Evaluating Medication Optimization in Heart Failure: A Pharmacist's Perspective

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ABSTRACT

Introduction:

This study is a multidisciplinary quality improvement initiative which aims to evaluate the appropriateness of physician-led care in the initiation of guideline-directed medical therapy (GDMT) for patients with heart failure with reduced ejection fraction (HFrEF) within the Oklahoma State University Medical Center (OSUMC) Cardiology Clinic.

Methods:

A retrospective chart review was conducted for physician-managed patients enrolled in the clinic during the 6 months prior to establishment of pharmacist-led services. Participants included English-speaking adults who had a diagnosis of HFrEF documented by an echocardiogram, were patients at the OSUMC clinic, or were recently discharged from the OSUMC emergency department or inpatient services for new onset HFrEF or acute exacerbation in the previous 30 days. Data were analyzed to identify the proportion of patients on appropriate GDMT.

Results:

A total of 86.3% of patients were appropriately initiated on an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or angiotensin receptor blocker/neprilysin inhibitor, with 62.3% of those patients achieving optimal doses. A total of 95.0% of patients were appropriately initiated on beta blockers, with 71.1% of those patients achieving optimal doses. A total of 54.4% of patients with a left ventricular ejection fraction (LVEF) ≤ 40% and an indication for an aldosterone antagonist also prescribed spironolactone; 96.8% of these patients achieved optimal doses.

Conclusion:

While the majority of patients were appropriately initiated on GDMT, there is additional need for further titration of GDMT, initiation of indicated supplemental GDMT, and patient education. Further study on the benefit of multidisciplinary practice following the recent implementation of a pharmacist-managed HF service is recommended.

INTRODUCTION

Previous research has observed a potential association between positive patient outcomes and the implementation of multidisciplinary approaches to the management of patients with heart failure (HF). Specifically, the management of medications after hospitalization plays a fundamental role in ensuring and optimizing patient safety and outcomes. This period of time for a discharged patient is highlighted as a vulnerable period for the continuation of consistent care and management of medications, and is often accompanied by poor adherence, poor communication with healthcare providers, poor understanding of medications prescribed, or inadequate monitoring of adverse effects.[1] Medication-related problems in these types of care transitions have been demonstrated as a major barrier to appropriate patient care in recent studies.[1-4] One fifth of all hospitalizations were associated with post-

discharge adverse events within 30 days post-discharge, 72% of which were specifically identified as drug-related problems.[5]

These types of post-discharge issues are often associated with hospital readmissions, which account for an immense amount of hospital expenditure. It is well known that heart failure re-admissions in particular are major contributions to these rising healthcare costs in the US.[6] Therefore, avoiding re-hospitalization has become a priority for policy makers in the U.S., including the Joint Commission (JC)[6] and the Center for Medicare & Medicaid Services (CMS). These organizations have created and proposed a set of *core measures*, which are researched and evidence-based standards of care that have shown to result in the improvement of the care and clinical outcomes of patients in National Clinical Focus Areas including heart failure, acute myocardial infarction (MI), pneumonia, venous thromboembolism (VTE), and others.[6,7]

Adherence to these standards and attainment of these core measures is the responsibility of all providers to ensure quality patient care. In order to ensure that patients receive the appropriate care with the attainment of these measures, multidisciplinary approaches may be implemented as supplementary services to primary care. In this domain, providers who may provide supplement services to regular physician care may include the use of nurses, nurse practitioners (NPs), physician assistants (PAs), and pharmacists (PharmDs). Existing evidence has shown an expanding role for PharmDs emerging for assisting in this post-discharge process.[1] In order to strengthen the multidisciplinary approach to care for heart failure patients, a pharmacist heart failure service was piloted in heart failure patients within the Oklahoma State University Medical Center (OSUMC) Cardiology clinic. In order to better focus the efforts for the incoming PharmD staff, it was necessary to analyze the ability of the current clinical staff to achieve the heart failure core measures, prior to the initiation of PharmD services. Therefore, the aim of this quality improvement initiative was to evaluate the appropriateness of physician led care in the initiation of guideline-directed medical therapy (GDMT) as defined by the 2017 ACC/AHA/HFSA heart failure guidelines for patients with heart failure with reduced ejection fraction (HFrEF).

METHODS

A retrospective chart review was conducted of patients who were referred or established outpatients afflicted by other previous cardiovascular diagnoses, but now with heart failure with reduced ejection fraction (HFrEF) at the OSUMC clinic, an outpatient cardiology clinic in Tulsa, Oklahoma. This study was approved by Oklahoma State University Medical Center Institutional Review Board (IRB) and the requirement for an informed consent was waived. All patient records and clinical data were collected without patient identifiers and maintained confidentially.

Retrospective chart review was completed for patients enrolled in the clinic during the 6 months prior to the establishment of pharmacist-led services (March 1, 2020 – September 30, 2020). Patients included for analysis met the following criteria: English-speaking adults at least 18 years of age or older, with a diagnosis of HFrEF defined by a LVEF $\leq$ 40% documented by an echocardiogram, were referred or established outpatients at the OSUMC clinic, or were recently discharged from the OSUMC emergency department or adult inpatient services for new onset HFrEF or acute exacerbation in the previous 30

days. This included patients who were started on GDMT agents for HF for the first time in the clinic, and it also included those started on these agents during their hospital admission, because these were considered newly initiated patients who now need management at the clinic for further titration or additional agents. Patients documented as pregnant or deceased at any point during the study period, diagnosis of diastolic HF or heart failure with preserved ejection fraction (HFpEF) alone, and significant renal impairment including diagnosis of chronic kidney disease (CKD) with or without dialysis were excluded from this study. Demographic information obtained from the Electronic Medical Record (EMR) included: patient age (years), gender, race, ethnicity, LVEF (%), grade of diastolic dysfunction, diagnosis of HFrEF, diagnosis of combined systolic and diastolic HF, NYHA class documentation, tobacco, alcohol, or drug use, insurance status, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), weight (kg), body mass index (BMI) (kg/m^2), serum creatinine, glomerular filtration rate (GFR), blood urea nitrogen (BUN), B-type natriuretic peptide (BNP), N-terminal-pro hormone BNP (NT-proBNP), and patient co-morbidities.

Data were analyzed to identify the proportion of patients on appropriate GDMT. The following clinical data were collected from an EMR and subsequently analyzed: proportion of patients seen by cardiology attending, cardiology fellow, and cardiology physician assistant(s), average length of follow-up time between appointments for providers, proportion of patients who received diet, activity recommendations, proportion of patients with advanced directive in place or received education or referral, proportion of patients with an EF < 35% and an indication for device therapy with an implantable cardioverter-defibrillator/cardiac resynchronization therapy (ICD/CRT), proportion of patients with an EF < 35% and an indication plus insertion or referral for device therapy with an ICD/CRT, proportion of patients on appropriate pharmacologic GDMT, the mean dose of the utilized pharmacologic GDMT agent, proportion of patients who achieved goal or maximally tolerated doses of their pharmacologic GDMT agents. Pharmacologic GDMT agents were defined as: angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), or angiotensin receptor blocker/neprilysin inhibitors (ARNIs), beta blockers (BBs), or aldosterone antagonists.

RESULTS

Baseline Characteristics

Of the 221 patients identified for review, a total of 80 patients were included in the final analysis. The resulting demographic data and clinical characteristics are shown in Table 1. The majority of the patient population consisted of Caucasian (63.8%) males (76.3%) at a mean age of 63 years, with a mean LVEF of 26%. The majority of patients had combined systolic and diastolic heart failure (61.3%). NYHA class was undocumented in the majority of patients (53.8%), with NYHA Class II (31.33%) representing the largest proportion of those with documentation completed. Most prevalent patient co-morbidities were hypertension (88.8%) and coronary artery disease (CAD) (53.8%). Patients were overweight with a mean weight of 90.2 kg and a mean body mass index (BMI) of 29.9 kg/m^2.

Table 1 Patient Demographics

Patient Characteristic	No. Patients (%) (N=80)
Age (years)	63 (mean)
Gender, male	61 (76.3%)
Caucasian	51 (63.8%)
LVEF (%)	26% (mean)
Diastolic Dysfunction	72 (90.0%)
-Unassessed	8 (10.0%)
-Grade 1	36 (45.0%)
-Grade 2	14 (17.5%)
-Grade 3	22 (25.5%)
HFrEF	31 (38.7%)
Combined systolic/diastolic dysfunction	49 (61.3%)
NYHA Class	
-Undocumented	43 (53.8%)
-NYHA Class I	1 (1.2%)
-NYHA Class II	25 (31.3%)
-NYHA Class III	10 (12.5%)
-NYHA Class IV	1 (1.2%)
Tobacco user	24 (30.0%)
Alcohol user	22 (27.5%)
Drug user	16 (20.0%)
-Marijuana	16 (20.0%)
-Methamphetamines	1 (1.2%)
-Cocaine	1 (1.2%)
Insurance status	
-Uninsured	16 (20.0%)
-Private insurance	33 (41.2%)
-Medicare/Medicaid	31 (28.8%)
Co-Morbidities	
Ischemic cardiomyopathy	21 (26.3%)
Non-ischemic cardiomyopathy	29 (36.3%)
Atherosclerosis	28 (35.0%)
HTN	71 (88.8%)
DLD	41 (51.3%)
DM	27 (33.3%)
Afib/Aflutter	23 (28.8%)
CVA/TIA	5 (6.25%)
COPD	15 (18.8%)
OSA	11 (13.8%)
CAD	43 (53.8%)
PVD	6 (7.5%)

MI	15 (18.5%)
CABG	22 (27.5%)
PCI	49 (61.3%)

Vitals & Laboratory Values	Mean Value
Systolic blood pressure (mmHg)_	121
Diastolic blood pressure (mmHg)	77
Heart rate (bpm)	76
Weight (kg)	90.2
Body mass index (BMI) (kg/m^2)	29.9
Serum creatinine (mg/dL)	1.10
Glomerular filtration rate (mL/min)	67
Blood urea nitrogen (mg/dL)	17
B-type natriuretic peptide (ng/L)	919

LVEF left ventricular ejection fraction, *HFrEF* heart failure with reduced ejection fraction, *NYHA* New York Heart Association, *HTN* hypertension, *DLD* dyslipidemia, *DM* diabetes mellitus, *Afib* atrial fibrillation, *Aflutter* atrial flutter, *CVA* cerebrovascular accident, *TIA* transient ischemic attack, *COPD* chronic obstructive pulmonary disease, *OSA* obstructive sleep apnea, *CAD* coronary artery disease, *PVD* peripheral vascular disease, *MI* myocardial infarction, *CABG* coronary artery bypass graft, *PCI* percutaneous coronary intervention

Provider Follow-Up

The data for provider follow-up is shown in Table 2. On average, attending physicians saw the highest percentage of patients (46.3%), closely followed by residents or fellows (38.7%). Approximately 15.0% of patients were seen by a physician assistant. The mean time elapse between visits for attending physicians, residents or fellows, and physician assistants were 3.2 months, 3.0 months, and 2.2 months, respectively.

Table 2 Provider Follow-Up

Provider Type	No. Patients Seen (%)	Total No. Visits	Total No. Follow-Ups (%)	Mean Time Elapse Between Visits
Attending Physician	37 (46.3%)	46	13 (28.3%)	3.2 months
Resident/Fellow	31 (38.7%)	45	15 (33.3%)	3.0 months
Physician Assistant	12 (15.0%)	22	10 (45.5%)	2.2 months

Lifestyle Modifications

The data for achievement of lifestyle modifications as core measures is shown in Table 3. On average, diet and activity recommendations were completed about half of the time (53.8% and 51.2%, respectively). Recommendations for advanced directives were completed approximately 20% of the time.

Table 3 Lifestyle Modifications

Provider Type	Total No. Patients (%)
Diet Recommendations	43 (53.8%)
Activity Recommendations	41 (51.2%)
Advanced Directives	16 (20.0%)

Device Therapy

The data for device therapy recommendations as core measures is shown in Table 4.[6,7,9,10] On average, 50 of the 51 patients (98.0%) indicated for device therapy with an ICD or CRT were appropriately referred, counseled, or already placed on the appropriate therapy.

Table 4 Device Therapy

	Total No. Patients (%)
EF < 35% + Indication for ICD/CRT	51 (63.8%)
EF < 35% + Indication/Insertion/Referral for ICD/CRT	50 (62.5%)
ICD/CRT Device in Place	37 (46.3%)

Pharmacologic Guideline-Directed Medical Therapy

The data for achievement of pharmacologic GDMT are shown in Tables 5, 6, and 7. Approximately 86.3% of patients were appropriately prescribed an ACEI, ARB, or ARNI. Of these patients, 62.3% were documented as achieving a goal or maximally tolerated dose of an agent from this category. Lisinopril was the most prevalently (and only) prescribed ACEI (32.5%), with losartan representing the most prevalently prescribed ARB (92.3%). Eleven patients were not on ACEI, ARB, or ARNI therapy; six (7.5%) of those patients were not prescribed a drug from this category for an unknown reason, and 5 (6.3%) of those were not prescribed a drug from this category due to a listed contraindication.

Table 5 Achievement of Pharmacologic GDMT: *ACEIs, ARBs, ARNIs*

Agent(s)	Total No. Patients (%)	Mean Total Daily Dose	Total No. Achieved Goal or Max Tolerated Dose (%)
All Agents (ACEI, ARB, ARNIs) (N=69)	69 (86.3%)	---	43 (62.3%)
Lisinopril	26 (32.5%)	12.0 mg	21 (80.8%)
Losartan	12 (92.3%)	47.9 mg	3 (25.0%)
Valsartan	1 (7.7%)	320 mg	1 (100.0%)
Sacubitril/Valsartan	30 (37.5%)	43.4 mg/46.3 mg	18 (60.0%)
No Agent (ACEI, ARB, ARNIs) -Indicated, not prescribed -Indicated, contraindication	11 (13.8%) 6 (7.5%) 5 (6.3%)	---	

Approximately 95.0% of patients were appropriately prescribed a heart failure indicated BB. Of these patients, 71.1% were documented as achieving a goal or maximally tolerated dose of an agent from this category. The distribution of patients appropriately initiated on carvedilol (51.3%) and metoprolol succinate (48.7%) were similar. Approximately 4 (5.0%) patients were not prescribed a BB, with 3 of them documented as being prescribed a non-heart failure approved BB, and 1 of them not prescribed a drug from this category for an unknown reason.

Table 6 Achievement of Pharmacologic GDMT: *BBs*

Agent(s)	Total No. Patients (%)	Mean Total Daily Dose		Total No. Achieved Goal or Max Tolerated Dose (%)
All Agents (N=76)	76 (95.0%)	---		54 (71.1%)
Carvedilol	39 (51.3%)	12.9 mg		29 (74.4%)
Metoprolol succinate	37 (48.7%)	62.2 mg		25 (67.6%)
No Agent -Indicated, not prescribed -Indicated, non-HF BB used	4 (5.0%) 1 (1.3%) 3 (3.8%)	---		

Approximately 38.8% of patients were appropriately prescribed an aldosterone antagonist, with spironolactone representing 100% of the agent used for this category. Of these patients, 100% were documented as achieving a goal or maximally tolerated dose of spironolactone. Approximately 61.4% of patients were not appropriately prescribed an aldosterone antagonist. Of these patients, 71.4% of them were not prescribed a drug from this category for an unknown reason, and 28.6% of them were not prescribed a drug from this category due to a listed contraindication.

Table 7 Achievement of Pharmacologic GDMT: *Aldosterone Antagonists*

Agent(s)	Total No. Patients (%)	Mean Total Daily Dose	Total No. Achieved Goal or Max Tolerated Dose (%)
Spironolactone	31 (38.8%)	26.6 mg	31 (100.0%)
No Agent -Indicated, not prescribed -Indicated, contraindication **Hypotension* **Arrhythmia*	49 (61.4%) 35 (71.4%) 14 (24.6%) 11 (73.3%) 3 (21.4%)	---	

DISCUSSION

Several studies have highlighted the importance of medication management and post-discharge care for patients with heart failure.[1,5,8-11] There is growing evidence from these analyses that a multidisciplinary approach in particular may contribute to a higher level of patient care, ability to more easily achieve goals such as the JC and CMS core measures, and even improvement in patient outcomes. Therefore, this quality improvement initiative and observational analysis sought to evaluate the appropriateness of physician-led care in the initiation of GDMT for patients with HFrEF. The purpose of this analysis was to identify areas of improvement within the current physician-led model within the OSUMC Cardiology Clinic, in order to better focus the efforts of incoming pharmacists in a newly implemented PharmD Heart Failure Service.

We observed that most patients were appropriately initiated on pharmacologic GDMT including ACEIs, ARBs, ARNIs, BBs, and aldosterone antagonists over the 6-month period that was studied. Our results align with those of previous studies.[1, 5,8-11] Within the pharmacologic GDMT data, our analysis also revealed that there is a need for further improvement of the continued titration of these medications, specifically the ACEI, ARB, ARNI, and BB agents, to aim for achievement of goal or maximally tolerated doses of agents. Our data also revealed that there may be a need for further initiation of additional pharmacologic agents that would be considered 'supplemental' to the 'backbone' of ACEI, ARB, ARNI, and BBs – such as aldosterone antagonists. Due to the relatively small sample size of this study, and lack of analysis of other 'supplemental' agents such as nitrates, hydralazine, ivabradine, digoxin etc., this should be interpreted with caution and true clinical implications likely require further and more expanded study.

Our study also revealed an additional need for focus on non-pharmacologic GDMT and core measure recommendations, such as lifestyle modifications including diet and exercise recommendations. With these data, the newly implemented pharmacist heart failure service was able to focus efforts on these aspects of patient care and education. The pharmacist services were also able to focus on medication titration to achieve goal or maximally tolerated doses, which were completed with close follow-up time, typically in weekly or two-week intervals. The expectation of this study is to be expanded into a second part, including the 6-month period after the establishment of pharmacist-led services in addition to the current physician-led practices in place.

There are several limitations to our analysis of achievement of GDMT in this study. Firstly, this study has possible biases related to its observational design. Additionally, our analysis did not evaluate other potential 'supplemental' pharmacologic GDMT such as nitrates, hydralazine, ivabradine, digoxin, etc. Lastly, the 6-month period during which this data was collected occurred during the beginning of global pandemic with COVID-19, which may have affected the number of patients included and therefore contributed to a smaller sample size. Although our results were consistent with currently available literature, the impact and clinical implications of our findings require further study with the addition of data from the 6-month period post implementation of pharmacist-led services.

CONCLUSION

Our analysis suggestions that the majority of patients were appropriately initiated on GDMT upon diagnosis with physician-led care. Our findings raise the possibility that there is additional need for further titration of GDMT to achieve goal or maximally tolerated doses in patients, as well as initiation of indicated supplemental GDMT such as additional pharmacologic therapy, and patient education including lifestyle modifications. It is possible that these measures may be better attainted through the use of supplementary care in the form of a multidisciplinary approach to practice, such as a pharmacist managed HF service, which may be able to provide closer follow-up than regular physician-led care. A continuation of this study evaluating the addition of pharmacist-led care to regular physician-led care is recommended.

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