Thrombosis and Prognosis Following ST-Elevation Myocardial Infarction

Left Ventricular Thrombus Assessment by Cardiac Magnetic Resonance

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Acute ST-segment-elevation myocardial infarction (STEMI) is estimated to occur in over 3 million patients each year.1 Left ventricular (LV) thrombus is a serious complication of STEMI, which has been attributed to blood stasis resulting from LV contractile dysfunction and altered geometry (aneurysm). Advances in STEMI management bear particular relevance to LV thrombus: improved coronary reperfusion has augmented myocardial salvage, resulting in improved LV function and remodeling. Newly adopted standard of care therapies, such as thienopyridines, inhibit platelet aggregation, thereby potentially decreasing risk for thrombus. However, despite widespread changes in post-STEMI care, limited data exists concerning LV thrombus in the current era. Given that LV thrombus provides a substrate for embolic events and a rationale for anticoagulation, better understanding of prevalence, predictors, and prognostic significance of post-STEMI LV thrombus is of substantial importance.

Beyond changes in clinical management, advances in noninvasive imaging provide a strong rationale for revisiting post-STEMI LV thrombus. Echocardiography (echo) has traditionally been used as the primary modality for evaluating STEMI patients because it is widely available, inexpensive, and supported by ample data demonstrating that echo-based quantification of LV structure and function stratifies post-STEMI prognosis.2,3 However, echo can be limited with respect to LV thrombus. Image quality can be compromised by near field artifacts that obscure the LV apex, a location in which thrombus is often suspected. More broadly, echo limitations may stem from the approach by which thrombus is diagnosed. Echo identifies thrombus based on morphology. This approach can be straightforward when thrombus is large or protuberant, but challenging when thrombus is small or flat (mural). Consistent with these concepts, echo studies have reported marked variability in thrombus prevalence and prognostic significance4,5 and reported substantial inter-reader variability concerning diagnosis of LV thrombus.6 Given that even small or mural thrombus provides an embolic substrate, improved imaging strategies for LV thrombus detection are warranted.

Cardiac magnetic resonance (CMR) enables thrombus to be identified based on tissue properties related to vascularity. Using the technique of delayed-enhancement (DE) CMR, which is commonly used to discern viable from infarcted myocardium based on gadolinium contrast distribution, thrombus can be identified by absence of contrast uptake. As DE-CMR identifies thrombus based on tissue characteristics rather than morphological appearance, it enables thrombus to be delineated from myocardium and blood pool irrespective of thrombus location or morphology. LV thrombus identification by DE-CMR has been validated based on pathology findings and clinical embolic events.7,8 Several studies have reported CMR to yield improved diagnostic performance versus echo for LV thrombus.7,9–12 Notably, DE-CMR has been shown to yield improved detection of LV thrombus compared with both contrast-echo and cine-CMR (which both provide excellent image quality), supporting the concept that limitations of these techniques are not modality-specific, but instead attributable to intrinsic features of imaging strategies that identify thrombus based on morphology rather than tissue characterization.10 CMR has been widely used to study LV thrombus in patients with heart failure or in heterogeneous cohorts,7,9–11 although uncertainty remains with respect to utility of CMR for LV thrombus in post-STEMI patients.

In this issue of Circulation: Cardiovascular Imaging, Pöss et al use CMR to assess prevalence, determinants, and prognostic significance of LV thrombus among a multicenter post-STEMI cohort.13 To do so, CMR was performed within 1 week post-STEMI among 738 patients undergoing primary angioplasty at 8 sites. CMR was analyzed by a central core laboratory blinded to patient characteristics. Clinical follow-up (with blinded event adjudication) was performed in a standardized manner for assessment of adverse outcomes, including embolic events. LV thrombus was present in 3.5% of patients; prevalence was increased 2-fold (7.1%) among patients with anterior MI. Regarding markers of thrombus, findings confirm a strong association with markers of myocyte injury, as evidenced by larger LV infarct size, decreased myocardial salvage, and increased frequency of microvascular obstruction among patients with thrombus (all \(P \leq 0.01\)). Consistent with this, patients with thrombus had lower average LV ejection fraction (EF) and larger LV chamber volumes than did those without thrombus (both \(P < 0.001\)). Regarding outcomes, LV thrombus was independently associated with a 1 year combined...
end point of death, reinfarction, or heart failure (hazard ratio = 2.73 [95% confidence interval 1.11–6.73], P = 0.03) even after controlling for infarct size, angiographic, and clinical variables. However, incremental prognostic value of thrombus was minimal, as evidenced by nonsignificant increases in model fitting (c-index) when LV thrombus was analyzed together with infarct size and microvascular obstruction. Moreover, thrombus-associated adverse events more strongly associated with heart failure (P < 0.001), rather than mortality (P = 0.11) or reinfarction (P = 0.63). Despite the association between thrombus and overall adverse outcomes, embolic events did not significantly differ between patients with and without LV thrombus (3.8% [1/26] versus 0.7% [5/712], P = 0.12).

Taken together, these data provide clear evidence that despite advances in coronary reperfusion, LV thrombus continues to occur in a small but substantial number of post-STEMI patients, especially in individuals with anterior wall infarction. Data are especially remarkable in context of the fact that all study participants presented within 12 hours of symptom onset underwent rapid triage (median door to balloon time 30 minutes [interquartile range 22–42]) and were treated via primary angioplasty with adjunctive glycoprotein IIb/IIIa receptor antagonists. Regarding structural markers of thrombus, it is important to note that despite lower overall LVEF among patients with thrombus, median LVEF in this group was 36% (interquartile range 31%–47%), supporting the notion that thrombus can occur even in the absence of advanced global LV dysfunction. Thrombus location, apical contraction, and aneurysmal dilation were not specified in this study. However, given the fact that LV thrombus tends to localize to the apex, it is tempting to speculate that apical contractile abnormalities or aneurysm would be more strongly associated with thrombus than would global parameters of LV function, thereby providing a more effective means of identifying (via echo or other conventional tests) those patients in whom LV thrombus is most likely. Consistent with this concept, recent data by our group has shown echo-evidenced apical dysfunction to perform superiorly to LVEF for identifying post-STEMI patients with DE-CMR–evidenced thrombus.

Although the current study provides multiple important insights concerning post-STEMI LV thrombus, several issues should be noted. Prevalence of LV thrombus in this study (3.5%) was substantially lower than that reported in 2 recent CMR studies, including multicenter data by Delewi et al (8.8%) and single center data by our group (8%). It is possible that thrombus prevalence in the current study may be under-representative of that in post-STEMI patients undergoing routine care, a setting in which symptom duration and door to balloon time can vary. All patients in this cohort underwent rapid coronary reperfusion, thereby minimizing infarct size, contractile dysfunction, and aneurysm—known predictors of thrombus formation. Moreover, although prior studies using serial echo have suggested that maximum incidence of thrombus occurs at least 2 weeks post STEMI, CMR was performed within 1 week post STEMI (median 3 days)—25% of participants underwent CMR within 2 days of STEMI. In this context, prevalence of LV thrombus in this study would not be expected to reflect patients in whom LV thrombus develops at later time points (because of persistent contractile dysfunction and blood stasis). It is also important to note that this study focused exclusively on CMR. Thus, it is uncertain as to whether additive utility of CMR over less costly techniques, such as contrast echo (as has been shown in heterogeneous cohorts), extends to post-STEMI patients—a group in which LV systolic dysfunction and chamber geometry may be relatively preserved.

Beyond prevalence and predictors, one key study observation relates to the link between thrombus and prognosis. The reported association between thrombus and adverse events and is certainly novel, representing a new finding pertinent to post-STEMI management. What remains uncertain is the actual pathophysiological mechanism explaining this clinical observation. It is not straightforward as to how thrombus itself would directly augment heart failure–related adverse events, as was observed in this study. One possibility is that LV thrombus is a marker for other indices that impair cardiac performance. For example, patients with thrombus may have particular patterns of regional LV contractile dysfunction or more advanced diastolic dysfunction (secondary to MI-related LV noncompliance), each of which would contribute to heart failure symptoms. LV thrombus was the primary measure of cardiac performance analyzed for this study. One notion that cannot be fully excluded is that the observed link between thrombus and adverse events was because of unexamined confounding variables or other factors, for example, multivariate modeling used TIMI risk score (an aggregate variable that includes anterior MI together with several other factors) rather than anterior MI alone (a solitary variable that has been linked to both thrombus and prognosis). Regardless of mechanism, current data support the concept that patients with post-STEMI thrombus represent a high-risk cohort warranting close monitoring for heart failure and other adverse events.

In summary, findings by Pöss et al provide important groundwork for further investigation because LV thrombus continues to occur in STEMI patients receiving state-of-the-art care, in particular among patients with anterior infarction. In addition, Pöss et al show that LV thrombus is linked to adverse clinical events; although the exact mechanism for this association remains to be clarified, one can speculate that LV thrombus is likely a generalized marker of impaired cardiac performance. Finally, observed absence of an association between stroke and LV thrombus should be taken in the context of low stroke rates in this population, perhaps influenced by uniform use of dual antiplatelet therapy and IIb/IIIa inhibitors, as well as anticoagulant therapy for patients with LV thrombus. Further research is ongoing to elucidate mechanistic links between thrombus and adverse prognosis, as well as to test whether anticoagulant treatment of CMR-evidenced thrombus—or prophylactic therapy in individuals with high-risk markers for thrombus— is effective for improvement of post-STEMI outcomes.

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References


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