**Editorial Comment**

**Left Ventricular Thrombus and Stroke After Myocardial Infarction: Toward Prevention or Perplexity?**

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Cardiogenic cerebral thromboembolism is responsible for about 15% of all cases of ischemic stroke—not as many as attributed to thrombotic or embolic complications of cerebrovascular disease, but still the cause of disabling stroke in >75,000 Americans annually (1). As we recently reviewed (2), cardiac diseases underlying these events involve atrial fibrillation in about half the cases and valvular heart disease or left ventricular mural thrombus in the remainder (1,3). Sixty percent of emboli of left ventricular origin are a consequence of acute myocardial infarction (1,4), accounting for 15,000 to 25,000 embolic strokes each year. Several studies suggest that the risk is highest in the first 1 to 3 months after infarction and perhaps even greater in the first 10 days for patients with a large anterior infarct who have a 30% to 40% chance of developing ventricular thrombus and about a 5% risk of embolism (4,5). In addition, those who survive become part of a larger population of patients with chronic ventricular dysfunction in whom the potential for embolism is persistent (6).

**Left ventricular thrombus in acute myocardial infarction.** In patients with myocardial infarction, >90% of ventricular thrombi occur when the anterior wall becomes hypokinetic or akinetic, enlarging the apical zone of intraventricular stasis. Inflammatory changes at the endocardial surface and enhanced thrombogenicity are additional reasons thromboembolism occurs most frequently within the first 10 days of a coronary event, although the tendency to thrombus formation may persist during the first 1 to 3 months. Infarct size seems directly related to thromboembolic risk, and the incidence of left ventricular thrombus during the early postinfarction period exceeds 50% in those with anteropical infarction, producing peak serum creatine kinase concentrations >2,000 U/liter (4,5).

**Pathophysiology of cardiogenic thromboembolism.** The pathophysiology involves a balance between the factors favoring thrombus formation within the ventricular cavity—endocardial injury, regional circulatory stasis and activation of the intrinsic coagulation system—and the dynamic forces of the circulation that must project thrombotic material out of the ventricular cavity and into the systemic circulation to produce clinical morbidity. For example, when left ventricular aneurysm is present remote from myocardial infarction, mural thrombus formation is frequent, but the embolic risk is low. On the other hand, embolism seems to occur most frequently in patients with echocardiographically evident mobility of the thrombotic mass within the ventricular chamber (5,7,8). Overall, the published data suggest that cerebral embolism occurs clinically in about 10% of those with echocardiographically evident mural thrombus within the first 3 months after myocardial infarction, although it is often difficult to classify acute ischemic events as embolic in patients with advanced atherosclerotic disease.

**Treatment.** The effect of antithrombotic medication on the occurrence and natural history of left ventricular thromboembolism is difficult to surmise. In the past 5 years, several studies (9-11) involving patients with acute myocardial infarction have addressed the relation between cerebral embolism and left ventricular thrombus detected by echocardiography. Although no clinical trial has had sufficient sample size to detect significant differences in embolism, in aggregate thrombus formation has been reduced by >50% with anticoagulant therapy (12-14). Other trials involving patients with acute inferior and anterior myocardial infarction demonstrated that initial treatment with heparin followed by administration of an oral anticoagulant agent for a few months in relatively low doses reduced the occurrence of cerebral embolism to 1% from the 3% rate obtained with no anticoagulation (15). A recently reported randomized prospective trial (16), involving more than 200 patients with a large anterior infarct, found that thrombus was detected in 11% of the group given the higher heparin dose of 12,500 U every 12 h compared with 32% of those receiving the lower dose of 5,000 U every 12 h during the first 10 days. The impact of adding platelet inhibitor medication to an anticoagulant agent has not been evaluated in a large scale study (17).

**Present study.** In this issue of the Journal, Nihoyannopoulos et al. (18) offer data that challenge several basic assumptions regarding left ventricular mural thrombus formation after acute myocardial infarction. Because the prognosis for survival was better in patients with evidence of thrombus formation and the risk of stroke was no greater...
than in those without thrombus, the authors conclude that such thrombi may offer a protective effect and that antithrombotic medication may not be needed in such patients.

Three aspects of the report (18) warrant particular comment. First, each of the patients received antithrombotic medication in the form of heparin subcutaneously plus aspirin and dipyridamole orally; one cannot be sure what impact this intervention may have had on the natural history of thromboembolic events. Second, early in-hospital mortality was greater in patients without a thrombus than in those in whom a thrombus occurred, leading the authors to suggest that the mural thrombus might offer mechanical support to infarcted myocardium and protect against rupture. Although this hypothesis is intriguing, it may take about a week for thrombus to be detectable by standard transthoracic echocardiography. In the study by Nihoyannopoulos et al. (18), 5 (42%) of 12 early deaths occurred within 3 days of admission, yet a detectable thrombotic mass did not usually develop before the 6th day. An alternative hypothesis, therefore, is that patients at highest risk may not have survived long enough for ventricular thrombus to form (19).

The third aspect is that a clear-cut stroke occurred in only one patient before hospital discharge, and this patient had an inferior myocardial infarction without evident intraventricular thrombus. Neurologic symptoms in 11% of the other patients were transient and difficult to interpret, but no infarct was apparent on computed tomographic scans of the brain in these patients.

After hospital discharge, only one definite stroke occurred in a patient without thrombus. Although thrombus remained echocardiographically apparent 1 year after myocardial infarction in 38% of those patients in whom the diagnosis was initially made, and 24% still had evidence of thrombus after 2 years, it appears that no early or late embolic events occurred in these patients.

The implied benignity of the echocardiographic finding of left ventricular thrombus formation after myocardial infarction in this study may reflect the limited number of cases of large anterior infarction studied, because only two or three embolic events would be expected to occur in a clinical sample of this size. Furthermore, some cases of cerebral embolism may involve transient cerebral ischemia without clinical or tomographic evidence of infarction, perhaps taking a cumulative rather than an abrupt toll in terms of brain function, and these events may not be detected without careful neurologic observation (3).

Implications. The best approach to prevention of embolism in patients with acute myocardial infarction cannot yet be defined on the basis of sound data, but it seems reasonable to administer heparin to those with a large anterior infarct during the early phase (15). Among the many questions left unanswered is whether to perform regularly investigations like echocardiography to detect left ventricular thrombus. Other considerations are how long to continue prophylactic anticoagulant medication in patients without thrombus formation and when to withdraw anticoagulant medication when thrombus is identified—at the time of the patient’s discharge from the hospital or after 3 months? Another issue is whether thrombolytic therapy will, in fact, reduce the likelihood of developing ventricular thrombus.

In addition to the problem of left ventricular thromboembolism, patients with myocardial infarction present a complex situation in which antithrombotic therapy may have implications for the prevention of future coronary events. The best approach for the prevention of both left ventricular thrombus and complications of underlying coronary atherosclerotic disease remains to be defined on the basis of a prospective clinical trial. The advocacy of “masterly inactivity” by Nihoyannopoulos et al. (18) seems premature.

References


