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Cardiac Imaging

Detection of Left Ventricular Thrombus by Delayed-Enhancement Cardiovascular Magnetic Resonance

Prevalence and Markers in Patients With Systolic Dysfunction

Jonathan W. Weinsaft, MD,*† Han W. Kim, MD,*† Dipan J. Shah, MD,*§ Igor Klem, MD,*†
Anna Lisa Crowley, MD,*† Rhoda Brosnan, MD,*† Olga G. James, MD,*§ Manesh R. Patel, MD,*†
John Heitner, MD,*† Michele Parker, MS, RN,* Eric J. Velazquez, MD,†
Charles Steenbergen, MD, PHD,‡ Robert M. Judd, PHD,*† Raymond J. Kim, MD*†

Durham, North Carolina; and Brentwood, Tennessee

Objectives This study sought to assess the prevalence and markers of left ventricular (LV) thrombus among patients with systolic dysfunction.

Background Prior studies have yielded discordant findings regarding prevalence and markers of LV thrombus. Delayed-enhancement cardiovascular magnetic resonance (DE-CMR) identifies thrombus on the basis of tissue characteristics rather than just anatomical appearance and is potentially highly accurate.

Methods Prevalence of thrombus by DE-CMR was determined in 784 consecutive patients with systolic dysfunction (left ventricular ejection fraction [LVEF] <50%) imaged between July 2002 and July 2004. Patients were recruited from 2 separate institutions: a tertiary-care referral center and an outpatient clinic. Comparison to cine-cardiovascular magnetic resonance (CMR) was performed. Follow-up was undertaken for thrombus verification via pathology evaluation or documented embolic event within 6 months after CMR. Clinical and imaging parameters were assessed to determine risk factors for thrombus.

Results Among this at-risk population (age 60 ± 14 years; LVEF 32 ± 11%), DE-CMR detected thrombus in 7% (55 patients) and cine-CMR in 4.7% (37 patients, $p < 0.005$). Follow-up was consistent with DE-CMR as a better reference standard than cine-CMR, including 100% detection among 5 patients with thrombus verified by pathology (cine-CMR, 40% detection), and logistic regression analysis testing the contributions of DE-CMR and cine-CMR simultaneously, which showed that only the presence of thrombus by DE-CMR was associated with follow-up end points ($p < 0.005$). Cine-CMR generally missed small intracavitary and small or large mural thrombus. In addition to traditional indices such as low LVEF and ischemic cardiomyopathy, multivariable analysis showed that increased myocardial scarring, an additional parameter available from DE-CMR, was an independent risk factor for thrombus.

Conclusions In a broad cross section of patients with systolic dysfunction, thrombus prevalence was 7% by DE-CMR and included small intracavitary and small or large mural thrombus missed by cine-CMR. Prevalence increased with worse LVEF, ischemic etiology, and increased myocardial scarring. (J Am Coll Cardiol 2008;52:148–57)

Patients with heart failure are at increased risk for thromboembolic events that may result in major clinical sequelae. Left ventricular (LV) thrombus provides a substrate for events and a rationale for anticoagulation (1). However, prior echocardiography studies have yielded discordant results regarding thrombus prevalence. Among populations with similar degrees of systolic dysfunction, studies have reported over a 20-fold difference in prevalence, ranging from 2.1% to 50% (2–4). Moreover, when thrombus is identified, discordant findings have been reported concerning the risk of future embolic events (4–7). One potential reason for these disparate findings may relate to limitations of echocardiography, which has been the predominant modality used to identify LV thrombus. Prior echocardiography studies have reported significant interobserver variability in diagnosing LV thrombus (8). Others have shown

From the *Duke Cardiovascular Magnetic Resonance Center, †Department of Medicine, and the ‡Department of Pathology, Duke University Medical Center, Durham, North Carolina; and the §Nashville Cardiovascular Magnetic Resonance Institute, Brentwood, Tennessee. Supported by R01-HL64726 (Dr. Kim), R01-HL63268 (Dr. Judd), and a Doris Duke Clinical Scientist Development Award (Dr. Weinsaft). Drs. Kim and Judd are inventors of a U.S. patent on delayed-enhancement magnetic resonance imaging, which is owned by Northwestern University.

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that up to 46% of echocardiograms may be diagnostically inconclusive for thrombus (9). As the benefits of anticoagulation for treatment of thrombus are counterbalanced by hemorrhagic risk, patient management and outcome may be improved by a better understanding of the prevalence and risk factors for LV thrombus.

Cardiovascular magnetic resonance (CMR) provides high-resolution images of anatomy with improved reproducibility as compared with echocardiography (10). However, a simple anatomical approach may be relatively insensitive for thrombus because thrombus may be indistinguishable from surrounding myocardium (11). Delayed-enhancement cardiovascular magnetic resonance (DE-CMR) using gadolinium contrast has been well validated as a means of characterizing viable and infarcted myocardium on the basis of contrast uptake patterns (12). More recently, this technique has also shown promise as a sensitive method for detecting LV thrombus (13,14); DE-CMR differentiates thrombus from surrounding myocardium as thrombus is avascular and thus characterized by an absence of contrast uptake (13,14). In studies of selected groups, DE-CMR identified thrombus not detected by anatomical imaging using either cine-CMR or echocardiography (13,14). At present, however, DE-CMR has not been used to study thrombus in a general, unselected population at risk for thrombus, such as patients with systolic dysfunction. The aims of the current study were 3-fold: first, to assess the prevalence of thrombus using DE-CMR among a broad cross section of patients with systolic dysfunction; second, to compare DE-CMR to anatomical imaging using cine-CMR; and third, to determine predisposing risk factors for LV thrombus formation by evaluating numerous clinical and imaging parameters.

Methods

Population. The study population consisted of consecutive patients with systolic dysfunction who underwent cine- and DE-CMR during a single imaging session between July 2002 and July 2004. Patients were recruited from the Duke Cardiovascular Magnetic Resonance Center (Durham, North Carolina), a tertiary-care referral center, or the Nashville Cardiovascular Magnetic Resonance Institute (Brentwood, Tennessee), a clinical outpatient facility. Systolic dysfunction was defined as a left ventricular ejection fraction (LVEF) below 50% measured quantitatively on cine-CMR. Patients were referred to CMR most commonly for evaluation of myocardial viability, assessment of myocardial infarction, or evaluation of scar patterns in cases of suspected cardiomyopathy. Institutional review board approval was obtained at both participating sites; all patients provided written informed consent.

On the day of the CMR procedure, a complete medical history including cardiac risk factors, medication regimen, and information regarding prior coronary revascularization, myocardial infarction, and thromboembolic events, was obtained to assess potential predictors of thrombus. Additionally, clinical records were reviewed including prior X-ray coronary angiography results, and established criteria were used to classify the etiology of systolic dysfunction as ischemic or nonischemic: patients were considered to have ischemic cardiomyopathy if there was angiographically significant disease (≥70% stenosis of a major epicardial artery or ≥50% of the left main artery [15]), history of biomarker proven myocardial infarction, or evidence of ischemia on clinical stress testing (16). All other patients were classified as having nonischemic cardiomyopathy. The majority of patients (86%) had previously undergone coronary angiography.

Abbreviations and Acronyms

CMR = cardiovascular magnetic resonance
CVA = cerebrovascular accident
DE-CMR = delayed-enhancement cardiovascular magnetic resonance
LV = left ventricle/ventricular
LVEF = left ventricular ejection fraction
TI = inversion time
TIA = transient ischemic attack

Clinical follow-up and validation of imaging. Follow-up was performed prospectively in all patients to provide data regarding the choice of a truth standard for the diagnosis of LV thrombus. Specifically, all records were carefully reviewed in patients who had direct inspection and pathology evaluation of the left ventricle (i.e., patients who underwent heart transplantation, LV aneurysmectomy, or post-mortem necropsy) within 6 months after CMR without intervening events. Additionally, all specimens were re-examined thoroughly by a cardiovascular pathologist (C.S.). Follow-up was also performed for identification of clinical embolic events that were highly suggestive of the presence of LV thrombus. These events consisted of a documented cerebrovascular accident (CVA) or transient ischemic attack (TIA) that prompted the initial clinical workup or occurred within 6 months after CMR. A relatively short follow-up time of 6 months was chosen to increase the likelihood that clinical events were related to findings at the time of imaging. Clinical information was obtained via: 1) telephone interview with the patient, or, if deceased, with family members; 2) contact with the patient's physician; and 3) hospital records. Death was not considered evidence of LV thrombus unless directly linked to a cerebrovascular embolic event.

Image acquisition. MAGNETIC RESONANCE IMAGING. 1.5-T clinical scanners (Siemens Sonata, Siemens, Malvern, Pennsylvania) with phased-array coil systems were used. In all patients, CMR consisted of 2 components as previously described (17). Briefly, cine-CMR was performed for anatomical and functional assessment using a steady-state free-precession sequence (repetition time, 3.0 ms; echo time, 1.5 ms; in-plane spatial resolution, 1.7 × 1.4 mm; temporal resolution, 35 to 40 ms), and DE-CMR was performed for tissue characterization using a segmented inversion-recovery sequence (18) (in-plane spatial resolution, 1.8 × 1.3 mm; temporal resolution, 160 to 200 ms) 10 min after contrast administration (gadoverset-