Left ventricular thrombus in acute myocardial infarction

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Introduction

Catastrophic morbidity or mortality from cardiogenic cerebral embolism occurs in approximately 2000 cases each year in the Netherlands. Left ventricular thrombus after myocardial infarction is a source of such emboli which is largely preventable by systemic anticoagulation. However, anticoagulants induce a bleeding risk and must be given only when the risk of embolism is increased. Two-dimensional echocardiography has played a pivotal role in defining the natural history of thrombus formation in patients with acute myocardial infarction. The role of echocardiography has recently been expanded by use of Doppler echocardiography since it has been shown that study of intraventricular flow patterns provides a unique and pathophysiologically rational means of estimating the risk of thrombus formation with potentially important implications for the management of anticoagulant drugs.

This review will first discuss the diagnosis left ventricular thrombus. Second, the natural history of left ventricular thrombus will be outlined, including the prediction of thrombosis risk by clinical markers and two-dimensional or Doppler echocardiography. Third, the prognostic importance of left ventricular thrombus will be outlined. Finally, the practical strategies to prevent embolic complications of myocardial infarction will be reviewed.

Diagnosis of left ventricular thrombus

Angiocardiography

The sensitivity of left ventriculography for the detection of thrombus is unacceptably low (26–31%) Further-. more, cardiac catheterization has the potential for precipitating emboli by manipulation of the thrombus. Coronary angiography showed an association of ventricular thrombus with subtotal or complete occlusion of the left anterior descending artery, in conjunction with increased ventricular volumes, filling pressures and shape change, i.e. ventricular remodelling.

Indium-III platelet scanning

This technique detects haematologically active thrombi with a sensitivity of 71% and a specificity of 100%, compared with aneurysmectomy or autopsy. Operative material had high indium activity at the surface of thrombi and low activity in adjacent tissues. Although its accuracy is acceptable, platelet scintigraphy is not applied widely, possibly because it is time consuming and expensive, not universally available and involves radiation exposure.

Echocardiography

Echocardiography enables reliable and non-invasive detection of intracardiac masses. Two-dimensional echocardiography from the apical window has a sensitivity and specificity of approximately 90% compared with aneurysmectomy or autopsy. Specificity should be optimized by adherence to strict echocardiographic criteria. Thrombus is universally associated with abnormal motion of the underlying myocardium and has margins distinct both from the endocardium and the ventricular lumen. Presence of mobile parts as well as variations on serial study are also helpful. False-positive studies result from either technical artifact (reverberations, side lobe or near-field artifacts) or failure to differentiate thrombus from other cardiac structures, such as muscle trabeculation, chordal structures and tangentially-cut left ventricular wall. Varying gain settings and depth of field, as well as using transducers with different carrier frequencies in multiple positions and orientations, are helpful to minimize such false-positive studies.
evidence of pump failure, severe apical asynergy (i.e. Table I). Most studies found an association of 28-32 thrombus with increased enzymatic infarct size, clinical pared to 0-5% in non-anterior myocardial infarctions anterior wall infarction, with a frequency of 39%, com- echocardiographic studies in a total of 2018 patients, the formation. Thrombus was found almost exclusively in acute myocardial infarction is 27% (Table 1). reported frequency of left ventricular thrombus after healed infarction, larger pathological infarct size and association with anteriorly located, acute (as opposed to acute or healed myocardial infarction'). Thrombi were defined at post mortem. In studies from the beginning of this century the frequency of left ventricular thrombus during life, its natural history was frequency in a more recent study of 327 autopsies of [23-24], comparable to the 33% this time course has been ascribed to concomitant inflammatory endocardial changes and a systemic hypercoagulable state in early myocardial infarction[41]. Formation of thrombi during long-term follow-up is rare and associated with recur- ent infarction, heart failure during the index admission, aneurysm formation, decreased left ventricular ejection fraction and deterioration of ventricular function during follow-up[27].

**Prognosis in left ventricular thrombus**

Mortality is increased in patients with left ventricular thrombus, especially when these develop within 48 h[34,36,37] (Fig. 1). In contrast, one study found a mortality of 34% in patients without thrombus, com- pared to 9% in patients with thrombus (29%). These authors postulated that splinting of the infarcted segment by thrombus prevented remodelling and dilatation. No other investigation found a survival benefit of left ventricular thrombus.

Although many of the factors associated with thrombus formation decrease survival, none of the prognostic studies corrected for these confounders. The independent contribution of thrombus to mortality (i.e. by fatal embolic complications) is therefore unknown. Nevertheless, in clinical practice the presence of thrombus marks a dubious prognosis.

**Risk of embolism due to left ventricular thrombosis**

The frequency of arterial embolic events was 18% in the pooled data of 921 patients with left ventricular thrombus, compared to 2% in patients without thrombus[27-29,31-40,42]. The risk of embolism is not only dependent on the presence of thrombus but also on its morphology, such as mobility or protrusion into the ventricular lumen. Approximately 55% of mobile thrombi will embolize, compared to 10% of non-mobile thrombi[32,33,42-44]. Similarly, the embolic risk of pro- truding thrombi was estimated at 45%, compared to a 7% incidence in flat thrombi[32,33,42-44]. Of note[35], changes in thrombus shape occurred in 41% (15/38 protruding thrombi became mural, and 9/21 mural thrombi became protruding) and changes in mobility occurred in 30% (mobility disappeared in 5/8 and appeared in 12/51) in one study following patients not on platelet inhibitors or anticoagulants. Changes were found up to more than 1 year after the first detection. A much lower variability was found in another study[45] where changes in thrombus morphology occurred in 16% of 60 thrombi and changes in mobility in 10%.

**Table 1 Summary of major studies of left ventricular thrombosis frequency in acute myocardial infarction**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Anterior MI with LVT (%)</th>
<th>Inferior MI with LVT (%)</th>
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<td>40</td>
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<td>—</td>
<td>49</td>
</tr>
<tr>
<td>Total</td>
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MI=myocardial infarction, LVT=left ventricular thrombus.

**Magnetic resonance imaging**

Magnetic resonance imaging can detect ventricular thrombus[19-22]. The widespread availability of echocardiography, with its advantages in terms of portability and examination times, has relegated magnetic resonance imaging to a supporting role for this indica- tion, at least at present.

**Natural history of left ventricular thrombus**

Before the availability of techniques to diagnose left ventricular thrombus during life, its natural history was defined at post mortem. In studies from the beginning of this century the frequency of left ventricular thrombus was approximately 30%/23,24] comparable to the 33% frequency in a more recent study of 327 autopsies of acute or healed myocardial infarction[25]. Thrombi were noted most often at the apex of the left ventricle, in association with anteriorly located, acute (as opposed to healed) infarction, larger pathological infarct size and clinical evidence of congestive heart failure.

Combining the results of the most important echocardiographic studies in a total of 2018 patients, the reported frequency of left ventricular thrombus after acute myocardial infarction is 27% (Table 1).

Several factors are associated with thrombus formation. Thrombus was found almost exclusively in anterior wall infarction, with a frequency of 39%, com- pared to 0-5% in non-anterior myocardial infarctions (Table 1)[17,28-32]. Most studies found an association of thrombus with increased enzymatic infarct size, clinical evidence of pump failure, severe apical asynergy (i.e. presence of either akinesis or dyskinesia), increased left ventricular volumes and decreased global left ventricular function[17,26-29,31,34,36,37,39,40].

Most thrombi (>75%) develop in the first week after infarction[28,35-37]. This time course has been ascribed to concomitant inflammatory endocardial changes and a systemic hypercoagulable state in early myocardial infarction[41]. Formation of thrombi during long-term follow-up is rare and associated with recur- ent infarction, heart failure during the index admission, aneurysm formation, decreased left ventricular ejection fraction and deterioration of ventricular function during follow-up[27].

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Modification of embolic risk by anticoagulants

Administration of antiplatelet agents or anticoagulant drugs have both been shown to considerably decrease the number of cardiac and other vascular events after myocardial infarction. Although only limited data are available regarding their relative efficacy, one study comparing aspirin to oral anticoagulants found no significant difference in protective effect. Indiscriminate administration of anticoagulants to all patients after myocardial infarction does not seem advisable. For instance, it can be calculated that 185 patients were anticoagulated during 1 year to prevent one cerebral infarct in the recently conducted placebo controlled ASPECT trial. This benefit was obtained at a cost of almost two intracerebral or major extracerebral bleedings induced by the anticoagulants. This unfavourable risk-to-benefit ratio is explained by the exclusion of patients at highest risk of left ventricular thrombus from this trial.

Thus, at the state of our present knowledge, aspirin appears to be the drug of first choice for the secondary prevention of cardiovascular events after myocardial infarction, with oral anticoagulants reserved for those patients appearing at increased risk of cardiogenic embolism. For such an approach, accurate risk assessment of embolic complications after myocardial infarction is essential. In the pooled results of echocardiographic studies in which oral anticoagulants were given to patients with left ventricular thrombus, the relative risk of embolism in anticoagulant-treated patients may be estimated at 0-3 (95% confidence interval, range 0-1-0-5). Thus, in patients with echocardiographic evidence of left ventricular thrombus, anticoagulants reduce the risk of embolic complications by 70%.

Modification of left ventricular thrombus incidence by anticoagulants

Prevention of thrombus formation by oral anticoagulants

Pooling two studies, patients with anterior Q-wave infarction randomized within 12 h of admission to heparin followed by warfarin had an incidence of thrombus of 11%, compared to 29% in the controls, a relative risk of 0-4 (95% confidence interval, range 0-1-0-9). Although heparin followed by oral anticoagulants is effective, the 95% confidence interval is wide and the size of the effect cannot be accurately estimated.

Established thrombus

In patients with established thrombus randomized to oral anticoagulants at discharge or several weeks thereafter, 65% showed thrombus resolution during 1 to 2 years follow-up, compared to 11% of the placebo-treated controls. The relative risk of thrombus persisting...
under anticoagulants was 0.4 (95% confidence interval, range 0.2-0.6). In patients with persistent thrombi, thrombus thickness progressively decreased in the anticoagulated group but not in the controls\[^{31,32}\].

**Platelet inhibitors**

Two studies of the effect of antiplatelet drugs found no effect on echocardiographic thrombus size, and a varying effect on platelet deposition as assessed by indium-III scanning\[^{53,54}\]. Thus, these drugs appear not be effective in this regard.

**Reperfusion therapy**

Ventricular function is preserved by thrombolysis or direct angioplasty\[^{55-59}\]. This decreases the incidence of thrombus after myocardial infarction\[^{60-66}\]. The relation between ventricular function and thrombosis risk is, however, unchanged after thrombolytic therapy\[^{60,61}\], suggesting that the decreased incidence of thrombus is not due to a direct lytic effect but results from improved global ventricular function and less severe apical asynergy. Myocardial infarction cannot be fully prevented by thrombolytics due to pre-hospital time delays and failed reperfusion in some patients. Therefore, left ventricular thrombosis will continue to be a challenge in the thrombolytic era.

**Stratification of left ventricular thrombus risk based on left ventricular flow pattern**

To select patients for anticoagulant prophylaxis, empirical algorithms based on, for example enzymatic infarct size, global left ventricular function and presence of apical akinesis or dyskinesia, have been proposed\[^{61,67,68}\].

Abnormal flow is one of the key determinants of thrombosis and can be investigated by Doppler echocardiography. Abnormal spatial patterns of inflow in impaired ventricles have been characterized both in experimental and clinical studies\[^{3,69-77}\]. In a computer model we have shown that abnormal flow causes apical stasis. The observation that abnormal flow precedes thrombus formation lends further support to the pathogenetic significance of abnormal flow patterns as detected by Doppler echocardiography\[^{3,44}\]. Doppler-flow had superior predictive accuracy compared to conventional predictors of thrombus risk and was the only independent correlate of thrombosis on stepwise logistic regression\[^{41}\].

The incidence of thrombus is negligible in patients with normal flow\[^{3,41}\] in whom anticoagulants can safely be withheld. Although the risk of left ventricular thrombus in patients with abnormal flow is clearly increased (63%), the best approach to their management has not been formally tested. It appears prudent to anticoagulate patients with abnormal flow and without contraindications to anticoagulants, in view of the potentially devastating nature of embolic complications.

**Treatment of ventricular thrombus**

In patients presenting left ventricular thrombus, three management options to prevent embolism are available. In determining the optimal treatment strategy, the perceived risk of embolism as estimated by two-dimensional echocardiography following the criteria outlined above must be used as a guide.

First, a course of intravenous heparin followed by oral anticoagulants is appropriate\[^{78}\]. The response to treatment, i.e. size and shape of the thrombus, should be controlled by frequent echocardiographic examinations. Although this has not been described for this indication in the literature, concomitant platelet inhibition by aspirin should be considered\[^{41}\].

Thrombolysis of ventricular thrombus has been tried but increased mobility of apical clot has been documented\[^{27}\], together with sometimes fatal embolic phenomena\[^{27,79}\]. Thus, the safety of this approach appears questionable.

Finally, surgical removal may be indicated in patients sustaining embolic events, especially when recurrent. Prophylactic surgery has been described when thrombus morphology suggested a high risk of embolism\[^{80,81}\].

**Conclusion**

The embolic risk of left ventricular thrombus after myocardial infarction will continue to be present despite the success of thrombolysis. In selecting patients for anticoagulant prophylaxis, Doppler examination of intraventricular flow appears a promising alternative to the conventional clinical and two-dimensional echocardiographic indicators.

**References**


