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Predictive Modeling Pilot Project for Readmissions in Heart Failure Patients with Preserved Ejection Fraction

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Predictive Modeling Pilot Project for Readmissions in Heart Failure Patients with Preserved Ejection Fraction

by

By Pin Xiang

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Dedication

This thesis is dedicated to my family. My mother and father who raised me. My brother who I care for. My wife who I love deeply and our daughters who I will always cherish. I couldn't have done it without your unconditional love and support. Wish to continue our happy and simple life.

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Abstract

Predictive Modeling Pilot Project for Readmissions in Heart Failure Patients with Preserved Ejection Fraction

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Objectives: To pilot a predictive model evaluating hospital readmissions for heart failure with preserved ejection fraction (HFpEF) patients and the association with management by a cardiologist, number of comorbidities, and type of treatment.

Methods: This is a retrospective, observational study of claims data to evaluate the effect of various factors: age, gender, provider, baseline inpatient admissions, comorbidities and baseline drug treatment classes (e.g. antiarrhythmic, beta blocker, calcium channel blocker, diuretic, RAAS-inhibiting agents) on number of readmissions, time to readmission, and odds of readmission. Patients ≥18 years of age with an inpatient admission with a primary discharge diagnosis of HFpEF between October 1, 2011 and September 30, 2014 were identified and data were assessed 1-year pre- and post-hospitalization. Patient characteristics were described, and patients treated by a cardiologist were compared to those who were not. Multivariate regression and Cox

proportional hazard models were used to assess the association of all-cause and heart failure-related readmissions adjusting for demographic and clinical covariates.

Results: A total of 264 patients with HFpEF were identified (60.2% female; mean age of 79 years (SD 10.8) of which 77 [29%] did not see a cardiologist. Patients who saw a cardiologist were more likely to be male and had a greater number of comorbidities including diabetes, dyslipidemia, hypertension, coronary heart disease, cardiomyopathy, and valvular heart disease than those without cardiologist. Overall, 51% of the patients had an all-cause readmission and 15% had an HF-related readmission. Patients who had a cardiologist were associated with more all-cause readmissions (IRR of 2.21, p=0.0003) and a shorter time to all-cause readmissions (HR of 1.91, p=0.004). Being on diuretics was associated with more heart failure-related readmissions (IRR of 2.84, p=0.0301). A higher number of all-cause readmission was associated with patients having more comorbidities (IRR of 1.19, p=0.0038).

Conclusion: This study demonstrated that all-cause and heart failure-related readmission is high in patients with HFpEF. The pilot predictive models show that various factors associated with higher risk patients, such as those with cardiologist management, more comorbidities, and use of diuretics, may be associated with increased hospital readmissions.

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CHAPTER 1: INTRODUCTION

1.1 Background

Heart failure (HF) or congestive heart failure (CHF) is characterized by the inability of the heart to pump blood well enough to meet the body's need for blood and oxygen.[1] There is a significant unmet need in the management of heart failure indicated by the high rate of hospitalization in the United States. Approximately 60% of all direct healthcare cost for heart failure is associated with hospitalization.[2] Once hospitalized, patients are often rehospitalized for heart failure. This has become a point of focus in recent years as heart failure hospital readmissions have been implemented as a quality measure. In 2012, the Affordable Care Act established the Hospital Readmission Reduction Program, which penalized hospital with higher than expected 30-day readmission rates for acute myocardial infarction, heart failure, and pneumonia.[3]

The 2013 ACCF/AHA Heart Failure Guideline characterized heart failure (HF) into two groups: those with reduced ejection fraction (HFrEF) or with preserved ejection fraction (HFpEF). HFrEF is commonly referred to as systolic HF and occurs when the ejection fraction is less than 40%. HFpEF is referred to as diastolic HF and occurs when ejection fraction is more than 50%. Those with EF between 41-49% is considered borderline HFpEF.[1,4-8] Table 1.1 provides an in-depth description.

Table 1.1 - Definitions of HFrEF and HFpEF[1]

Classification	EF (%)	Description
I. Heart failure with reduced ejection fraction (HFrEF)	≤ 40	Randomized controlled trials have mainly enrolled patients with HFrEF, and it is only in these patients that efficacious therapies have been demonstrated to date.
II. Heart failure with preserved ejection fraction (HFpEF)	≥ 50	Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.
a. HFpEF, borderline	41 to 49	These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF
b. HFpEF, improved	> 40	It has been recognized that a subset of patients with HFpEF previously had HFrEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients.

EF- ejection fraction; HF, heart failure; HFpEF- heart failure with preserved ejection fraction; and HFrEF- heart failure with reduced ejection fraction

While symptoms of both types of heart failure often includes shortness of breath, fatigue or swelling in leg, the clinical characteristics and management of HFrEF and HFpEF is quite different. While HFrEF usually indicates a pumping problem where the left ventricle can't contract vigorously enough (thus reduced ejection fraction), HFpEF is a filling problem where the left ventricle can't relax or fill fully. Furthermore, most randomized controlled trials have predominantly enrolled patients with HFrEF and all proven efficacious treatments have only been demonstrated in this group. With no clear efficacious treatment identified, those with HFpEF is a highly underserved patient group and will be the focus of this study.[5,9-11]

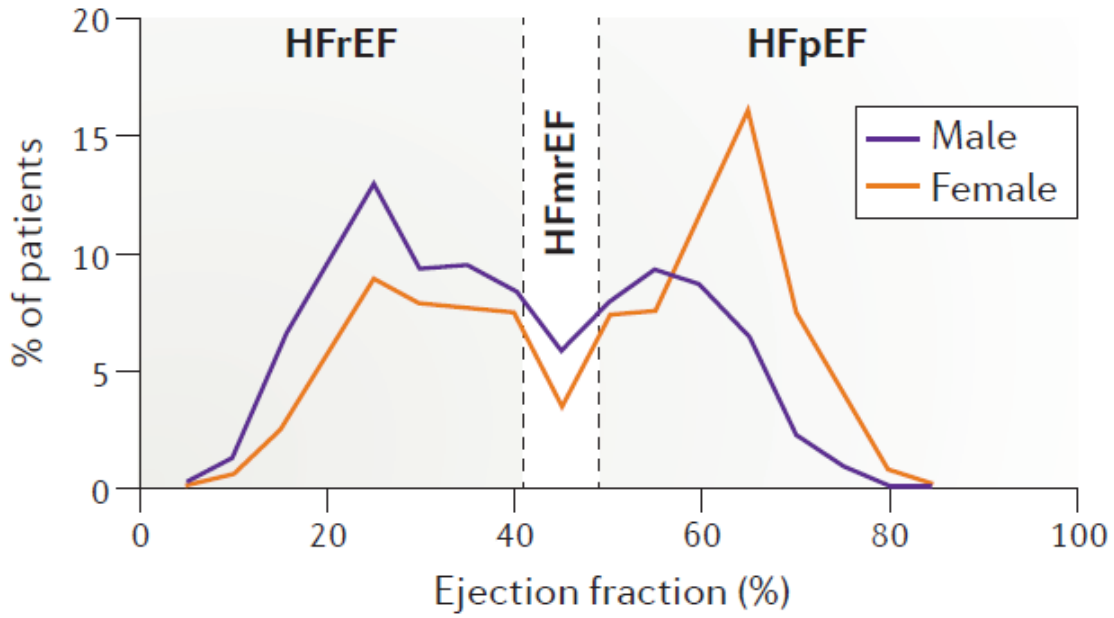
1.2 Epidemiology and Prevalence of Heart Failure

The lifetime risk of developing heart failure (HF) is 20% for both men and women at age of 40 years and older.[12] This burden is especially high among the elderly where the incidence and prevalence of Medicare patients (aged ≥ 65 years) with HF is approximately 29 and 121 per 1,000 per years, respectively.[13] Based on the 2017 Heart Disease and Stroke statistics put out by the American Heart Association, there is 960,000 new cases of HF annually. Based on 2011-2014 NHANES data, approximately 6.5 million people greater than 20 years of age in the US have heart failure. It is projected that the total number of Americans living with HF will increase by 46% from 2012 to 2030, which is over 8 million people.[14]

There were over 1 million hospital stays that had a principal diagnosis of HF in 2011 and over 500,000 emergency room visits the following year. Approximately 25% of hospitalized patients with HF are readmitted within 30 days of discharge and HF is the leading cause of rehospitalization in patients on Medicare. This leads to an estimated direct annual cost of $60 billion when considered in isolation and $115 billion when considered as part of a syndrome.[14-18]

While more research has been conducted in patients with HFrEF, approximately 50% of the HF patients suffer from HFpEF (Figure 1.1). The latest data suggest that age-specific incidence of HF may be decreasing, but to a lesser extent in HFpEF than HFrEF. Furthermore, the risk of HFpEF increases sharply with age, which is a concern given the aging US population. Finally, multimorbidity is common in both types of HF but slightly more severe in HFpEF, where 50% of patients have five or more comorbidities.[19-20]

Figure 1.1 – Distribution of left ventricular ejection fraction in incident heart failure[20]



HFrEF- heart failure with reduced ejection fraction; HmrEF- heart failure with mid-range ejection fraction; HFpEF- heart failure with preserved ejection fraction.

The distribution of ejection fraction in 1,223 patients with incident heart failure (defined by Framingham criteria) from Olmsted County, Minnesota, USA, according to sex.

1.3 Pathophysiology of Heart Failure

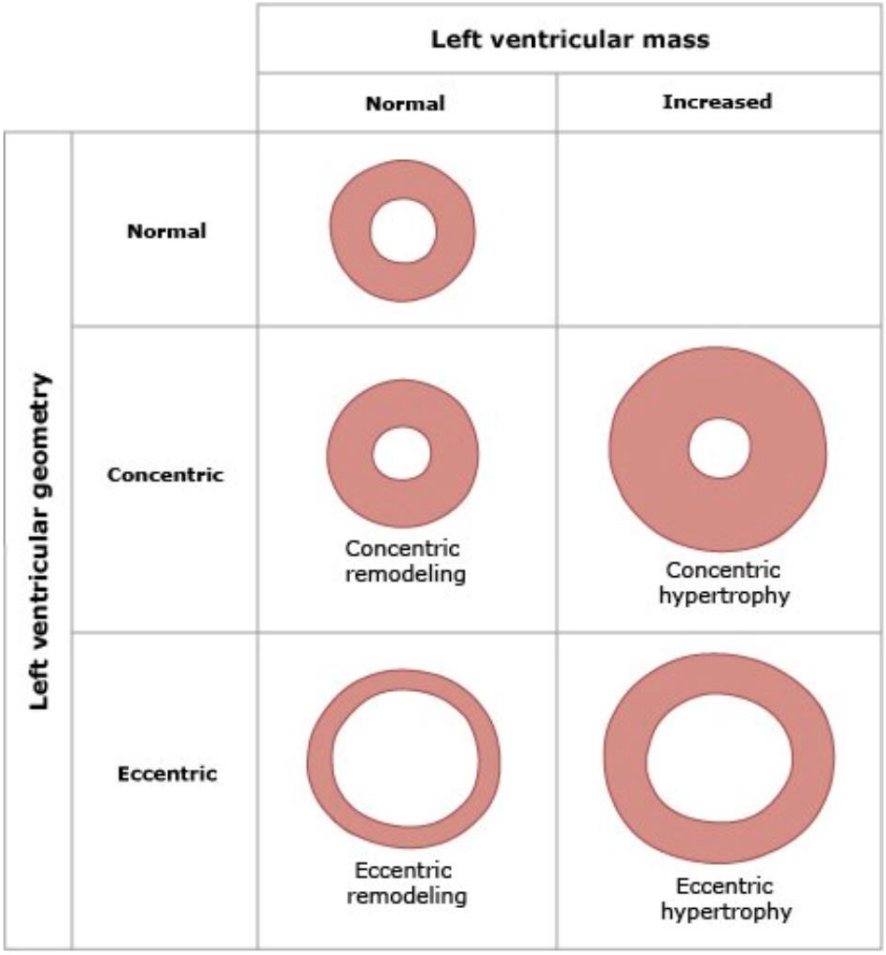
Heart failure, by its name, may suggest the disorder of the heart but it is a multisystem disorder characterized by abnormalities of the heart muscle, skeletal muscle, endothelial function, renal function, sympathetic nervous system, and neurohormonal changes.[21] It can be defined by the inability to provide sufficient blood output to meet the requirements from tissues while maintaining filling pressure. This can occur in two ways:

- Systolic dysfunction (HFrEF) where there is impaired cardiac contractility – pumping problem
- Diastolic dysfunction (HFpEF) where there is abnormal cardiac relaxation – filling problem

The cause for heart failure from the damage of the heart muscle can be from a wide number of conditions such as myocardial infarction (heart attack), hypertension (high blood pressure), and amyloidosis (stiffening of heart muscle from protein deposits).[22-26]

More specifically, for heart failure with preserved ejection fraction, these patients often have significant remodeling that affects the left ventricular and left arterial chambers, the cardiomyocytes, and the extracellular matrix. Many patients with HFpEF undergo a concentric pattern of left ventricular chamber remodeling and a hypertrophic process (see Figure 1.2).[27-30]

Figure 1.2 Pattern of left ventricular remodeling



- The schematic demonstrates the relationship between left ventricular (LV) end-diastolic volume (LVEDV, represented here by the size of the inner circle) and LV mass (LV mass, represented here by the size of the shaded region) for various patterns of remodeling.
- Relative wall thickness (RWT) is the ratio of wall thickness to left ventricular diastolic dimension (RWT = 2x [diastolic posterior wall thickness]/left ventricular internal diastolic dimension).
- With concentric remodeling, LVEDV is normal or reduced, LV mass is normal, and RWT is increased (and LV mass/LVEDV is increased).
- With concentric hypertrophy, LVEDV is normal or reduced, LV mass is increased, and RWT is increased (and LV mass/LVEDV is increased).
- With eccentric remodeling, LVEDV is increased, LV mass is normal to reduced, and RWT is normal to reduced (and LV mass/LVEDV is normal to reduced).
- With eccentric hypertrophy, LVEDV is increased, LV mass is increased, and RWT is normal to reduced (and LV mass/LVEDV is normal to reduced).

1.4 Diagnosis of Heart Failure

The most common symptoms of heart failure are shortness of breath, fatigue, and fluid retention. This may lead to pulmonary congestion (difficulty breathing) and peripheral edema (swelling of the leg).[1] The American College of Cardiology Foundation and the American Heart Association groups HF into 4 stages based on risk and progression[31]:

A. At high risk for HF but without structural heart disease or symptoms of HF
B. Structural heart disease but without signs or symptoms of HF
C. Structural heart disease with prior or current symptoms of HF
D. Refractory HF requiring specialized interventions

Whereas the New York Heart Association groups HF in 4 classes based on severity[31]:

I. No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF
II. Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF
III. Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF
IV. Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest

As discussed in the background, HFpEF and HFrEF are commonly differentiated based on the ejection fraction (EF) where EF $\leq$ 40% are HFrEF patients, EF$\geq$50% are HFpEF patients, and EF between 41-49% are borderline HFpEF patients.[1] However, HFpEF should be distinguished from other causes of HF with EF$\geq$50% such as valvular heart disease, cardiomyopathy,

pericardial disease, and high output HF. Table 1.2 highlights differential diagnoses of HFpEF, where the signs and symptoms may be present but not included in the definition of HFpEF.

Table 1.2 – Differential Diagnosis of HFpEF[19]

Categories and Diagnosis	
Uncorrected primary left-sided valvular heart disease - Aortic stenosis - Aortic regurgitation - Mitral stenosis - Mitral regurgitation	**Pericardial disease** - Tamponade - Constrictive pericarditis

Isolated right ventricular failure
- WHO group 1,3,4, or pulmonary hypertension
- Genetic
  o Arrhythmogenic right ventricular dysplasia
- Congenital heart disease
- Isolated primary pulmonary or tricuspid valvular disease
- Right ventricular infarction
	Specific cardiomyopathies
	- Infiltrative (amyloidosis)
	- Infectious/inflammatory
	  o Sarcoidosis
	  o Viral
	- Genetic
	  o Hypertrophic cardiomyopathy
	  o Restrictive cardiomyopathy

HFpEF is typically associated with hypertension, aging, coronary heart disease, diabetes, sleep disordered breathing, obesity, kidney disease, lung disease and anemia.[32-36] While the signs and symptoms of all heart failure is similar, a HFpEF diagnosis should be considered in patients without significant epicardial coronary disease.[37-39]

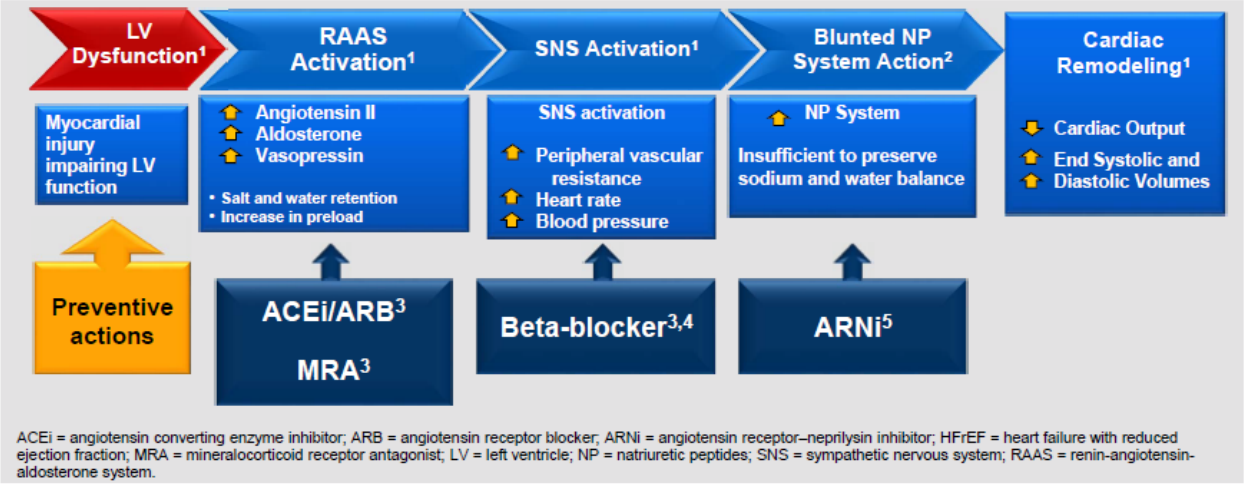
1.5 Treatment Guidelines for Heart Failure

The goals of treatment in heart failure are to control symptoms, improve health-related quality of life, and prevent hospitalization and death. In the past, most randomized control trials have predominantly enrolled patients with HFrEF, and all currently proven efficacious treatment options have only been demonstrated in this group. The US treatment guidelines recommend a combination of pharmacologic therapies for HFrEF patients.[1] These treatments include:

- Angiotensin-converting enzyme inhibitors (ACEI) or Angiotensin II-receptor blocker (ARB)
- Beta-blocker
- Diuretic
- Mineralocorticoid receptor antagonist (aldosterone antagonists)
- Certain vasodilators (hydralazine and isosorbide dinitrate)
- Angiotensin receptor-neprilysin inhibitor (ARNI)
- Sinoatrial node modulator

The use of ACEI or ARB with beta-blocker in all patients with stable heart failure with reduced ejection fraction is recommended to reduce hospitalization and death. Diuretics and aldosterone antagonists can be added depending on the symptoms and severity of HF. Hydralazine and isosorbide dinitrate has been shown to be more effective in African Americans. In more recent years, ARNIs and sinoatrial node modulators have been approved for use. Figure 1.3 describes where the various treatment options affect the HFrEF disease pathway.[1]

Figure 1.3 – Pharmacological Approach to Different Disease Pathway in HFrEF[1,40-41]



ACEI - Angiotensin-converting enzyme inhibitors; ARB - Angiotensin II-receptor blocker; ARNI - Angiotensin receptor-neprilysin inhibitor; and HFrEF- heart failure with reduced ejection fraction; MRA - mineralcorticoid receptor antagonist; LV – left ventricle; natriuretic peptides; SNS – sympathetic nervous system; RAAS – renin-angiotensin aldosterone system

Additionally, calcium channel blockers may be used to treat heart failure caused by high blood pressure, and antiarrhythmic agents may be used for patients with symptomatic ventricular arrhythmia.

No clear efficacious treatment has been identified in the HFpEF population, thus far, and the completed clinical trials have only produced neutral results to date. Most treatments are largely directed toward associated conditions such as hypertension and symptoms such as edema. In the 2013 American College of Cardiology / American Heart Association heart failure guidelines and the 2016 European Society of Cardiology heart failure guidelines, the recommendations for patients with HFpEF were limited due to lack of high quality data.[1,42] The 2013 ACA/AHA HF guidelines states that:

- Systolic and diastolic hypertension should be controlled in accordance with published clinical guidelines to prevent morbidity.
- Diuretic should be used to relieve symptoms due to volume overload

However, with the high prevalence of HF and half of the patients suffering from HFpEF, there is an incredible opportunity for new treatment options in development to show clinical benefits in this patient group.

1.6 Study Rationale

Heart failure (HF) is a chronic disease with acute exacerbation that affects more than 5.8 million people in the United States and more than 23 million worldwide. Despite advancement in medical therapy, the number of heart failure hospitalizations remains high, indicating a lack of disease control. With the increase in health care costs in general, the cost of heart failure treatment is predicted to increase by approximately 150% from 2012 to 2013.[43] With 1.8 million physician office visits and 1 million hospital discharges for heart failure in 2010, it is the leading cause of hospitalization and 30 day readmission for the US elderly population.[1,17,44] Approximately 25% of patients hospitalized for heart failure are readmitted for any cause within 1 month and 10% die of any cause within 30 days.[45,46] In 2012, the Affordable Care Act established the Hospital Readmission Reduction Program which penalized hospitals with higher than expected 30-day readmission.[3] Both the social and economic impact drives the need for a deeper understanding of heart failure and how to curb the disease burden.

Furthermore, HF with preserved ejection fraction (HFpEF) is becoming a predominant form of HF in the developed world. It is also a disease that is poorly understood and under managed. In a previous study, healthcare resource utilization and medication use were described

in patients with heart failure (both HFrEF and HFpEF) in Central Texas. This study will be an extension of the previous study to pilot a predictive model to evaluate readmission for HFpEF patients based on the cohort identified. This model can be later applied to other cohorts to help providers make more informed decisions related to the disease management of HF.

CHAPTER 2: METHODOLOGY

2.1 Study Objectives and Hypotheses

To pilot a predictive model to evaluate hospital readmission for HFpEF patients:

1. To determine whether being managed by a cardiologist affected the number of, time to, and odds of readmission (HF-related and all-cause)

- $H_0$1.1 The difference in the number of readmissions (HF-related and all-cause) experienced by patients managed by a cardiologist and patients not managed by a cardiologist is not statistically significant.
- $H_0$1.2 The difference in time to first readmission (HF-related and all-cause) experienced by patients managed by a cardiologist and patients not managed by a cardiologist is not statistically significant.
- $H_0$1.3 The difference in odds for HF-related readmission experienced by patients managed by a cardiologist and patients not managed by a cardiologist is not statistically significant.

2. To determine whether the number of comorbidities affect the number of, time to, and odds of readmission (HF-related and all-cause)

- $H_0$2.1 The number of readmissions (HF-related and all-cause) experienced by patients will not differ significantly based on the number of comorbidities.
- $H_0$2.2 The time to first readmission (HF-related and all-cause) experienced by patients will not differ significantly based on the number of comorbidities.
- $H_0$2.3 The odds for HF-related readmission experienced by patients will not differ significantly based on the number of comorbidities.

3. To determine whether the type of treatment (antiarrhythmics, beta-blockers, calcium channel blocker, renin-angiotensin aldosterone system inhibitor, or diuretic) affects the number, time, and odds of readmission (HF-related and all-cause)

- $H_0$3.1 The number of readmissions (HF-related and all-cause) experienced by patients will not differ significantly based on the type of treatments (Antiarrhythmic, BB, CCB, RAAS inhibitor or Diuretic).
- $H_0$3.2 The time to first readmission (HF related and all cause) experienced by patients will not differ significantly based on the type of treatments (Antiarrhythmic, BB, CCB, RAAS inhibitor or Diuretic).
- $H_0$3.3 The odds for HF-related readmission experienced by patients will not differ significantly based on the type of treatments (Antiarrhythmic, BB, CCB, RAAS inhibitor or Diuretic).

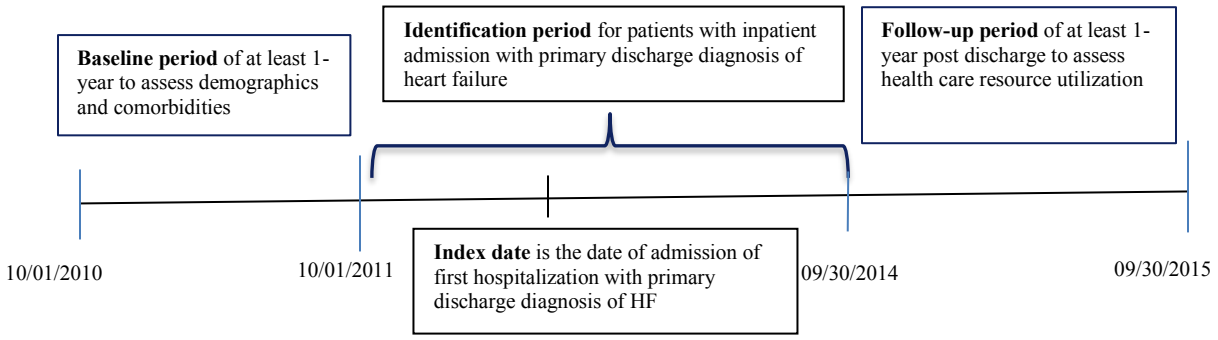
2.2 Study Design and Data Source

In the previous study, data from existing Scott and White Health Plan (SWHP) medical and pharmacy claims, and electronic medical record (EMR) were utilized. SWHP is part of the Baylor Scott & White Health (BSWH) system, a non-profit integrated health system with 48 acute care hospitals, 900 patient care sites, and approximately 6,000 physicians or other health care providers. The date of admission of first hospitalization with a primary discharge diagnosis of HF was referred to as the index date. Baseline data from one year prior to the index date, details of the index admission, and healthcare resource utilization and costs for at least 1 year after discharge were analyzed. An ejection fraction measurement from an echocardiogram during index hospitalization was used to determine the patients with reduced versus preserved EF status.

Patients were followed until death, end of health plan enrollment, or end of study period (Oct 2010 to Sept 2015).

This is a retrospective, observational study of existing pharmacy and medical claims data to determine and specifically evaluate the effect of various factors: age, gender, provider, baseline number of inpatient admissions, number of comorbidities and baseline drug treatment classes (e.g. antiarrhythmic, beta blocker, calcium channel blocker, diuretic, RAAS-inhibiting agents) on number of readmissions, time to readmission, and odds of readmission. The summary of the study design is described in Figure 2.1.

Figure 2.1 - Study Design Schema



The primary study endpoints are:

- Number of Readmissions: All-Cause
- Number of Readmissions – HF-related

The secondary study endpoints are:

- Time to First Readmission: All-Cause
- Time to First Readmission: HF-related
- Odds of HF-related Readmission

This study was approved by the University of Texas at Austin and the Baylor Scott & White Institutional Review Board following expedited review.

2.3 Sample Selection

Patients at least 18 years of age with an inpatient admission with a primary discharge diagnosis of HF (ICD-9-CM 428.xx) between October 1, 2011 and September 30, 2014 were identified (fiscal years FY2012-FY2014). The target population was health plan members that have heart failure with preserved ejection fraction. To be included in the study, patients had to be enrolled for 1 year prior to and at least 1 year after the index HF admission; the number of enrolled days was included as a covariate for patients with less than 2 full years of enrollment. In addition, patients were required to have a recent EF measurement from an echocardiogram that was ≥ 50%. Patients were excluded if they had an index length of stay (LOS) greater than 30 days, a prior heart transplant or LV atrial defibrillator. A detailed list of inclusion and exclusion criteria is summarized below in Table 2.1.

Table 2.1 - Patient Inclusion/Exclusion Criteria

Inclusion	Exclusion
• ≥ 18 years of age • Hospital admission with primary discharge diagnosis of HF (International Classification of Diseases, Ninth Edition [ICD-9-CM] 428.xx) • Continuous enrollment for 1 year prior to index admission, and at least 1 year after discharge • EF measurement from echocardiogram during index hospitalization >/= 50%	• Previous HF hospitalization in preceding 12 months • Index Length of stay >30 days • Patients with reduced EF (EF < 50% during index hospitalization • Patients who are heart transplantation (history of heart transplant V42.1, heart transplantation ICD-9-A code 37.5x and CPT-4 code 33945) or LVAD recipients (V43.21, 37.66, 37.52, 37.54, 37.55, 37.63; 33975-33983, 33993, 93750)

2.4 Study Variables

Medical and pharmacy claims, and electronic medical record (EMR) data were captured from one-year pre-index to the end of the follow-up period. Baseline patient characteristics such as demographics, previous diagnosis of HF, and comorbidities were captured. The length of stay, costs, and ejection fraction (EF) measurement was described at index admission, and health care resource utilization (numbers, types, and costs of pharmacy and medical claims) was captured during follow-up for at least one-year post hospital discharge. Table 2.2 provides a detailed list of study variables, as well as health plan enrollment start and end dates for the HFpEF cohort.

All patient-identifying data remained strictly confidential. All data were maintained on secure, password protected Baylor Scott & White computers and only study investigators weregranted access to the study data.

Table 2.2 - Study Variables

Baseline (one year prior to index)	**Index admission**	**Follow-up** (≥1 year after discharge)
• Age • Gender • Previous diagnosis of HF • Race/ethnicity • Comorbidities, including: – Coronary heart disease (ICD-9-CM: 410.x to 414.x, also CPT codes for stent placement [G0291, C9600 to C6908], and coronary bypass surgery [S2205 to S2209]) – Diabetes mellitus (ICD-9-CM 250.xx) – Hypertension (ICD-9-CM: 401.x to 405.x, and/or presence of anti-hypertensive medications) – Depression (ICD-9-CM: 296.2 to 296.8, 300.4, 309.1, and 311) – Dyslipidemia (ICD-9-CM: 272.xx) – Valvular heart disease (ICD-9-CM: 424.0 to 424.3) – Cardiomyopathy (ICD-9-CM: 425.x) – Tobacco use disorder (ICD-9-CM: 305.1) – Cardiac dysrhythmias (ICD-9-CM: 427.x)	• Length of stay • Cost of hospitalization • Ejection fraction measurement from echocardiogram	• Number of inpatient admissions • Hospital days • Outpatient visits • Emergency room visits • Pharmacy dispenses (30 day supply; # of unique meds overall, then anti-arrhythmics, anti-hypertensives, digoxin, anticoagulants, calcium channel-blockers, beta-blockers, anti-lipidemic) • Costs (inpatient, outpatient, pharmacy)

2.5 Statistical Analysis

Descriptive statistics were calculated for all variables. Continuous variables are described using means and standard deviations (SD). Categorical variables are described using frequencies with percentages. Two sample t-test and Chi-square tests were also used to conduct bivariate analyses, specifically comparing the group of patients treated by a cardiologist those who are not treated by cardiologist.

Multivariate regression and Cox proportional hazard models were used to assess the association of the all-cause or heart failure-related readmission adjusting for demographic and clinical covariates. An estimated coefficient associated with readmission whose 95% confidence interval of the incident rate ratio (IRR) which excludes 1.0 highlights a significant association. A poisson regression model was selected to assess the associations with the number of readmissions, while the cox-proportion hazard model was used for time to first readmission. A logistic regression model was selected to determine the odds of heart-failure related readmissions. The covariates for all models included age and gender for demographics, provider (Non-Cardiologist/Cardiologist) for objective 1, baseline number of inpatient admissions to adjust for severity, the number of comorbidities for objective 2, and various medications including antiarrhythmics, beta-blockers, calcium channel blockers, RAAS-inhibiting agents (ACEI/ARBs), and diuretics for objective 3. These are detailed in Table 2.3. All analyses were performed using SAS version 9.4 software (SAS institute, Cary, North Carolina) with an alpha < 0.05 as the criterion for statistical significance.

Table 2.3 - Predictive Models:

Model 1: Poisson Regression (or related approach appropriate to the distribution such as negative binomial regression) for Number of Readmission All Cause = Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)
Model 2: Cox Proportional Hazards Regression** for Time to First Readmission All Cause = Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)
Model 3: Poisson Regression (or related approach) for Number of HF related Readmission = Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)
Model 4: Cox Proportional Hazards Regression** for Time to First Readmission HF= Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)
Model 5: Logistic Regression for odds of HF related Readmission (yes/no)= Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)

*Comorbidities includes: Diabetes, Dyslipidemia, Hypertension, Coronary Heart Disease, Cardiomyopathy, Dysrhythmia, Valvular heart disease, Depression, Tobacco, Alcohol/other drug use

** if proportional hazards assumptions are not met, Accelerated Failure Time models will be applied

CHAPTER 3: RESULTS

3.1 Study Sample

For the timeframe of October 2010 to September 2015, a total of 831 patients with a primary diagnosis of heart failure were identified. Among them, 601 (72%) had an index admission between October of 2011 and September of 2014 to allow for at least 1year pre- and post-index periods. After excluding minors (age <18) or those that met other exclusion criteria, a total of 264 patients were identified with preserved heart failure. Table 3.1 reports the sample attrition.

Table 3.1 - Sample Selection

Selection Criteria	**n (%)**
Inpatient admission with primary diagnosis of heart failure between Oct 1, 2010 and Sept 30, 2015	831 (100%)
Index admission between Oct 1, 2011 to Sept 30, 2014	601 (72%)
Inclusion and Exclusion Criteria Met	438 (53%)
Ejection fraction ≥ 50	**264 (32%)**

3.2 Baseline Demographics and Clinical Characteristics

Table 3.2 describes the baseline demographic and clinical characteristics for the 264 patients meeting the inclusion criteria. 159 (60.2%) of the studied population were women, with a mean age at index of 79 years (SD 10.8). The average length of stay at index was 4.1 days with an average LV EF of 61.8%. Patients managed by a cardiologist were more likely to be male and had greater number of comorbidities, including diabetes, dyslipidemia, hypertension, coronary heart disease, cardiomyopathy, and valvular heart disease, than those without cardiologist.

Table 3.3 describes the baseline healthcare resource utilization and medication use for the HFpEF patients. Overall, the patients had an average of 2.4 (SD 3.7) inpatient admissions, which equates to 5.4 hospital days (SD 9.9) one year before the index date. A total of 8% of patients were on antiarrhythmics, 56% were on beta-blockers, 37% were on calcium channel blockers, 49% were on ACE/ARBs, and 55% were on diuretics. Patients who visited a cardiologist during the baseline period had a higher number of inpatient admissions, inpatient hospital days, primary care visits, and ED visits than those without a cardiologist. They were also more likely to be on antiarrhythmic and beta blocker medications.

Table 3.2 - Baseline Demographic and Comorbidities

	All HFpEF (n=264)	*HFpEF w/o Card (n=77)*	*HFpEF w/ Card (n=187)*	*p-value*
Female, n	159 (60.2)	58 (75.3)	101 (54.0)	**0.0013**
Age, years	79.0 (10.8)	79.5 (11.3)	78.83 (10.7)	0.4807
Index admission length of stay, day	4.1 (3.2)	4.3 (4.0)	4.0 (2.8)	0.9678
Comorbidities, number of	3.7 (1.7)	2.3 (1.5)	4.3 (1.4)	**<0.0001**
Diabetes, n	125 (47)	29 (37.7)	96 (51.3)	**0.0431**
Dyslipidemia, n	178 (67%)	35 (45.5)	143 (76.5)	**<0.0001**
Hypertension, n	236 (89%)	59 (76.6)	177 (94.7)	**<0.0001**
Coronary heart disease, n	133 (50%)	14 (18.2)	119 (63.6)	**<0.0001**
Cardiomyopathy, n	18 (7%)	1 (1.3)	17 (9.1)	**0.0283**
Dysrhythmia, n	156 (59%)	22 (28.6)	134 (71.7)	**<0.0001**
Valvular heart disease, n	53 (20%)	4 (5.2)	49 (26.2)	**<0.0001**
Depression, n	45 (17%)	9 (11.7)	36 (19.3)	0.1374
Tobacco use, n	21 (8%)	5 (6.5)	16 (8.6)	0.8027
Alcohol/other drug use , n	9 (3%)	0 (0.0)	9 (4.8)	0.0624

Table 3.3 – Baseline Healthcare Resource Utilization and Medication Use

	All HFpEF (n=264)	*HFpEF w/o Card (n=77)*	*HFpEF w/ Card (n=187)*	*p-value*
Number of Inpt Admission	2.4 (3.7)	0.8 (2.2)	3.1 (4.0)	**<0.0001**
Inpt Hospital days	5.4 (9.9)	1.8 (4.3)	6.9 (11.1)	**<0.0001**
Primary care visits	13.2 (14.5)	5.9 (5.2)	16.3 (15.9)	**<0.0001**
ED visits	1.4 (2.0)	0.3 (0.6)	1.8 (2.3)	**<0.0001**
Anticoagulant	62 (23.5)	13 (16.9)	49 (25.2)	0.1044
Antiarrhythmics	21 (8.0)	2 (2.6)	19 (10.2)	**0.0447**
Beta-blockers	148 (56.1)	34 (44.2)	114 (61.0)	**0.0124**
Calcium channel blockers	97 (36.7)	27 (35.1)	70 (37.4)	0.7168
ACEI/ARBs	130 (49.2)	35 (45.5)	95 (50.8)	0.4296
Diuretics	146 (55.3)	38 (49.4)	108 (57.8)	0.2119

ACEI- Angiotensin-converting enzyme inhibitors, ARB- Angiotensin II-receptor blocker, ED- emergency department, Inpt- inpatient

3.3 Follow-up Healthcare Resource Utilization and Hospital Readmission

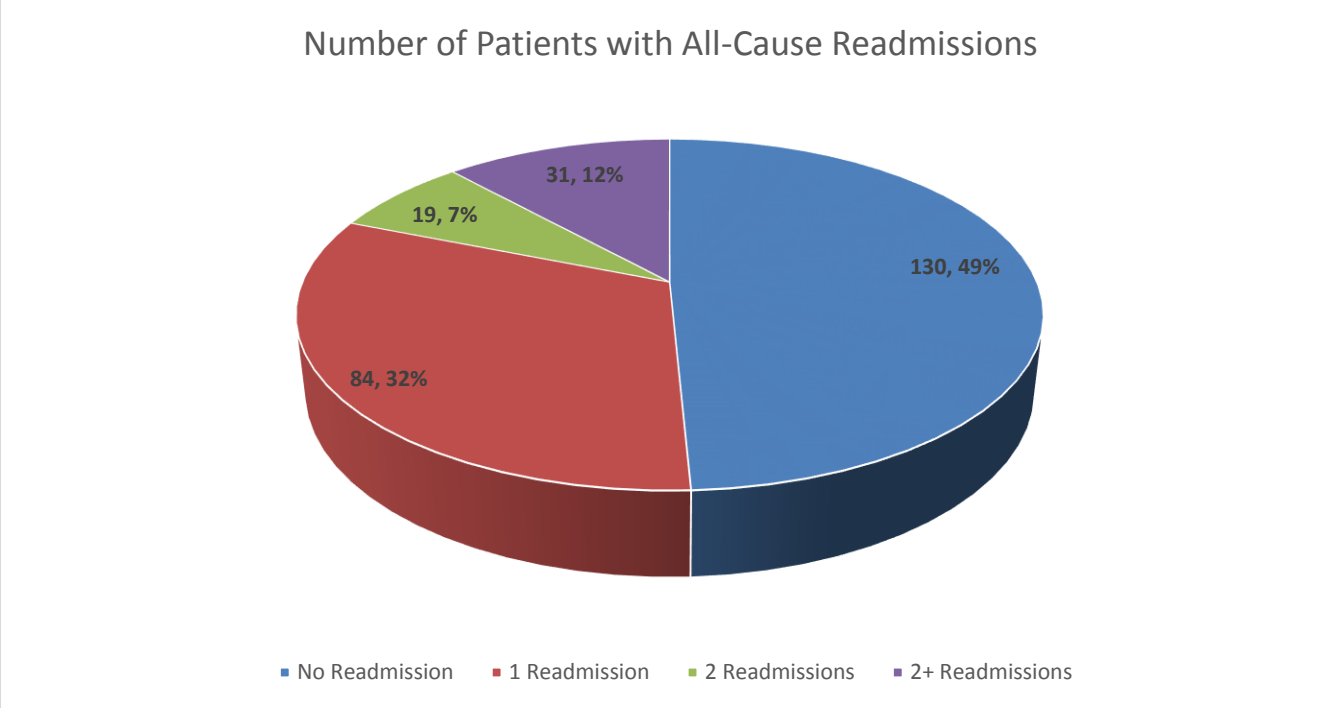
Table 3.4 describes the one-year follow up healthcare resource utilization and readmissions. The HFpEF patients had an average of 3.8 (SD 5.0) inpatient readmissions, which equates to 7.3 hospital days (SD 12.1) one year after the index date. Nearly 51% of the patients had an all-cause readmission and 14% of patients had a HF-related readmission. Patients who saw a cardiologist during the pre-index period had a higher number of inpatient readmissions, inpatient hospital days, primary care visits, cardiologist visits, ED visits, and all-cause readmissions than those without a cardiologist.

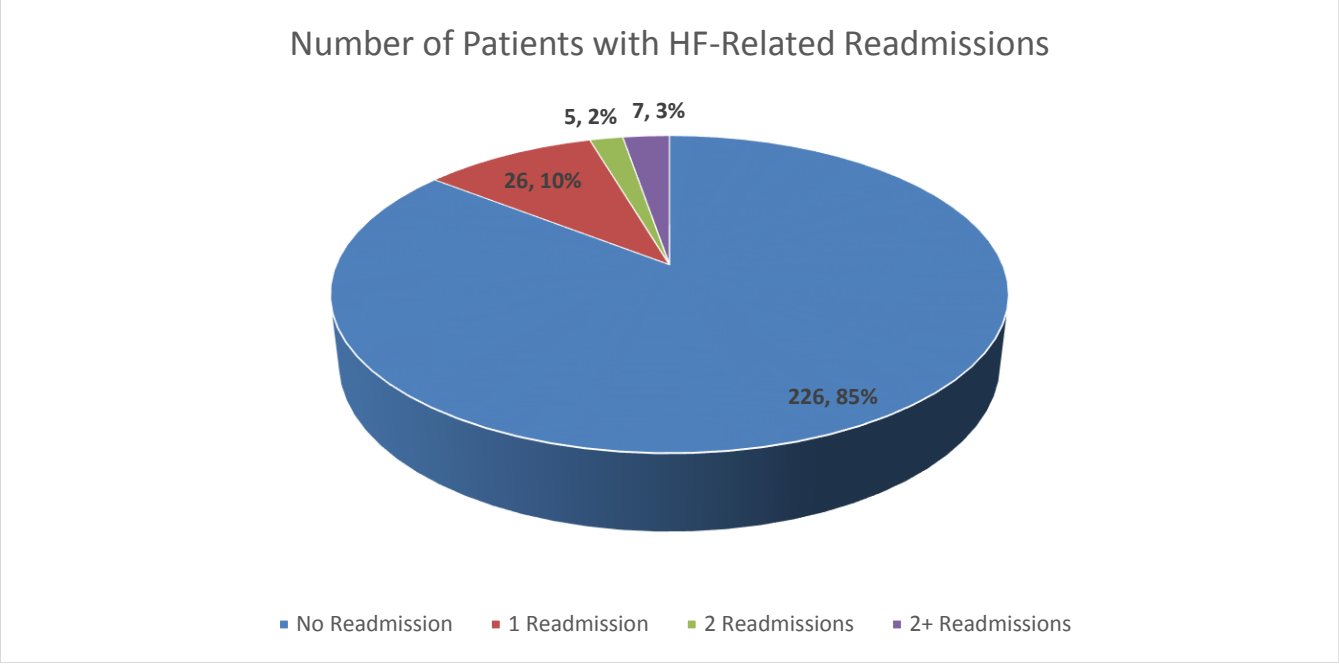
Figure 3.1 shows the breakdown of the number of patients with readmissions. Nearly 51% of the HFpEF patients (n=134) had an all-cause readmission during the 1-year post index, with 31 patients having 3 or more readmissions. About 15% of the patients had a HF-related readmission (n=38) and 7 patients had 3 or more HF-related readmissions.

Table 3.4 – One Year Follow Up Healthcare Resources Utilization and Readmission

	All HFpEF (n=264)	*HFpEF w/o Card (n=77)*	*HFpEF w/ Card (n=187)*	*p-value*
Number of Inpt Admission	3.8 (5.0)	2.9 (2.9)	4.2 (5.6)	**0.0374**
Inpt Hospital days	7.3 (12.1)	5.1 (7.2)	8.2 (13.5)	**0.0222**
Primary care visit	19.9 (14.3)	16.6 (13.4)	21.3 (14.4)	**0.0014**
Cardiologist visits	5.8 (7.5)	3.3 (3.2)	6.69 (8.4)	**<0.0001**
ED visits	2.3 (2.6)	1.6 (1.8)	2.6 (2.8)	**<0.0001**
All cause readmitted	134 (50.8%)	27 (35.1%)	107 (57.2%)	**0.0011**
HF readmitted	38 (14.4%)	7 (9.1%)	31 (16.6%)	0.1152

Figure 3.1 - Number of Patients with Readmission





3.4 Predictive Modeling

Table 3.5 shows the results of the Poisson regression models for predictors of the number all-cause readmissions. Being older (by 10 years) is associated with lower number of all- cause readmission with an incidence rate ratio (IRR) of 0.81 (p-value=0.0092). Having a cardiologist and having more comorbidities at baseline is associated with higher number of all-cause readmissions with an IRR of 2.21 (p-value=0.0003) and 1.19 (p-value=0.0038) respectively.

Table 3.6 shows the results of the Cox Proportional Hazard models for predictors of the time to first all-cause readmission. Patients who have cardiologists were 91% more likely to be readmitted at any time point during the study period (HR of 1.91, p-value=0.0040). The Kaplan-Meier curve of time to first all-cause readmission for those with and without a cardiologist is illustrated in Figure 3.2.

Table 3.7 shows the results of the Poisson regression models for predictors of the number of heart failure-related readmissions. Being on a diuretic at baseline is associated with higher number of heart failure-related readmissions, with an incidence rate ratio of 2.84 (p-value=0.0301).

Table 3.8 shows the results of the Cox Proportional Hazard models for predictors of the time to first HF-related readmission. Patients who use beta-blockers were 83% less likely to be readmitted at any time point, while those who used calcium channel blockers were 71% less likely to be readmitted at any time point during the study period (HR of 0.17, p-value=0.0012 and HR of 0.29, p-value=0.0054). The Kaplan-Meier curve of time to first HF-related readmission for those with and without a cardiologist is illustrated in Figure 3.3.

Table 3.9 shows the results of the logistic regression models for predictors of the odds of heart failure-related readmissions. None of the variables were predictive of the odds of having another heart failure-related readmission.

Table 3.5 – Model 1 to Evaluate Predictors of Number of All-Cause Readmission
Poisson Regression (or related approach appropriate to the distribution such as negative binomial regression) for Number of Readmission All Cause = Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)

Variable	*IRR*	*95% CI*	*Chi-Square*	*p-value*
Age (10 year)	0.81	0.69-0.95	6.78	**0.0092**
Female	1.05	0.74-1.51	0.08	0.7720
Cardiologist	2.21	0.49-0.05	12.89	**0.0003**
Number of Inpt admission	1.04	0.99-1.10	2.87	*0.0851*
Number of comorbidities	1.19	1.06-1.34	8.39	**0.0038**
Antiarrhymic use	0.81	0.42-1.54	0.42	0.5157
Beta-blocker use	0.95	0.62-1.45	0.07	0.7969
CC blocker use	0.91	0.52-1.33	0.25	0.6144
ACEI/ARB use	1.20	0.82-1.75	0.88	0.3474
Diuretic use	1.15	0.76-1.74	0.44	0.5056

ACEI- Angiotensin-converting enzyme inhibitors, ARB- Angiotensin II-receptor blocker, BB- Beta blocker, CCB- Calcium Channel blocker, Inpt- Inpatient

Table 3.6 – Model 2 to Evaluate Predictors of Time to First All-Cause Readmission

Cox Proportional Hazards Regression** for Time to First Readmission All Cause = Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)

Variable	*HR*	*95% CI*	*Chi-Square*	*p-value*
Age (10 year)	0.87	0.75-1.02	3.09	*0.0789*
Female	1.04	0.72-1.51	0.05	0.8247
Cardiologist	1.91	1.23-2.96	8.30	**0.0040**
Number of Inpt admission	1.03	0.98-1.07	1.18	0.2770
Number of comorbidities	1.12	0.99-1.26	3.25	*0.0712*
Antiarrhythmic use	1.07	0.59-1.92	0.05	0.8300
Beta-blocker use	0.80	0.51-1.23	1.06	0.3034
CC blocker use	0.91	0.62-1.33	0.26	0.6109
ACEI/ARB use	1.20	0.80-1.78	0.78	0.3767
Diuretic use	1.49	0.95-2.33	3.06	*0.0803*

ACEI- Angiotensin-converting enzyme inhibitors, ARB- Angiotensin II-receptor blocker, BB- Beta blocker, CCB- Calcium Channel blocker, Inpt- Inpatient

Figure 3.2 – Time to First All-Cause Readmission by Cardiologist Status

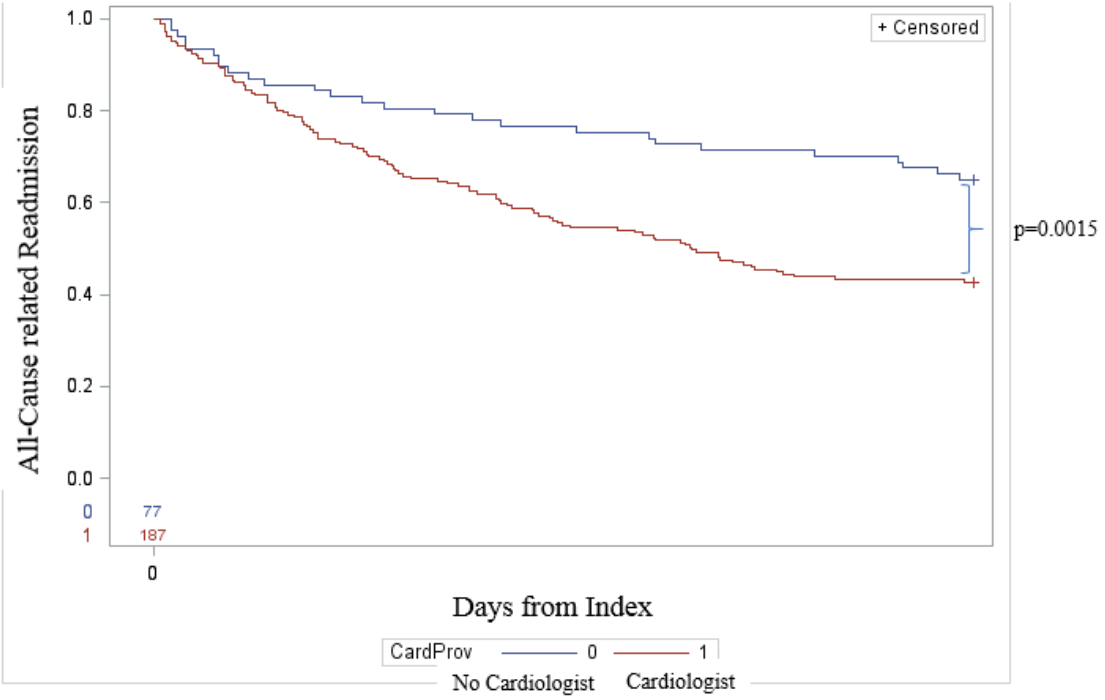


Table 3.7 – Model 3 to Evaluate Predictors of Number of HF-Related Readmission
Poisson Regression (or related approach) for Number of HF related Readmission = Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)

Variable	*IRR*	*95% CI*	*Chi-Square*	*p-value*
Age (10 year)	0.89	0.65-1.22	0.54	0.4612
Female	1.07	0.50-2.31	0.03	0.8631
Cardiologist	1.69	0.70-4.07	1.38	0.2404
Number of Inpt admission	0.98	0.88-1.10	0.09	0.7685
Number of comorbidities	1.31	0.99-1.73	3.63	*0.0568*
Antiarrhythmic use	0.85	0.22-3.35	0.05	0.8155
Beta-blocker use	0.74	0.30-1.83	0.43	0.5112
CC blocker use	1.04	0.47-2.32	0.01	0.9160
ACEI/ARB use	0.74	0.33-1.67	0.54	0.4639
Diuretic use	2.84	1.11-7.29	4.70	**0.0301**

ACEI- Angiotensin-converting enzyme inhibitors, ARB- Angiotensin II-receptor blocker, BB- Beta blocker, CCB- Calcium Channel blocker, Inpt- Inpatient

Table 3.8 – Model 4 to Evaluate Predictors of Time to First HF-related Readmission
Cox Proportional Hazards Regression** for Time to First Readmission HF= Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N)

Variable	*HR*	*95% CI*	*Chi-Square*	*p-value*
Age (10 year)	0.76	0.55-1.06	2.56	0.1096
Female	1.24	0.54-2.84	0.26	0.6087
Cardiologist	2.56	0.83-7.88	2.69	0.1007
Number of Inpt admission	1.02	0.88-1.17	0.06	0.8063
Number of comorbidities	1.16	0.81-1.67	0.64	0.4226
Antiarrhythmic use	2.40	0.69-8.30	1.89	0.1685
Beta-blocker use	0.17	0.06-0.50	10.42	**0.0012**
CC blocker use	0.29	0.12-0.69	7.75	**0.0054**
ACEI/ARB use	2.48	0.91-6.72	3.16	*0.0754*
Diuretic use	2.08	0.84-5.17	2.50	0.1135

ACEI- Angiotensin-converting enzyme inhibitors, ARB- Angiotensin II-receptor blocker, BB- Beta blocker, CCB- Calcium Channel blocker, Inpt- Inpatient

Figure 3.3 – Time to First HF-Related Readmission by Cardiologist Status

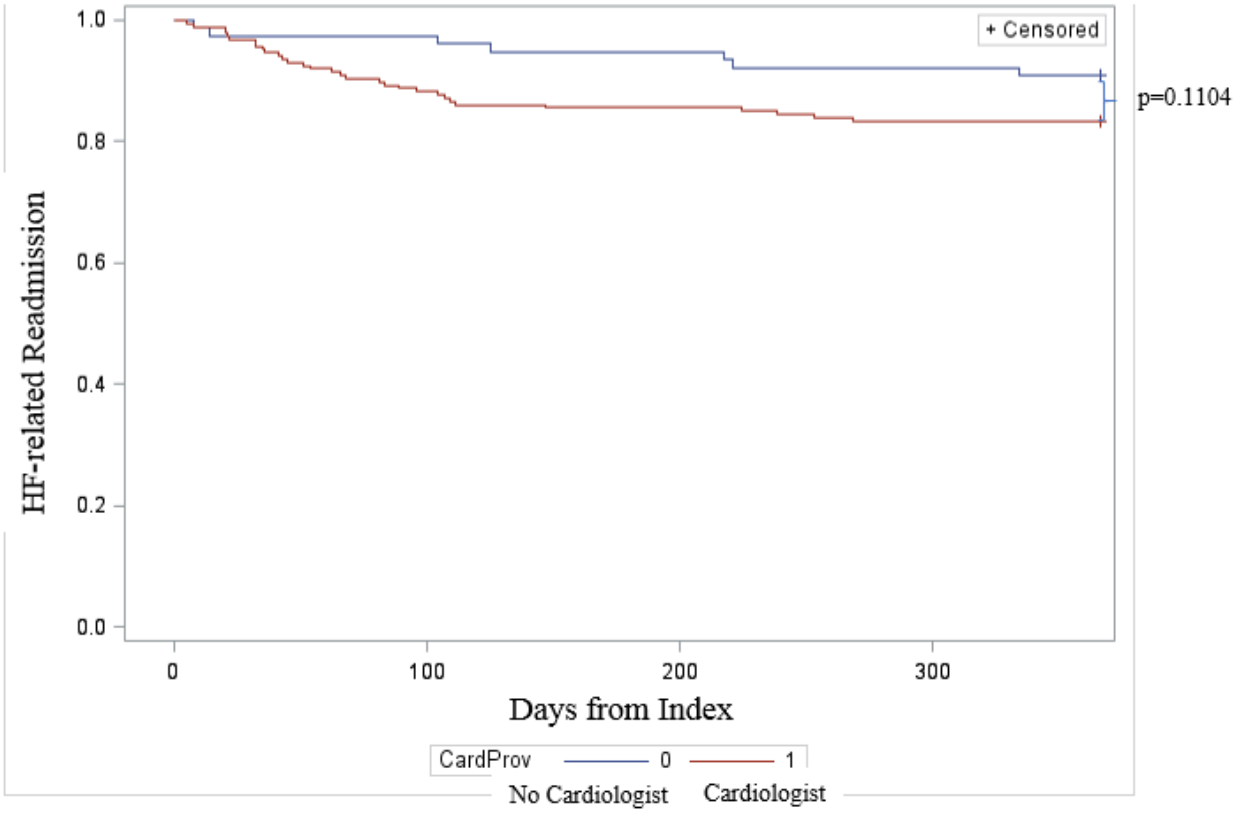


Table 3.9 – Model 5 to Evaluate Predictors of Odds of HF-Related Readmission
Logistic Regression for Number of HF related Readmission (yes/no)= Age (#) + Gender (M/F) + Provider (Non-Cardiologist/Cardiologist) + Baseline Number of Inpt Admissions + Comorbidity* (#) + Antiarrhythmic (Y/N) + Beta-Blocker (Y/N) + Calcium Channel Blocker (Y/N) + RAAS-inhibiting agents (Y/N) + Diuretics (Y/N);

Odds Ratio Estimates

Effect	OR	95% Confidence Limits		p-value
Age (10 year)	0.782	0.570	1.073	0.1278
Female	0.711	0.333	1.516	0.3776
Cardiologist	1.748	0.703	4.345	0.2291
Number of Inpt admission	1.001	0.902	1.109	0.9901
Number of comorbidities	1.221	0.949	1.571	0.1213
Antiarrhythmic use	1.333	0.401	4.432	0.6394
Beta-blocker use	0.863	0.356	2.092	0.7436
CC blocker use	1.429	0.649	3.145	0.3752
ACEI/ARB use	0.847	0.389	1.842	0.6748
Diuretic	2.238	0.867	5.778	0.0959

ACEI- Angiotensin-converting enzyme inhibitors, ARB- Angiotensin II-receptor blocker, BB- Beta blocker, CCB- Calcium Channel blocker, Inpt- Inpatient

3.5 Summary of Results

Results of all hypothesis tested are reported in Table 3.10. A higher number of and shorter time to all-cause readmissions was associated with patients who have a cardiologist (Objective 1). Being on a diuretic at baseline was associated with a higher number of heart failure-related readmissions while being on beta-blockers and calcium channel blockers was associated with a longer time to first heart failure-related readmission (Objective 2). A higher number of all-cause readmissions was associated patients having more comorbidities (Objective 3)

Table 3.10 – Results of Hypothesis Test

Objectives and Alternate Hypothesis (H_1)	**Results**
Objective 1: To determine whether being managed by a cardiologist affected the number of, time to, and odds of readmission (HF-related and all-cause)	
$H_1$1.1 The difference in the number of readmissions (HF-related and all-cause) experienced by patients managed by a cardiologist and patients not managed by a cardiologist is statistically significant.	Failed to Reject (all-cause readmission)
$H_1$1.2 The difference in time to first readmission (HF-related and all-cause) experienced by patients managed by a cardiologist and patients not managed by a cardiologist is statistically significant.	Failed to Reject (all-cause readmission)
$H_1$1.3 The difference in odds for HF-related readmission experienced by patients managed by a cardiologist and patients not managed by a cardiologist is statistically significant.	Rejected

Table 3.10 – Results of Hypothesis Test (continued)

Objective 2: To determine whether the number of comorbidities affect the number of, time to, and odds of readmission (HF-related and all-cause)	
H_I2.1 The number of readmissions (HF-related and all-cause) experienced by patients will differ significantly based on the number of comorbidities.	Failed to Reject (all-cause readmission)
H_I2.2 The time to first readmission (HF-related and all-cause) experienced by patients will differ significantly based on the number of comorbidities.	Rejected
H_I2.3 The odds for HF-related readmission experienced by patients will differ significantly based on the number of comorbidities.	Rejected
Objective 3: To determine whether the type of treatment (antiarrhythmics, beta-blockers, calcium channel blocker, renin-angiotensin aldosterone system inhibitor, or diuretic) affects the number, time, and odds of readmission (HF-related and all-cause)	
H_I3.1 The number of readmissions (HF-related and all-cause) experienced by patients will differ significantly based on the type of treatments (Antiarrhythmic, BB, CCB, RAAS inhibitor or Diuretic).	Failed to Reject (HF readmission for Diuretics)
H13.2 The time to first readmission (HF related and all cause) experienced by patients will differ significantly based on the type of treatments (Antiarrhythmic, BB, CCB, RAAS inhibitor or Diuretic).	Failed to Reject (HF readmission for BB and CCB)
H_I3.3 The odds for HF-related readmission experienced by patients will differ significantly based on the type of treatments (Antiarrhythmic, BB, CCB, RAAS inhibitor or Diuretic).	Rejected

CHAPTER 4: DISCUSSION AND CONCLUSION

4.1 Discussion

The purpose of this study was to assess the effects of demographic, clinical characteristics, healthcare resource utilization and medication on number of readmissions, time to readmission, and odds of readmission for patients with HFpEF. The study focuses on patients with HFpEF due to the limited research and treatment options in this cohort compared to HFrEF.[1,19,20,42] The study is consistent with current literature where HFpEF patients were more likely to be female (60%) and older (mean age at index of 79 years) given the pathophysiology of the disease which increases with age.[47-49] Patients had an average of 3.7 comorbidities, with 67% suffering from dyslipidemia, 89% from hypertension, and 59% from dysrhythmia. The number of comorbidities were higher among those treated by cardiologists, which is supportive of previous findings where multimorbidity is common in HFpEF patients.[19-20] Furthermore, HFpEF is typically associated with hypertension, aging, coronary heart disease, diabetes, sleep disordered breathing, obesity, kidney disease, lung disease and anemia.[32-36] Thus, it is no surprise that a higher number of all-cause readmissions was associated with patients having more comorbidities.

This studied shows that patients who have a cardiologist were associated with a higher number all-cause readmissions and a shorter time to all-cause readmissions. While this may be a predictive factor, it is not believed to be causative. Based on the bivariate analysis, patients with cardiologist care appear to be at higher risk and with greater number of comorbidities, including diabetes, dyslipidemia, hypertension, coronary heart disease, cardiomyopathy, and valvular heart disease than those without a cardiologist. Although our model adjusted for various factors such as age, number of comorbidities, and treatments, it was not able to account for severity of conditions.

A study of 275 patients showed that patients under generalist care had less severe cardiac disease than those cared for by cardiologist. The study suggested that any differences in outcomes between the two groups of patients were likely due to the severity of underlying disease and co-morbidites rather than quality of care that was provided by the physicians. [51] Furthermore, another study of 1,298 patients based out of the San Francisco Bay area found that patients were less likely to receive care from a cardiologist if they were black, had less income, or were older. [52] These socioeconomic factors are well-established factors for access to healthcare resources, which were not in our predictive models for hospital readmission.

None of the typical HF treatments were associated with the number of all-cause readmissions. While the ACEI or ARB with beta-blockers are recommended in all patients with stable heart failure with reduced ejection fraction, there is no proven treatment for HF patients with preserved EF. This is evident in the study where ACEI/ARBs, beta-blockers, calcium channel blockers, and diuretics were utilized by only half of the patients. The best guidance from the ACC/AHA is to manage hypertension to prevent morbidity and use diuretics to relieve symptoms. There was evidence that suggests being on diuretic at baseline is associated with higher number of heart failure-related readmission. However, this may also be confounded by patient disease severity since diuretics and aldosterone antagonists are added to help manage the symptoms and severity of HF.[1]

Just over half of the patients suffered from an all-cause readmission, which is consistent with the hospitalization rate from the OPTIMIZE HF Registry, a large national registry and performance improvement program for patients hospitalized for HF.[50] This illustrates a significant unmet need and opportunity for improvement, especially given the payment incentive from the Hospital Readmission Reduction Program. In a study evaluating strategies to reduce 30-day

readmissions in older patients hospitalized with heart failure, the author recognizes that predictors and strategies are limited.[53] It's clear that readmission may not be readily explained by simple deterministic understanding of risk, and our pilot supports this conclusion. Thus, an integrated view of patient risk, recovery after hospitalization, and innovative treatment for patients with HFpEF is needed to effectively manage the disease.

4.2 Limitations

Due to the nature of the retrospective observational study, limitations should be taken into consideration for the interpretation of findings. First, data utilized in this study were collected for hospital administrative purposes and not for research. Therefore, administrative data may not always accurately capture patient and clinical characteristics. In addition, it is well known that studies using administrative data cannot confirm ingestion of prescribed medications; the current study can only determine that the prescription was filled at the pharmacy. Multivariate regression and Cox proportional hazard models are common methodologies to analyze associations, but causations may require more intensive prospective randomized control studies. Finally, the patient population is predominantly made up of a small set of patients in central Texas, which may not be representative or generalizable to broader population. The small sample size limits the number and depth of predictive factors tested in the analysis. Thus, there may be confounding factors not considered and the results are hypothesis generating in nature.

4.3 Conclusion

As the United States population continues to age and healthcare cost rises, innovative management of the prevalent HFpEF condition is needed to curb the progression of the disease and the strain on the healthcare system from readmission. This study demonstrated that all-cause and heart failure-related readmissions signify an unmet need. The pilot predictive models show that various factors associated with higher risk patients such as those with cardiologist management, more comorbidities and use of diuretics may be associated with increased hospital readmissions. Further research is needed to take a more comprehensive look at the predictors of hospital readmissions over a larger patient cohort while controlling for more confounding factors to identify opportunities for improvement.

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