Title of Research
Extended-Duration Thromboprophylaxis with Direct-Acting Oral Anticoagulants After Hospitalization for Heart Failure: A Meta-Analysis

Lead Researcher
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Summary of Research
Heart failure is the leading cause of hospitalization in older adults in the United States, accounting for over 1 million admissions annually. Within a year of hospitalization, roughly 50% of patients are readmitted and 30% have died. Venous thromboembolism (VTE) – when a blood clot breaks loose and travels in the bloodstream – during or after hospitalization for heart failure may contribute to these poor post-discharge outcomes. Although inpatient treatment to prevent formation of blood clots, known as thromboprophylaxis, is an effective and recommended strategy in patients hospitalized for heart failure, many such patients develop VTE shortly after hospital discharge. Large, multi-center randomized controlled trials have shown mixed results regarding the safety and efficacy of extended-duration thromboprophylaxis in a broad population of medically-ill hospitalized patients. The most recent guidelines do not support the routine use of prolonged VTE prophylaxis in medically-ill patients.

Limited data are available on the risk-benefit profile of extended-duration thromboprophylaxis in patients hospitalized for heart failure. In addition, currently available injectable anticoagulants – intended to prevent blood clots – are burdensome, and their utilization is suboptimal even during hospitalization for heart failure.

Direct-acting oral anticoagulants (DOACs) have been shown to be safe, efficacious, and cost-effective in patients diagnosed with VTE, but their role in extended-duration prophylaxis in high-risk patients remains uncertain.

The event-driven, placebo-controlled COMMANDER-HF trial (NCT01877915) aims to evaluate low-dose rivaroxaban, a DOAC, for prevention of thrombotic events in patients following hospitalization for heart failure and significant coronary artery disease. The results are awaited.

Study Design
The study aims to determine whether extended-duration thromboprophylaxis with direct-acting oral anticoagulants reduces the risk of post-discharge venous thromboembolism with a favorable bleeding profile in patients hospitalized for heart failure compared to standard of care.

A meta-analysis will be carried out of the four large randomized controlled clinical trials evaluating utility of extended-duration thromboprophylaxis in subgroups of patients hospitalized for heart failure. The researchers have data from the subset of heart failure patients from EXCLAIM (Extended Clinical Prophylaxis in Acutely Ill Medical Patients), MAGELLAN (Multicenter, Randomized, Parallel Group Efficacy and Safety Study for the Prevention of Venous Thromboembolism in Hospitalized Acutely Ill Medical Patients Comparing Rivaroxaban with Enoxaparin), and APEX (Acute Medically Ill Venous Thromboembolism Prevention with Extended Duration Betrixaban) trials.

Data on the clinical profile, safety, and efficacy outcomes of heart failure patients included in the ADOPT (Apixaban Dosing to Optimize Protection from Thrombosis) trial will be added to these. The ADOPT data will be crucial to the meta-analysis since ADOPT included the highest number of heart failure patients (2,516) of the four trials. The primary efficacy outcome in ADOPT was a 30-day composite of death related to venous thromboembolism, pulmonary embolism, symptomatic deep-vein thrombosis, or asymptomatic proximal-leg deep-vein thrombosis, as detected with the use of systematic bilateral compression ultrasonography on day 30. The primary safety outcome was bleeding.

Two reviewers will independently extract data from the included studies.

Study Population
Patients for whom the reason for hospitalization was "Congestive Heart Failure" in the ADOPT trial (n=2,516)

Funding Source of Research
Not provided

Requested Study
CV185-036 (NCT00457002)
Study of Apixaban for the Prevention of Thrombosis-related Events in Patients With Acute Medical Illness (ADOPT)