seen on gadolinium-enhanced CMR.

Note the adjacent white appearing areas indicating infarcted myocardium. CMR indicates cardiac magnetic resonance; and LV, left ventricular.

from the adjacent endocardium and it protrudes into the LV cavity. Mural LV thrombi are often undetected by echocardiography performed without intravenous administration of an ultrasound-enhancing agent (eg, Definity, Optison, Lumason). Although administration of an ultrasound-enhancing agent increases sensitivity, close approximation of a small thrombus to the adjacent akinetic wall (which also lacks enhancing agent uptake) can limit detection. Delayed-enhancement CMR offers the best sensitivity and specificity specifically for this thrombus subtype (Figure 3).¹³

Studies using echocardiography have historically identified mural LV thrombi to be associated with a lower risk of embolism compared with protuberant or mobile LV thrombi.^{23,82} Despite a lack of correlative pathological imaging studies, mural thrombi detected by imaging are often considered organized (and thus with lower thromboembolic potential than protuberant or mobile thrombi). However, the risk of thromboembolism with mural thrombus is not negligible. Up to 40% of thromboembolic events in patients with LV thrombus occur in the mural subtype.⁸² In a large contemporary observational study using CMR (with modern medical therapy and anticoagulation; $n=155$, 32% mural LV thrombus), the risk of long-term embolic events (stroke, TIA, or extracranial systemic arterial embolism) was not significantly different between patients with mural and those with protuberant LV thrombi ($P=0.39$).³ However, in this analysis, the small number of patients limited the power to detect significant differences, and protuberant thrombi had a numerically higher risk of embolism.

Limited data also suggest that protuberant thrombi may resolve earlier than mural thrombi (OR, 3.2 [95% CI, 1.1–8.89]; $P=0.026$),⁸³ which may affect long-term thromboembolic potential. Consistent with this, it is not

uncommon for repeated echocardiograms over the course of months or years to continue to show small residual mural thrombus, which is likely well organized by that point with a lower risk of thromboembolism.

This writing group suggests the following approach to mural thrombus; based more on consensus than study data. For a newly diagnosed mural thrombus, although the risk of embolization may be less than for a protuberant thrombus, it is likely not trivial, and it would be prudent to anticoagulate for this thrombus similarly to a protuberant thrombus. For persistent mural thrombus after a course of OAC, particularly if organized or calcified, the risk of embolization is likely low, and in such cases, a shared decision-making approach seems appropriate, weighing the small but likely nonzero risks of cardioembolic stroke against the risks and inconveniences of OAC.

The key relevant studies on mural (laminated) LV thrombus are summarized in the [Study Summary Tables Supplement](#).

DOAC AS AN ALTERNATIVE TO WARFARIN FOR THE TREATMENT OF LV THROMBUS

VKAs, predominantly warfarin, have traditionally been used and recommended for the prevention and treatment of LV thrombus. OAC with warfarin, however, requires dietary consistency, frequent INR monitoring, and vigilance with regard to drug-food (and drug-drug) interactions that can be challenging for many patients. Failure to maintain a therapeutic INR (TTR <50%) appears to increase the risk of stroke in patients with LV thrombus.^{16,63} These challenges have led to increased adoption of DOAC for oral anticoagulation treatment in atrial fibrillation and venous thromboembolism.⁸⁴ In current practice, some practitioners have extrapolated the results of studies of DOAC for atrial fibrillation and venous thromboembolism to LV thrombus and are using DOAC for such treatment.

The 2013 ACC/AHA STEMI guideline recommendation on anticoagulation for LV thrombus calls out a VKA and does not mention DOAC, although this recommendation was formulated a decade ago.¹ The 2017 European Society of Cardiology STEMI guideline on anticoagulation for LV thrombus states simply that “anticoagulation should be administered” but mentions neither warfarin nor DOAC.³ The 2021 AHA/ASA stroke guideline contains a Class IIb recommendation that in patients with stroke or TIA and new LV thrombus, the safety of anticoagulation with a DOAC to reduce risk of recurrent thrombus is uncertain, citing 2 retrospective studies.^{85,86} Thus, at present, there is little organizational guidance on whether DOAC is a reasonable alternative to warfarin for the treatment of LV thrombus.

Several retrospective studies, randomized trials, and meta-analyses comparing DOAC with warfarin for the

treatment of LV thrombus provide some, although not always consistent, results.^{86–97} Three small randomized controlled trials found DOACs to be noninferior to VKAs.^{90–92} The major limitation of these trials was the small sample size. A meta-analysis of these 3 randomized controlled trials, which consisted of a total of 139 patients, found DOACs to be noninferior to VKA with respect to mortality, stroke, or LV thrombus resolution.⁹³ Pooled analysis also showed that major bleeding was significantly lower with DOACs (2.86% with DOACs versus 13.2% with warfarin; OR, 0.16 [95% CI, 0.02–0.82]).⁹³ A second meta-analysis, which included 8 randomized and nonrandomized studies with a pooled sample of ≈1200 patients, also found DOACs to be noninferior to VKA, again with lower bleeding rates.⁹⁴ Another meta-analysis, consisting of 2 randomized trials and 16 cohort studies in 2666 patients, found a statistically significant reduction in stroke with DOAC compared with VKA (OR, 0.63 [95% CI, 0.42–0.96]; $P=0.03$).⁹⁵ However, no significant difference was noted in mortality, bleeding, systemic embolism, and the combined end point of systemic embolism or stroke and LV thrombus resolution. A meta-analysis of 8 retrospective studies with pooled data on 1955 patients found that DOACs were noninferior to or at least as effective as VKAs in the treatment of LV thrombus, but no other benefit was found, including bleeding complications.⁹⁶ Yet another meta-analysis of 12 studies and 2322 patients found no difference between DOACs and VKAs in the resolution of LV thrombus or bleeding complications.⁹⁷ Taken as a whole, these studies and meta-analyses seem to suggest that DOACs is at least as good as VKAs in terms of ischemic and bleeding events.

To further assess all available current data, we conducted an updated and comprehensive meta-analysis comparing the effectiveness and safety of DOACs and VKAs for the treatment of LV thrombus (see [Study Summary Tables Supplement](#), Section IX for methodology and individual studies). This analysis combined the data of randomized clinical trials, prospective studies, and retrospective studies from inception to January 19, 2022. Pooled data from these 21 studies included 3057 patients with LV thrombus, of whom 824 were treated with DOAC and 2233 treated with VKA. The median follow-up time (according to data from 19 studies) was 12 months (interquartile range, 6–24 months). The median duration of anticoagulation in each arm (provided in only 4 studies) was 222 days (interquartile range, 125.2–417 days) for DOAC and 345.5 days (interquartile range, 253–575 days) for VKA. This meta-analysis found no differences in therapeutic efficacy and safety in the treatment of LV thrombus between DOAC and VKA treatment in stroke or systemic embolization (OR, 0.94 [95% CI, 0.70–1.25]; $P=0.65$; Figure 4), as well as in all-cause mortality (OR, 0.92 [95% CI, 0.64–1.30]; $P=0.63$), thrombus resolution (OR, 1.21 [95% CI, 0.89–1.64]; $P=0.22$), and bleeding complications (OR, 0.79 [95% CI, 0.56–1.11]; $P=0.17$). (Additional forest plots of these 3

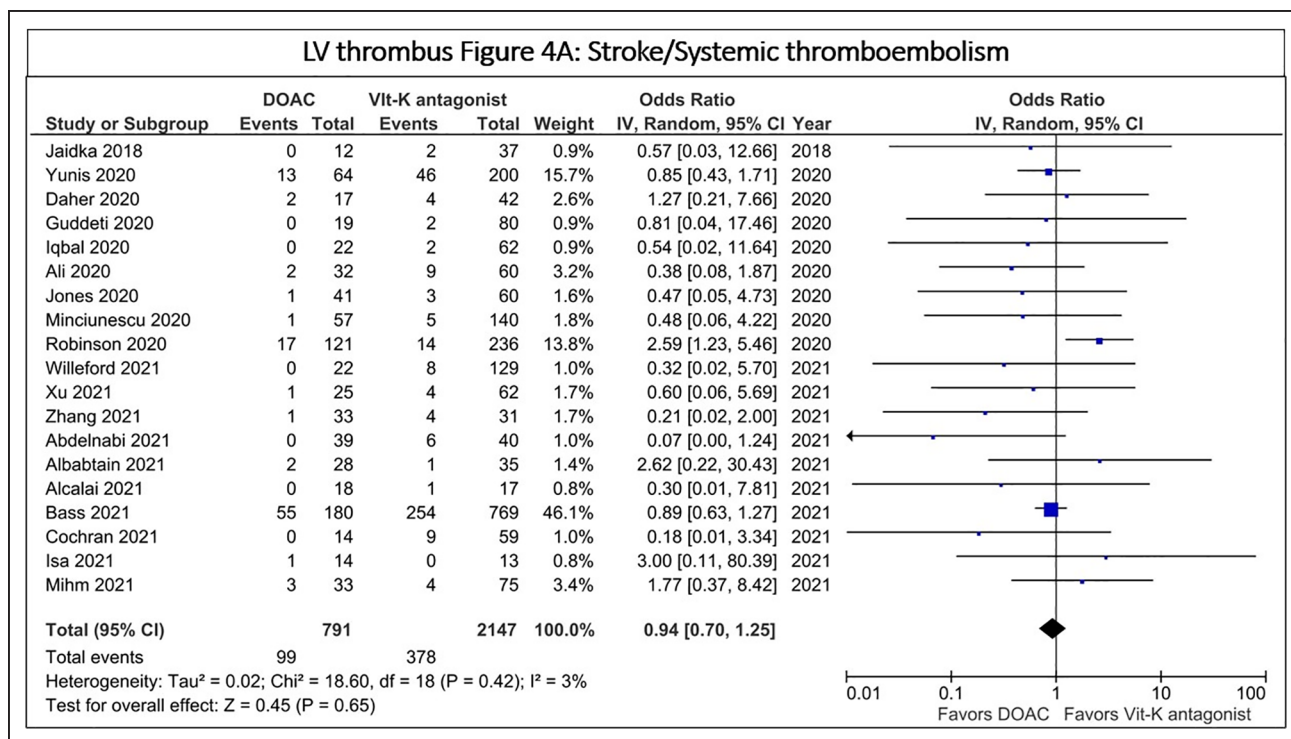


Figure 4. Updated meta-analysis of randomized studies of warfarin vs DOAC in patients with LV thrombus, with end points of stroke and systemic thromboembolism.

Similar analyses for the end points of all-cause mortality, thrombus resolution, and bleeding are given in Section VIII of the [Study Summary Tables Supplement](#). DOAC indicates direct oral anticoagulant; IV, instrumental variable; and Vit-K, vitamin K.

analyses are given in Section VIII of the [Study Summary Tables Supplement](#)). Separate meta-analyses using only randomized controlled trials and randomized controlled trials plus prospective studies did not find statistically significant differences between the 2 treatment strategies in therapeutic efficacy and favored DOAC in terms of bleeding outcome (see [Study Summary Tables Supplement](#)).

Thus, according to all currently available data, DOACs are considered by this writing group to be a reasonable alternative to VKA in patients with LV thrombus and may be particularly attractive as a therapy in patients in whom a therapeutic INR range is difficult to achieve consistently or in whom frequent INR checks are impractical (eg, lack of transportation). At present, there are no data on the use of DOACs for either prophylaxis or treatment of LV thrombus in patients with end-stage renal disease. Thus, the choice of OAC in such patients must be based on best clinical judgment and shared decision-making.

The key relevant studies on DOACs as an alternative to warfarin for the treatment of LV thrombus are summarized in the [Study Summary Tables Supplement](#).

OAC IN PATIENTS TREATED WITH ANTIPLATELET THERAPY

Combining OAC and antiplatelet therapy significantly increases bleeding risk.⁹⁸ Over the past decade, multiple

studies have explored the best treatment strategies in patients undergoing PCI with an indication for antiplatelet therapy and who also have an indication for OAC.⁹⁸ Although in these studies LV thrombus was rarely the indication for OAC, it would seem reasonable to extrapolate the results of these studies, as well as resultant expert and organizational recommendations, to patients with indications for OAC for the prevention or treatment of LV thrombus. On the basis of these studies and consistent with current practice and guideline recommendations,^{99–101} when oral anticoagulation is added to antiplatelet therapy in patients who have undergone PCI, a general strategy of double (dual) therapy, with OAC (preferably a DOAC) and a P2Y₁₂ inhibitor (preferably clopidogrel), after 1 to 4 weeks of triple therapy, is preferred over longer-term triple therapy consisting of an OAC plus DAPT.

DAPT FOR THE PREVENTION OF LV THROMBUS

The pathophysiology of thrombus formation provides the rationale for the use of anticoagulants, rather than antiplatelet drugs, for the prevention or treatment of LV thrombus.^{16,102} No randomized clinical trials have examined the impact of DAPT alone (without OAC) for the prevention of LV thrombus after an acute MI. In a database analysis of patients with anterior wall STEMI with

apical akinesis or dyskinesis (on echocardiography performed within 7 days of hospitalization), those treated with warfarin plus clopidogrel-based DAPT had a greater incidence of composite ischemic and bleeding adverse cardiac events than those treated with clopidogrel-based DAPT alone; there was only 1 ischemic stroke in each treatment group.⁴⁶ One observational study found that ticagrelor-based DAPT was associated with a lower incidence of LV thrombus compared with clopidogrel-based DAPT.¹⁰³ A study comparing a treatment strategy of ticagrelor-based DAPT at 1 hospital with triple antithrombotic therapy at another hospital in patients treated with primary PCI for anterior STEMI with “apical dysfunction” found no difference in a composite end point of ischemic and bleeding events, although only 1 patient in the study had a stroke or TIA.¹⁰⁴ There are overall insufficient high-quality study data to assess whether DAPT alone has any protective effects for the formation of LV thrombus or whether a more potent P2Y₁₂ inhibitor such as ticagrelor might be preferable if DAPT alone is used to treat patients at risk of LV thrombus formation.

FIBRINOLYSIS FOR LV THROMBUS

There are very limited data on the efficacy and safety of fibrinolysis for LV thrombus. In 1 small series, 16 patients with MI 3 to 12 weeks previously and found to have large LV thrombi were treated with 2- to 8-day courses of urokinase. Lyses of the thrombus were deemed successful in 10 patients (predominantly in those with more recent MI), with no evidence of embolic events in any patient. All patients were subsequently treated with 6 months of OAC.¹⁰⁵ A few small reports address the use of fibrinolysis for the acute treatment of stroke in patients who also had LV thrombus.^{106–109} Although in most such cases no clinical emboli resulted, at least 1 such case was well documented, resulting in embolization of the LV thrombus and severe stroke in the hemisphere contralateral to the initial stroke. The 2019 AHA/ASA guideline for the early management of patients with acute ischemic stroke states that in patients with major ischemic stroke likely to produce severe disability and known LV thrombus, treatment with IV alteplase may be reasonable (Class of Recommendation IIb; Level of Evidence C-LD).¹¹⁰ On the basis of consensus opinion, given the very limited safety data and small but likely nonzero risk of embolization, we do not generally suggest fibrinolytic treatment for the primary purpose of treating LV thrombus.

SURGICAL EXCISION OF LV THROMBUS

There are only a few anecdotal reports and retrospective small case series of surgical excision of LV thrombus.^{111–115} Most such cases are in the setting of another indication for cardiac surgery such as multivessel coronary artery

disease or aortic stenosis. At present, there are insufficient data to recommend surgical excision (without other indications for surgery) for the treatment of LV thrombus. Because of the risks of surgery and lack of supportive data, such an approach should be limited to rare circumstances such as inability to tolerate anticoagulation therapy (other than that briefly administered during surgery) when there is perceived to be a high risk of embolization or cardioembolic stroke despite anticoagulation.

LV THROMBUS SIZE, LV THROMBUS REGRESSION, AND EMBOLIC RISK

Multiple studies have found that the most important risk factor for LV thrombus embolization is a mobile or protruberant thrombus.^{16,23,59–61,82} LV thrombus size rarely appears in studies as a risk factor for embolization, and when it does, it is a lesser risk factor.⁸² Thus, for most thrombi, size per se should not factor strongly into decisions about OAC. In 1 study, smaller baseline thrombus size was associated with a greater likelihood of LV thrombus regression, and total LV thrombus regression was associated with a lower risk of mortality.¹⁷ In a second study, failure of initial thrombus resolution and thrombus recurrence were independent predictors of stroke.⁵⁹ The management of thrombi that do not resolve or regress in size with OAC is addressed in the LV Thrombus Persistence Despite Anticoagulation Therapy section.

MANAGEMENT OF MASSIVE LV THROMBUS

There are only a few anecdotal reports on the management of giant, huge, massive, or obliterating thrombus, including treatment with DOAC, fibrinolytic therapy, and surgical resection.^{116–120} In unusual circumstances, thrombus size may affect diastolic ventricular volume or obstruct either mitral inflow or aortic outflow. There are insufficient data to preferentially recommend any one approach to large or massive LV thrombi, and these rare scenarios are best addressed with a multidisciplinary approach to therapeutic intervention.

LV THROMBUS PERSISTENCE DESPITE ANTICOAGULATION THERAPY

LV thrombus persistence despite ongoing anticoagulation and recurrence after completion of anticoagulation are understudied phenomena. Observational research suggests that persistence of LV thrombus is not uncommon. In a contemporary report, 157 of 159 patients with LV thrombus (79% of whom had coronary artery disease) were treated with oral anticoagulation for a median of 1.4 years (VKA, DOAC, or heparin). Concomitant antiplatelet

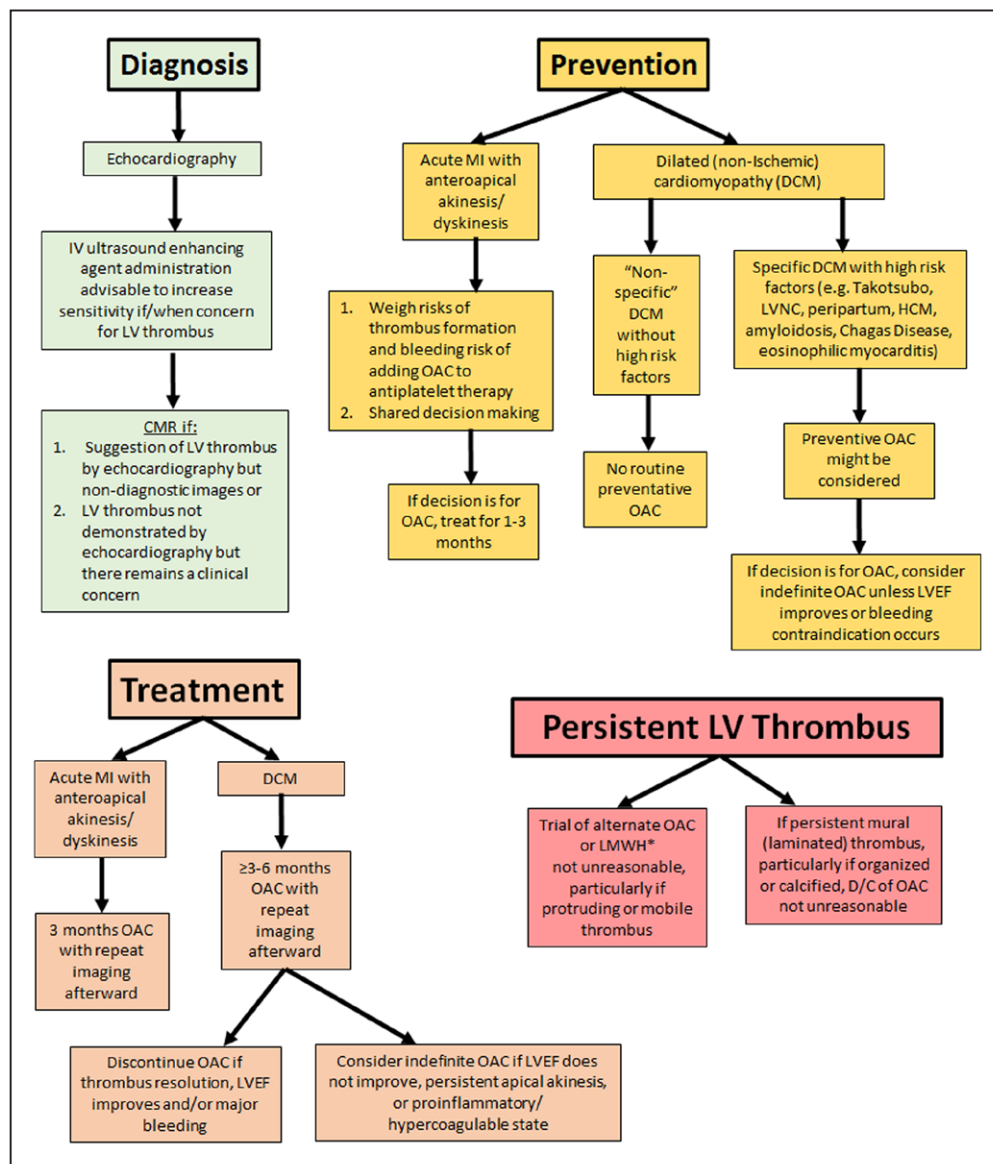


Figure 5. Overview of suggested strategies for the prevention and management of LV thrombus.

CMR indicates cardiac magnetic resonance; D/C, discontinuation; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LMWH, low-molecular-weight heparin; LV, left ventricular; LVEF, left ventricular ejection fraction; LVNC, left ventricular noncompaction; MI, myocardial infarction; OAC, oral anticoagulation; and VKA, vitamin K antagonist. *Trial of VKA if persistent LV thrombus despite dual OAC; trial of dual OAC if persistent LV thrombus in the setting of consistent subtherapeutic international normalized ratio; and trial of LMWH if persistent LV thrombus in the setting of consistent therapeutic international normalized ratio.

therapy was prescribed in 67.9%. Serial echocardiography was conducted per usual clinical care. Complete thrombus resolution was achieved in 62.3% ($n=99$) at a median of 103 days (interquartile range, 32–392 days).¹⁷ Recurrence of thrombus or an increase in LV thrombus area was observed in 14.5% ($n=23$), a finding associated with poor adherence, prothrombotic conditions, and increased mortality.¹⁷

In another report of 35 patients with STEMI complicated by LV thrombus, a higher rate of resolution was reported on serial echocardiography using a predefined assessment protocol (65% resolution at 2 months, 87% at 4 months, 81% at 12 months, and 100% at 18 months).

All participants received warfarin-based anticoagulation (46% with concomitant clopidogrel) for at least 4 months or until thrombus resolution. Again, there was a recurrence rate of 14% after OAC discontinuation.¹²¹

Although trial data informing the treatment of persistent or recurrent LV thrombus are lacking, prolonged anticoagulation and repeated imaging assessment are generally recommended. Treatment adherence should be assessed, and anticoagulation should generally be continued until resolution.¹⁰ Although there are no good trial data on changing the anticoagulation approach, we suggest, on the basis of consensus opinion, a trial of an alternative OAC in some patients with persistent LV thrombus, particularly a protruding or

Table 3. Suggested Practical Management of Patients at Risk for or With LV Thrombus

1. We suggest that CMR may be most appropriate when (1) there is the suggestion of a possible LV thrombus on echocardiogram but echocardiography imaging even with an ultrasound-enhancing agent is not diagnostic and (2) echocardiography does not demonstrate LV thrombus but a clinical concern remains (for example, cardioembolic stroke).
2. We suggest that, given the relatively weak data supporting prophylactic (preventive) OAC in patients with acute anteroapical STEMI treated with reperfusion therapy (usually primary PCI) and anteroapical akinesis, any such consideration of OAC should weigh and incorporate the perceived risk of thrombus formation and bleeding and involve shared decision making. If OAC is initiated, a treatment duration might be 1–3 mo, depending on bleeding risk.
3. We suggest that, on the basis of reasonable study data, post-MI patients with LV thrombus should be treated with OAC, typically for a duration of 3 mo.
4. We suggest that, given reasonably randomized data, patients with DCM should not be prophylactically treated with OAC, with the possible exception of those with specific cardiomyopathies (for example, takotsubo syndrome, LV noncompaction, eosinophilic myocarditis, peripartum cardiomyopathy, and cardiac amyloidosis) with associated factors that increase the risk of LV thrombus formation, in which cases OAC could be considered.
5. We suggest that, on the basis of limited data, patients with NICM with LV thrombus should be treated with OAC for at least 3–6 mo, with discontinuation if LVEF improves to >35% (assuming resolution of the LV thrombus) or if major bleeding occurs. There are insufficient study data to determine whether OAC should be continued indefinitely.
6. We suggest that, on the basis of limited data, it may be prudent to treat patients with OAC for newly diagnosed mural (laminated) LV thrombus as one would a patient with a protruding or mobile thrombus.
7. We suggest that, on the basis of supportive though insufficiently powered randomized data, in patients with LV thrombus, DOAC seems to be a reasonable alternative to warfarin.
8. We suggest that, on the basis of consensus opinion, in some patients with persistent LV thrombus, particularly a protruding or mobile thrombus, a trial of an alternative OAC or LMWH (for example, VKA if on DOAC, DOAC if on VKA with repeatedly subtherapeutic INR, LMWH if on VKA with therapeutic INRs) is not unreasonable. On the other hand, also on the basis of consensus opinion, discontinuation of OAC in patients with persistent mural (laminar) thrombus, particularly if the thrombus becomes organized or calcified, is not unreasonable.

CMR indicates cardiac magnetic resonance; DCM, dilated cardiomyopathy; DOAC, direct oral anticoagulant; INR, international normalized ratio; LMWH, low-molecular-weight heparin; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NICM, nonischemic cardiomyopathy; OAC, oral anticoagulant; PCI, percutaneous coronary intervention; STEMI, ST-segment-elevation myocardial infarction; and VKA, vitamin K antagonist.

mobile thrombus. For example, individuals who are compliant with DOAC but have persistent LV thrombus could be treated with a trial of VKA; those who are unable to maintain therapeutic INRs with VKA and have persistent LV thrombus could be treated with a trial of DOAC; and patients with confirmed therapeutic INRs on VKA who nonetheless have persistent LV thrombus might be treated with a trial of low-molecular-weight heparin. On the other hand, in patients with persistent mural (laminar) thrombus, particularly if the thrombus becomes organized or calcified, the risk of embolization may be low, and discontinuation of OAC is not unreasonable after a risk/benefit discussion with the patient.¹⁰ However, given the lack of high-quality data to confirm this opinion, decisions on mode and duration of anticoagulation should be on a case-by-case basis.

Table 4. Factors to Assess and Reassess in Patients With LV Thrombus That Support the Continuation of OAC and Factors That May or Do Not Favor Continued OAC

Factors that favor continued OAC
Anteroapical MI with persistent akinesis
Protruding/mobile thrombus
Suspected or known cardioembolic event
Not high bleeding risk
Proinflammatory or hypercoagulable states
Recurrent LV thrombus
Factors that may or do not favor continued OAC
High bleeding risk
Concomitant antiplatelet therapy
Improvement in LVEF or focal akinesis
Persistent mural (laminated) thrombus, particularly if organized or calcified, despite therapeutic OAC

LV indicates left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; and OAC, oral anticoagulant.

Last, there is no evidence that surgery for persistent LV thrombus has net efficacy.

The key relevant studies on persistence of LV thrombus despite treatment are summarized in the [Study Summary Tables Supplement](#).

PRACTICAL MANAGEMENT SUGGESTIONS

Only AHA/ACC guidelines can in general make formal recommendations. That said, so as not to make this document merely an academic exercise, the writing group has striven to generate some practical management suggestions that are based on careful and critical review of actual study data, as well as existing guidelines and expert opinion, that address the 8 key questions that served as the rationale for this scientific statement and the assembly of this multispecialty writing group. These suggestions are given in Table 3 and summarized in Figure 5. Factors to assess and reassess in patients with LV thrombus that support the continuation of OAC and factors that may or do not favor continued OAC are given in Table 4.

CONCLUSIONS

Despite advances in reperfusion therapy for acute MI and pharmacological and device treatments for patients with cardiomyopathy with depressed LVEF, LV thrombus continues to be a not uncommon and challenging medical condition. In addition, despite decades of research, treatment recommendations are often based on limited, often noncontemporary studies, with a paucity of study data in some settings to guide informed treatment. Accordingly, contemporary clinical trials are needed to inform the

outstanding uncertainty of whether the benefit of prophylactic anticoagulation in reducing the incidence of LV thrombus formation outweighs the risks in some settings. Future research should investigate (1) the natural history of mural (laminated) LV thrombus and whether the duration of anticoagulation should be tailored to the morphology of the LV thrombus; (2) the benefits of OAC in addition to antiplatelet therapy in patients with STEMI who have undergone primary PCI; (3) whether indefinite anticoagulation is merited in patients with DCM or with prior (not acute or recent) MI who develop LV thrombus; and (4) the optimal anticoagulants (eg, VKA, DOAC, low-molecular-weight heparin) in specific clinical settings. As of this writing, several trials (NCT03764241, NCT04970381, NCT05028777, NCT04970576, NCT03786757, NCT05077683) are in progress that are investigating management issues addressed in this scientific statement, and future such trials are strongly encouraged.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a

personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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Disclosures

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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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