Introduction:

Heart failure (HF) is a complex clinical syndrome that results in the impairment of the heart's ability to fill or to pump out blood. As of 2013, an estimated 5.8 million people in the United States (1) were living with HF. Patients with HF have varying signs and symptoms that are often nonspecific and have a wide differential diagnosis, making diagnosis by presentation very challenging. Some of the symptoms are due to congestion such as dyspnea on exertion (DOE), orthopnea, paroxysmal nocturnal dyspnea (PND), and fluid retention while other symptoms are due to lack of adequate cardiac output that include fatigue, exercise intolerance, and weakness. This diversity of presentation often results in delays in definitive diagnosis and treatment, and such delays are linked with poor prognosis.(2)

Cardiac function may be assessed by echocardiography or radionuclide ventriculography however, there is no specific diagnostic test for HF.(3) Cardiovascular physical examination is used commonly as a basis for diagnosis and therapy in congestive heart failure. Patients diagnosed with HF require constant observation to identify hemodynamic deterioration that might warrant adjustments to their therapy.

There are two basic pathophysiologic mechanisms that cause reduced cardiac output and HF: heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF). HFrEF and HFpEF may be due to a variety of etiologies and effective management is often dependent upon establishing the etiology. The most common causes of HFrEF are coronary (ischemic) heart disease, idiopathic dilated cardiomyopathy, hypertension, and

valvular disease. While HFpEF can be induced by many of the same conditions, the most common causes are uncontrolled hypertension, ischemic heart disease, hypertrophic obstructive cardiomyopathy, and restrictive cardiomyopathy.(3) Clinical trials of HF therapies have typical inclusion criteria with the majority of patients being younger males of HFrEF with no other life-threatening comorbidities such as unstable angina or heart failure due to valvular heart disease. Consequently, few data are available in patients with HFpEF that describe outcomes or guide management strategies; this lack of evidence is problematic because these patients are frequently hospitalized for HF.

We have proposed a single center (UNC), pilot study to take a contemporary snapshot of the acute HF patient population with a retrospective and prospective chart review to characterize patients hospitalized for heart failure. We proposed to focus on specific biomarkers as described below.

Background:

Nearly a decade ago, two national heart failure registries were conducted- Acute Decompensated Heart Failure National Registry (ADHERE) and Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). Both were designed to bridge the gap in knowledge and care by prospectively studying patient characteristics, management, and outcomes in a broad sample of patients hospitalized with ADHF. In the ADHERE study (Oct 2001-July 2004), one of the characterizations of HF patients was to compare patients with HFpEF to patients with HFrEF.(4) What they found was that the characteristics between patients enrolled in heart failure clinical trials often differed from the patient characteristics in the community. Almost half of the sample size

included patients with HFpEF, females, and patients with other comorbidities such as coronary artery disease (CAD), myocardial infarction (MI), and diabetes.(5) Most clinical trials predominantly include younger males with no other comorbidities with HFrEF. OPTIMIZE-HF (Mar 2003---Dec 2004) also confirmed the observations from ADHERE, that a large portion of patients with HF are ones with HFpEF. From clinical trials, it was thought that patients with HFpEF would be more likely to survive a HF hospitalization than patients with HFrEF. However, OPTIMIZE-HF found that patients with HFpEF remain at equally high risk for mortality and re-hospitalization compared to patients with HFrEF in the first 60 to 90 days after index hospitalization.(6)

Biomarkers:

One of the advances in the last decade that has aided in the diagnosis and treatment of heart failure has been the utilization of biomarkers, especially b-type natriuretic peptide (BNP) and N-terminal pro B-type natriuretic peptide (NT-proBNP). Although most of the data collected between ADHERE and OPTIMIZE-HF was similar, one of the differences was that the OPTIMIZE-HF trial also collected data on BNP.

Another new biomarker that may provide additional information in HF patients is soluble ST2 (sST2). Compared to other biomarkers, such as natriuretic peptides, advantages of sST2 include that its concentration is not affected by age, renal function, or body mass index.(7) Our study will focus on these two biomarkers in addition to other characteristics outlined above. With the addition of these biomarkers, we hope to gain a better understanding of ADHF so that newer therapies can be developed.

Purpose:

Describe the biomarker profile, demographics, clinical characteristics, treatments, quality indicators, and outcomes of patients hospitalized at UNC for ADHF. We will then use these results to compare it to previous/older HF registry studies to identify new trends in the characteristics of patients hospitalized for ADHF.

Significance:

If any new trends in the characteristics of patients with ADHF exist, it would be important to identify new potential ways to improve the quality of care for these patients in the future. This could either be in the diagnosing or treatment process of HF.

Methods:

Study description: This is a single-center, hospital-based, observational, retrospective and prospective study, conducted at the University of North Carolina, Chapel Hill, North Carolina. To characterize the HF population, we propose to retrospectively review clinical information from patient medical records between July 2014 and July 2015. Then all HF patients would be tracked prospectively for re-admissions or discharges. Medical records of all hospitalized adult patients with symptoms or complications of heart failure were eligible for the inclusion and exclusion criteria.

Inclusion criteria: All patients admitted to the UNC Health System for symptoms or complications of heart failure between July 2014 and July 2015 were to be screened. Computerized clinical records on about 600 patients admitted during the study period would be retrieved and analyzed to find eligible patients who met the following

Inclusion criteria:

- Primary diagnosis of ADHF on admission
- Signs and symptoms consistent with ADHF
- 18 years of age or older

Exclusion criteria:

- Scheduled hospitalizations or hospitalizations in the context of cardiac surgery
- In order to avoid duplicate records, readmissions to the hospital during the study period were not counted as new cases

Data collection: Data on patients would include clinical information on demographics, drug prescription(s) before and following admission, etiology, and the possible precipitating factors of HF, ejection fraction (%), Pro-BNP levels, ST2 levels, relevant comorbidities, and outcomes such as the number of re-hospitalizations within 1-2 years.

Data analysis: Using descriptive analysis, categorical variables would be presented as counts and percentages, while quantitative variables as means and standard deviation (SD) or medians and 25^{th} percentile-75^{th} percentile as appropriate, depending on the empirical distribution of the variable. All tests would be two-sided and p-values less than 0.05 would be considered statistically significant. Subgroups of patients would be compared using the chi-square test or Fisher's exact test for categorical variables and the t-test.(8) The analysis was to be performed using SAS software.

Hypothesis and Specific Aims:

Compared to data collected from ADHERE and OPTIMIZE-HF approximately a decade ago, we hypothesized that contemporary snapshot of patients hospitalized for ADHF would show that there is an even greater population of

patients with HFpEF, longstanding hypertension as the etiology of HF, as well as a younger presentation. The primary objective of this study was to describe the biomarker profile, clinical characteristics, hospital management, and outcomes of patients hospitalized with ADHF. The secondary objectives were to compare this data collected to previous HF registries, ADHERE and OPTIMIZE-HF, to see if there was a new trend in the characteristics that patient's presenting with HF currently.

Results: Results are not available due to the study not being completed.

Discussion:

There are a number of important obstacles facing investigators conducting research. These obstacles include locating funding, responding to multiple review cycles, obtaining Institutional Review Board (IRB) approval, recruiting patients, data collection challenges, and completing large amounts of associated paperwork. As a result of these challenges, many who attempt clinical investigation quit or have incomplete results. One of the biggest challenges to my project was obtaining IRB approval. Since the project was to retrospectively review charts, it was assumed IRB approval to have remote access to the electronic medical records at UNC after having EPIC training would be expedited. Unfortunately, there were unexpected stipulations preventing IRB approval and furthermore the IRB decision making process can be lacking in timeliness and accountability.(9) One of the most important lessons I have learned about conducting research includes being highly tenacious, being persistent, and having exceptional motivation to complete the process. The key to success is to learn from past failures and to put those lessons learned into action.

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