Original Article

Influence of Patient Characteristics on Provider Deviation from Guideline-Directed Medical Therapy of Heart Failure with Reduced Ejection Fraction in Primary Care Clinics

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Abstract

Background: Heart failure with reduced ejection fraction (HFrEF) is a significant cause of morbidity and mortality in the United States. Although data have demonstrated that guideline-directed medical therapy (GDMT) improves clinical outcomes, hospitalizations, and death due to HFrEF remain common.

Objective: To identify GDMT gaps for patients with HFrEF.

Methods: This retrospective cohort study evaluated adults with HFrEF at an academic internal medicine (IM) or family medicine (FM) clinic between 1/1/2018 and 2/29/2020. A chart review was conducted to characterize patient demographics, characteristics, and GDMT. Descriptive statistics and chi-squared tests were used to describe GDMT regimens and factors associated with improved guideline adherence.

Results: A total of 596 patients were evaluated and 96 included. Overall, 20% of patients were prescribed three GDMT agents (β-blocker+angiotensin converting enzyme inhibitor [ACEi]/angiotensin receptor blocker [ARB]/angiotensin receptor-neprilysin inhibitor [ARNI]+mineralocorticoid receptor antagonist [MRA]), 43.8% two agents (β-blocker + ACEi/ARB/ARNI), 27% one agent, and 9% no GDMT. Those with a payor status defined as commercial insurance were more likely to be on three GDMT agents than those with no commercial insurance (34.8% vs. 15.1%; p=0.039). Patients ≥65 years were less likely to be on three agents compared to those <65 years (8.3% vs. 32%, p=0.029), but more likely to be on a combination of a β-blocker+ACEi/ARB/ARNI (52.8% vs. 32%, p=0.01) or a β-blocker+MRA (11% vs. 2%; p=0.044).

Conclusions: GDMT was underutilized in these academic clinics. Differences in provider prescribing were identified based on age and funding status. Differences in prescribing could be due to demographics or other factors.

Keywords: HFrEF, GDMT, provider deviation, guideline-based treatment, primary care

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Background

Heart failure with reduced ejection fraction (HFrEF) is a significant cause of morbidity and mortality in the United States. Although data have demonstrated that guideline-directed medical therapy (GDMT) improves clinical outcomes, hospitalization and death remain common.[1]

A critical component of GDMT in HFrEF includes the utilization of agents demonstrated to reduce morbidity and mortality. When the study was conducted in 2020 the 2013 ACC/AHA Guideline for Management of Heart Failure, along with the 2016/2017 focused updates to the guidelines, outlined optimized GDMT as an angiotensin-converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARB), or angiotensin II receptor blocker-neprilysin inhibitor (ARNI), with an evidence-based β-blocker (i.e., bisoprolol, metoprolol succinate, carvedilol), and a mineralocorticoid receptor antagonist (MRA).[2-5] In 2022, the ACC/AHA Guideline for the Management of Heart Failure added sodium-glucose-like peptide-2 inhibitors (SGLT-2 inhibitor) as standard GDMT, along with recommending ARNI therapy over ACEi/ARB therapy in class C/D (NYHA Class II-III) heart failure, to optimize morbidity reduction.[5]

In addition to these guideline-based medications, it is critical that optimal doses are utilized.[2-5] These optimal, or "target doses", are those used in clinical trials that demonstrated improved clinical outcomes. With ACEis, ARBs, and β-blockers, these "target doses" are typically much higher than those used for other indications (e.g., high blood pressure). Available literature indicates that patients with HFrEF are frequently not on GDMT medications or at an optimal dose.[1,6-8]

It is currently unclear why many patients with HFrEF may not be on optimal therapy. Some studies suggest patient factors like contraindications, poor tolerability of recommended medications, or poor patient adherence as causes for suboptimal GDMT use.[1] Studies with HFrEF patient registries such as the CHAMP-HF, QUALIFY, and ASIAN-HF have found that women, older patients, different racial groups, and those with lower socioeconomic status are less likely to be prescribed guideline-based treatment or reach optimized doses of medication.[1,6-8] According to the CHAMP-HF study, among patients eligible for therapy, 27%, 33%, and 67% were not prescribed ACEI/ARB/ARNI, evidenced-based beta-blockers, and MRA respectively. Additionally, when medications were prescribed, very few patients received target doses of those medications. Finally, CHAMP-HF found that of patients on all classes of medication, only 1% of them were on target doses of all agents.[1]

There is little information known regarding possible HFrEF GDMT treatment gaps in academic teaching clinics. To address this knowledge gap, provider deviation rates from HFrEF GDMT (i.e., ACEi, ARB, ARNI, β-blocker, and MRA) were assessed in family medicine and internal medicine academic teaching clinics.

Objective

The primary outcome of this study was to describe the use of GDMT in this patient population and assess various factors (e.g., race, sex, age, payor status, healthcare

access, medication choice, and dosing) associated with guideline adherence. The secondary outcomes were to determine the percentage of patients on optimal and suboptimal HFrEF therapeutic regimens at each clinic independent of patient characteristics and identify a recommendation to improve care.

Methods

Study Design and Participants

This is a retrospective cohort analysis of outpatients who had an appointment addressing their heart failure condition at Texas Tech Family and Community Medicine (FM) and Internal Medicine (IM) clinics between 01/01/2018 and 02/29/2020. Medication data and labs that were from their most recent visit during this index period were collected. Patients were included if they were ≥18 years of age and diagnosed with chronic, acute on chronic, or unspecified HFrEF (I50.22; I50.23; I50.20), congestive HF (I50.9), HF due to hypertension (I11.0), or end-stage HF (I50.84) and had a left ventricular ejection fraction (EF) of ≤40%. Exclusion criteria included pregnancy, comfort care or hospice, recipients of a heart transplant, using a left ventricular assistive device, on dialysis, prisoners, or wards of the state, or had inadequate documentation in the medical record to meet inclusion criteria.

Data Collection

Patient data were extracted from the electronic health record after a manual record review and maintained in a Microsoft Excel (Redmond, WA) spreadsheet. Individuals responsible for collecting data were trained in the use of the database and audits on the individuals were conducted randomly to provide quality assurance. Subjects were identified by an Allscripts EHR query. These patients were then reviewed to ensure they met inclusion criteria. Baseline characteristics collected included age, race, sex, height, weight, body mass index (BMI), payor status, employment status, distance from home to clinic, left-ventricular ejection fraction, and clinic (FM or IM). Other data collected included the subject's past medical history, recent labs, vital signs, and laboratory values (e.g., chemistry panel, kidney function) to evaluate possible contraindications. Data were also collected on the medication prescribed including the medication name, dose, and dosing frequency. Finally, data on contraindications were also collected, including if the patient had hypotension (blood pressure <90/60 mmHg), bradycardia (heart rate <60 bpm), eGFR<30 mL/min/1.73m^2, or hyperkalemia (K>5 mEq).

Statistical Analysis

Descriptive statistics (i.e., mean, standard deviation, percentages) were used for the primary objective of characterizing the use of GDMT in HFrEF patients. Fisher's Exact test and chi-squared test were performed on the following patient categories (i.e., male vs. female; clinic type [FM vs. IM clinic], distance to clinic [<10 miles vs. ≥10 miles], age ≥65 vs <65, with a payor status defined as commercial insurance [private insurance] vs. non-commercial insurance [Medicare, Medicaid, or self-pay], and race [non-minority vs. minority]) to assess for differences in prescribing of GDMT in different patient demographic groups. The distance of radius of 10 miles is due to Amarillo being a mid-size city where most businesses and residences are within a 10-mile radius. The racial categories are defined as non-minority (Caucasian) and minority (Asian, African American, non-white Hispanic, unknown/unlisted, and other). For

all analyses conducted the *a priori* level of significance was 0.05 on Microsoft Excel (Redmond, WA).

To assess different GDMT regimens, patients were stratified and compared by grouping. Three-agent regimens were an evidence-based β-blocker + ACEi/ARB/ARNI + MRA, two-agent regimens were an evidence-based β-blocker + ACEi/ARB/ARNI, β-blocker + MRA, or an ACEi/ARB/ARNI + MRA, and one-agent regimens were an evidence-based β-blocker, ACEi/ARB/ARNI, or MRA. At the time the study was conceived and conducted, sodium glucose-like peptide-2 inhibitors (SGLT-2 inhibitors) were not recommended in the national guideline, and therefore, quadruple GDMT regimens were not assessed. Chi-squared test or Fisher's exact tests were used, depending on sample size, to compare the usage of these regimens based on patient characteristics.

Results

Five hundred ninety-six patients between January 1, 2018, to February 29, 2020, were identified by the electronic health records query. A total of 500 patients were excluded; 160 for an ejection fraction (EF) >40%, 130 because they had no recent laboratory values within the time frame of review, 116 for an unknown LVEF, 40 were deceased or dismissed from the clinic, 29 due to not being seen in clinic during the pre-specified dates, 15 due to hospice care, and 10 due to dialysis. The 29 patients excluded from the study were included in the query due to them having communication with an internal medicine or family medicine physician or resident during the index date. This left a study population of 96 patients for evaluation. Patient demographics are listed in Table 1.

Table 1. Demographic and Clinical Information for Patient Cohort

Characteristic	**Total (n=96)**
Male, No. (%)	60 (62.5)
Age (mean ± SD), y	60.8 (13.4)
BMI (mean ± SD), kg/m^2	31.6 (7.4)
Distance from clinic (mean ± SD), miles	12.4 (19)
Race, No. (%)	
Caucasian	67 (69.8)
Asian	0 (0)
African American	10 (10.4)
Hispanic	17 (17.7)
Other	1 (1.0)
Unknown/Unlisted	1 (1.0)
Vital Signs	
Systolic BP (mean ± SD), mmHg	129.2 (19.8)
Diastolic BP (mean ± SD, mmHg	77.4 (12.6)
Heart rate (mean ± SD), bpm	81.7 (14.3)
Laboratory Values	
Potassium (mean ± SD), mEq/L	4.2 (0.5)
Sodium (mean ± SD), mEq/L	139 (4)
Serum creatinine (mean ± SD), mg/dL	1.4 (0.7)
Patients with an eGFR >60 mL/min/1.73m^2 (%)	43.8
Payor Status, No. (%)	
Commercial insurance	23 (24.0)
Non-commercial insurance	
• Medicare/Medicaid	52 (54.2)
• Multiple insurances (Medicare/Medicaid primary)	15 (15.6)
• Self-pay (no insurance coverage)	6 (6.3)
Clinic site, No. (%)	
Internal Medicine Clinic	64 (66.7)
Family Medicine Clinic	32 (33.3)

For the primary outcome, there was no significant difference in prescribing patterns between sex, ethnicities, distances from clinic, or clinic type (See Table 2). HFrEF patients on GDMT with a payor status defined as commercial insurance were more likely to be on 3 GDMT agents than those without commercial insurance (34.8% vs. 15.1%; p=0.039). Compared with patients <65 years of age, those ≥65 years were less likely to be on 3 GDMT agents (8.3% vs. 32%, p=0.029), but were more likely to be on a combination of an evidence-based β-blocker + ACEI/ARB/ARNI (52.8% vs. 32%, p=0.01) or an evidence-based β-blocker + MRA (11% vs. 2%, p=0.044; see Figure 1.) No patients in the study were prescribed eplerenone for their MRA, thus it can be concluded that whenever a patient has an MRA in their regimen it's spironolactone.

The secondary outcome of this study found that of 96 patients included in this study, 19.8% were prescribed 3 GDMT agents (an evidence-based β-blocker + ACEi/ARB/ARNI + MRA), 43.8% were prescribed 2 GDMT agents (an evidence-based β-blocker + ACEi/ARB/ARNI, an evidence-based β-blocker + MRA, or an ACEi/ARB/ARNI + MRA). Twenty-seven percent (27.1%) were on a single GDMT agent and 9.4% were on no GDMT. Of 87 patients on GDMT agents with no contraindications to therapy or optimization, only 5 patients (6.1%) received optimized GDMT regimens. The percentage of patients on individual GDMT agents was collected (see Figure 1) along with the percentage of patients optimized on each GDMT agent (see Figure 2). For patients not on 3 GDMT medications, the majority (71%) had no contraindications to therapy. The remaining had an eGFR<30 ml/min (11%), hypotension (7%), hyperkalemia (5%), or bradycardia (3%).

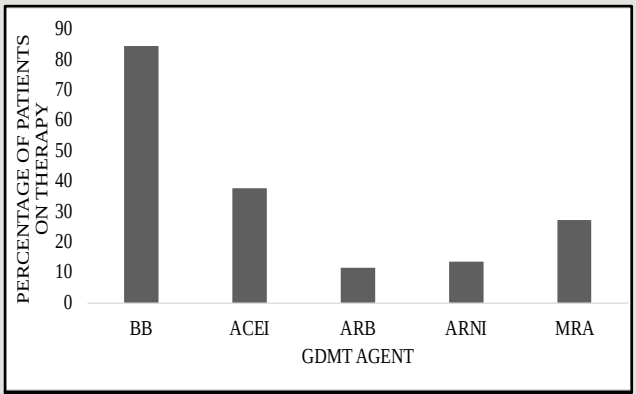

Figure 1. Percentage of patients on each respective GDMT agent

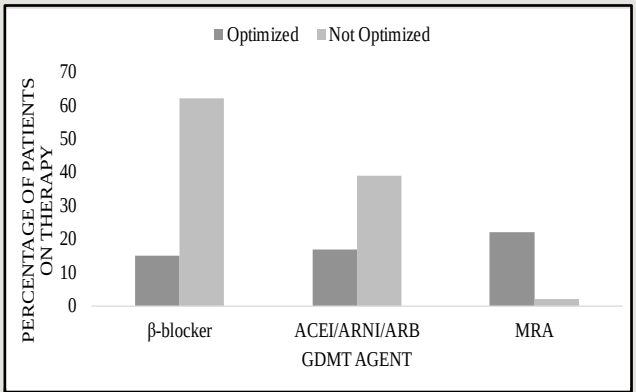

Figure 2. Percentage of patients on optimized versus non-optimized therapy

Table 2. Primary objective findings of inter-group comparisons of medication regimens

Medication Regimen	Comparison Group on Regimen, No. (%)	Comparison Group on Regimen, No. (%)	p-value
	Females	Males	
BB+ACEI/ARB/ARNI+MRA	7 (19.4)	12 (20)	0.947266
BB+ ACEI/ARB/ARNI	11 (30.5)	24 (40)	0.351975
BB+MRA	2 (5.5)	3 (5)	0.905592
ACEI/ARB/ARNI+MRA	1 (2.8)	1 (1.7)	0.712118
Single agent	12 (33)	14 (23.3)	0.285792
None	3 (8.3)	6 (10)	0.786218
	Non-minority	Minority	
BB+ACEI/ARB/ARNI+MRA	14 (20.6)	5 (17.9)	0.76016
BB+ ACEI/ARB/ARNI	26 (38.2)	9 (32.1)	0.572947
BB+MRA	2 (2.9)	3 (10.7)	0.119241
ACEI/ARB/ARNI+MRA	2 (2.9)	0 (0)	1
Single agent	16 (23.5)	10 (35.7)	0.222045
None	7 (10.3)	2 (7.1)	0.63018
	Commercial Insurance	Non-Commercial Insurance	
BB+ACEI/ARB/ARNI+MRA	8 (34.8)	11 (15.1)	**0.039521**
BB+ ACEI/ARB/ARNI	7 (30.4)	28 (38.4)	0.491279
BB+MRA	0 (0)	5 (6.8)	1
ACEI/ARB/ARNI+MRA	2 (8.7)	0 (0)	0.0555
Single agent	5 (21.7)	21 (28.8)	0.508363
None	1 (4.3)	8 (11)	0.342858
	Distance <10 miles	Distance ≥ 10 miles	
BB+ACEI/ARB/ARNI+MRA	11 (15.7)	8 (30.8)	0.074833
BB+ ACEI/ARB/ARNI	27 (38.6)	8 (30.8)	0.590201
BB+MRA	4 (5.7)	1 (3.8)	0.714307
ACEI/ARB/ARNI+MRA	2 (2.9)	0 (0)	1
Single agent	21 (30)	5 (19.2)	0.29135
None	6 (8.6)	3 (11.5)	0.657611
	Family Medicine	Internal Medicine	
BB+ACEI/ARB/ARNI+MRA	5 (15.6)	14 (21.9)	0.468738
BB+ ACEI/ARB/ARNI	15 (46.9)	20 (31.3)	0.133766
BB+MRA	0 (0)	5 (7.8)	1
ACEI/ARB/ARNI+MRA	1 (3.1)	1 (1.6)	1
Single agent	7 (21.9)	19 (29.7)	0.41679
None	5 (15.6)	4 (6.3)	0.137395
	≥ 65 Years Old	< 65 Years Old	
BB+ACEI/ARB/ARNI+MRA	3 (8.3)	16 (32)	**0.029062**
BB+ ACEI/ARB/ARNI	19 (52.8)	16 (32)	**0.010074**
BB+MRA	4 (11)	1 (2)	**0.043779**
ACEI/ARB/ARNI+MRA	0 (0)	2 (4)	0.5263
Single agent	12 (33.3)	14 (28)	0.285792
None	3 (8.3)	6 (12)	0.786218

Discussion

The current study highlights significant opportunities for quality improvement initiatives around GDMT for HFrEF patients in academic teaching clinics. Only 6.1% of patients were documented to be on optimized GDMT therapy. Significant differences between GDMT therapeutic regimens and patient characteristics were found in this study, including differences based on age groups and payor status. There may be several reasons for the low percentage of patients on documented optimized GDMT, including lack of cardiologist management, lack of follow-up documentation, missing data elements in the electronic health record, and undocumented contraindications or adverse effects.

Findings from this study are consistent with other research demonstrating treatment gaps with GDMT in HFrEF despite the availability of evidence-based guidelines.[1,6-8] Advanced age (i.e., ≥65 years of age) was associated with poorer provider adherence to GDMT agent triple therapy (i.e., ACEI/ARB/ARNI + an evidence-based β-blocker + MRA) compared to those <65 years old. Those ≥65 years of age, however, were more likely to be on dual therapy (an evidence-based β-blocker + ACEI/ARB/ARNI or an evidence-based β-blocker + MRA). This could be due to older patients having more comorbidities or being less able to tolerate more aggressive GDMT therapy than younger patients. However, consistent with other data, due to the lack of documentation, the exact reason(s) cannot be elucidated.[1] It was also found that those with commercial insurance were more likely to be on three GDMT agents than those with non-commercial insurance. Reasons for this difference could be cost or issues with being able to afford follow-up visits.

The secondary outcome of determining the percentage of patients on optimal and suboptimal HFrEF therapeutic regimens at each clinic independent of patient characteristics also yielded interesting results. Despite having a relatively low number of patients with contraindications to therapy optimization or specific GDMT agents (e.g., abnormal electrolytes, impaired kidney function) the majority (71%) were still on sub-optimal therapy. The most common contraindication to a GDMT agent was an eGFR <30 mL/min/1.73m^2, preventing patients from receiving an MRA. A small number of patients (7%) of patients had hypotension (blood pressure <90/60 mmHg), which could slow or limit the ability to up-titrate therapy but likely not result in a contraindication to use. Again, it is impossible to know precisely why specific agents were not used in certain patients due to a lack of documentation and the nature of a retrospective chart review.

There are several possible reasons why few patients were on optimized GDMT. First, many of these patients were seen and managed by outside cardiologists. If any of these patients had their HF regimens managed through their cardiologist, it is possible the medications in the primary care provider's records were not up to date despite the standard practice of nurses conducting medication reconciliations at each office visit. Also, many primary care providers may feel uncomfortable adjusting medications an outside specialist has been managing. Another reason for this treatment gap could be the lack of documentation on the type of heart failure. Many patients had a general diagnosis of heart failure without specific categorization regarding ejection fraction or other sub-categories (i.e., HFrEF, HFpEF, HFmrEF, HFimpEF). The lack of a specific diagnosis makes management difficult. Lastly, the electronic medical record

used in the FM and IM clinics lack a field for documentation of the patient's most recent LVEF, making documentation of the type of heart failure the patient has even more difficult.

There have been several studies conducted evaluating methods to improve provider adherence to GDMT. One study found that chart reminders within the electronic health record (EHR) led to an increase in the number of patients prescribed an indicated agent. Clinical pathways have also been shown to improve provider adherence to GDMT as they provide them with a resource to help navigate the treatment guidelines. Changes to EHR systems to address limitations were also shown to increase the percentage of patients prescribed their indicated GDMT agents.[9]

One approach, found to be particularly effective, utilized a team-based care approach with pharmacists. In a general cardiology (GC) clinic, the use of outpatient pharmacists to manage HFrEF patients in a medication titration assistance clinic (MTAC) was associated with a greater number of patients being prescribed an ACEi or ARB and an evidence-based β-blocker, and a higher likelihood of reaching the target, or maximally tolerated, doses compared to usual care. Of the patients previously stated 64% in the MTAC versus 40% in GC reached target or max tolerated doses (p=0.01). The MTAC was also found to be more likely than the GC clinic to achieve >50% of target doses for ACEi/ARBs (83% vs. 69%, p=0.04) and evidence-based β-blockers (64% vs. 41%, p=0.003).[10] In the IMPROVE-HF study, the impact of multidimensional, practice-specific performance improvement interventions on the use of GDMT in outpatient cardiology practices was evaluated. The intervention included incorporating a guideline-based clinical decision tool kit, educational materials, practice-specific data reports, and evidence-based best-practices algorithms. Participation in this study yielded statistically significant & clinically relevant improvements in the proportion of eligible patients treated at target doses for evidence-based β-blockers (20.5% vs. 30.3% at the 24-month mark, p<0.001). Similar improvements were not seen in other medication classes, however. This study suggests that enhanced systems of care are needed to better educate patients to expect dose up-titration even if HF symptoms are improving, to provide decision support tools to physicians for dose titration, and to ensure outpatient follow-up visits are set at certain intervals until target doses are achieved.[11]
There were several limitations to our study including the small sample size and limited sites, retrospective design, and limits of the EHR system used. Another limitation was that when comparing commercial insurance to non-commercial insurance, it was difficult to determine whether patients with Medicare coverage had Medicare Part D. If patients had Medicare Part D coverage, the reasoning behind the lack of adherence to GDMT may be less likely due to affordability issues. The clinic EHR (Allscripts) presented limitations as well, with no defined field for documentation of the most recent ejection fraction.

Improving the specificity of heart failure diagnosis in the electronic health record is imperative in improving the treatment and utilization of GDMT. This can be done by obtaining the most recent echocardiogram and having dedicated areas for it in the medical record. Communication with the patient's cardiologist and obtaining current medical records is also imperative to help optimize heart failure regimens. Lastly, thorough documentation behind the reasons for the lack of adherence to optimized GDMT

is important to aid in the continuity of care and dose optimization in the future.

Conclusion

GDMT was significantly underutilized in IM and FM academic clinics, particularly for older patients and those without commercial insurance. Results from this study suggest several challenges related to GDMT utilization, including the lack of documentation of heart failure type, ejection fraction, and outside medical records from specialists. Multidimensional efforts including improved documentation of HFrEF diagnosis, whether the patient is being managed by a cardiologist or only primary care, echocardiogram results, and reasons for not using GDMT agents and/or optimized doses are warranted in our clinics.

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