MAYO CLINIC

ORIGINAL ARTICLE

Anticoagulation in Ischemic Left Ventricular Aneurysm

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Abstract

Objective: To evaluate the role of systemic anticoagulation using warfarin in patients with post–myocardial infarction left ventricular (LV) aneurysm formation with or without definite LV thrombus formation.

Patients and Methods: This study included 648 patients with post–myocardial infarction LV aneurysm formation diagnosed retrospectively by 2-dimensional echocardiography from December 1, 1994, to February 29, 2012. Of these 648 patients, 106 patients received warfarin and 542 patients did not. We studied a composite of death, nonfatal myocardial infarction, cerebrovascular accident, and systemic embolization as the primary outcome and a composite of cerebrovascular accident and systemic embolization as the secondary outcome by using propensity score–adjusted multiple Cox proportional hazards regression analysis.

Results: In patients with LV aneurysm, LV thrombus was observed in 89 patients (13.7%) and it was associated with a higher incidence of adverse secondary events (hazard ratio [HR], 3.63; 95% CI, 1.12-11.8; P=.03) in unadjusted analysis. However, in adjusted analysis, anticoagulation did not predict either a better or a worse outcome for primary outcomes (HR, 1.05; 95% CI, 0.67-1.64; P=.84) or for secondary outcomes (HR, 1.52; 95% CI, 0.670-3.46; P=.31). The benefit of anticoagulation was also not established in patients with LV thrombus (HR, 1.38; 95% CI, 0.32-5.97; P=.66).

Conclusion: In patients with ischemic LV aneurysms, oral anticoagulation therapy with warfarin may not be effective enough to reduce cardiac and cerebrovascular events including systemic embolism. Further studies are needed to confirm this finding.

 ■ Mayo Clin Proc. 2015;90(4):441-449

There is controversy surrounding the best management of patients with post–myocardial left ventricular aneurysm (LVA) formation and left ventricular (LV) thrombus formation, specifically regarding whether anticoagulation therapy is beneficial, and if so when does it need to be initiated and for how long. Anticoagulation therapy is no longer routinely recommended for patients with reduced LV ejection fraction if the patients do not have another thromboembolic risk factor such as atrial fibrillation, a previous thromboembolic event, or a cardioembolic source.[1] According to previous reports, about a third of postinfarct LVA cases are associated with systemic thromboembolism without systemic anticoagulation in their natural course.[2,3] It is estimated that about 26% to 68% of post–myocardial infarction (MI) LVAs were accompanied by LV thrombus, a possible cardioembolic source.[3-6] However, there is a controversy as to whether postinfarct LVA should be considered as a cardioembolic source that would require therapeutic anticoagulation. Although the 2013 American College of Cardiology Foundation/American Heart Association ST-segment elevation myocardial infarction guidelines state that anticoagulation with a vitamin K antagonist may be considered in anteroapical akinesis or dyskinesis, there have been few clinical outcome studies to prove the benefits of anticoagulation treatment in patients with documented ischemic LVA.[7] Hence, we tested the hypothesis that anticoagulation using warfarin was beneficial in patients after MI in an observational study of patients with LVA formation.

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PATIENTS AND METHODS

Study Design and Patients

This was a single-center retrospective study. We reviewed the database of 2-dimensional transthoracic echocardiographs acquired at Samsung Medical Center, Seoul, Korea, from December 1, 1994, to February 29, 2012, and identified patients with 1 or more aneurysmal segments by using a 17-segment model in echocardiography.[8] *Aneurysm* was defined as a thin-walled bulging LV contour during both diastole and systole.[9] Among these, only patients with post-MI LVA were included in our study. *Ischemic LVA* was defined to be definite with previously diagnosed MI or at the time of diagnosis of LVA. If we could not ascertain the previous MI, hypokinesia or akinesia in LV segments adjacent to LVA without global hypokinesia was considered a sign of probable ischemic etiology. Exclusion criteria were as follows: (1) LV ballooning syndrome; (2) burnout stage of hypertrophic cardiomyopathy; (3) infiltrative cardiomyopathy including amyloidosis or sarcoidosis; (4) treated or untreated congenital heart disease; (5) previously diagnosed dilated cardiomyopathy; or (6) previous valve replacement surgery due to substantial valvular disease.

Laboratory Data

Two-dimensional echocardiography was performed according to the guidelines of the American Society of Echocardiography. Basically, LV ejection fraction in echocardiography was attained by using a biplane modified Simpson's method.[8] In the limited cases having a poor echo window, visual estimation of the ejection fraction was allowed. The presence of LV thrombus was determined by multiple views in echocardiography in which LVA was first identified. Since 2009, if the presence of LV thrombus is not conclusive, contrast echocardiography has also been performed with SonoVue (Bracco Imaging S.p.A.) or Definity (Lantheus Medical Imaging) to confirm the presence of LV thrombus.[10] The level of N-terminal prohormone of brain natriuretic peptide (NT-proBNP) at the time of diagnosis of LVA was analyzed in a portion of patients because the test was unavailable in the early period of our study. The data of the patients with chronic kidney disease (serum creatinine >2.0 mg/dL [to convert to mmol/L, multiply by 0.0259] or dialysis) were excluded in the analysis of NT-proBNP levels because of its impaired excretion in renal dysfunction. Consequently, NT-proBNP levels of 349 of the 648 patients were available.

Primary and Secondary Outcomes

The primary outcome in this study was a composite of cardiac and cerebrovascular events (all-cause death, nonfatal MI, cerebrovascular accident [CVA], and systemic embolization). Cerebrovascular accident included stroke and transient ischemic attack. Systemic embolization included acute limb ischemia, renal infarction, splenic infarction, and mesenteric infarction. The secondary outcome was a composite of CVA and systemic embolization. We followed the included patients to June 2013, and all included patients were followed for more than a year after the first detection of LVA. The median follow-up duration was 38.7 months (interquartile range, 20.2-71.0 months).

This retrospective study was approved by our institutional review board (#2012-12-047), and informed consent was waived for the retrospective study.

Statistical Analyses

Data are expressed as frequencies, means ± SDs, or median values with interquartile ranges (25th-75th percentiles), where appropriate. Categorical variables were compared using the chi-square test. Continuous variables were compared using the Student *t* test if the variables were normally distributed or the Mann-Whitney test if they were not. Normal distribution was verified using the Kolmogorov-Smirnov test. Unadjusted event-free survivals according to anticoagulation status were evaluated using Kaplan-Meier curves and log-rank tests. The estimated incidence of events at a specific point in time was calculated by using estimates and the *z* score obtained from the Kaplan-Meier curve. To control selection bias in allocating the patients to anticoagulation therapy, a covariate adjustment of the propensity score was executed using multiple Cox proportional hazards regression models. The propensity score was calculated as a predicted probability by using a logistic regression model based on the following

Mayo Clin Proc. ■ April 2015;90(4):441-449 ■ http://dx.doi.org/10.1016/j.mayocp.2014.12.025
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