ADHERENCE TO EVIDENCE-BASED PHARMACOLOGICAL GUIDELINES AND OUTCOMES FOR HEART FAILURE IN PRIMARY CARE PROVIDERS

by

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A DNP Project Submitted to the Faculty of the

COLLEGE OF NURSING

In Partial Fulfillment of the Requirements

For the Degree of

DOCTOR OF NURSING PRACTICE

In the Graduate College

THE UNIVERSITY OF ARIZONA

2014
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ACKNOWLEDGEMENTS

I would like to acknowledge my family, particularly my wife Eden; this project could not have been possible without her love and support during the entire process. Eden and my two beautiful kids’ smiles and humor made the completion of this project possible. I would like to thank my mother-in-law and extended family members for your understanding when I was not available for many holidays and the times away because of this project. Additionally, I am fortunate to have my two brothers who encouraged and supported me to focus during this educational endeavor.

I am sincerely grateful to my advisor Dr. Shu-Fen Wung for her patience, responsiveness and phenomenal presence during this special journey. Your insight and ideas during this process have shaped me into a doctorally-prepared clinician. I am sincerely grateful to my doctoral committee members Dr. Carrie Merkle and Dr. Anne G. Rosenfeld during the entire project.

I wish to extend my acknowledgement to all staff at Providers Direct primary care practice, particularly to Dr. John Schmaling, Carrie Catalano and Monica Villaescusa for their invaluable support during data collection process.
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ABBREVIATIONS

AHA - American Heart Association
ACCF - American College of Cardiology Foundation
ACEI - Angiotensin converting enzyme inhibitors
ACS - Acute coronary syndrome
ARB - Angiotensin receptor blocker
ASCVD - Atherosclerotic cardiovascular disease
AST - Aspartate aminotransferase
ALT - Alanine aminotransferase
BNP - Brain natriuretic peptide
BMI - Body mass index
CDC - Centers for Disease Control and Prevention
CHADS - Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, previous Stroke/transient ischemic attack
EMR - Electronic medical record
ESC - European Society of Cardiology
EF - Ejection fraction
GFR - Glomerular filtration rate
HF - Heart failure
HFrEF - HF with reduced ejection fraction
HFpEF - HF with preserved ejection fraction
HbA1C - Hemoglobin A1C

HDL - High density lipoprotein

ICD - International Classification of Disease

LDL - Low high-density lipoprotein

LVEF - Left ventricle ejection fraction

LVSD - Left ventricular systolic dysfunction

NYHA - New York Heart Association

PI - Principal Investigator

RAAS-I - Renin angiotensin aldosterone system inhibitors

TIA- Transient ischemic attack
LIST OF ILLUSTRATION

Figure 1

Study Flow Chart of Sample Selection for the Analysis of Adherence to Pharmacologic Treatment

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ABSTRACT

Background: Heart failure (HF) is a major public health problem in the United States and accounts for a large burden in rising health care expenditures. Appropriate use of evidence-based pharmacological treatment, including the use of renin-angiotensin-aldosterone inhibitors and beta-blockers can slow progression of the disease and reduce the need for hospitalization.

Objectives: In a sample of individuals with HF in a primary care setting, the objectives of this study were to determine the level of providers’ adherence to evidence-based pharmacological guidelines and the rate of cardiovascular-related emergency department or hospital visits.

Methods: A convenience sample of patients 18 years of age and older with a diagnosis of HF was included. A retrospective chart review of 54 HF subjects was done between April and September 2014, using the American College of Cardiology Foundation and American Heart Association outpatient performance measurement set for HF.

Results: Adherence to guideline recommendations for beta-blocker, angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blocker ARB), anticoagulation for atrial fibrillation, statin, and aldosterone receptor antagonist therapy was present in 81%, 77.8%, 78%, 80.7% and 23.1% of eligible subjects, respectively. The use of ACEIs/ARBs (OR=8.853, CI 1.212-64.66, p= 0.032) and beta-blockers (OR= 9.24, CI 1.212-70.438, p =0.031) was significantly associated with reduced number of (≤ 1) cardiovascular-related emergency department or hospital visits after adjusted for confounders including age, sex, body mass index, and comorbidities.
**Conclusion:** The use of ACEIs/ARBs and beta-blockers among primary care providers was comparable or higher than similar studies conducted in the primary care settings. However, despite the available evidence and recommendations, the use of aldosterone receptor antagonists in HF patients with myocardial infarction and diabetes mellitus was still low in the absence of any contraindications. These findings can be used by primary care providers to assess the existing gap in the use of HF guideline-recommended therapy and develop interventions to improve the utilization of evidence-based guidelines.
CHAPTER 1

INTRODUCTION

Heart failure (HF) continues to be a major public health problem in the United States. Every year, more than 650,000 Americans are newly diagnosed with HF. The incidence of HF approaches 10 per 1,000 in the elderly population 65 years of age and older. According to the American Heart Association (AHA) report, there were nearly 670,000 new cases of HF diagnoses in individuals over the age of 45 (AHA, 2012; Yancy et al., 2013). In addition to these staggering statistics, HF also accounts for more than 6.5 million hospital stays and 12-15 million office visits annually (American College of Cardiology Foundation [ACCF], AHA, 2009). Since 1980, there has been a steady increase in the hospitalization rates of patients with HF; this increase in hospitalization and office visit rates is likely to continue. There were no significant changes in hospital discharges for HF between 1999 and 2009 and HF was listed as the primary discharge diagnosis in 975,000 and 1,094,000 individuals, respectively. In 2009, there were 3,041,000 office visits with a primary diagnosis of HF and 668,000 emergency department visits due to HF (AHA, 2012). Between 1980 and 2006, HF hospitalization rates have significantly increased with an average annual increase of 1.2% for men and 1.55% for women (Liu, 2011). Finally, HF is the primary or contributory cause of death in approximately 300,000 patients annually. The number of deaths has increased steadily, despite technological advances and improved treatments in care for HF patients (AHA, 2012).

HF currently claims more lives yearly than any other common chronic disease such as cancer, chronic lower respiratory disease, and accidents combined. A recent study suggests a decrease in deaths related to cardiovascular disease from 1998 to 2008 and almost half of this
decrease is a result of the increased use of evidence-based therapies as well as lifestyle and environmental changes in our culture (AHA, 2012). In the United States, even death rates from heart disease have decreased in recent decades; mortality rates continue to be high, particularly for people living in the Southeast region, those with low socioeconomic status, and members of certain racial and ethnic groups (Centers for Disease Control and Prevention [CDC], 2011).

High mortality due to HF alone cannot fully convey the burden of heart disease and associated health problems (AHA, 2012). HF also accounts for a large burden in rising health care expenditures (AHA, 2012; Calvin et al., 2012). Due to the co-occurrence of two or more comorbidities with HF, patients take on an average of six HF-related medications, and 78% have at least two hospital admissions per year, leading to an annual cost of $10–38 billion (Calvin et al., 2012; Liu, 2011; Rosamond et al., 2007). In the United States, in 2010, an estimated $444 billion dollars was spent treating cardiovascular and other related diseases. Approximately 1 of every 6 dollars in health care spending is for treatment of these diseases. As our population ages, the economic impact of cardiovascular disease on our country’s health care system will continue to rise (CDC, 2011).

According to a report by the CDC, HF accounts for much of the rising costs in healthcare, translating into 3.4 million office visits and 1 million hospital days per year. In 2010, the total cost of HF treatment in the United States has risen to $34.4 billion (CDC, 2011). Because of the high mortality rates and large expense associated with HF treatment, it is crucial that practitioners adhere to evidence-based therapy guidelines (Calvin et al., 2012; Liu, 2011). The significant value of following these guidelines is supported by evidence, including medical therapy and lifestyle changes that effectively delay the progression of heart disease and
significantly improve survival rates (Calvin et al., 2012). Evidence-based guidelines have been developed by the ACCF/AHA for treatment of patients with HF (Calvin et al., 2012); however, little is known regarding the current adherence to these standard guidelines in the management of patients with HF among primary care providers. This study determined the overall adherence among primary care providers to HF treatment using the measures and treatment guidelines identified by the ACCF/AHA.
CHAPTER 2

LITERATURE REVIEW

HF is a complex medical problem resulting from structural or functional loss of ventricular filling or ejection of blood (AHA, 2013). This problem does not allow adequate blood flow to the vital organs. HF is associated with a wide spectrum of left ventricular function. Left ventricular ejection fraction (EF) is often used to classify HF into HF with reduced EF (HFrEF), also referred to as systolic HF, in which there is dysfunction of the left ventricle, and HF with preserved ejection fraction (HFpEF), also known as diastolic HF (Brashers, 2006).

Any damage to the heart muscles, vessels, and valves can cause HF. It can also result from metabolic abnormalities such as hypertriglyceridemia, low high-density lipoprotein, and fasting hyperglycemia that alter the normal cardiac functions (AHA, 2013; Yancy et al., 2013). Several factors and comorbidities are associated with an increased risk of structural heart disease (Yancy et al., 2013). According to ACCF/AHA, hypertension, diabetes mellitus, metabolic syndrome and atherosclerotic disease are significant risk factors for HF (AHA, 2013). Although obesity and systolic dysfunction are important risk factors for HF, about 75% of HF cases are related to hypertension (AHA, 2013).

According to ACCF/AHA there are four stages of HF (Table 1). The first stage, Stage A, includes those at a high risk for HF but do not have any structural disorder of the heart and those at risk due to certain comorbidities strongly associated with the risk of HF, including patients with a history of hypertension, coronary artery disease, diabetes mellitus, history of cardiotoxic drug therapy or alcohol abuse, rheumatic fever, and family history of cardiomyopathy. Stage B refers to patients with structural heart disease but no clinical signs or symptoms of HF. These
patients are at a higher risk of developing HF because of factors such as left ventricular hypertrophy or fibrosis, left ventricular dilatation or hypocontractility, asymptomatic valvular heart disease, or previous myocardial infarction. Stage C includes patients with symptoms caused by underlying structural heart problems. In Stage D, patients have refractory HF, requiring specialized treatment such as mechanical circulatory support, continuous inotropic infusions, cardiac transplantation, or hospice care (Yancy et al., 2013).

Table 1. ACCF/AHA Stages of HF (Yancy et al., 2013)

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<td>A</td>
<td>High risk for HF but without impaired left ventricular function, hypertrophy or chamber geometric changes and symptoms of HF, examples: patients with hypertension, diabetes, atherosclerotic disease, obesity, metabolic syndrome</td>
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<td>B</td>
<td>Structural heart disease with left ventricular hypertrophy and/or impaired function but without signs or symptoms of HF, this stage includes patients with previous myocardial infarction with left ventricular remodeling including left ventricular hypertrophy and low EF, and asymptomatic valvular disease</td>
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<tr>
<td>C</td>
<td>Structural heart disease with prior or current symptoms of HF. Stages C includes patients with known structural heart disease and shortness of breath and fatigue, reduced exercise tolerance</td>
</tr>
<tr>
<td>D</td>
<td>Refractory HF requiring specialized interventions. This stage includes patients who have marked symptoms at rest despite maximal medical therapy (examples: those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)</td>
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EF- Ejection fraction, HF- Heart failure

The ACCF and AHA have published guidelines for treatment and management of HF (AHA, 2012). Despite the recommendations of the ACCF/AHA, there is still substantial variation in the treatment of HF patients in different settings and communities (Schopfer, Whooley, & Stamos, 2012). With the intention of assisting primary care providers in making clinical decisions, practice guidelines describe a range of generally acceptable approaches for the
prevention, diagnosis, and management of HF and use of these evidence-based guidelines has been shown to be beneficial in the treatment of patients with HF (Calvin et al., 2012; Yancy et al., 2010). Current research demonstrates improved practitioner adherence to certain evidence-based guidelines for inpatients with symptoms of HF, but there is room for improvement (Yancy et al., 2010). According to the most recent research, observation of care provided to patients with HF in outpatient settings shows a low level of adherence to clinical guidelines (Yancy et al., 2010). More than 40% of providers failed to prescribe or document administration of statins and antiplatelet therapy for eligible patients in the absence of documented contraindications (Yancy et al., 2010).

According to a number of studies, most patients with HF are not diagnosed or treated according to published guidelines (Hickling, Nazareth, & Rogers, 2001; Naveiro-Rilo et al., 2012; Yancy et al., 2010). This indicates that there is a need for improvement in this area. Such improvements could reduce both mortality and morbidity from HF (Hickling et al., 2001; Richardson et al., 2010). For example, the mortality rate for those receiving an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) alone (6.1%), or a beta-blocker alone (5.9%) was higher compared to those receiving a combination of ACEI/ARB and a beta-blocker (5.3%). In contrast, among patients that did not use an ACEI, using an ARB or a beta-blocker yielded a mortality rate of 20% (p <0.0001) (Richardson et al., 2010). Based on majority of research findings, use of guideline-recommended cardiac medications in clinical practice effectively reduces mortality in HF population (Calvin et al., 2012; Peters-Klimm et al., 2012; Richardson et al., 2010).
Results from a study conducted in 10 diverse hospital settings showed that both physicians and patients have low rates of adherence (41%) to evidence-based guidelines and therapy (Calvin et al., 2012). According to this study, a majority of patients are not benefitting from life-saving drug therapy as a result of their providers’ non-adherence to these guidelines, which was adversely and independently correlated with a high number of comorbidities, older age, more advanced HF, and minority status. Patients’ non-adherence to guideline-recommended cardiac drugs was found to be primarily associated with minority status (Calvin et al., 2012).

Other reasons for the providers’ non-adherence to the recommended evidence-based guidelines can be attributed to factors such as knowledge and attitudes of providers. Providers’ knowledge and attitudes in the use of evidence-based guidelines were associated with difference in training, familiarity with guidelines, and lack of institutional systems to ensure that appropriate care was provided (Cabana et al., 1999; Calvin et al., 2012; Fonarow et al., 2010). More than 10% of providers were not aware of the available evidence-based guidelines (Cabana et al., 1999). Self-reported providers-related barriers to evidence-based prescribing of HF medications included a lack of knowledge regarding the evidence-based guidelines or confidence concerning the use of the guidelines (Kasje, Denig, De Graeff, & Haaijer-Ruskamp, 2005). Lack of knowledge, such as not knowing the target dose of ACEIs and beta-blockers, or lacks of awareness about the new practice guidelines, determine the providers’ adherence to evidence-based guidelines. Providers’ attitudes also play a role, such as lack of confidence, uncertainties about benefits for very old patients, fear for side effects or hesitancy to change the treatment in stable patients (Annema et al., 2009; Cabana et al., 1999; Kasje, et al., 2005).
Appropriate use of evidence-based pharmacological treatment, including the use of renin-angiotensin-aldosterone system inhibitors (RAAS-I) and beta-blockers, requires providers to be competent in prescribing medications and step-wise up-titration. Monitoring of typical side-effects such as low blood pressure, change in creatinine-clearance or potassium levels are also imperative (Peters-Klimm et al., 2012). In primary care settings, despite the agreement on clinical practice guidelines that recommend the use of RAAS-I in target doses, there are significant problems in transferring theory into practice. Most recent literature indicates that many patients actually do not receive RAAS-I due to provider uncertainty or lack of awareness on the usage of this drug therapy (Peters-Klimm et al., 2012). When providers are uncertain about implementation or have a lack of awareness of relevant research evidence, adherence to guidelines is decreased. Rapidly changing therapeutic guidelines are factors contributing to variations in usage and application of the clinical guidelines (Annema et al., 2009; Fuat, Hungin, & Murphy, 2003).

Drug therapies and lifestyle changes can reduce hospitalizations, but non-adherence is still a major factor (Annema et al., 2009; Peters-Klimm et al., 2012). A lack of adherence to suggested lifestyle changes, such as salt restriction, physical activity, and daily weighing, tends to be higher, ranging from 50 to over 80%, with the higher rates occurring in the more disadvantaged subgroups (Van der Wal & Jaarsma, 2008). Most studies found that worsening HF was the single most common reason for hospital readmission; however, 36% of caregivers, 56% of patients, and 63 to 65% of health care providers claimed that other factors, such as comorbidities, non-adherence, and non-optimal medications were also contributing factors (Annema et al., 2009; Luttik, & Jaarsma, 2009). According to a recent study, in only 34% of
readmissions did patients and their caregivers agree with health care providers on the underlying reason for increased readmissions rate (Annema et al., 2009). Another study conducted to determine HF-related hospitalization in California between 2007 and 2009 reports a 30-day readmission rate of 40% due to acute myocardial infarction and HF exacerbation (Ranasinghe et al., 2014).

Despite the significant improvement in use of evidence-based guidelines and medical technologies, more than 50% of HF patients were readmitted within six months of discharge according to the study conducted in California (Desai & Stevenson, 2012; Ranasinghe et al., 2014). Both health care providers and patients reported that 23 to 31% of the readmissions could probably have been prevented if there were stricter adherence to guidelines, if patients had requested help earlier, and adequate availability of multidisciplinary professionals had helped with effective discharge instructions, appropriate dose titration, education regarding HF, monitoring, and strict follow-up for use of guideline recommended treatments (Annema et al., 2009).

Physician identification of patients with HF adhering to evidence-based guideline was based on whether or not the patient chart audit showed the usage of a beta-blocker and ACEI/ARB (Calvin et al., 2012). Another recent study conducted by the primary care team of the Leon Health area revealed that the rate of adherence to evidence-based guidelines for prescribing ACEI and beta-blockers was 55.2% (Naveiro-Rilo et al., 2012). Another national study conducted in ambulatory veterans with HF and HFrEF, 87% of the study subjects were adherent to an ACEI/ARB, and 82% were adherent to a beta-blocker (Steinman et al., 2011).
Treatment with a combination of agents such as diuretic, digoxin, ACEI, and beta-blocker can provide relief of symptoms while also addressing specific pathophysiologic factors by allowing therapy to be tailored to the individual (Calvin et al., 2012; Pina, 2001). The multi-drug approach can slow progression of the disease, reduce or prevent the need for hospitalization, decrease health-care costs and mortality rates (Calvin et al., 2012; Naveiro-Rilo et al., 2012; Richardson et al., 2010). Evidence of the beneficial outcomes of the multi-drug approach has been drawn from numerous trials testing newer treatments guidelines for HF that have been evaluated in the context of the background therapy considered standard at the time of the trial (Richardson et al., 2010).

In order to provide HF patients with the best care available, providers must consider the potential benefits as well as the possible risks from the use of ACEIs/ARBs, beta-blockers, aldosterone receptor antagonists and anticoagulant for eligible patients (Calvin et al., 2012; Pina, 2001; Richardson et al., 2010).

**Clinical Guidelines**

A clinical practice guideline is a systematically developed guideline to assist providers and patient decisions about appropriate health care for specific clinical situations. Evidence-based medicine suggests that the recommendation has been developed based on unbiased and clear process of systematic review and using the best clinical research findings of the highest value to assist in the delivery of the best clinical care to patients (Watters, 2013).

**Pharmacological Therapy**

Appropriate use of ACCF/AHA guidelines, including the use of ACEIs/ARBs, beta-blockers, aldosterone receptor antagonists, statin, and digitalis, is associated with improved
quality of life, reduced mortality, and morbidity rates in HF patients (Calvin et al., 2012; Pina, 2001; Richardson et al., 2010; Yancy et al., 2013).

**ACEI/ARB**

The most recent guidelines published by the ACCF/AHA recommend the use of ACEI or ARB therapy in patients with Stage A HF and vascular disease or diabetes. In mild to moderate disease (Stage B HF), which includes structural heart disease, beta-blockers may also be introduced. ACCF and AHA recommended the use of ACEI or ARB in patients with HFrEF and left ventricular systolic dysfunction (LVSD). In addition, the use ACEI in patients with HF have shown an improvement in symptoms and functioning, a decrease in recurrent hospitalizations, and an increased survival rates (Calvin et al., 2012; Hickling et al., 2001; Richardson et al., 2010). ACEI/ARB significantly reduces the risk of death and recurrent hospitalization in HFrEF. ACEI/ARB benefits patients with all stages of HF and in patients with or without coronary artery disease. ACEI should be initiated in all patients with HFrEF unless contraindicated (Calvin et al., 2012; Hickling et al., 2001; Yancy et al., 2013). There are also potential drawbacks from ACEI. These risks include hypotension, decrease in renal function, and coughing. Hyperkalemia is also a risk, especially for patients with impaired renal function. In addition, ACEIs are contraindicated in patients with bilateral renal artery stenosis and angioedema (Pina, 2001). According to previous studies, fewer than half of patients with probable HF were given ACEI (Calvin et al., 2012; Hickling et al., 2001). It is perceived that the adverse effects of ACEIs are the largest barrier to their effective usage. ACEI or ARB should be used in all patients with HFrEF to prevent symptomatic HF (Yancy et al., 2013). As a result of research in this area,
emphasis on the importance of practicing evidence-based therapies and the concept of multi-drug therapy for HF patients must be addressed (Calvin et al., 2012; Hickling et al., 2001).

**Beta-Blockers**

Appropriate use of beta-blockers can lessen the symptoms of HF, improve the patient’s clinical status, and enhance the patient’s overall quality of life. Furthermore, use of a beta-blocker can reduce the risk of death and hospitalization like an ACEI (Calvin et al., 2012; Yancy et al., 2013). The guidelines advise providers to use beta-blockers in all patients with a reduced EF to prevent symptomatic HF, even if in the absence of previous history of myocardial infarction, unless contradicted (Yancy et al., 2013). These benefits of beta-blockers were seen in patients with or without coronary artery disease and in patients with or without diabetes mellitus, as well as in women and blacks. The use of a beta-blocker such as bisoprolol, carvedilol, and sustained release metoprolol succinate is recommended for all patients with current or prior symptoms of HFrEF, unless contraindicated, to reduce morbidity and mortality (Calvin et al., 2012; Gonzalez-Garcia et al., 2013; Yancy et al., 2013).

A recent study has shown that Carvedilol, a beta-blocker with vasodilator properties, significantly reduced the mortality risk by 65% (Pina, 2001). Similar findings on the beneficial impact of Carvedilol in reducing mortality and readmission rates have been reported (Calvin et al., 2012; Gonzalez-Garcia et al., 2013; Pina, 2001). There is consensus that a complementary treatment using a beta-blocker and an ACEI improves the outcome of HF patients (European Society of Cardiology [ESC], 2012; Yancy et al., 2013). Both should be started as soon as possible after diagnosis of HFrEF. This is due to the modest effect of ACEI on left ventricular remodeling and substantial improvement in EF from the use of beta-blockers. Additionally, beta-
blockers are more effective in reducing the risk of sudden cardiac death, and exhibit early reduction in overall mortality due to anti-ischemic action (ESC, 2012).

**Aldosterone Receptor Antagonists**

The addition of low-dose aldosterone receptor antagonists in carefully selected patients with moderate to severe HF symptoms and recent decompensation or with left ventricular dysfunction early after myocardial infarction should be considered to reduce cardiovascular disease death and recurrent hospitalizations (Nappi & Sieg, 2011; Pitt et al., 1999; Vizzardi et al., 2013). The ACCF/AHA guidelines recommend the use of aldosterone receptor antagonists in patients with NYHA class II–IV (Table 2) that have LVEF ≤ 35% and in those following an acute myocardial infarction that have LVEF ≤ 40% with symptoms of HF or diabetes mellitus (Yancy et al., 2013). Spironolactone is the most widely-used aldosterone receptor antagonists.

Several previous studies demonstrated that the addition of low doses of spironolactone to ACEI therapy for patients with NYHA class II-IV HF reduces cardiovascular disease-related death and hospitalization (Nappi & Sieg, 2011; Pitt et al., 1999; Vizzardi et al., 2013). According to a large-scale, long-term trial conducted in patients with NYHA class II-IV HF, the aldosterone receptor antagonists in patients being treated with an ACEI the risk of death was reduced from 46 to 35% over 2 years, with a 35% reduction in HF hospitalization and an improvement in functional class (Pitt et al., 1999).

According to recent data collected in the United States from 81,570 post-acute myocardial patients from 219 hospitals between 2006 and 2009, among eligible patients, only 9.1% were prescribed aldosterone receptor antagonists at discharge. Based on this study, the use of aldosterone receptor antagonists increased from 6.0 to 13.4% (p < 0.001) from 2006 to 2009.
(Rassi et al., 2013). Another study conducted at Durham Veterans Affairs medical center on patients with HF and EF ≤ 45%, aldosterone receptor antagonists were prescribed for 36% of the total 64 eligible patients (Atwater et al., 2012). The electronic medical record (EMR) system in the Veterans Administration health systems provides over 10 years of patient history, echocardiogram, imaging and medication history in a single user-friendly platform to alert providers to use guideline-recommended medications (Atwater et al., 2012). Despite the available evidence and recommendation to use aldosterone receptor antagonists in patients with HFrEF and myocardial infarction, their use is extremely low in the absence of any contraindications (Lew & DeMaria, 2013; Rassi et al., 2013; Vizzardi et al., 2013).
Table 2. New York Heart Association (NYHA) Functional Classification of Heart Failure (Yancy et al., 2013)

<table>
<thead>
<tr>
<th>Class</th>
<th>Patient Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (Mild)</td>
<td>No limitation or symptoms of physical activity. Ordinary physical activity does not cause symptom of HF such as fatigue, palpitation, dyspnea, or angina.</td>
</tr>
<tr>
<td>II (Mild)</td>
<td>Mild symptoms or slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.</td>
</tr>
<tr>
<td>III (Moderate)</td>
<td>Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.</td>
</tr>
<tr>
<td>IV (Severe)</td>
<td>Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency and the angina syndrome present at rest. Discomfort increased with any physical activity.</td>
</tr>
</tbody>
</table>

HF- Heart failure

**Statin**

Other comorbid conditions such as diabetes and dyslipidemia often exist in patients with HF (Annema et al., 2009; Calvin et al., 2012; Pina, 2001) and require the use of non-cardiac medications (Calvin et al., 2012; Pina, 2001; Richardson et al., 2010). Patients with atherosclerotic disease are at high-risk to develop HF. Providers should use the guideline-recommended medications to control vascular risk factors. Appropriate treatment of hyperlipidemia with statins and long-term treatment with ACEI in patients with atherosclerotic disease may also reduce the risk of HF (Yancy et al., 2013). Cholesterol-lowering statin therapy should be initiated for adults ≤75 years of age with atherosclerotic cardiovascular disease (ASCVD) such as, coronary heart disease, stroke, and peripheral arterial disease, patients with low density lipoprotein(LDL) \( \geq 190 \text{ mg/dL} \), diabetes age 40 to 75 years with LDL–C 70 to 189 mg/dL and without clinical ASCVD (Stone et al., 2013).

The treatment goal is to lower the LDL–C to < 70 mg/dL in individuals with a prior history of ASCVD (secondary prevention) and LDL–C to <100 mg/dL in patient with no prior
history of ASCVD (primary prevention) (Stone et al., 2013). For patients that do not experience frequent symptoms, compliance to multi-drug therapy may be challenging. It is imperative that the clinician ensures that the patient understands the importance of complying with the prescribed regimen in order to avoid the risk of more serious problems in the future. Close monitoring of patients is extremely important with multi-drug therapy to ensure that medication dosage provides maximum benefits and minimizes side effects (Annema et al., 2009; Calvin et al., 2012; Pina, 2001).

**Treatment of Hypertension**

Uncontrolled hypertension is another major independent risk factor for coronary artery disease, stroke, and HF. The overall goal of controlling high blood pressure is to reduce morbidity and preventable death. AHA established therapeutic targets for blood pressure to prevent complications and deaths related to uncontrolled hypertension. The current target blood pressure is less than 140/90 mm Hg for the general population and less than 130/80 mm Hg in individuals with diabetes mellitus, ASCVD, and chronic kidney disease (Rosendorff et al., 2007). For patients with left ventricular dysfunction, target blood pressure should be less than 120/80 mm Hg (Rosendorff et al., 2007). Failure to use ACEIs/ARBs, beta-blockers or aldosterone receptor antagonists for eligible patients according to ACCF/AHA guidelines by the practitioner in the absences of any clinical contraindications listed in Table 3 is considered non-adherence to evidence-based guidelines recommended by ACCF/AHA (AHA, 2009).

**Diuretics**

Nearly 90% of HF hospitalizations in the United States are due to complications related to excess sodium and fluid (Contanzo & Jessup, 2012). HF patients with evidence of fluid
overload should start a diuretic unless contraindicated to achieve an euvolemic state (AHA, 2005; Contanzo & Jessup, 2012). Diuretics act at the loop of Henle and distal portion of the renal tubule to inhibit the reabsorption of sodium or chloride to decrease fluid retention in patients with HF (Yancy et al., 2013). Initiation of diuretics produces more rapid symptomatic relief associated with fluid overload than any other drug for HF. Diuretics can relieve any central or peripheral fluid retention such as pulmonary and peripheral edema within hours; however, the apparent clinical effects of digitalis, ACEIs, or beta-blockers may require weeks or months (AHA, 2005; Contanzo & Jessup, 2012). Diuretics should generally be used in combination with an ACEI, beta-blocker and aldosterone receptor antagonist. The ACCF/AHA guidelines recommend the use of diuretics in patients with HFrEF that have evidence of fluid overload, unless contraindicated, to improve symptoms (Yancy et al., 2013).

**Anticoagulants, Digitalis, Hydralazine and Nitrates**

For patients with moderate to severe disease (Stage C, NYHA Class I – IV), additional drug therapy may include anticoagulants or digitalis, along with combination therapies including hydralazine and nitrates (AHA, 2005).

Patients with chronic HF with permanent and persistent paroxysmal atrial fibrillation who have a high risk factor for cardioembolic stroke such as history of hypertension, diabetes mellitus, and previous stroke or transient ischemic attack, or ≥ 75 years of age should receive chronic anticoagulant therapy (Yancy et al., 2013). The indication and selection of an anticoagulant agent for permanent/persistent/paroxysmal atrial fibrillation depends on the risk factors, cost, patient factors (age and tolerability), potential for drug interactions, and other clinical characteristics. The clinical effect of long-term anticoagulant use for the prevention of
stroke in patients with atrial fibrillation is well established. However, the ACCF/AHA guidelines recommend the use of the CHADS score [Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, previous Stroke/transient ischemic attack (doubled risk weight)] to assess patient risk for stroke and to assist in the selection of anticoagulant agent (Yancy et al., 2013). In patients with moderate to high risk of thromboembolic events (CHADS2 score ≥ 2), warfarin or other anticoagulants significantly reduce the incidence of stroke (Akao et al., 2013; Yancy et al., 2013).

In one study conducted in Japanese patients with atrial fibrillation, more than 50 % of the subjects had CHADS2 score 2 or more and 87.3 % of these subjects were taking warfarin (Atarashi et al., 2011). A community based survey conducted in Fushimi atrial fibrillation registry in Japanese patients with atrial fibrillation at 76 institutions, warfarin was prescribed in only 48.5 % of the study subjects (Akao et al., 2013). A study conducted in hospitalized patients with atrial fibrillations between 2003 and 2004 in the United States, only about 56% of the subjects received warfarin. Older age, certain risk of bleeding, such as liver disease and renal disease, were associated with lower likelihood of warfarin use in hospitalized patients (Agarwal, Bennett, & Smith, 2010).

Digoxin can be beneficial in patients with HFrEF, unless contraindicated, to decrease HF-related hospitalizations (Yancy et al., 2013). Providers may consider initiating digoxin in patients with persistent symptoms of HFrEF during guideline-directed medical therapy. Digoxin is occasionally indicated in patients with HFrEF and atrial fibrillation; however, beta-blockers are usually more effective in controlling the ventricular response when added to digoxin, particularly during exercise. Digoxin should not be prescribed if the patient has significant sinus
or atrioventricular block unless the block has been resolved with a permanent pacemaker.

Digoxin should be used with caution in patients taking other drugs that can suppress sinus or atrioventricular nodal function or affect digoxin levels such as amiodarone or beta-blockers (AHA, 2005; Yancy et al., 2013).

The ACCF/AHA guidelines recommends the combination of hydralazine and isosorbide dinitrate in African Americans with NYHA class III–IV HFrEF receiving optimal therapy with ACEI and beta-blockers to reduce morbidity and mortality, unless contraindicated (AHA, 2005; Yancy et al., 2013).
Table 3. Contraindications and commonly used drugs in HF (Yancy et al., 2013)

<table>
<thead>
<tr>
<th>Drug group</th>
<th>Contraindications</th>
</tr>
</thead>
</table>
| ACEIs/ARBs                  | • Chronic renal failure (serum creatinine > 2.5mg/dL), serum potassium > 5.5 mEq/L  
                                • Bilateral renal artery stenosis, severe aortic stenosis and angioedema |
| BBs                         | • Asthma, second or third degree heart block, sick sinus syndrome (in the absence of a permanent pacemaker), and systolic blood pressure < 80 mmHg and sinus bradycardia (≤ 45 bpm/min) |
| Statin                      | • CK greater than 10 times the upper limit of normal, AST or ALT > 3 times the upper limit of normal and active liver disease and myopathy |
| Loop diuretics              | • History of immediate allergic reaction  
                                • Serum creatinine is greater than 2.5 mg/dL in men or greater than 2.0 mg/dL in women, serum potassium level < 3.5 for thiazide and loop diuretics  
                                • GFR declines > 30% within 4 months without explanations |
| Aldosterone receptor antagonists | • Serum creatinine is greater than 2.5 mg/dL in men or greater than 2.0 mg/dL in women, serum potassium level > 5.0, GFR < 30% |
| Anticoagulant               | • Active bleeding and recent surgery or trauma and hypersensitivity to drug |
| Digitals                    | • Significant sinus or atrioventricular block, ventricular fibrillation  
                                • Hypersensitivity to drug |

AST-Aspartate aminotransferase, ALT-Alanine aminotransferase, bpm = beats per minute, CK-Creatine kinase, GFR- glomerular filtration rate

Dietary Recommendations

Dietary education is also highly recommended during any visit for patients with HF. Nutritional interventions that should be considered include dietary sodium restriction of less than two grams per day and, for some patients with serum sodium abnormalities, free water restriction (Arcand et al., 2005). Sodium restriction has been shown to provide reduced mean arterial blood
pressure and possibly prevent urinary potassium loss in patients taking diuretics for hypertension or HF (Graudal, Hubeck-Graudal, & Jurgens, 2012). Approximately 20% of patients with acute decompensated HF have excessive salt intake, which has been identified as the primary cause for exacerbation (Arcand et al., 2005). Evidence from other studies demonstrates that high salt intake not only increases blood pressure, but also affects cardiovascular structure and function, albuminuria and renal disease progression, and increases the risk of cardiovascular morbidity and mortality (Aaron & Sanders, 2013). Outpatient consultation with nutritionists or registered dieticians should be suggested by clinicians at every visit in order to assess and ensure patient adherence to and understanding of this key self-care behavior (Arcand et al., 2005).

**Significance of the Study**

Multi-drug therapy can provide a pathophysiologic approach that addresses most aspects of the disease process rather than the symptoms alone and can be beneficial for patients with HF (Calvin et al., 2012; Gonzalez-Garcia et al., 2013; Hickling et al., 2001). Use of multi-drug therapy can also reduce the risk of mortality, the need for hospitalization, and lower healthcare expenditure (Calvin et al., 2012; Pina, 2001). Achieving these goals requires providers to make a commitment to stringent follow-up care and ensuring proper dosage of all prescribed medications (Calvin et al.; Naveiro-Rilo et al., 2012; Pina, 2001). Based on research, many providers stray from the ACCF/AHA recommendations (Calvin et al., 2012; Pina, 2001). In addition, little is known about the providers’ adherence to evidence-based guidelines in primary care settings. Understanding the gap between evidence-based practice and actual adherence levels is essential for the development of strategies that aimed to improve the treatment of HF patients.
The baseline information on the use of evidence-based guidelines in management of HF can help to determine the level of providers’ adherence to current guidelines. This information may allow primary care providers to assess the existing gap in the use of HF guideline-recommended therapy and develop interventions to improve the utilization of evidence-based guidelines. Finally, use of evidence-based guidelines is associated with better quality of life and lowered mortality rates in patient with HF.
CHAPTER 3

METHODS

Specific Aims

The specific aims of this study are to:

Specific Aim 1. Assess the level of providers’ adherence to evidence-based pharmacological guidelines for individuals with HF in a primary care setting. Guideline-recommended pharmacological therapy includes the use of beta-blocker, ACEI/ARB, statin, anticoagulation, and aldosterone receptor antagonist to all eligible patients according to ACCF/AHA recommendations.

Specific Aim 2. Determine the rate of cardiovascular-related emergency department or hospital visits within six months of medical record review.

Research Design

A descriptive study design was used to assess providers’ adherence to ACCF/AHA evidence-based guidelines in the pharmacological management of HF patients. A convenience sample of patients 18 years of age and older with diagnosis of HF was included.

Setting

The setting for this project was a private primary care setting in Tucson, Arizona. This practice provides primary health care in the clinic as well as in the community, including residents who are homebound, residing in assisting living, adult care homes, or nursing homes. Currently, six nurse practitioners are working in this primary care setting. The staff includes two geriatrics nurse practitioners, one acute care nurse practitioner, two women’s health care nurse practitioners, and one family nurse practitioner.
Study Sample

The sample for this doctor of nursing practice (DNP) project was 54 patients with HF under the care of this practice. Patient records were reviewed between April and September 2014 for this study descriptive study. Inclusion criteria for this study were: patients 18 years of age or older with an International Classification of Disease (ICD-9) Codes for HF (Table 4) and patients with stages C and D HF according to ACCF/AHA classification. Patients on hospice or palliative care were excluded due to the providers’ philosophy of care that focus on the palliation of chronically and terminally ill patients’ pain and symptoms.

Human Subject Protection

This retrospective chart review was approved by the human subject protection program from the University of Arizona institutional review board before data collection. There were no known risks to participants and all information obtained was treated in an anonymous and confidential manner. This research study involved only retrospective medical chart review and no patients, family members or providers were recruited. No identifiable information was included in data analysis.

Data Collection Instrument and Protocol

After receiving human subject protection approval from the University of Arizona institutional review board, a list of patients with ICD 9 codes meeting the inclusion criteria was provided by the practice. The Principal Investigator (PI) accessed the electronic database using a secure web-based interface, and was required to login using a secured password and user name.

The investigator used the electronic database to enter the assigned patient identification number. Patients’ paper-based health record was reviewed for any missing information from the
electronic database. Retrospective data were collected using ACCF/AHA provider’s measurement check lists (Appendix A) (ACCF/AHA, 2009; AHA, 2005). Performance measures regarding diet counselling, physical activity, and global coronary heart disease risk estimation were excluded as they are beyond the scope of this study.

The outpatient performance measurement set for HF was developed, reviewed, and accepted through joint efforts between the ACCF, AHA, and the physician consortium (ACCF/AHA, 2009; AHA, 2005). The ACCF/AHA HF outpatient performance measures reflect the quality of care and intended to enhance the quality improvement process. The measures are designed with the intent to use either for retrospective or prospective data collection using clinical criteria. Additionally, the data elements needed to create the performance measures are identified and associated to current ACCF/AHA clinical data standards to encourage the standardization of cardiovascular measurement (Bonow et al., 2005).

The study variables were recorded in the Excel (Microsoft, USA) spreadsheet, which includes study code numbers, patient demographic and clinical variables. Demographic characteristics included age, gender, and living arrangement (home, long term care faccility, skilled nursing facility, and acute rehabilitation). Clinical variables such as ejection fraction, medications, height, weight, comorbidity (such as history of diabetes, hyperlipidemia, hypertension, and atrial fibrillation), drug allergy, smoking status (never smoked, former smoker, and current smoker), history of hospitalization or emergency department visits within six months of initial medical record review, and previous history of any coronary artery bypass graft (CABG), previous pacemaker or implantable cardioverter defibrillator were recorded. Most recent lab results, including brain natriuretic peptide (BNP), blood urea nitrogen (BUN), serum
creatinine level, serum potassium level, estimated glomerular filtration rate, hemoglobin A1C (HbA1C), fasting low-density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides and total cholesterol for all eligible patients were collected. Vital signs such as heart rate and blood pressure were also obtained.

Use of ACEIs/ARBs and beta-blockers was evaluated against recommendations from AHA guidelines for HF treatment (AHA, 2012). For patients not prescribed ACEIs/ARBs, documentation of contraindications including chronic renal failure (serum creatinine > 2.5mg/dL), hyperkalemia (serum potassium > 5.5 mEq/L), bilateral renal artery stenosis, severe aortic stenosis and angioedema was determined. For patients not prescribed beta-blockers, contraindications include asthma, second or third degree heart block, sick sinus syndrome (in the absence of a permanent pacemaker), systolic blood pressure < 80mmHg and sinus bradycardia (≤ 45beats/min) were recorded. Use of anticoagulant for HF patient with atrial fibrillation and/or flutter was documented. Patient should not use anticoagulants if there is active bleeding, hypersensitivity to drug, and within five to six days of recent surgery or trauma (Yancy et al., 2013).

The outcome variables for this study included percentage of providers’ adherence level to evidence-based guidelines and the number of HF patients’ emergency department or hospital visits within six months prior to data collection which was between October 2013 and March 2014. All the data extraction was conducted by the PI. Following the extraction of data from patients’ charts and electronic medical records, no patient identifying information was included in the data set.
**Assessment of Non-adherence**

The ACCF/AHA guideline for the management of HF was used to assess the level of adherence to evidence-based guidelines by providers. The provider adherence was determined based on the patient current and active medications during data collection. Provider’s non-adherence was defined as when a pharmacologic agent was not prescribed, in the absence of contraindications, in any of the following medications to eligible patients: ACEI/ARB; beta-blocker, and statin (Yancy et al., 2013). In the case of beta-blockers, a heart rate of ≤45 beats per minute, a systolic blood pressure < 80 mmHg, and the presence of asthma severe enough to require the use of one asthma medication are contraindications (AHA, 2009; Calvin et al., 2012). In addition, patients should not be given ACEI or ARB if a systolic blood pressure is < 80 mmHg, they are pregnant, they have a previous history of angioedema, when there is the presence of bilateral renal artery stenosis, or levels of serum potassium > 5.0 mEq/L or serum creatinine are elevated ≥2.5 mg/dL (Yancy et al., 2013). Use of aldosterone receptor antagonists should be avoided if serum creatinine level > 2.5 mg/dL in men or > 2.0 mg/dL in women (or estimated glomerular filtration rate < 30 mL/min/1.73 m²), and if potassium level > 5.0 mEq/L (AHA, 2009, Calvin et al., 2012). Statins should be avoided in patients with creatine kinase (CK) greater than 10 times the upper limit of normal, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 times the upper limit of normal, active liver disease and myopathy (Yancy et al., 2013).

HFrEF or left ventricular systolic dysfunction (LVSD) is HF with reduced EF ≤40%. Patients with HF and preserved EF (> 40%), normal left ventricular function, or mild LVSD, referred to as HFP EF (Yancy et al., 2013).
The providers’ adherence was determined for each guideline-recommended drug. The providers’ adherence for each pharmacologic therapy is calculated by dividing all patients who currently prescribed the therapy by all eligible patients in the absence of contraindications.

**Operational Definitions**

**Smoking Status:** An adult who had smoked 100 cigarettes in his or her lifetime and actively smoked cigarettes either every day or some days were defined as a current smoker. Patients who reported a history of smoking at least 100 cigarettes in their lifetime and who, at the time of medical record review, did not smoke at all were defined as a former smoker. Patients that had never smoked, or had smoked less than 100 cigarettes in his or her lifetime were defined as a never smoker (CDC, 2009).

**Emergency department or hospital visit:** Emergency department (ED) or hospital visit determined by the number of ED or hospital visits due to cardiovascular-related reasons such as chest pain, abnormal or elevated BNP, and HF exacerbations was obtained from discharge summary in the six months prior to data collection, from October 2013 to March 2014.
Table 4. ICD-9 codes for HF (ACCF/AHA, 2005)

<table>
<thead>
<tr>
<th>ICD-9</th>
<th>Short description</th>
</tr>
</thead>
<tbody>
<tr>
<td>402.01</td>
<td>Hypertensive heart disease, malignant, with heart failure</td>
</tr>
<tr>
<td>402.11</td>
<td>Hypertensive heart disease, benign, with heart failure</td>
</tr>
<tr>
<td>402.91</td>
<td>Hypertensive heart disease, unspecified, with heart failure</td>
</tr>
<tr>
<td>404.01</td>
<td>Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified</td>
</tr>
<tr>
<td>404.03</td>
<td>Hypertensive heart and chronic kidney disease, malignant, with heart failure and with chronic kidney disease stage V or end stage renal disease</td>
</tr>
<tr>
<td>404.11</td>
<td>Hypertensive heart and chronic kidney disease, benign, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified</td>
</tr>
<tr>
<td>404.13</td>
<td>Hypertensive heart and chronic kidney disease, benign, with heart failure and chronic kidney disease stage V or end stage renal disease</td>
</tr>
<tr>
<td>404.91</td>
<td>Hypertensive heart and chronic kidney disease, unspecified, with heart failure and with chronic kidney disease stage I through stage IV, or unspecified</td>
</tr>
<tr>
<td>404.93</td>
<td>Hypertensive heart and chronic kidney disease, unspecified, with heart failure and chronic kidney disease stage V or end stage renal disease</td>
</tr>
<tr>
<td>428.0</td>
<td>Congestive heart failure, unspecified CHF</td>
</tr>
<tr>
<td>428.1</td>
<td>Left heart failure</td>
</tr>
<tr>
<td>428.20</td>
<td>Unspecified systolic heart failure</td>
</tr>
<tr>
<td>428.21</td>
<td>Acute systolic heart failure</td>
</tr>
<tr>
<td>428.22</td>
<td>Chronic systolic heart failure</td>
</tr>
<tr>
<td>428.23</td>
<td>Acute on chronic systolic heart failure</td>
</tr>
<tr>
<td>428.30</td>
<td>Unspecified diastolic heart failure</td>
</tr>
<tr>
<td>428.31</td>
<td>Acute diastolic heart failure</td>
</tr>
</tbody>
</table>

**CHF-Congestive heart failure**

**Data Management and Statistics**

Data were entered into the Excel spreadsheet and then transferred into a Predictive Analytical Software (PASW) 18th edition student version database (SPSS Inc., Chicago IL.).

After the Excel data were uploaded into PASW, the PI verified the accuracy and completeness of each entry to avoid any errors during data transfer. Missing values for any of the variables were coded as missing.
Quantitative data collected were compiled and analyzed using SPSS 23.0 statistical package. Both categorical and continuous variables were presented with frequencies (N) and percentage (%). The frequency and percentage of patients that received ACEI/ARB, beta-blocker or aldosterone receptor antagonist, anticoagulant and statin among eligible patients were obtained. The frequency and percentage of ED or hospital visits six months prior to data collection was calculated. Frequency and percentage of the study participate by age, sex, body mass index (BMI), smoking history, alcohol use and EF was determined.

Chi-square test was used to test for significance difference in the number of patients receiving ACEI/ARB and beta-blocker, and the number of ER or hospital visits. Any missing variable was excluded from the analysis. Multivariate analysis using binary logistic regression was done to determine the effect of patient factors such as age and sex, comorbidity, and use of ACEI/ARB and beta-blocker to determine their relationship with frequent ER or hospital visits. A $p$ value of less than 0.05 was considered statistically significant.
CHAPTER 4

RESULTS

Sample Characteristics

Medical records of 57 study subjects with a diagnosis qualifying the ICD-9 codes for HF (Table 4) between April and September 2014 were retrospectively reviewed. Of the 57 subjects reviewed, three study subjects on hospice or palliative care were excluded (Figure 1). From the remaining 54 eligible HF study subjects, 22 (40.7%) had reduced EF \( \leq 40\% \).

Among 54 eligible HF study subjects, 36 (66.7%) were female. The majority of the study subjects (n=41; 75.9%) with HF were older than 65 years and the ages ranged from 40-99 years (mean age: 76.4 \( \pm \) 17.8 years). Nearly one-fourth of the study subjects (n=12; 22.2%) were current smokers, while (n=19; 35.5%) were former smokers. The majority of subjects were residents of assisted living (n=24; 44.4%). More than half of subjects were either overweight (31.5%) or obese (22.2%). The most frequent comorbidities were hypertension (n=48; 88.9 %), peripheral vascular disease (n=45; 88.3%), dyslipidemia (n= 36; 66.7%), asthma (n= 23; 42.6%) and diabetes mellitus (n=23; 42.6%). At least two comorbidities were reported in the majority of subjects (n= 51; 94.4%) (Table 6).
Figure 1- Study Flow Chart of Sample Selection for the Analysis of Adherence to Pharmacologic Treatment

n=3 with hospice or palliative care were excluded

n=57 with a diagnosis qualifying the ICD-9 codes for HF

n=22 with an ejection fraction ≤40% with or without history of myocardial infarction

n=54 eligible

n=22 with an ejection fraction ≤40% with or without history of myocardial infarction

n=4 with end stage kidney disease (serum creatinine > 2.5 mg/dl) were excluded

n=18 eligible for ACEI/ARBs

n=45 ACS, PVD, stroke, TIA, diabetes with LDL-C between 70-189 mg/dl, LDL-C ≥190 mg/dl

n=1 with sinus bradycardia was excluded

n=21 eligible for beta blockers

n=4 with end stage kidney disease (serum creatinine > 2.5 mg/dl) were excluded

n=20 diabetes, n = 6 myocardial infarction and EF ≤40%

n=26 eligible for aldosterone receptor antagonist

n=19 over 75 years of age

n=26 eligible for statin
Table 5. Demographic and clinical characteristics of the study subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall n=54, n (%)</th>
<th>EF ≤ 40 %, n=22</th>
<th>EF ≥40 %, n=24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (33.3)</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Female</td>
<td>36 (66.7)</td>
<td>11</td>
<td>19</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-52</td>
<td>4 (7.4)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>53-65</td>
<td>9 (16.7)</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>66-78</td>
<td>13 (24.1)</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>79-91</td>
<td>21 (38.9)</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>92-104</td>
<td>7 (13.0)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>45 (83.3)</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>1-2 drinks a day</td>
<td>7 (35.2)</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>3 or more drinks a day</td>
<td>2 (22.2)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Smoking history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>23 (42.6)</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Former</td>
<td>19 (35.2)</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Current</td>
<td>12 (22.2)</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Patient Residence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult care home</td>
<td>24 (44.4)</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Clinic patients</td>
<td>6 (11.1)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Homebound</td>
<td>19 (35.2)</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Nursing home</td>
<td>5 (9.3)</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight (&lt; 18.5)</td>
<td>6 (11.1)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Normal (18.5-24.9)</td>
<td>11 (20.4)</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Over weight (25-29.9)</td>
<td>17 (31.5)</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Obese (&gt; 30)</td>
<td>12 (22.2)</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Unavailable</td>
<td>8 (14.8)</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>
Table 6. Comorbidities and ejection fraction of the study subjects

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Overall n=54, n (%)</th>
<th>EF &lt; 40 %, n=22</th>
<th>EF &gt; 40 %, n=24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>23 (42.6)</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Hypertension</td>
<td>48 (88.9)</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>36 (66.7)</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>20 (37.0)</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>10 (18.5)</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Stroke</td>
<td>12 (22.2)</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>COPD</td>
<td>21 (38.9)</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Asthma</td>
<td>23 (42.6)</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>19 (35.2)</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>12 (22.2)</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>PVD</td>
<td>45 (83.3)</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>18 (33.3)</td>
<td>10</td>
<td>7</td>
</tr>
</tbody>
</table>

COPD= Chronic obstructive pulmonary disease, BMI= Body mass index; EF = ejection fraction, PVD = Peripheral vascular disease

Among the study subjects, 15 (27.8%) had a pacemaker or implantable cardioverter-defibrillator and 10 (18.5%) had previous coronary artery bypass. The majority of subjects (n=32, 59.3%) had BNP > 300 pg/ml (Table 7). Cardiac echocardiogram data were available in 46 (85.2%) subjects. Twenty-two subjects (40.7%) had an ejection fraction ≤ 40% and 24 (44.4%) had ejection fraction > 40%.
Table 7. Most recent blood B-type natriuretic peptide (BNP) values among the study subjects

<table>
<thead>
<tr>
<th>BNP pg/ml</th>
<th>Frequency</th>
<th>Percent of all subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>100-300</td>
<td>9</td>
<td>16.7</td>
</tr>
<tr>
<td>301-600</td>
<td>13</td>
<td>24.1</td>
</tr>
<tr>
<td>601-900</td>
<td>12</td>
<td>22.2</td>
</tr>
<tr>
<td>&gt; 900</td>
<td>7</td>
<td>13.0</td>
</tr>
<tr>
<td>Unavailable</td>
<td>13</td>
<td>24.1</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>100</td>
</tr>
</tbody>
</table>

**Beta-Blockers**

Of the total 54 patients, 22 (40.7%) with an ejection fraction ≤ 40% were eligible to receive beta-blockers before accounting for contraindications. Contraindication to beta-blocker therapy was present in 1 out of 22 subjects due to sinus bradycardia (HR < 45 bpm/min). Adherence to guideline recommendations for beta-blocker therapy was present in 17 of 21 (81%) subjects with ejection fraction ≤ 40%.

**ACEI/ARB**

Of the 22 subjects with an ejection fraction ≤ 40%, 14 (66.3%) received ACEI or ARBs before accounting for contraindications. Contraindications to ACEIs or ARBs were documented in 4 out of 22 subjects due to end stage kidney disease (serum creatinine > 2.5 mg/dl).
Adherence to guideline recommendations for ACEI/ARB was found in 14 of 18 (77.8%) subjects.

**Aldosterone Receptor Antagonists**

Of the total 54 subjects, 20 diabetes patients with no prior history of myocardial infarction and 6 subjects with a history of myocardial infarction and EF ≤ 40% were included to determine adherence to aldosterone receptor antagonist (Figure 1). Adherence to aldosterone receptor antagonist was found in only 6 of 26 (23.1%) eligible study subjects, and no contraindications or other medical reasons were recorded (Table 8).

**Lipid-lowering Medications**

Of all the study subjects, 45 (83.3%) had a history of peripheral vascular disease, 18 (33.3%) had a history of coronary artery disease, 12 (22.2%) had a history of TIA or stroke, 15 subjects had a history of diabetes with LDL-C between 70-189 mg/dl, and 21 (38.9%) non-diabetic subjects with LDL-C ≥ 190 mg/dl were included to determine the use of statin or other lipid-lowering drugs. Subjects with two or more comorbidities were counted in one of the above categories to determine eligibility for statin or other lipid-lowering drugs. After accounting for subjects with two or more morbidities, 45 (83.3%) were eligible to receive statin or other lipid-lowering drugs. Among the 45 subjects, 19 over 75 years of age were further excluded according to ACCF/AHA eligibility criteria (Yancy et al., 2013). After excluding the study subjects with contraindications to recommended treatment guidelines, adherence to statin and other lipid-lowering drugs was found in 21 of 26 (80.7%) eligible subjects.
Anticoagulation

Among 20 subjects with atrial fibrillation, one patient with a history of warfarin allergy was excluded. Adherence to anticoagulation for atrial fibrillation was found in 15 of 19 (78%) eligible subjects. All of the study subjects with history of atrial fibrillation had CHADS2 score of 2 and more, correlating with a ≥ 4.0 % annual stroke risk. Among all patients with atrial fibrillation, 10 (50%) had CHADS2 score of 3 and an estimated annual stroke risk of 5.9%. The mean CHADS2 score was 3.55 (Table 9).

Table 8. The ACCF/AHA HF guideline adherence before and after contraindications were considered

<table>
<thead>
<tr>
<th></th>
<th>Guideline adherence before accounting contraindications and other patient factors*</th>
<th>Contraindication or other patient factors to therapy</th>
<th>Guideline adherence after accounting contraindications and patient factors*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers</td>
<td>17/22 (77.3%)</td>
<td>1/22 (4.6%)</td>
<td>17/21 (81%)</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>14/22 (63.6%)</td>
<td>4/22 (18.2%)</td>
<td>14/18 (77.8%)</td>
</tr>
<tr>
<td>Aldosterone receptor antagonist</td>
<td>6/26 (23.1%)</td>
<td>0</td>
<td>6/26 (23.1%)</td>
</tr>
<tr>
<td>Anticoagulation for atrial fibrillation</td>
<td>15/20 (75%)</td>
<td>1/20 (5%)</td>
<td>15/19 (78%)</td>
</tr>
<tr>
<td>Statin or other lipid-lowering drugs</td>
<td>21/45 (46.7%)</td>
<td>19*/45 (42.2%)</td>
<td>21/26 (80.7%)</td>
</tr>
</tbody>
</table>

All values expressed as number (%), ACEI-Angiotensin converting enzyme inhibitors

ARB-Angiotensin receptor blocker

* 19 patients over 75 years of age were excluded from statin group according to ACCF/AHA eligibility criteria, (ACCF/AHA 2013).
Table 9. Calculated CHADS2 score for the study subjects with history of atrial fibrillation

<table>
<thead>
<tr>
<th>CHADS2 Score</th>
<th>n (%)</th>
<th>Literature-supported stroke risk % per year</th>
<th>Use of anticoagulant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>2 (10%)</td>
<td>4.0</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>10 (50%)</td>
<td>5.9</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>3 (15%)</td>
<td>8.5</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>5 (25%)</td>
<td>12.5</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>20 (100%)</td>
<td></td>
<td>15 (75%)</td>
</tr>
</tbody>
</table>

Mean CHADS2 score = 3.55

CHADS - Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, previous Stroke/transient ischemic attack

**HF-Related ER Visits or Hospitalization**

Among 54 study subjects, 45 (83.3%) visited the ER or hospital at least one time between October 2013 and March 2014. Among all the study subjects, 34 (63%) had a history of < 2 ER visits or hospitalization and the remaining 20 (37%) subjects had 2 or more ER visits or hospitalization due to chest pain, abnormal BNP and HF exacerbation, and shortness of breath. Among 45 subjects that visited the ER or were hospitalized, the majority of the subjects (n=35; 77.8%) were due to shortness of breath and chest pain, 7 (15.5%) subjects had chest pain alone, and 3 (6.7%) subjects had abnormal BNP and HF exacerbation. The use of guideline-recommended therapies, beta-blockers (n=54, \( \chi^2 = 4.4, p=0.04 \)) and ACEIs/ARBs (n=54, \( \chi^2 = 7.2, p=0.01 \)), were significantly associated with a fewer number of cardiovascular-related ER
visits or hospitalizations compared to those subjects that were not on beta-blockers and ACEIs/ARBs (Table 10).

Multivariate analysis using binary logistic regression was used to determine the effect of patient factors such as age and sex, comorbidity and use of ACEIs/ARBs and beta-blockers to determine their relationship with frequency of ER visits or hospitalization. Age, sex, BMI and comorbidity such as history of hypertension, hyperlipidemia, COPD and diabetes mellitus were not significantly associated with the number of ER visits or hospitalization (Table 11). Use of guideline-recommended medications, ACEIs/ARBs (OR=8.853, CI 1.212-64.66, p= 0.032) and beta-blockers (OR= 9.24, CI 1.212-70.438, p=0.031) were independently associated with fewer number of hospitalization or ER visits after adjusting for confounders such as age, sex, BMI, and comorbidities.

Table 10. Cardiovascular-related emergency room visits or hospitalization within six months of medical record review

<table>
<thead>
<tr>
<th>Guideline-recommended medications</th>
<th>Hospitalization or emergency room visits</th>
<th>Total</th>
<th>p-value</th>
<th>Chi-square ($\chi^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 2 visits</td>
<td>2 or more visits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-blockers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>9 (16.7%)</td>
<td>11 (20.4%)</td>
<td>20 (37.0%)</td>
<td>.04</td>
</tr>
<tr>
<td>Yes</td>
<td>25 (46.3%)</td>
<td>9 (16.7%)</td>
<td>34 (63.0%)</td>
<td>4.4</td>
</tr>
<tr>
<td>ACEIs/ARBs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>11 (20.4%)</td>
<td>14 (25.9%)</td>
<td>25 (46.3%)</td>
<td>.01</td>
</tr>
<tr>
<td>Yes</td>
<td>23 (42.6%)</td>
<td>6 (11.1%)</td>
<td>29 (53.7%)</td>
<td>7.2</td>
</tr>
<tr>
<td>Total</td>
<td>34 (63.0%)</td>
<td>20 (37.0%)</td>
<td>54 (100%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 11. The effect of patient factors, comorbidities and guidelines recommended medications on cardiovascular related ER or hospital visits

<table>
<thead>
<tr>
<th></th>
<th>Hospital or ER visits</th>
<th>Adjusted odd ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 2 visits</td>
<td>2 or more visits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-52</td>
<td>3</td>
<td>1</td>
<td>0.609</td>
<td>0.211-1.755</td>
</tr>
<tr>
<td>53-65</td>
<td>5</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>66-78</td>
<td>7</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>79-91</td>
<td>15</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>92-04</td>
<td>4</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>14</td>
<td>0.285</td>
<td>0.023-3.564</td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of beta-blockers</td>
<td></td>
<td></td>
<td>9.240</td>
<td>1.212-70.438</td>
</tr>
<tr>
<td>No</td>
<td>9</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of ACEIs/ARBs</td>
<td></td>
<td></td>
<td>8.853</td>
<td>1.212-64.660</td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td>3.275</td>
<td>0.366-29.325</td>
</tr>
<tr>
<td>No</td>
<td>18</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td>0.824</td>
<td>0.034-20.044</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>32</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
<td></td>
<td>0.485</td>
<td>0.071-3.331</td>
</tr>
<tr>
<td>No</td>
<td>10</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td>0.963</td>
<td>0.370-2.505</td>
</tr>
<tr>
<td>&lt;18</td>
<td>4</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>6</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-29.9</td>
<td>15</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;= 30</td>
<td>6</td>
<td>6</td>
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<td></td>
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</table>
CHAPTER 5

DISCUSSION

This study showed that in a primary care practice, adults with HF and reduced systolic function, 81% of the subjects were prescribed an ACEI or ARB and 77.8% were prescribed a beta-blocker. Several previous studies reported a substantial variation and underutilization of the ACCF/AHA HF guideline-recommended therapies in the management of HF patients (Schopfer, Whooley, & Stamos, 2012; Calvin et al., 2012; Yancy et al., 2010). Our findings are similar to data reported in a study in the hospital setting, where 82% of the study subjects received a beta-blocker and 87% of subjects received an ACEI or ARB (Steinman et al., 2011). A recent study conducted by the primary care team of the Leon Health area in 9 urban and 19 rural primary care settings revealed that the rate of adherence to evidence-based guidelines for prescribing ACEIs and beta-blockers was 55.2% (Naveiro-Rilo et al., 2012). This suggests that there is inconsistency and substantial variation in use of ACEIs/ARBs and beta-blockers among primary care providers. Lack of knowledge, such as not knowing the target dose of ACEIs/ARBs and beta-blockers, or lack of awareness and providers’ attitudes about the new practice guidelines may affect the providers’ adherence to evidence-based guidelines (Annema et al., 2009; Cabana et al., 1999; Kasje, et al., 2005).

In the present study, only 23.1% of HF subject with diabetes mellitus or myocardial infraction and LVEF ≤40% received aldosterone receptor antagonists. In primary care settings, despite the agreement on the use of RAAS-I, there are significant problems in transferring this theory into practice (Peters-Klimm et al., 2012). Most recent literature indicates that many patients actually do not receive RAAS-I according to ACCF/AHA recommendations (Peters-
Klimm et al., 2012; Rassi et al., 2013). Rassi and colleagues (2013) conducted a study on 81,570 patients post-acute myocardial infarction with LVEF ≤ 40% or with diabetes mellitus from 219 hospitals between 2006 and 2009 and found that only 9.1% of eligible subjects received aldosterone receptor antagonists at hospital discharge. Similarly, another study conducted at Durham Veterans Affairs medical center on patients with HF and EF ≤ 45%, aldosterone receptor antagonists were prescribed to only 23 of the 64 (36%) eligible subjects (Atwater et al., 2012). The use of aldosterone receptor antagonists among Durham Veterans Affairs medical center was higher than the present study and other previous studies (Nappi & Sieg, 2011; Pitt et al., 1999). This is possibly due to the EMR systems in the Veterans Administration health system providing > 10 years of patient history, echocardiogram, imaging, and medication history in a single user-friendly platform to alert providers on the use of guideline-recommended drugs (Atwater et al., 2012). Furthermore, their study used subjects with HF and EF ≤ 45% compared to EF ≤ 40% used in this study to determine the use of aldosterone receptor antagonists according to ACCF/AHA.

The addition of low-dose aldosterone receptor antagonists in HF patients with NYHA class II–IV (Table 2) that have LVEF ≤ 35% and those with a myocardial infarction and LVEF ≤ 40% with symptoms of HF or diabetes mellitus should be considered to reduce cardiovascular disease death and recurrent hospitalizations (Nappi & Sieg, 2011; Pitt et al., 1999; Vizzardi et al., 2013). However, the use of aldosterone receptor antagonists was low in the present study. This is possibly due to lack of awareness and/or knowledge about the available evidence-based guidelines among providers. According to a previous study, more than 10% of providers are not aware of the available evidence-based guidelines (Cabana et al., 1999). Data from several
previous studies have showed that lack of knowledge on the target dose of guideline-
recommened drugs and unawareness of practice guidelines are the main providers-related
barriers to use evidence-based guidelines (Cabana et al., 1999; Calvin et al., 2012; Fonarow et
al., 2010).

In this study, 80.7% of eligible subjects (those with history of peripheral vascular disease,
coronary artery disease, TIA or stroke, diabetes mellitus with LDL-C of 70-189 mg/dl, or non-
diabetic subjects with LDL-C ≥ 190 mg/dl) received statin or other lipid lowering drugs. A study
conducted in 10 hospitals to determine the providers’ level of adherence to evidence-based
guidelines and therapy showed a low rate of adherence (41%) to statin, ACEI/ARB (Calvin et al.,
2012). In another study conducted in outpatient settings, more than 40% of providers failed to
prescribe or document statins and antiplatelet therapy for eligible HF patients in the absence of
contraindications (Yancy et al., 2010). Results from prior studies showed higher rates of
underutilization of statins and warfarin; however, both studies failed to account for therapeutic
contraindications and patient refusal to determine the true adherence to guideline-recommended
drugs (Annema et al., 2009; Hickling et al., 2001; Richardson et al., 2010).

In the present study, we found a higher level of adherence (78%) in the use of warfarin
among patients with HF and atrial fibrillation compared to previous studies (Agarwal, Bennett,
& Smith, 2010; Akao et al., 2013). In a similar study conducted in Japanese patients with atrial
fibrillation, 87.3% of the subjects were taking warfarin and more than 50% of the subjects had a
CHADS2 score of 2 or more (Atarashi et al., 2011). However, in another community-based
survey conducted in Fushimi AF registry among 76 institutions in Japanese patients with atrial
fibrillation, warfarin was only prescribed in 48.5% of the study subjects (Akao et al., 2013).
Another recent study conducted in United States hospitalized patients with atrial fibrillation between 2003 and 2004 showed that only 56% of the subjects received warfarin (Agarwal, Bennett, & Smith, 2010). In this study by Agarwal et al., the low adherence rate of using warfarin in patients with atrial fibrillation in hospitalized patients was attributed to older age with 50% of the study subjects older than 75 years and had certain risks of bleeding such as liver disease and end stage renal disease (Agarwal, Bennett, & Smith, 2010).

In the present study, 37% of HF patients visited the ER or were hospitalized at least twice between October 2013 and March 2014, due to cardiovascular-related reasons such as chest pain and shortness of breath due to HF exacerbation. This finding was similar to the 25-40% 30-day readmission rates due to cardiovascular-related reasons, such as acute MI and HF exacerbation, among HF patients (Ranasinghe et al., 2014)(Gheorghiade et al., 2006; Ross et al., 2010). Another recent study conducted in California reported more than 50% of HF patients were readmitted to the hospital within six months of discharge (Desai & Stevenson, 2012; Ranasinghe et al., 2014).

According to the ACCF/AHA report in 2009, 668,000 ED visits were made due to HF annually (AHA, 2012). Recurrent hospitalization by patients with HF is associated with worsening disease condition.

Readmission rates might be reduced if ACCF/AHA guidelines recommended interventions such as use of an alert system, patient and provider education regarding the importance of guideline-recommended drugs fully instituted by all providers (Gheorghiade et al., 2006). Based on several studies conducted in outpatient HF patients, the use of guideline-recommended medications can slow progression of the disease and reduce or prevent the need
for hospitalization (Calvin et al., 2012; Naveiro-Rilo et al., 2012; Richardson et al., 2010).

Providers’ non-adherence was adversely and independently correlated with worsening of HF and recurrent hospital visits (Calvin et al., 2012; Naveiro-Rilo et al., 2012).

The use of guideline-recommended medications was associated with reduced ER or hospital visits in the present study. Specifically, the use of guideline-recommended therapy was significantly associated with reduced number of cardiovascular-related ED or hospital visits. ACEIs/ARBs (OR=8.853, CI 1.212-64.66, p= 0.032) and beta-blockers (OR= 9.24, CI 1.212-70.438, p=0.031) were independently associated with ER visits and hospitalization, after adjusting for confounders such as age, gender, and comorbidities. Similarly, several previous studies conducted in outpatient HF patients also reported an association between the use of guideline-recommended drugs such as ACEIs/ARBs and beta-blockers and reduced hospitalizations (Naveiro-Rilo et al., 2012; Richardson et al., 2010). The use of guideline-recommended therapies can slow progression of the disease, reduce or prevent the need for hospitalization, decrease health care costs and mortality rates (Calvin et al., 2012; Naveiro-Rilo et al., 2012; Richardson et al., 2010).

**Limitations**

Our study was performed in only 54 HF patients and was limited to one primary care practice, so the results cannot be generalized to other primary care settings. Due to the retrospective nature of this study, it was not possible to obtain complete information regarding EF and BNP in all study subjects. Another limitation in this retrospective study was that we were unable to classify patients according to NYHA functional classification to determine eligibility for aldosterone receptor antagonist. NYHA functional classification requires direct patient
assessment to collect HF-related symptoms to determine functional classification. Selection bias is possible since the PI is one of the providers in this clinical setting; however the study aim was not to determine individual provider’s adherence level. No identifying data or information about the providers were collected or used for data analysis. Other ACCF/AHA recommended performance measures, such as diet counselling, physical activity, and global coronary heart disease risk estimation, were not determined in this study.

**Future Studies**

This small retrospective descriptive study provides baseline information regarding the use of ACCF/AHA evidence-based guidelines for management of HF patients among providers in a primary care setting. Future longitudinal research to improve the use of ACCF/AHA evidence-based guidelines in a larger sample of HF patients will provide valuable contributions to improve the use of evidence-based, guideline-recommended drugs among primary care providers. Furthermore, determining the providers’ knowledge and awareness regarding the available evidence-based guideline in primary care setting will provide valuable information to improve the use of guideline recommended drugs.

**Clinical Implication**

HF accounts for more than 6.5 million hospital stays and 12-15 million office visits annually. The significant value of using ACCF/AHA evidence-based guidelines for treatment and management of HF patient is supported by multiple studies (Calvin et al., 2012; Yancy et al., 2010). The gap in the use of evidence-based guidelines among providers requires determining the practitioners’ awareness of ACCF/AHA guidelines in the clinical setting. This study revealed that providers’ adherence in the use of beta-blockers, ACEIs/ARBs, angiotensin receptor
antagonists, anticoagulation, and statins. The use of ACEIs/ARBs, anticoagulants, and statins is comparable or higher than similar studies conducted in the primary care settings. In the present study, the use of guidelines recommended drugs is significantly associated with fewer ($<1$) ER or hospital visits. Result from this study indicates a low level of provider adherence to angiotensin receptor antagonists. Therefore, understanding the gap between evidence-based practice and actual adherence is essential for the development of strategies aimed to improve the treatment of HF patients.

**Conclusion**

Treatment with a combination of cardiovascular drugs and use of ACCF/AHA guidelines, such as ACEIs/ARBs, beta-blockers and aldosterone receptor antagonists can slow progression of HF, and reduce or prevent the need for hospitalization. The use of ACEIs/ARBs and beta-blockers was acceptable. However, despite the available evidence and recommendation of the use of aldosterone receptor antagonists in patients with diabetes mellitus or myocardial infarction with LVEF $\leq 40\%$, the use of aldosterone receptor antagonists in this group of HF patient remains low. Therefore, this information will allow primary care providers to assess the existing gap in the use of HF guideline-recommended therapy and develop interventions to improve the utilization of evidence-based guidelines.
APPENDIX A

LETTER OF SUPPORT FROM THE STUDY SETTING
March 10, 2014

Institutional Review Board for the Protection of Human Subjects
University of Arizona
1618 E. Helen Street
Tucson, AZ 85721

Dear Members of the Committee:

On behalf of the providers Direct PLL medical practice, I am writing to formally indicate my awareness of the research proposed by Masresha Akalu, a student at University of Arizona, College of Nursing. I am aware that Masresha Akalu intends to conduct his research Title: “Adherence to Evidence-Based Pharmacological Guidelines and Outcomes for Heart Failure in Primary Care Providers” using our electronic medical record and other patient records to collect retrospective medication and clinical data. I give Masresha Akalu a full permission to conduct his research in our clinical setting.

If you have any questions or concerns, please feel free to contact my office at 520-722-2400

Sincerely

John Schmaling, DNP, GNP-BC, Director of the Practice
APPENDIX B

THE UNIVERSITY OF ARIZONA-IRB APPROVAL LETTER FOR THE PROPOSED PROJECT
Date: April 22, 2014

Principal Investigator: Masresha Akalu

Protocol Number: 1404295644

Protocol Title: Adherence to Evidence-Based Pharmacological Guidelines and Outcomes for Heart Failure in Primary Care Providers

Level of Review: Expedited

Determination: Approved

Expiration Date: April 17, 2015

This submission meets the criteria for approval under 45 CFR 46.110, 45 CFR 46.111 and/or 21 CFR 50 and 21 CFR 56.

- The University of Arizona maintains a Federalwide Assurance with the Office for Human Research Protections (FWA #00004218).
- All research procedures should be conducted in full accordance with all applicable sections of the Investigator Manual.
- The current consent with the IRB approval stamp must be used to consent subjects.
- The Principal Investigator should notify the IRB immediately of any proposed changes that affect the protocol and report any unanticipated problems involving risks to participants or others.
- For projects that wish to continue after the expiration date listed above please submit an F212, Continuing Review Progress Report, forty-five (45) days before the expiration date to ensure timely review of the project.
- All documents referenced in this submission have been reviewed and approved. Documents are filed with the HSPP Office. If subjects will be consented the approved consent(s) are attached to the approval notification from the HSPP Office.

This project has been reviewed and approved by an IRB Chair or designee.
No changes to a project may be made prior to IRB approval except to eliminate apparent immediate hazard to subjects.
APPENDIX C

QUESTIONNAIRE
**Appendix C: American College of Cardiology Foundation and American Heart Association Performance Measurements**

<table>
<thead>
<tr>
<th>Patient code________</th>
<th>Medical history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age_____ years</td>
<td>Vascular disease__(Y/N)</td>
</tr>
<tr>
<td>Gender:</td>
<td>(peripheral vascular disease,</td>
</tr>
<tr>
<td>o Male</td>
<td>Carotid artery disease, or</td>
</tr>
<tr>
<td>o Female</td>
<td>abdominal aortic aneurism)</td>
</tr>
<tr>
<td>ICD code used________</td>
<td>History of stroke ___(Y/N)</td>
</tr>
<tr>
<td>Diabetes____ (Y/N)</td>
<td>History of Transient ischemic</td>
</tr>
<tr>
<td>Hypertension___ (Y/N)</td>
<td>attack (TIA) ____ (Y/N)</td>
</tr>
<tr>
<td>Hyperlipidemia___ (Y/N)</td>
<td>COPD___ (Y/N)</td>
</tr>
<tr>
<td>Atrial Fibrillation____( Y/N)</td>
<td>Asthma___(Y/N)</td>
</tr>
<tr>
<td>sinus bradycardia___(Y/N)</td>
<td>Chronic renal failure___(Y/N)</td>
</tr>
<tr>
<td>Myocardial infarction___ (Y/N)</td>
<td></td>
</tr>
<tr>
<td>Bilateral renal artery</td>
<td></td>
</tr>
<tr>
<td>stenosis___(Y/N)</td>
<td></td>
</tr>
<tr>
<td>Severe aortic stenosis___(Y/N)</td>
<td></td>
</tr>
<tr>
<td>Angioedema___( Y/N)</td>
<td></td>
</tr>
</tbody>
</table>

**Lifestyles Factors**

*Tobacco use:*
- o Never smoked
- o Former smoker

Date quit___/____/____
- o Current smoker

**Alcohol use**
- o Never
- o 1-2 drinks/day
- o > 2 drinks per day

1 drink= 4oz wine, 2oz spirits, or 1 beer

**Patient type**
- o Clinic
- o Homebound
- o Nursing Home

**Assisting living**

**Drug allergy**
- o Yes
- o No

Specify__________

**Physical exam findings**

Height______ inches

Weight______ lbs

BMI________kg/m²

**Most recent Blood pressure___/___mmHg,**

Heart Rate____beat/minute

**Complete if BP is > 140/90: Two or more antihypertensive medications prescribed**

- o Yes
- o No

**Recent labs**

**Fasting lipid profile**

Total cholesterol_____mg/dl

LDL-C_____mg/dl

HDL-c_____mg/dl

Triglyceride______mg/dl

**Check all that apply**

- o Total cholesterol is ≥ 240mg/dl
- o LDL-C is ≥ 130mg/dl

HDL-C is ≤ 40mg/dl if patient is male OR < 55mg/dl, if patient is female

**At least 1 lipid lowering medication prescribed at maximum tolerated dose**

- o Yes
- o No

**Medical or patient reason(s) no lipid-lowering medications was prescribed_______**

**Most recent renal function Test**

- o Serum creatinine______
- o Blood urea nitrogen level___
- o Potassium level____

Glomerular filtration rate (GFR)____

**If diabetic HbA1c____**

**Last Brain Natriuretic peptide (BNP) _________**

**Left ventricular systolic(LVS)**

**Volume overload recorded**
function assessment- Ejection fraction (EF) _______

Last LVS assessment date/Echo___/___/

- Dyspnea
- Orthopnea
- Peripheral edema
- Ascites

Patient with volume overload was diuretics prescribed?
- Yes
- NO
- If yes specify ___

Patient with HF and LVSD was beta blockers prescribed?:
- Yes
- No

If no, documentation of medical or patient reasons:
- Yes (specify)___________
- No

Patient with HF and LVSD was ACE inhibitors/ARBS prescribed?
- Yes
- No

If no, documentation of medical or patient reasons:
- Yes (specify)___________
- No

Patients who have LVEF ≤40% and following an acute MI who with symptoms of HF or Diabetes mellitus (DM) was Aldosterone receptor antagonists prescribed?
- Yes
- No

If no, documentation of medical or patient reasons:
- Yes (specify)___________
- No

Warfarin Therapy for patients with atrial fibrillation (AF)
- Yes
- No

If no, documentation of medical or patient reasons:
- Yes (specify)___________
- No

Hospitalization in the last 6 months
- Never
- 1
- 2-4
- > 4

Previous coronary artery bypass graft (CABG)
- Yes
- No

Previous pacemaker or implantable cardioverter defibrillator (ICD)
- Yes
- No

*Tobacco use

- Current smoker: An adult who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes either every day or some days
• Former smoker: Patients who reported history of smoking at least 100 cigarettes in their lifetime and who, at the time of the survey, did not smoke at all were defined as former smoker.

• Never smoker: Patients who has never smoked, or who has smoked less than 100 cigarettes in his or her lifetime were defined as never smoker.
REFERENCES


