Original Work

Addition of Pharmacist versus Usual Care Impact on Heart Failure with Reduced Ejection Fraction Management in a Cardiology Clinic

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Abstract

Objectives: Well-studied heart failure with a reduced ejection fraction (HFrEF) medications reduce morbidity and mortality when titrated to evidence-based target or maximally tolerated doses. External studies showed benefits when pharmacists manage HFrEF medications, but internal validation at Froedtert & the Medical College of Wisconsin (F&MCW) had not been done. This study aimed to describe the differences in HFrEF medication-related management between patients who were and were not followed by a pharmacist.

Methods: A retrospective chart review was conducted of patients who were followed by an F&MCW Cardiology Clinic provider and prescribed a new HFrEF medication over a one-year period. Patients were stratified into the provider or pharmacist group and were compared based on reaching target or maximally tolerated doses for prescribed HFrEF medications; appropriate lab monitoring; number of visits; time between visits; number of heart failure admissions and re-admissions; and change in left ventricular ejection fraction (LVEF).

Results: Patients in the pharmacist group met their target or maximally tolerated doses at a higher rate than the provider group for four of seven HFrEF medications. There was no appreciable difference in appropriate lab monitoring. Patients in the pharmacist group had more visits and were seen more frequently. The pharmacist group saw a larger average LVEF increase and fewer admissions and re-admissions.

Conclusions: These results suggest that when pharmacists are included in a patient's care team, the team provides superior, more efficient medication-related care to patients with HFrEF. Pharmacists can effectively titrate HFrEF medications because they are able to focus on a patient's medications.

In the United States, heart failure costs $30.7 billion in health care and missed work annually. A large source of this cost is admissions and re-admissions with the primary diagnosis of heart failure. On average, 25% of all patients with heart failure will be re-admitted to the hospital within 30 days of being discharged. Additionally, the five-year mortality rate for patients diagnosed with heart failure is about 50%.[1] Fortunately, there are well-studied, effective medication therapies available for use in heart failure, specifically heart failure with a reduced ejection fraction (HFrEF), that reduce morbidity and mortality. To achieve clinical benefits, these medications must be titrated to target doses. When patients cannot tolerate target doses, these medications should be titrated to maximally tolerated doses. There are a total of seven HFrEF medication classes that are considered Guideline-Directed Medical Therapies (GDMT) as outlined in the American College of Cardiology (ACC)/American Heart Association (AHA) Guideline for the Management of Heart Failure.[2,3] The GDMT are: beta blockers (BB), angiotensin receptor neprilysin inhibitor (ARNI), angiotensin-converting enzyme inhibitor (ACEi), angiotensin II receptor blocker (ARB), aldosterone receptor antagonists (ARA), vasodilators (i.e. hydralazine and isosorbide), and ivabradine.

Titrating patients to goal or maximally tolerated doses of GDMT in a timely and safe manner requires close follow-up and monitoring. Because of this, a multidisciplinary approach to heart failure management can improve the quality of medication-related care. Pharmacists are particularly well-positioned to optimize heart failure medication therapies as the medication experts on the healthcare team. Several previous studies showed that when patients with heart failure are managed by a pharmacist in addition to the rest of their care team, versus a more typical care model, the patients with pharmacist support had better heart failure outcomes. These outcomes included a reduction in admissions, reduction in mortality, and an improvement in reaching goal or maximally tolerated heart failure medication doses.[4-6]

Froedtert & the Medical College of Wisconsin's (F&MCW) Center for Advanced Care (CFAC) Cardiology Clinic manages patients with heart failure, among other cardiovascular disease states. Pharmacists in this clinic work under a

collaborative practice agreement (CPA) to assist providers in heart failure medication titrations and general medication management. Pharmacists follow up with patients regularly to titrate HFrEF medication doses, monitor relevant vitals and labs, educate patients on their medications and disease state, and manage adverse drug reactions based on guidance from national heart failure treatment guidelines and expert consensus reports.[2,3,7]

The benefit of having pharmacists take part in HFrEF medication management has been proven in external studies, but no internal validation of this concept had been conducted at F&MCW. This study aims to add to the existing evidence regarding the pharmacist's impact in heart failure medication management while also providing internal validation of existing pharmacist services.

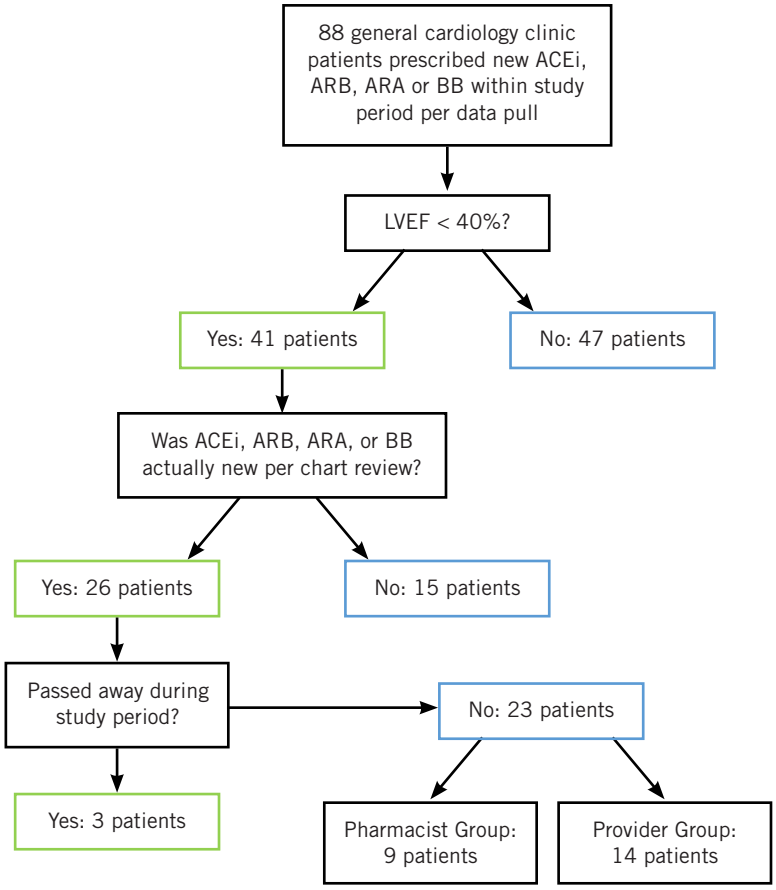
Methods

Study Site

The F&MCW health system is a regional network of one academic medical center, four community hospitals, and more than 45 clinics located in southeastern Wisconsin. This study took place at F&MCW's CFAC Cardiology Clinic on the Froedtert Hospital campus. This clinic encompasses both general cardiology and advanced heart failure clinics. This study focused on HFrEF patients that follow with general cardiology only, as the advanced heart failure clinic functions under a medical home model with increased provider and staff support.

Pharmacists in this clinic work alongside physicians, advanced practice providers, nurses, and medical staff. They work under robust CPAs to see patients independently for heart failure, hyperlipidemia, hypertension, and tobacco abuse disease states. Cardiology providers refer patients to the pharmacist for a pre-specified reason, and the pharmacist can start, adjust, or discontinue medications, monitor relevant vitals, order labs, and educate patients on their medications and disease states. The pharmacist follows patients primarily via in-person office visits but can also provide follow-up care via telephone and MyChart when preferred by the patient or to increase access to care. For heart failure management, the pharmacist prefers to follow up with the patient every 2 weeks when possible to ensure efficacy and tolerability of the medication regimen. Once the patient has reached their medication-related disease state goals or the pharmacist has exhausted available resources, the pharmacist discharges the patient back to the referring cardiology provider and no longer follows up with the patient. Cardiology providers typically follow patients indefinitely and prefer to see patients via in-person office visits every few months.

FIGURE 1. Screening Patients for Inclusion and Exclusion Criteria



Abbreviations: angiotensin-converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARB), angiotensin receptor antagonist (ARA), beta blocker (BB), left ventricular ejection fraction (LVEF)

Study Design

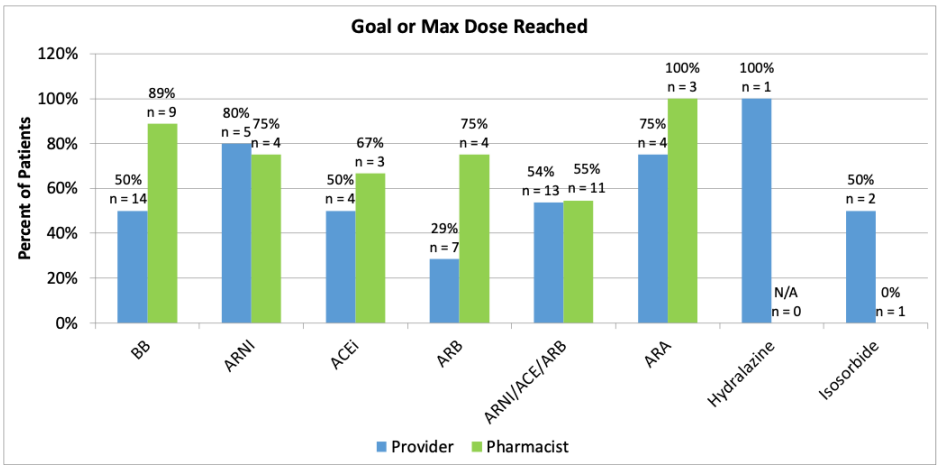
This was a single-center, retrospective chart review of patients with HFrEF followed by a cardiology provider at F&MCW's CFAC Cardiology Clinic. This project was deemed a quality improvement

TABLE 1. Baseline Characteristics

	All (N=23)	*All (N=14)*	*Pharmacist Group (N=9)*	*p-value*
Mean Age (SD)	64.83 (14.62)	65.29 (16.23)	64.11 (12.60)	0.729
Gender				0.214
Male	11 (47.8%)	5 (35.7%)	6 (66.7%)	
Female	12 (52.2%)	9 (64.3%)	3 (33.3%)	
Average Baseline LVEF	32.5%	33.9%	29.6%	

Abbreviations: left ventricular ejection fraction (LVEF)

FIGURE 2. Goal or Maximally Tolerated Dose Reached



Abbreviations: beta blocker (BB), angiotensin receptor neprilysin inhibitor (ARNI), angiotensin-converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARB), angiotensin receptor antagonist (ARA)

project by the F&MCW Pharmacy Research Committee in August of 2019. The index event qualifying patients for inclusion into the study cohort was being prescribed a new angiotensin-converting enzyme inhibitor (ACEi), angiotensin II receptor blocker (ARB), angiotensin receptor neprilysin inhibitor (ARNI), or beta blocker (BB) medication between December 1, 2017 and December 1, 2018.

Patients were included if their left ventricular ejection fraction (LVEF) was 40% or less based on any type of cardiac imaging done before the date the new medication that triggered patient inclusion was first prescribed. Charts of patients who met inclusion criteria were reviewed to determine whether the patient was referred to and seen by a clinical cardiology pharmacist for heart failure medication titration. Patients were then stratified into two groups: those referred to the clinical pharmacist for medication titration (pharmacist group) and those not referred to the clinical pharmacist (provider group). The study period for the pharmacist group lasted from the time of the first visit with the pharmacist to the last visit. The study period for the provider group was a standard six months, starting with the date the new medication that triggered patient inclusion was first prescribed. This six-month time period was based on the presumed length of time that pharmacists follow HFrEF patients, as providers typically follow patients indefinitely.

Patients were excluded if they were followed by an F&MCW advanced heart failure provider, not seen by an F&MCW cardiology clinical pharmacist or F&MCW cardiology provider during the study period, or seen by a cardiology clinical pharmacist for a referral reason other than heart failure medication titration. Medication-related outcomes were reviewed for the following seven groups of GDMT: beta blockers (BB), angiotensin receptor neprilysin inhibitor (ARNI), angiotensin-converting enzyme inhibitor (ACEi), angiotensin II receptor blocker (ARB), aldosterone receptor antagonists (ARA), hydralazine, and isosorbide. Medication-related outcomes, such as medication adjustments and lab monitoring, were counted when they were completed by any cardiology clinic team member for both groups, as long as they occurred within the study period. This was done to capture the overall team's impact on HFrEF outcomes. Medication adjustments and lab monitoring completed by a non-cardiology clinic health care professional were not counted for either group.

Outcomes

The overall objective of this study was to describe differences in medication-related management between patients in the pharmacist group and provider group. The primary outcome was the number and percent of patients in each group who reached a target or maximally tolerated dose for each individual as well as the sum of all GDMT they were prescribed.

Several secondary outcomes were assessed during the retrospective review. The percent of patients in each study group with appropriate medication-related lab monitoring was assessed. Appropriate lab monitoring was defined as having a basic metabolic panel (BMP) lab ordered within 2 weeks of ACEi, ARB, ARNI, or aldosterone receptor antagonist (ARA) initiation, or when the medication dose was increased was assessed. The average number of office visits, telephone encounters, MyChart encounters, and total encounters was tracked. Groups were compared based on the average time between office visits. The average change in LVEF based on cardiac imaging completed before the start of the study period and the first cardiac imaging completed within 6 months of the end of the study period was assessed. The

TABLE 2. Primary Outcome

Medication	All (N=23)	Provider Group (N=14)	Pharmacist Group (N=9)	p-value
BB	15 (65.2%)	7 (50.0%)	8 (88.9%)	0.086
ARNI	7 (77.8%)	4 (80.0%)	3 (75.0%)	> 0.999
ACEi	4 (57.1%)	2 (50.0%)	2 (66.7%)	> 0.999
ARB	5 (45.5%)	2 (28.6%)	3 (75.0%)	0.242
ARA	6 (85.7%)	3 (75.0%)	3 (100.0%)	> 0.999
Hydralazine	1 (100.0%)	1 (100.0%)	0 (–%)	
Isosorbide	1 (33.3%)	1 (50.0%)	0 (0.0%)	

Abbreviations: beta blocker (BB), angiotensin receptor neprilysin inhibitor (ARNI), angiotensin-converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARB), angiotensin receptor antagonist (ARA)

FIGURE 3. Goal or Maximally Tolerated Dose Reached for All GDMT Patient Taking

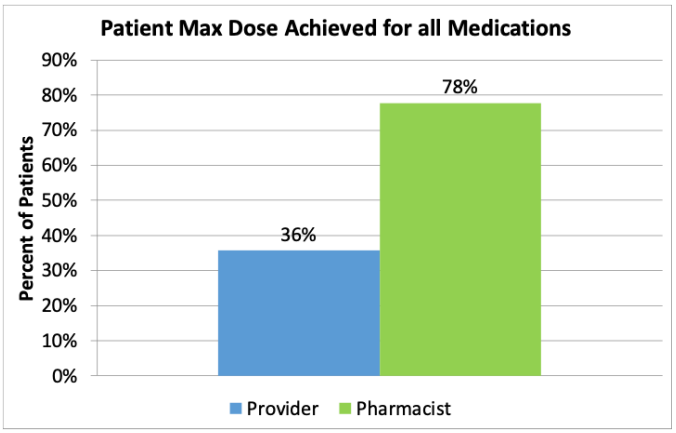
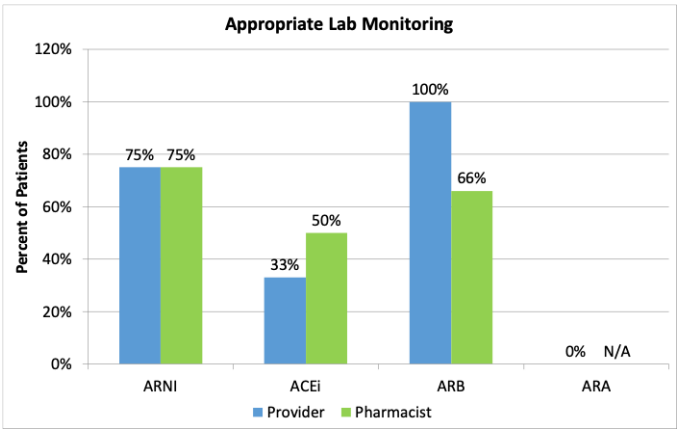


FIGURE 4. Appropriate Lab Monitoring



Abbreviations: angiotensin receptor neprilysin inhibitor (ARNI), angiotensin-converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARB), angiotensin receptor antagonist (ARA)

type of LVEF imaging varied from patient to patient, but imaging was only included for comparison if the patient's pre-intervention and post-intervention LVEF imaging modality was the same. Additional secondary outcomes included the total number of patients admitted and total number of patients re-admitted with heart failure as the primary diagnosis during the study period.

Descriptive statistics were employed. Study variables were summarized by the mean and standard deviation for continuous variables. Frequency and percentage were used for categorical variables. Baseline characteristics and outcomes were compared between groups using Wilcoxon rank-sum tests for continuous variables and Fisher's exact tests for categorical variables. All statistical analyses were performed using R version 3.6.0 (R Foundation for Statistical Computing, http://www.R-project.org). All tests were two-sided and $p < 0.05$ was considered statistically significant. All analyses employed an "available-case" approach to missing data. No adjustments were made for multiple testing.

Results

Patient Population

A total of 88 patients were screened for inclusion and exclusion criteria. Results of the screening process are outlined in Figure 1. After screening, 23 patients were included for retrospective analysis. There were 14 patients in the provider group and 9 patients in the pharmacist group. Baseline characteristics for the included patient number of each encounter type and total clinical encounters per patient are outlined in Figure 5. Patients in the pharmacist group had statistically significantly more total clinical encounters over the course of the study period compared to the provider group. The average times between office visits are outlined in Figure 6. Pharmacist patients were followed for 4.11 months on average, which was less than the standard six-month period that patients in the provider group were followed. The pharmacist group saw patients more frequently, and this result was statistically significant.

The average baseline, end, and change in LVEF are displayed in Table 4. The pharmacist group saw slightly more LVEF improvement than the provider group on average. None of the patients in the pharmacist group were admitted or re-admitted to the hospital with heart failure as the chief concern. There were 3 hospital admissions and 0 re-admissions in the provider group. One patient in the provider group was admitted twice, but these

TABLE 3. Secondary Outcome

Variable	*All (N=23)*	*Provider Group (N=14)*	*Pharmacist Group (N=9)*	*p-value*
Mean # cardiology office visits during study period (SD)	3.30 (1.84)	3.14 (1.92)	3.56 (1.81)	0.678
Mean # cardiology telephone encounters during study period (SD)	3.48 (3.76)	2.57 (2.47)	4.89 (5.04)	0.170
Mean # cardiology MyChart encounters during study period (SD)	0.48 (0.99)	0.43 (0.76)	0.56 (1.33)	0.838
Mean # total cardiology encounters during study period (SD)	7.26 (4.29)	6.14 (2.77)	9.00 (5.70)	0.405
Mean # cardiology encounters with pharmacist during study period (SD)	1.78 (3.06)	0.29 (0.73)	4.11 (3.86)	0.004
Average time elapsed between office visits in weeks (SD)	8.59 (6.80)	10.54 (6.91)	5.56 (5.70)	0.021

Abbreviations: standard deviation (SD)

FIGURE 5. Average Number of Encounters per Patient

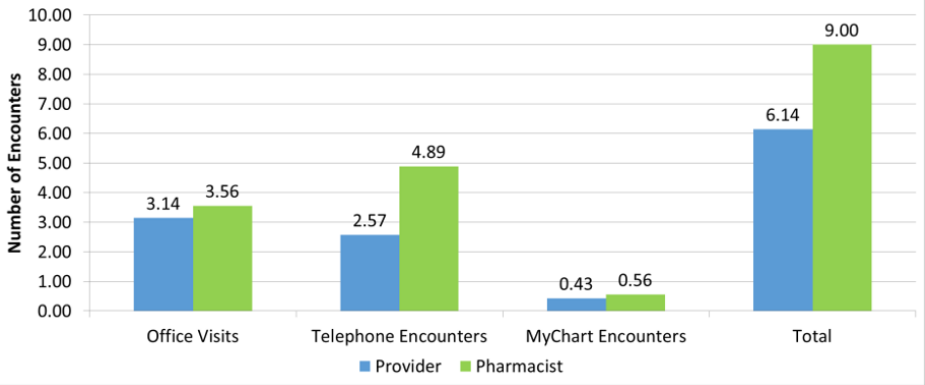
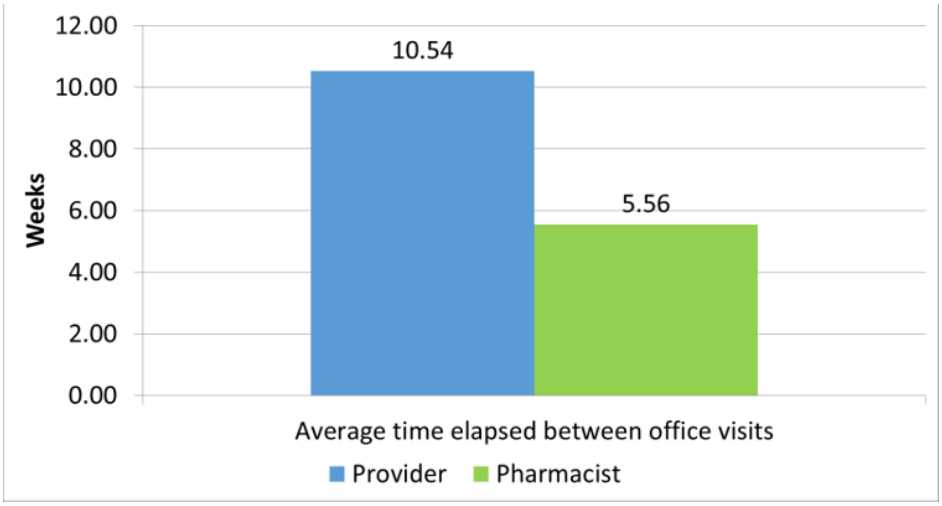


FIGURE 6. Average Time between Visits



population are outlined in Table 1. There was a non-statistically significantly higher percentage of males in the pharmacist group than in the provider group. The average age was similar for both groups, with an average age of 64.83 years for all included patients. The average baseline LVEF was slightly lower in the pharmacist group.

Outcomes

Results for the primary outcome are outlined in Figures 2 and 3. Statistical analysis of the primary outcome is outlined in Table 2. The pharmacist group achieved a higher percent of patients on target or maximally tolerated doses for four of seven GDMT categories. The pharmacist group also achieved a higher percent of patients on target or maximally tolerated doses for all the GDMT each patient was prescribed. None of the primary outcome components reached statistical significance.

Table 3 outlines the statistical analyses for all secondary outcomes. The difference between the pharmacist and provider groups in ordering appropriate lab monitoring for each applicable type of medication is outlined in Figure 4. This outcome did not reach statistical significance. The two groups varied in their rates of appropriate lab monitoring for each individual medication type but had overall similar rates of lab monitoring when considering all medications where lab monitoring is beneficial. The average admissions were more than 30 days apart, so they did not meet the criteria to be considered a re-admission. Neither of these outcomes reached statistical significance.

Discussion

The primary outcome was impacted by a couple of factors. There were no patients in the pharmacist group on hydralazine, so there is no meaningful comparison for hydralazine. Also, there was only one patient in the pharmacist group who was prescribed isosorbide, and this patient did not reach a target or maximally tolerated dose. This study found that there is room for improvement regarding ordering labs when appropriate, as well as ensuring patients follow through on having ordered labs drawn, as neither group had complete adherence for all relevant medication classes.

The average number of office visits and MyChart encounters patients had with their cardiology care team were about the same in both groups. However, patients in the pharmacist group had more telephone encounters, and thus had more total encounters. This was not surprising, since pharmacists are well-positioned to be able to conduct clinical visits via the phone due to billing constraints and frequency of encounters. Patients in the pharmacist group had more frequent follow-up than the provider group, even though this metric was based on time between office visits only and did not include telephone encounters. If all visit types were considered, it is likely this difference would be larger.

Although the number of office visits was not very different between the groups, the total time the pharmacist followed patients was only 4.11 months, while provider group patients were followed for a standard six months. This means that the pharmacist

TABLE 4. Left Ventricular Ejection Fraction

	Provider Group (N=14)	*Pharmacist Group (N=9)*	*p-value*
Average Baseline LVEF	33.9%	29.6%	
Average End LVEF	38.9%	37.2%	
Change in LVEF	5.0%	7.6%	0.767

Abbreviations: left ventricular ejection fraction (LVEF)

group fit more visits into a shorter period of time. This variance in study period length is a limitation of the study. The study period length varied because pharmacists in the cardiology clinic only follow patients until they reach their medication-related disease state goals or the pharmacist has exhausted available resources, while cardiology providers typically follow their patients indefinitely. At the beginning of the study it was estimated that pharmacists follow patients with HFrEF for six months on average; therefore, the standard six-month study period was established for the provider group. This ended up being an over-estimation and resulted in a difference in study period lengths. If these time periods were better matched, it is possible the results would have more accurately reflected pharmacist contribution.

A limitation to this study is the small sample size, which limited the ability to show statistical significance. The sample size was limited because patients were only included if they were prescribed a new ACEi, ARB, ARNI, or BB during the study period. This was done because the study needed to have the same inclusion trigger for both the pharmacist and provider groups in order to minimize bias when assessing analytical statistics. In a cardiology clinic, many patients are prescribed an ACEi, ARB, or BB for an indication other than heart failure even before they are diagnosed with heart failure, so this eliminated many patients. It was not possible to use a diagnosis of HFrEF as the inclusion trigger, because the way diagnoses are entered in the electronic health record is unreliable for data collection purposes.

Conclusion

This study suggests that when pharmacists are involved in the care team for patients with HFrEF, it leads to similar or possibly better outcomes compared to providers alone. These findings are similar to studies done outside F&MCW. Pharmacists are well-positioned to effectively titrate HFrEF medications because they can dedicate time to focus on a patient's medications. This information can and will be used to support existing pharmacist services in the cardiology clinic as well as to encourage continued pharmacist referrals from cardiology providers.

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