# Embolic Stroke in Cardiomyopathy
## Should Patients be Anticoagulated?

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**KEYWORDS**

• Heart failure • Stroke • Anticoagulation • Warfarin • Prevention

**KEY POINTS**

- A number of studies have shown that patients with heart failure have greater incidence of stroke when compared with patients without heart failure.
- The combination of endothelial dysfunction, a relative hypercoagulable state, and static blood flow (from cardiac remodeling) predisposes patients with heart failure to develop thrombus that leads to cardioembolic stroke. This is mediated by the release of prothrombotic factors.
- To date, 4 major randomized trials have investigated the role of anticoagulation in patients with heart failure (in sinus rhythm). Data pooled from these studies suggested the risk for bleeding with anticoagulation counterbalanced the small benefit observed in preventing strokes with anticoagulation.
- The decision to anticoagulate patients with heart failure with atrial fibrillation should be based on the $CHADS_2$-VASC score. The choice of anticoagulation (warfarin or a novel oral anticoagulant) should be individualized for each patient.

## INTRODUCTION

Heart failure (HF) is a growing public health concern. The aging population and advancements in medical therapies have led to the increased prevalence of HF. Recent survey data from the American Heart Association estimated that at least 5.1 million American adults have HF.[1] Worldwide, approximately 23 million people are thought to have HF.[2] Additionally, the economic burden of HF is significant. By 2030, the total direct medical costs of HF in the United States are projected to exceed $50 billion,[3] with an average lifetime expenditure of more than $100,000 per patient.[4]

Despite the use of interventions that improve outcomes in HF (resynchronization therapy and neurohormonal modulation with β-blockers, renin-angiotensin inhibitors, and aldosterone antagonism), mortality is still substantial. Nearly half of the patients with HF will die within 5 years of diagnosis.[5] A significant contribution to the overall mortality in HF is the predisposition of these patients to experience stroke and thromboembolic disease.

This review focuses on the role of anticoagulation in patients with HF. The epidemiology and pathogenesis of embolic stroke in HF will be discussed. In addition, we review the outcomes data available for anticoagulation in patients with HF.

## EPIDEMIOLOGY OF STROKE IN HEART FAILURE

Patients with HF have higher rates of thromboembolic events compared with the general population

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(Fig. 1). Several studies lend insight into the risk HF poses for stroke.

In a large Danish prospective study of 51,553 adults between the ages of 50 and 64 years who were followed for 14 years, 1239 patients with incident HF (and no concomitant atrial fibrillation) were identified. In the initial 30 days following the diagnosis of HF, patients experienced a greater risk for death (Hazard Ratio [HR] 42.8) or the composite of death and stroke (HR 38.4) compared with patients without HF. At more than 6 months after the diagnosis of HF, the risk for death or death and stroke remained elevated (HR 4.9 and 4.0, respectively). When adjusted for previous use of vitamin K antagonists, gender, and systolic blood pressure, HF continued to pose a greater risk for death (HR 2.9), death and stroke (HR 2.3), and ischemic stroke (HR 3.2) compared with patients without HF.[6]

In the Rotterdam study, 7546 patients aged 55 years or older without a history of stroke were followed for an average of 9.7 years. A total of 1014 patients developed HF, whereas strokes occurred in 827 patients (470 ischemic, 75 hemorrhagic, and 282 unclassified). In the first 30 days after the diagnosis of HF, an increased risk for ischemic stroke was observed (HR 4.6) even after adjusting for a number of risk factors, including age, gender, smoking, diabetes, ankle-brachial index, hypertension, use of antithrombotics, presence of atrial fibrillation, or history of myocardial infarction (MI). After 6 months, unlike what was observed in the Danish study, HF did not confer additional risk for stroke compared with patients without HF.[7]

Older community-based studies also have demonstrated the impact of HF on stroke. In the initial cohort from the Framingham Heart Study, composed of 5184 adults aged 30 to 62 years for which 24-year follow-up data are available, the relative risk (adjusted for age, systolic blood pressure, cholesterol, and smoking) for having an ischemic stroke in patients with HF was 2.7 for men and 2.1 for women.[8] In the Olmsted County Study of 630 patients with incident HF, a significant relative risk (17.4) for ischemic stroke was noted when compared with the general population in the first 30 days after the diagnosis of HF. The risk for ischemic stroke between patients with and without HF did not equalize at 5 years.[9]

Population and community-based studies often rely on diagnosis coding and lack complete information on left ventricular ejection fraction (LVEF) as it pertains to stroke. Analyses of several trials have shed light on the impact of LVEF and stroke incidence in patients with HF.

In a retrospective analysis of the SOLVD trial (6378 patients), the overall incidence of thromboembolic events (stroke, pulmonary embolism, and peripheral embolism) in patients with LV dysfunction (mean LVEF 27%) in sinus rhythm was 1.8% in men and 2.4% in women. In a multivariate analysis, a decrease in LVEF (per 10% intervals) remained an independent predictor of thromboembolic events in women but not in men.[10]

The SCD-HeFT trial also demonstrated a similar incidence of thromboembolism in patients with HF. When 2114 patients with New York Heart Association (NYHA) functional class II or III (mean LVEF 25%) and in sinus rhythm were examined for a median follow-up of 46 months, the annual risk of thromboembolism was approximately 1% per year.[11]

Similarly, when the V-HeFT I and II cohorts (1446 men with a mean LVEF or 29%) were examined retrospectively after a follow-up period of approximately 2.5 years, the incidence of all

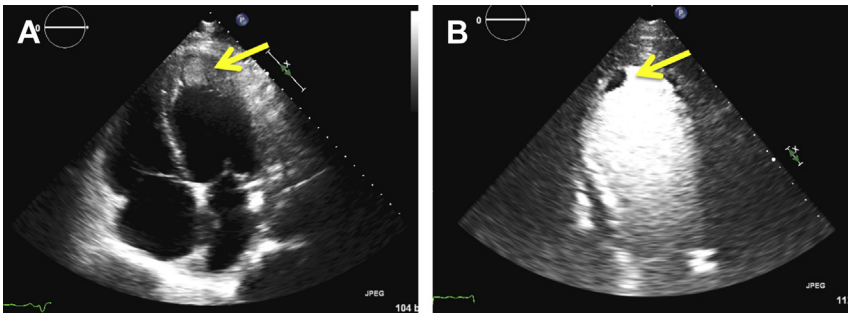


**Fig. 1.** (*A*) A 70-year-old man with a history nonischemic cardiomyopathy presented with acute decompensated HF. Transthoracic echocardiography demonstrated apical thrombus (*arrow*). (*B*) A 61-year-old man with a history of ischemic cardiomyopathy and acute lymphocytic leukemia presented in septic shock. Hospital course was complicated by left frontal ischemic stroke. Contrast transthoracic echocardiography demonstrated apical thrombus (*arrow*).