

Left Ventricular Thrombus and Dilated Cardiomyopathy: Role of Anticoagulation in Prevention of Thromboembolic Events

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A. Study Purpose and Rationale

Recent literature has reported increased thromboembolic events in patients with dilated cardiomyopathy. In particular, a study by Fuster et al. described an incidence of 18%. Recent analyses of larger studies such as the Vasodilators in Heart Failure (V-HeFT) study and Studies of Left Ventricular Dysfunction (SOLVD) have shown rates of 2.7/100 patient years and 2.4/100 patient years respectively. For the dilated cardiomyopathy population, there is an increased risk of developing an intracardiac thrombus secondary to stasis of blood. These thrombi are thought to predispose to thromboembolic events such as stroke and peripheral artery occlusion. In clinical practice, a majority of patients with intracardiac thrombi are anticoagulated with systemic agents such as heparin or coumadin to prevent such events. However, studies regarding the effectiveness of this clinical practice have not been conclusive. A study by Gottdiener et al. showed no significant increase in systemic emboli in patients with a known left ventricular thrombus. On the other hand, while other studies such as those by Katz et al and Falk et al. showed an increased incidence of embolic events in patient with a thrombus, the patient populations were too small to draw solid conclusions. Furthermore, these studies also failed to investigate the effectiveness of anticoagulation. A recent attempt at a retrospective analysis by Sharma et al likewise had too few patients to draw significant conclusions. The purpose of this study is to investigate the incidence of thromboembolic events in patients with dilated cardiomyopathy and a left ventricular thrombus. Furthermore, we will attempt to identify risk factors for embolic events and the protective role of anticoagulation and/or aspirin and/or clopidogrel therapy. Because Columbia Presbyterian Medical Center is a tertiary referral center for patients with heart failure, we expect to have records on a significantly larger population than previously studied.

B. Study Design and Statistical Analysis

Because of physician reluctance to randomize patients with a left ventricular thrombus to placebo, a prospective randomized design would be difficult to implement. Thus, the design of this study will be a retrospective cohort analysis. Using the Data Warehouse service provided by the WebCIS database, we will attain records on all patients satisfying inclusion and exclusion criteria from January 1997 until the present. Inclusion criteria will be a history of chronic dilated cardiomyopathy as defined by clinical history and echocardiographic findings of decreased ejection fraction or increased left ventricular end-diastolic dimension. Exclusion criteria will include a history of atrial fibrillation, previous thromboembolic event, chronic coumadin use, prosthetic valve, acute myocardial infarction within six months, previous thrombus on echocardiogram. All eligible patients must also have available records for 24 months of follow-up.

Based on an approximate overall incidence of thromboembolic events of 15% in patients with a thrombus and 6% in patients without a thrombus, for a power of 80%, with testing at $p=0.05$, for a chi-square analysis, approximately 200 patients will be needed in each study group. Taking at least 400 patients that satisfy the above criteria, patients will be evaluated for the following:

1. Age
2. Gender
3. Hypertension
4. Diabetes
5. Cholesterol: Total cholesterol and LDL level
6. Smoking
7. Ejection Fraction: mild, moderate, severely reduced, normal
8. Left ventricular end diastolic dimension
9. Presence of left ventricular thrombus by echocardiography
 - a. characteristics of thrombus: mobile, pedunculated, flat
10. Presence of left atrial thrombus
11. Drug therapy: coumadin, heparin, aspirin, clopidogrel
12. Reason for drug therapy

Patients will then be followed until an endpoint is achieved. Endpoints are 24 months of follow-up, death, or thromboembolic event which include embolic stroke or evidence of peripheral embolism. Thromboembolic stroke will be defined by CT scan or MRI, excluding hemorrhagic stroke. Transient ischemic attacks will be defined a clinical grounds of neurological compromise persisting for less than 24 hours.

Statistical analysis will be performed using chi-square analysis for dichotomous variables and analysis of variance for continuous variables. Logistic regression analysis will be used to evaluate risk factors for thrombus formation and thromboembolism.

C. Study Procedures

There will be no procedures performed.

D. Study Drugs/Medical Devices

No drugs or devices will be used.

E. Study Subjects

Inclusion Criteria: All of the participants' data will be obtained from medical records or computer data independent of race, religion, or ethnic background. Inclusion criteria will include history of chronic dilated cardiomyopathy as defined by clinical history and ejection fraction < 40%, or echocardiographic findings of a left ventricular end diastolic volume > 5.8cm. Exclusion criteria will include history of atrial fibrillation, chronic coumadin or heparin use, previous thromboembolism, recent myocardial infarction within six months, prosthetic valve, previous thrombus on echocardiogram.

F. Recruitment of Subjects

Subjects and subject data will be obtained from a review of patient histories through the WebCIS database and patient charts.

G. Confidentiality of Study Data

All study data will remain confidential. A unique numeric code will be assigned to each study subject.

H. Compensation or Costs to Subjects

There will be no compensation or costs to subjects.

I. References

1. Koniaris, Lauren S. et al. "Anticoagulation in Dilated Cardiomyopathy" *Journal of the American College of Cardiology* 1998; 31: 745-8.
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3. Katz, SD et al. "Low incidence of stroke in ambulatory patients with heart failure: A prospective study" *American Heart Journal* 1993;126:141-6
4. Gottdiener, JS et al. "Frequency and Embolic Potential of Left Ventricular Thrombus in Dilated Cardiomyopathy: Assessment by 2-Dimensional Echocardiography" *American Journal of Cardiology* 1983;52:1281-1285.
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6. Sharma, ND et al. "Left Ventricular Thrombus and Subsequent Thromboembolism in Patients with Severe Systolic Dysfunction" *Chest* 2000;117:314-320.