CARDIOLOGY Rounds®

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Left Ventricular Thrombus: Diagnosis, Prevention, and Management

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Left ventricular thrombus (LVT) is a well-recognized complication of acute myocardial infarction (AMI) and congestive heart failure (CHF) due to severely impaired LV systolic function. While the current use of antiplatelet and anticoagulant medications in these patient populations may have reduced the prevalence of LV thrombi, the prevention, recognition, and appropriate treatment of this condition remain important because of the potential risk of systemic embolization. This issue of *Cardiology Rounds* reviews the diagnostic modalities and criteria used to detect LV thrombi and the existing evidence for their prevention and management.

Left ventricular thrombus formation is a frequent complication observed in patients following an AMI and in those with systolic CHF. Previously, the incidence of LVT was reported to be as high as 30%-40% in patients with an anterior AMI. For patients with a non-anterior AMI, the risk of LVT was lower (<5%).[1] Although controversial, in the contemporary era of routine early revascularization and more aggressive anticoagulation, the incidence of LVT complicating an anterior AMI is likely reduced and is currently estimated at 5% to 15%.[2-4] In patients with dilated cardiomyopathy and CHF, the reported frequency of LVT varies from 10%-30%, depending on the series.[5,6] The prevention, diagnosis, and appropriate treatment of LVT are important because of the increased risk of systemic embolization, particularly, cardioembolic stroke.

Diagnosis of LVT

Echocardiography

Transthoracic echocardiography (TTE) remains the most common imaging modality to make a diagnosis of LVT. Advantages of TTE include convenience, portability, wide availability, relatively low cost compared to other imaging modalities, and the ability to provide important ancillary information on cardiac structure and function. When images are technically adequate, TTE has a sensitivity of 90%-95% and a specificity of 85%-90% for detection of LVT in studies where the presence of thrombi was confirmed at surgery or autopsy.[7,8] Echocardiographic criteria for LVT include:

- a distinct echogenic mass within the LV cavity (may be sessile/layered or protruding/mobile) that is contiguous with, but acoustically distinct from the underlying endocardial surface. It is seen throughout the cardiac cycle and visualized on at least 2 orthogonal views,
- an associated underlying region of severe wall motion abnormality, usually severe hypokinesis, akinesis, dyskinesis, or aneurysmal dilatation[7-10]

Rarely, LVT forms in regions of stunned myocardium that has recovered normal wall motion at the time of detection. Spontaneous echo contrast (SEC) or "smoke" is commonly seen within the LV of patients with intracardiac thrombi and is believed to be due to the interaction of red cells and plasma proteins in situations of low, stagnant flow.[11] The presence of SEC in association with marked wall motion abnormalities should warrant a high suspicion for the presence of LVT.

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Figure 1: Large echogenic mass (arrow), most likely a thrombus, filling an apical aneurysm in a patient after a recent anterior MI.

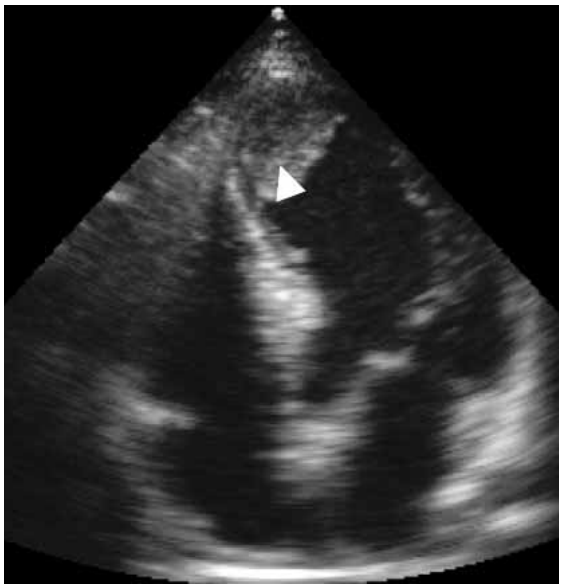
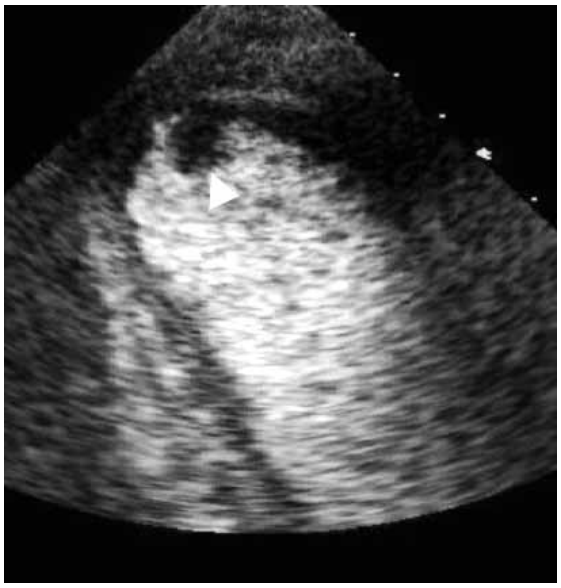


Figure 2: Filling defect (arrow) at the apex seen only during intravenous microbubble contrast enhancement of the LV cavity, compatible with a small apical thrombus.



Given the propensity for thrombi to form at the apex of the LV, the best imaging planes to visualize LVT are the apical views, where the transducer is closest to the region of interest. Figure 1 illustrates a large apical thrombus in a patient who developed an apical aneurysm after an anterior MI. Certain normal anatomic structures (papillary muscles, false tendons, trabeculations) and technical artifacts (reverberations, near-field artifacts) will result in false positive diagnoses of LVT.[9] The use of higher frequency transducers has been shown to overcome some of these limitations due to higher spatial resolution and reduced artifacts. More recently, in the setting of suboptimal images or potential imaging artifacts, the use of commercially available ultrasound contrast agents to opacify the LV cavity and better delineate the endocardial border have been shown to improve the detection of LVT by TTE.[12] Figure 2 depicts a contrast-enhanced TTE image, showing an apical filling defect compatible with an apical thrombus that was not apparent on non-contrast enhanced imaging. Finally, newer real-time 3D-echocardiographic techniques may allow for better characterization and delineation of the extent of LVT.[13]

Cardiac CT and MRI

Newer imaging techniques, such as cardiac computerized tomography (CT) and magnetic resonance imaging (MRI), have produced promising results for detection of LVT.[14-16] Contrast-enhanced MRI, in particular, has demonstrated more sensitivity than TTE, especially in the setting of small thrombi and poor acoustic windows, due to its higher spatial resolution and lack of attenuation artifacts.[18,19] This improved sensitivity of MRI versus TTE has to be weighed against higher costs, lower availability, and the inability to use cardiac MRI in patients with pacemakers and cardiac defibrillators.

Pathophysiology of LVT – Assessment of risk

The pathophysiologic mechanisms for LV thrombus formation is the so-called "Virchow's triad" that commonly exists in patients after AMI or in those with dilated cardiomyopathy and CHF. The triad consists of:

- stasis of blood
- endothelial injury or dysfunction
- a hypercoagulable state.

In general, LVT occurs within the first 1-2 weeks after an AMI.[4] Late occurrence of LVT is usually associated with adverse chamber remodeling, dilatation, reduced global function, and aneurysm formation. Factors associated with a higher risk of developing LVT have been well-studied, particularly in the post-MI setting, and are listed in Table 1.[17,18] The main risk of LVT remains systemic embolization, particularly in cerebral circulation. In a meta-analysis of studies performed in patients after anterior MI, the estimated odds ratio (OR) for increased risk of emboli in the presence of echocardiographically demonstrated LVT (11 studies, 856 patients) was 5.45 (95% confidence interval (CI), 3.02 – 9.83).[19]

While clinical features have not been found to be predictive of risk, the following echocardiographic characteristics of LVT are associated with a higher risk of embolization (Figure 3):

- mobility
- protrusion
- central echolucency. [20,21]

Table 1: High risk echocardiographic features for the development of LVT

- Large infarct size and extent
- Anterior >>inferior
- Severe global and regional LV systolic dysfunction, presence of CHF
- Elevated LV end-systolic volume, LV dilatation
- Spontaneous echo contrast
- Abnormal flow patterns within the LV
- Apical rotating flow
- Vortex ring formation

In comparison, the risk of emboli in the setting of CHF/dilated cardiomyopathy and LVT is less well-established, with several studies failing to demonstrate an increased risk of future embolization, despite the presence of LVT.[22,23]

Prevention and management of LVT

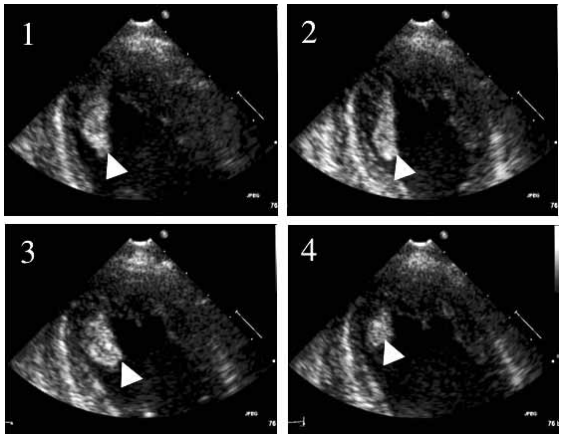
Post-MI

The 2004 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Management of Patients with ST-elevation (STE) MI recommend the use of oral anticoagulation, targeted to an international normalized ratio (INR) of 2.0-3.0, for at least 3 months (Class I, Level of Evidence B) and perhaps, indefinitely in patients without an increased risk of bleeding (Class I, Level of Evidence C) in post-STEMI patients with *documented* LVT.[24] This recommendation is based primarily on observational studies demonstrating that patients with LVT treated with heparin and warfarin had better outcomes and fewer cerebral emboli.

In a meta-analysis of published studies in patients with LVT post-MI,[19] the odds ratio (OR) of anticoagulation versus no anticoagulation in preventing embolization (7 studies, 270 patients) was 0.14 (95% CI, 0.04 - 0.52). Additional therapeutic interventions, such as thrombolysis or surgery, are rarely needed. In clinical practice, echocardiographic imaging is routinely used to follow patients being treated for LVT. The resolution of thrombi and improvement in regional wall motion abnormalities (RWMA) may allow discontinuation of systemic anticoagulation.

The 2004 ACC/AHA Guidelines for the Management of Patients with ST-elevation MI (STEMI) also addressed the issue of anticoagulation for prevention of LVT, with a recommendation for warfarin in post-STEMI patients with LV systolic dysfunction and extensive RWMA (Class IIa, Level of Evidence A). This was primarily based on observational studies, which revealed that late thromboembolism was reduced by systemic anticoagulation in the setting of LV aneurysms post-STEMI. In the previously mentioned meta-analysis,[19] the OR of anticoagulation versus control in preventing mural thrombus formation (4 studies, 307 patients) was 0.32 (95% CI, 0.20 - 0.52), and the event rate difference was -0.19 (95% CI, -0.09 to -0.28). However, the absolute number of ischemic strokes prevented with this strategy may only be marginal, given the anticoagulation risk, particularly if antiplatelet agents are used concurrently. In clinical practice, a common strategy is echocardiographic evaluation following anterior MI to determine the risk for developing LVT, with therapeutic anticoagulation reserved for those patients with a demonstrable thrombus and/or severe wall motion abnormality who are at high risk for developing LVT. The efficacy of this strategy, however, has not been proven in a randomized clinical study.

Figure 3: Pedunculated apical thrombus (arrows) at high risk for embolization, seen protruding into the LV cavity, with mobility throughout the cardiac cycle (frames 1-4).



CHF and dilated cardiomyopathy

Similar to the post-MI patient, a documented LVT in the setting of CHF and dilated cardiomyopathy likely warrants anticoagulation, especially if embolic potential is high and bleeding risk is low. Currently, no evidence exists for anticoagulation of chronic, layered, organized, mural thrombi. While there are no trials of systemic anticoagulation for prevention of LVT in patients with CHF and dilated cardiomyopathy, there are randomized controlled trials of antiplatelet and antithrombotic regimens in this population that examine broader clinical outcomes including stroke.

The Warfarin/Aspirin Study in Heart failure (WASH) trial[25] was an open-label, randomized, controlled trial comparing no antithrombotic regimen, aspirin (325 mg/day), and warfarin (targeted to an INR 2.5) in patients with CHF and LV systolic dysfunction (LV ejection fraction (LVEF) ≤35%). The patients (total N=279) were randomized, with a mean follow-up of 27±1 months. There were no significant differences in the composite primary

Table 2: Clinical and safety outcomes in the WATCH trial

Outcome	Aspirin (n=523)	Warfarin (n=540)	Clopidogrel (n=524)
Death, MI, or stroke (%)	20.5	19.8	21.8
HF hospitalizations (%)	22.2*	16.1	18.3
Minor bleeding (number of episodes)	696*	860	695*
Major bleeding (number of episodes)	19	30	13**

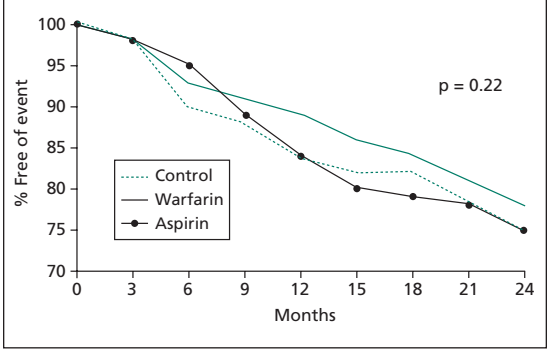
* p=0.01 vs warfarin
** p=0.012 vs warfarin

outcome of death, non-fatal MI, or non-fatal stroke (Figure 4). While the on-treatment analysis revealed a trend towards fewer primary outcome events in patients on warfarin, this was balanced by a higher rate of hemorrhagic events.

The results of the Warfarin and AntiplateleT in Chronic Heart failure (WATCH) trial were presented at the Scientific Meeting of the American College of Cardiology, 2004. Although the trial was designed to accept 4500 patients, it was terminated 18 months prematurely in June 2003 because of poor enrollment. In total, 1,587 patients with chronic ischemic or non-ischemic CHF and LVEF ≤35% were randomized to open-label warfarin (INR 2.5-3.0) or double-blind aspirin (average dose 162 mg/day), or clopidogrel (75 mg/day). Over a mean follow-up of 23 months, there were no significant differences between treatment groups for death, MI, stroke, or the composite endpoint (Table 2). Given the reduced statistical power of this study, no definite conclusions can be made.

Additional ongoing studies include the Warfarin vs Aspirin in ReduCed Ejection Fraction (WARCEF) trial comparing warfarin and aspirin in 2,860 CHF patients with the endpoints of death and stroke. It is hoped that this study will provide additional information about the relative effectiveness of these 2 agents. A combined analysis of the WARCEF and WATCH studies is planned.

Figure 4: Kaplan-Meier plot for the composite primary outcome of death, non-fatal MI, and stroke in the WASH trial.



Due to the current lack of definitive studies, the primary prevention of cardioembolic stroke through therapeutic anticoagulation remains controversial in patients with dilated cardiomyopathy and CHF. Despite the lack of supportive data, given that the greatest benefit would be expected for those with severe LV dysfunction (LVEF <20%) or a previous history of an embolic event, the use of anticoagulation in this select patient population may be reasonable.[26]

Conclusions

LVT remains an important complication in patients with ischemic heart disease after anterior AMI and in those with dilated cardiomyopathy and systolic heart failure. The diagnosis of LVT remains important, since anticoagulation will reduce the risk of systemic embolization and stroke. Despite advances in other imaging modalities, echocardiography remains the most important tool for diagnosis and risk stratification in patients predisposed to developing LVT. While the overall benefit of routine anticoagulation to prevent LVT and stroke remains controversial, in certain select patients who are at a very high risk for developing LVT and have no contraindications, systemic anticoagulation is generally recommended. The results of ongoing clinical trials will hopefully provide additional information about the therapeutic benefit of anticoagulation, if any, in the patient population with CHF and reduced LVEF.

References

1. Asinger RW, Mikell FL, Elsperger J, Hodges M. Incidence of left-ventricular thrombosis after acute transmural myocardial infarction. Serial evaluation by two-dimensional echocardiography. *N Engl J Med* 1981;305:297-302.
2. Kalra A, Jang IK. Prevalence of early left ventricular thrombus after primary coronary intervention for acute myocardial infarction. *J Thromb Thrombolysis* 2000;10:133-6.
3. Greaves SC, Zhi G, Lee RT, et al. Incidence and natural history of left ventricular thrombus following anterior wall acute myocardial infarction. *Am J Cardiol* 1997;80:442-8.
4. Nayak D, Aronow WS, Sukhija R, McClung JA, Monsen CE, Belkin RN. Comparison of frequency of left ventricular thrombi in patients with anterior wall versus non-anterior wall acute myocardial infarction treated with antithrombotic and antiplatelet therapy with or without coronary revascularization. *Am J Cardiol* 2004;93:1529-30.

5. Ciaccheri M, Castelli G, Cecchi F, et al. Lack of correlation between intracavitary thrombosis detected by cross sectional echocardiography and systemic emboli in patients with dilated cardiomyopathy. *Br Heart J* 1989;62:26-9.
6. Gottdiener JS, Gay JA, VanVoorhees L, DiBianco R, Fletcher RD. Frequency and embolic potential of left ventricular thrombus in dilated cardiomyopathy: assessment by 2-dimensional echocardiography. *Am J Cardiol* 1983;52: 1281-5.
7. Visser CA, Kan G, David GK, Lie KI, Durrer D. Two-dimensional echocardiography in the diagnosis of left ventricular thrombus. A prospective study of 67 patients with anatomic validation. *Chest* 1983;83:228-32.
8. Cacciapuoti F, Varrichio M, D'Avino M, Gentile S, Lama D, Cotrufo M. Post necrotic endoventricular thrombosis. Comparative evaluation of the diagnostic reliability of 2-dimensional echocardiography and cineventriculography. *G Ital Cardiol* 1986;16:344-349.
9. Asinger RW, Mikell FL, Sharma B, Hodges M. Observations on detecting left ventricular thrombus with two-dimensional echocardiography: emphasis on avoidance of false positive diagnoses. *Am J Cardiol* 1981;47:145-56.
10. Otto CM. *The Practice of Clinical Echocardiography*. Philadelphia, PA: WB Saunders Company; 2005.
11. Merino A, Hauptman P, Badimon L, et al. Echocardiographic "smoke" is produced by an interaction of erythrocytes and plasma proteins modulated by shear forces. *J Am Coll Cardiol* 1992;20:1661-8.
12. Ngai T, Atar S, Luo H, et al. The usefulness of second generation ultrasound contrast agents to identify intracardiac thrombus. *J Am Coll Cardiol* 1999;33:408A.
13. Chamoun AJ, McCulloch M, Xie T, Shah S, Ahmad M. Real-time three-dimensional echocardiography versus two-dimensional echocardiography in the diagnosis of left ventricular apical thrombi: preliminary findings. *J Clin Ultrasound* 2003;31:412-8.
14. Goldstein JA, Schiller NB, Lipton MJ, Ports TA, Brundage BH. Evaluation of left ventricular thrombi by contrast-enhanced computed tomography and two-dimensional echocardiography. *Am J Cardiol* 1986;57:757-760.
15. Barkhausen J, Hunold P, Eggebrecht H, et al. Detection and characterization of intracardiac thrombi on MR imaging. *AJR Am J Roentgenol* 2002;179:1539-1544.
16. Mollet NR, Dymarkowski S, Volders W, et al. Visualization of ventricular thrombi with contrast-enhanced magnetic resonance imaging in patients with ischemic heart disease. *Circulation* 2002;106:2873-2876.
17. Neskovic AN, Marinkovic J, Bojic M, Popovic AD. Predictors of left ventricular thrombus formation and disappearance after anterior wall myocardial infarction. *Eur Heart J* 1998;19:908-916.
18. Van Dantzig JM, Delemarre BJ, Bot H, Koster RW, Visser CA. Doppler left ventricular flow pattern versus conventional predictors of left ventricular thrombus after acute myocardial infarction. *J Am Coll Cardiol* 1995;25:1341-6.
19. Vaitkus PT, Barnathan ES. Embolic potential, prevention and management of mural thrombus complicating anterior myocardial infarction: a meta-analysis. *J Am Coll Cardiol* 1993;22(4):1004-9.
20. Haugland JM, Asinger RW, Mikell FL, Elsperger J, Hodges M. Embolic potential of left ventricular thrombi detected by two-dimensional echocardiography. *Circulation* 1984;70: 588-598.
21. Visser CA, Kan G, Meltzer RS, Dunning AJ, Roelandt J. Embolic potential of left ventricular thrombus after myocardial infarction: a two-dimensional echocardiographic study of 119 patients. *J Am Coll Cardiol* 1985;5: 1276-80.
22. Cleland JGF. Anticoagulant and anti-platelet therapy in heart failure. *Curr Opin Cardiol* 1997;12:276-287.
23. Katz SD. Left ventricular thrombus and the incidence of thromboembolism in patients with congestive heart failure; can clinical factors identify patients at increased risk? *J Cardiovasc Risk* 1995;2:97-102.
24. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004;44:E1-E211.
25. Cleland JG, Findlay I, Jafri S, et al. The Warfarin/Aspirin Study in Heart failure (WASH): a randomized trial comparing antithrombotic strategies for patients with heart failure. *Am Heart J* 2004;148:157-164.
26. Pulerwitz T, Rabbani LE, Pinney SP. A rationale for the use of anticoagulation in heart failure management. *J Thromb Thrombolysis* 2004;17:87-93.

Abstracts of Interest

Imaging and Pathologic Characteristics of Left Ventricular Thrombus: A Comparison of Contrast-Enhanced Magnetic Resonance Imaging, Transthoracic Echocardiography and Transesophageal Echocardiography with Surgical or Pathologic Validation

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BACKGROUND: Left ventricular (LV) thrombus formation is a frequent and potentially dangerous complication in patients with ischemic heart disease. We evaluated imaging and pathologic characteristics of confirmed LV thrombus and compared the diagnostic value of contrast enhanced magnetic resonance imaging (CE-MRI) with transthoracic echocardiography (TTE), and transesophageal echocardiography (TEE) for the diagnosis and exclusion of LV thrombi.

METHODS: Between November 1997 and December 2003, 361 patients with ischemic heart disease had surgical and/or pathologic confirmation of the presence or absence of LV thrombus. Surgical and pathologic reports were reviewed for presence or absence of thrombus, and if present, thrombus characteristics including size, location, and degree of organization. Pre-operative imaging study reports were retrospectively reviewed for detection of LV thrombus.

RESULTS: LV thrombus was present in 106 of 361 (29%) patients in this study. In 160 patients who underwent CE-MRI, TTE and TEE all within 30 days of their confirmation procedure, CE-MRI showed the highest sensitivity and specificity (88% and 99%, respectively), compared with TTE (23% and 96%, respectively) and TEE (40% and 96%, respectively) for the detection of LV thrombus. Detection of LV thrombus by TTE and TEE correlated with size and degree of organization of the thrombus, but was still inferior to evaluation of LV thrombus by CE-MRI, regardless of thrombus characteristics (Table 1).

CONCLUSIONS: CE-MRI provided the highest sensitivity and specificity for the diagnosis of LV thrombus when compared to TTE and TEE, and should be considered in the evaluation and management of patients at high risk of LV thrombus formation.

Table 1: Thrombus Characteristics

	Total n = 106	MRI detection n = 67	TTE detection n = 101	TEE detection n = 100
Any thrombus size	106	58/67 (87%)	27/101 (26%)	39/100 (39%)
Small (< 1cm)	36/106 (35%)	15/22 (68%)	3/33 (10%)	7/36 (19%)
Moderate (1-2 cm)	34/106 (32%)	24/26 (96%)	8/33 (24%)	13/31 (42%)
Large (>2 cm)	36/106 (34%)	19/20 (95%)	16/35 (46%)	19/33 (58%)
Location				
Apical location	75/106 (71%)	43/51 (84%)	18/71 (25%)	29/73 (40%)
Proximal location	31/106 (29%)	15/16 (94%)	9/30 (30%)	10/27 (37%)
Pathologic Characteristic				
Recent clot	16/76 (21%)	10/10 (100%)	2/16 (13%)	4/15 (27%)
Organizing clot	39/76 (51%)	24/27 (89%)	12/37 (32%)	15/36 (42%)
Chronic organizing clot	21/76 (28%)	10/10 (100%)	9/21 (43%0	12/20 (60%)

Circulation 2004;110(17):404(Suppl., abstract #1911).

Prevalence and Structural Risk Factors for Left Ventricular Thrombus in Patients with Systolic Dysfunction as Assessed by Cardiac MRI

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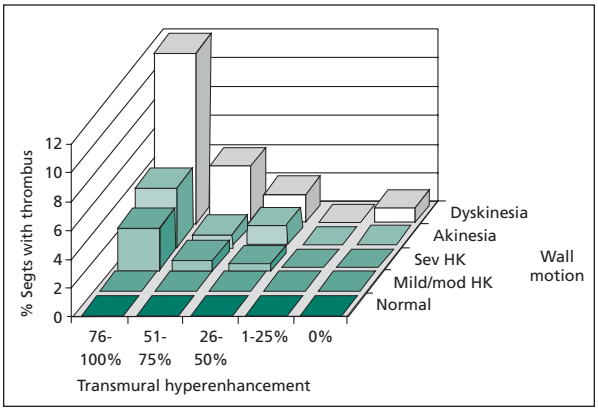
BACKGROUND: Delayed enhancement MRI (DE-MRI) offers tissue characterization that accurately identifies myocardial scarring (HE) and in small pilot studies has been shown to be superior to 2D echo for detecting left ventricular thrombus (LVT). We used DE-MRI to evaluate the prevalence and structural risk factors for LVT and to compare LVT detection with echo in a broad population of pts with systolic dysfunction.

METHODS: We prospectively enrolled consecutive pts referred for cardiac MRI with EF 45%. In a subgroup, echo was performed within 1 week of MRI. MRI and echo were scored for LVT blinded to the results of the other modality. Cine and DE-MRI were scored via a 17 segment model to quantify wall motion abnormalities (WMA) and HE.

RESULTS: 535 pts were studied (age 60 ± 15, 66% M, 61% HTN, 30% DM). 65% had CAD by clinical criteria. DE-MRI identified LVT in 42 pts (7.8%). The prevalence in CAD pts was 10.8% (n=37) and 2.7% (n=5) in non CAD pts (p=0.001). Among the subgroup with echo (n=232), 62% with LVT by DE-MRI were missed by echo and 48% were missed by cine MRI. 98% of LVT by DE-MRI were adjacent to myocardium with HE. In multivariate analysis including several clinical and imaging parameters, only severity of HE (RR 1.4, CI 1.2-1.5 p<0.0001) and WMA (RR 1.1, CI 1.0-1.3 p=0.02) were independent predictors of LVT. Figure illustrates the additive effects of HE and WMA on LVT prevalence on a segmental basis.

CONCLUSIONS: The prevalence of LVT by DE-MRI is dependent on the etiology of systolic dysfunction and includes a high proportion of pts missed by echo and cine MRI. Myocardial scar burden predicts LVT independent of the severity of contractile dysfunction and may be a useful index to determine thrombotic risk.



Circulation 2004;110(17):754(Suppl., abstract #3486).

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