Original Article

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Four-Year Impact of Including a Pharmacist in a Multidisciplinary Team on Guideline-Directed Medical Therapy for Heart Failure with Reduced Ejection Fraction: Experience at a Tertiary-Care Hospital in Thailand

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Abstract:

Objective: We evaluated the real-world data from Thailand regarding dosage optimization of guideline-directed medical therapy (GDMT) in patients with heart failure and reduced ejection fraction (HFrEF). We also assessed GDMT usage, drug-related problems (DRPs) over 4 years, and performance measures based on HF parameters and cardiac biomarkers. All were evaluated before and after a 1-year follow-up in the HF clinic, where pharmacists served on a multidisciplinary team.

Material and Methods: We conducted a retrospective chart review of patients with HFrEF who attended our HF clinic. Data on GDMT dosage optimization, usage, and DRPs were gathered from all patient visits between January 2020 and September 2023. Performance measures were collected from patients who completed a 1-year follow-up within the same period.

Results: Among 2907 patient visits over 4 years, the annual GDMT dose rates were 67.4% for beta-blockers, 92.6% for renin–angiotensin–aldosterone system (RAAS) blockade, 40.5% for sacubitril/valsartan, and 100.0% for mineralocorticoid receptor antagonists (MRAs) and sodium–glucose cotransporter-2 inhibitors (SGLT2i). The proportion of visits achieving more than 50% of the GDMT dose was 67.6%, 80.3%, 45.9%, 100.0%, and 100.0%, respectively. Overall, GDMT usage was 90.3% for beta-blockers, 72.0% for RAAS blockade, 78.7% for MRAs, and 35.3% for SGLT2i. Adverse drug reactions were the most frequent DRPs.

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Conclusion: The inclusion of a pharmacist on a multidisciplinary team in a heart failure clinic can improve GDMT optimization, increase GDMT usage, and resolve DRPs, thereby enhancing therapeutic outcomes and quality of life.

Keywords: drug-related problems, ejection fraction, guideline-directed medical therapy, heart failure clinic, heart failure pharmacist, heart failure with reduced, optimizing GDMT dose

Introduction

Heart failure (HF) is a complex clinical syndrome marked by breathlessness, fatigue, and peripheral edema. Etiologies include ischemic cardiomyopathy and nonischemic cardiomyopathy, both of which reduce cardiac output. Diminished cardiac output triggers neurohormonal activation, leading to cardiac remodeling and end-organ damage. HF is a major global public health concern, and its prevalence continues to rise worldwide. HF incurs substantial healthcare costs and imposes a heavy economic burden. According to the National Health and Nutrition Examination Survey in the Heart Disease and Stroke Statistics—2023 Update: A Report from the American Heart Association (AHA), approximately 6.7 million Americans aged 20 years or older had HF between 2017 and 2020. This figure is projected to reach 3.0% by 2030[1].

In Asia, HF prevalence has also grown substantially. A recent study, Epidemiology and Burden of Heart Failure in Asia, reported a 33% increase in HF prevalence in Central Asia and a 186% increase in East Asia from 1990 to 2019[2]. One-year mortality rates among Asian patients with HF also remain high. In Thailand, the age-adjusted HF prevalence remained elevated, ranging from 651.54 cases per 100,000 population in 1990 to 646.03 cases per 100,000 population in 2019[2].

In light of these trends, public health agencies in many countries should urgently implement multidisciplinary HF management programs or specialized HF clinics at tertiary-care centers. Such programs can help lower morbidity and mortality in HF and improve the standard of care. Current European and U.S. HF guidelines recommend guideline-directed medical therapy (GDMT) for patients with HF with reduced ejection fraction (HFrEF), defined as a left ventricular ejection fraction (LVEF) of 40% or less[3,4].

GDMT targets neurohormonal pathways and typically includes beta-blockers (BBs), renin–angiotensin–aldosterone system (RAAS) blockade or angiotensin receptor–neprilysin inhibitors (ARNIs), mineralocorticoid receptor antagonists (MRAs), and sodium–glucose cotransporter-2 inhibitors (SGLT2i). Optimizing GDMT helps patients reach the target or maximally tolerated dose, thereby improving therapeutic outcomes and advantages to reduce mortality and HF readmission[3,4].

Optimizing GDMT in patients with HFrEF was suboptimal due to many factors, such as patient inability to tolerate side effects, non-compliance, healthcare insurance access limitations to GDMT, and a lack of multidisciplinary-care teams[5].

An HF clinic that offers outpatient, multidisciplinary care can slow HF progression, prevent the risk of hospitalization[4], and enhance quality of life. Another benefit of enrolling the multidisciplinary team in HF clinics: Reduction in medical costs from the decreasing rate of HF hospitalizations. Within this setting, HF pharmacists collaborate with HF specialists to optimize GDMT, prevent adverse effects, reconcile medications, and educate patients. They also help patients adhere to therapies and thereby improve clinical outcomes.

Real-world data on optimizing GDMT doses for HFrEF patients at outpatient HF clinics in Thailand are

limited. Therefore, this study aimed to present real-world data on GDMT dose optimization, GDMT usage, and drug-related problems (DRPs) between January 2020 and September 2023. We also evaluated the performance of HF clinic measures by comparing LVEF and signs and symptoms of congestion in the same HFrEF patients before and after a 1-year follow-up at a tertiary-care hospital in Thailand.

Material and Methods

Study design

We performed a retrospective chart review of patients with HFrEF (LVEF ≤40%) who attended the Heart Failure (HF) Clinic at Siriraj Hospital in Bangkok, Thailand. The study period spanned January 2020 to September 2023.

This study was approved by the Siriraj Institutional Review Board (reference: Si-942/2023).

Our objectives were to characterize GDMT dose optimization, GDMT usage, and DRPs. We also compared key HF parameters, including LVEF and signs and symptoms of congestion, before and after 1 year of HF clinic follow-up. We considered BBs, RAAS blockade, MRAs, and SGLT2i as GDMT.

Data collection

We recorded GDMT dose optimization, usage, and DRPs from all patient visits between January 2020 and September 2023. Data were reported annually. We calculated the percentage of GDMT usage by dividing the total patient visits receiving GDMT by the total patient visits overall. We determined the annual GDMT dose rate by dividing the average dose of each GDMT agent by its target dose, based on the AHA/ACC/HFSA 2022 guidelines[4]. We also identified the percentage of patient visits that achieved more than 50% of the recommended target GDMT dose.

Definition of DRPs

We defined 4 types of DRPs. The first was "dosage too low," referring to any GDMT dose below standard recommendations. The second was the "need for additional drug therapy," referring to patients requiring another GDMT agent. The third was "noncompliance," defined as failure to continue GDMT as prescribed. The fourth was "adverse drug reactions," defined as any harmful or unintended response to GDMT. We reported DRP data annually, based on total patient visits during the study period.

Performance measures

We collected performance data on LVEF, New York Heart Association (NYHA) functional class (I-IV), and signs and symptoms of congestion, including orthopnea, paroxysmal nocturnal dyspnea, edema, and lung crepitations. These data were obtained from the same patients with HFrEF before and after 1 year of follow-up at the HF clinic.

Role of pharmacists in the heart failure clinic

Pharmacists performed medication reconciliation, reviewed all medications including GDMT, optimized doses, verified the actual dose taken, and identified DRPs before patients saw the doctors. They also provided relevant interventions to physicians. After physician consultation, pharmacists counseled patients on their home medications and made appointments for the tele-monitoring of any side effects from GDMT titration. All information was recorded in both the pharmacist's database and the hospital database.

Study population

We included patients diagnosed with HFrEF who were followed up at the HF Clinic for at least 1 year between January 2020 and September 2023. We excluded those who were lost to follow-up.

Study outcomes

The primary outcomes were the real-world characterization of GDMT dose optimization, usage, and DRPs at the HF clinic during the study period. The secondary outcomes were evaluations of the HF clinic's performance by comparing LVEF, NYHA functional class, and signs and symptoms of congestion before and after at least 1 year of follow-up.

Statistical analysis

We calculated the sample size based on the assumption that 10.0% of total patient visits would present with the DRP "dosage too low." A total of 1537 visits was sufficient to achieve 90.0% power at a 0.05 significance level. Categorical data are expressed as counts and percentages. We used paired t-tests, Wilcoxon signed-rank tests, and McNemar's tests to compare any differences between the groups. IBM SPSS Statistics (version 30) and Microsoft Excel 365 were used for all statistical and descriptive analyses. Statistical significance was set at p-value<0.050.

Results

Patient flow and characteristics

A total of 2907 patient visits to the HF clinic at Siriraj Hospital, a large tertiary-care center in Thailand, were enrolled between January 2020 and September 2023. Of these, 72.2% involved male patients. The mean age was 60.1±14.7 years, and ischemic cardiomyopathy was observed in 53.1% of patients. The mean LVEF was 28.2±12.0%. All patient visits received standard GDMT if there were no contraindications. These therapies included evidence-based BBs (90.2%), RAAS blockade (70.9%), MRAs (78.5%), and SGLT2i (28.5%). Table 1 summarizes the baseline characteristics of these patient visits.

Primary outcomes

From January 2020 to September 2023, 2907 patient visits were evaluated for GDMT dose optimization. Annual percentages of the target dose for BBs showed that carvedilol reached 70.0%, 61.2%, 73.4%, and 66.6% each year, while bisoprolol achieved 60.8%, 71.0%, 66.0%, and 70.0%. For RAAS blockade and neprilysin inhibitors, enalapril attained 90.0%, 81.0%, 90.0%, and 80.0% over the 4 years, whereas losartan consistently reached 100.0%. Sacubitril–valsartan increased modestly from 37.5% to 43.5% across the same timeframe. Meanwhile, spironolactone (an MRA) remained at 100.0% each year, and SGLT2i (dapagliflozin, empagliflozin) also achieved a full 100.0% from 2021 onward.

Table 1 Baseline characteristics of 2907 patient visits (January 2020–September 2023)

Baseline characteristics	Number (%) or mean±S.D.
Sex (%)	
Male	2099 (72.2%)
Female	808 (27.8 %)
Age (year), mean±S.D. (range)	60.1±14.7 (46–74)
Type of cardiomyopathy (%)	
Ischemic cardiomyopathy	1543 (53.1%)
Dilated cardiomyopathy	1364 (46.9%)
LVEF (%), mean±S.D. (range)	28.2±12.0
Standard medication therapy (%)	
Beta-blocker	2623 (90.2%)
Carvedilol	1411 (53.8%)
Bisoprolol	1212 (46.2%)
RASS-blockade	2060 (70.9%)
Sacubitril/valsartan	1006 (48.8%)
Enalapril	661 (32.0%)
Losartan	393 (19.0%)
MRA	2283 (78.5%)
Spironolactone	2283 (78.5%)
SGLT2i	829 (28.5%)
Empagliflozin	458 (55.2%)
Dapagliflozin	371 (44.8%)

LVEF=left ventricular ejection fraction, MRA=mineralocorticoid receptor antagonist, RASS=renin-angiotensin system, S.D.=standard deviation, SGLT2i=sodium-glucose cotransporter-2 inhibitors

The proportion of visits that exceeded 50% of the target dose generally mirrored these trends. Carvedilol

ranged from 61.5% in 2020 to 74.6% in 2022 and slightly decreased to 65.3% in 2023, while bisoprolol ranged from 65.3% to 73.5%. Enalapril rose from 64.6% to 74.5%, losartan remained above 98.0%, and sacubitril–valsartan climbed from 38.8% to 54.8%. Spironolactone remained above 93.4% in all years, and SGLT2i reported 100.0% of visits achieving at least half the target dose after their introduction in 2021.

Over the same period, GDMT usage rates (the percentage of all patient visits receiving each class) also evolved. Beta-blocker use increased from 86.7% in 2020 to 93.3% in 2022, settling at 89.3% in 2023. RAAS blockade and neprilysin inhibitor usage rose from 67.2% to 74.1%, while MRA use ranged between 74.6% and 81.3%. SGLT2i use began at 13.4% in 2021, climbed to 38.5% in 2022, and reached 51.9% in 2023.

During these 2907 visits, pharmacists recorded 448 DRPs in GDMT, for which they provided interventions to the doctors. The DRPs were classified into 4 categories. "Dosage too low" increased from 1.4% in 2020 to as high as 13.2% in 2021, "need additional drug therapy" varied between 4.4% and 8.4%, and "noncompliance" ranged from 3.1% to 8.7%. Adverse drug reactions rose from 4.2% in 2020 to a peak of 15.0% in 2022, before settling at 11.5% in 2023. The full details of the primary outcomes are presented in Table 2.

Secondary outcomes

In this study, we found that 79 patients were followed up for at least 1 year between January 2020 and September 2023. Of these, 70.9% were male, and ischemic cardiomyopathy was present in 60.8% of cases. Dilated cardiomyopathy accounted for 39.2%. At the one-year follow-up, these 79 patients showed significant improvements in LVEF (p-value<0.002), NYHA functional class (p-value<0.001), and signs and symptoms of congestion such as orthopnea, paroxysmal nocturnal dyspnea, edema, and lung crepitations (p-value=0.025, 0.034, 0.001, and 0.008, respectively). A total of 64 patients demonstrated an increase in LVEF from the baseline. Table 3 provides the full details of these secondary outcomes.

Discussion

Real-world data on GDMT dose optimization for HFrEF in tertiary-care hospitals in Thailand are limited. This study provides insights into GDMT dosage achievement, usage rates, and DRPs in a large HF clinic population. Our primary outcomes indicate that, from 2020 to 2023, the annual dose rates for BBs, RAAS blockade and neprilysin inhibitors, MRAs, and SGLT2i (from 2021) were 67.4%, 92.6%, 40.5% (for sacubitril–valsartan), 100.0%, and 100.0%, respectively. The proportion of visits achieving more than 50% of the target GDMT dose mirrored these rates. These findings partly align with the EVOLUTION HF study[6], which revealed relatively low target-dose achievement in large cohorts from Japan, Sweden, and the United States. In our study, sacubitril–valsartan dose optimization was lower than that of other agents, possibly due to patient age (mean 60 years) and its associated risk of orthostatic hypotension[7]. The access to drugs for patients is limited because of the drug policy. Interestingly, the EVOLUTION HF cohort in Japan included older patients (mean 76 years) who also exhibited lower sacubitril–valsartan dose achievement[6]. Meanwhile, GDMT usage in our cohort, particularly BBs (90.3%) and MRAs (78.7%), exceeded that reported in the CHAMP-HF registry[7], which found usage rates of 67.0% for BBs and 33.0% for MRAs. These data highlight the advantages of pharmacists being involved in multidisciplinary HF clinics, ensuring more consistent use of guideline-directed medications.

Notably, SGLT2i use remained comparatively low (35.3%) in part because of health insurance constraints and high drug costs. Although coverage barriers persist, patients who did receive SGLT2i successfully reached target doses,

potentially conferring maximal therapeutic benefits. Evidence in Asian populations supports SGLT2i for reducing HF hospitalizations and cardiovascular mortality[8]. Policymakers should thus consider revising health insurance criteria to improve cost-effectiveness and access to these agents.

Our results also underscore the importance of pharmacists in HF clinics. Over 4 years, pharmacists intervened in 448 DRPs related to GDMT, including underdosing, the need for additional therapy, noncompliance, and adverse drug reactions. These interventions by the pharmacists

Table 2 Characterization of GDMT dose optimization, GDMT usage, and DRPs in HFrEF patients (2020–2023)

Results	Year			
	2020	2021	2022	2023
Total HFrEF patient visits, n	558	716	857	776
1. Percentage of the annual dose of GDMT* (%)				
1.1 Beta-blockers				
Bisoprolol	193 (60.8)	307 (71.0)	399 (66.0)	313 (70.0)
Carvedilol	291 (70.0)	339 (61.2)	401 (73.4)	380 (66.6)
1.2 RASS blockade and neprilysin inhibitors				
Enalapril	130 (90.0)	138 (81.0)	178 (90.0)	216 (80.0)
Losartan	65 (100.0)	106(100.0)	124 (100.0)	98 (100.0)
Sacubitril and valsartan	180 (37.5)	260 (39.1)	305(42.0)	261 (43.5)
1.3 MRAs				
Spironolactone	441(100.0)	572(100.0)	639 (100.0)	631 (100.0)
1.4 SGLT2i				
Dapagliflozin and Empagliflozin	–	96 (100.0)	330 (100.0)	403 (100.0)
2. Percentage total patient visits achieved dose more than 50% of GDMT (%)				
2.1 Beta-blockers				
Bisoprolol	126 (65.3)	224 (73.0)	279 (69.9)	230 (73.5)
Carvedilol	179 (61.5)	190 (56.0)	299 (74.6)	248 (65.3)
2.2 RASS blockade and neprilysin inhibitors				
Enalapril	84 (64.6)	90 (65.2)	122 (68.9)	161 (74.5)
Losartan	64 (98.5)	106 (100.0)	124 (100.0)	96 (98.0)
Sacubitril and Valsartan	70 (38.8)	106 (40.8)	143 (46.9)	143 (54.8)
2.3 MRAs				
Spironolactone	433 (98.2)	551 (96.3)	328 (93.4)	593 (94.0)
2.4 SGLT2i				
Dapagliflozin and Empagliflozin	–	96 (100.0)	330 (100.0)	403 (100.0)
3. Percentage of GDMT usage (%)				
3.1 Beta-blockers	484 (86.7)	646 (90.2)	800 (93.3)	693 (89.3)
3.2 RASS blockade and neprilysin inhibitors	375 (67.2)	504 (70.4)	639 (70.7)	575 (74.1)
3.3 MRAs	441 (79.0)	572 (79.9)	639 (74.6)	631 (81.3)
3.4 SGLT2i	–	96 (13.4)	330 (38.5)	403 (51.9)
Total DRPs, n	286	318	359	460
Total DRPs in GDMT, n	65	106	108	169
4. Percentage DRPs of GDMT (%)				
4.1 Dosage too low	4 (1.4)	42 (13.2)	29 (8.1)	48 (10.4)
4.2 Need for additional drug therapy	24 (8.4)	14 (4.4)	14 (4.4)	35 (7.6)
4.3 Noncompliance	25 (8.7)	15 (4.7)	11 (3.1)	33 (7.2)
4.4 Adverse drug reaction	12 (4.2)	35 (11.0)	54 (15.0)	53 (11.5)

DRP=drug-related problem, GDMT=guideline-directed medical therapy, HFrEF=heart failure with reduced ejection fraction, MRA=mineralocorticoid receptor antagonist, RASS=renin-angiotensin system, SGLT2i=sodium-glucose cotransporter-2 inhibitors
*Percentage of the annual dose of GDMT was calculated based on the guidelines for the management of heart failure from the AHA/ACC/HFSA 2022[4]

Table 3 Changes in HF parameters and cardiac biomarkers in 79 patients before and after attending the HF Clinic 1 year (2020–2023)

	Before attending HF clinic 1 year	After attending HF clinic 1 year	p-value
LVEF: %; mean±S.D.	24.8±8.6	37.4±14.4	<0.002[†]
NYHA functional class: *n* (%)			<0.001[$]
I	1 (1.3)	14 (17.7)	
II	31 (39.2)	50 (63.3)	
III	39 (49.4)	15 (19.0)	
IV	8 (10.1)	0	
Signs/symptoms of congestion: *n* (%)			
Orthopnea			
Yes	5 (6.3)	0	0.025[$]
No	74 (93.7)	79 (100.0)	
Paroxysmal nocturnal dyspnea			
Yes	8 (10.1)	2 (2.5)	0.034[$]
No	71 (89.9)	77 (97.5)	
Edema			
Yes	33 (41.8)	5 (6.3)	0.001[$]
No	46 (58.2)	74 (93.7)	
Lung crepitation			
Yes	7 (8.9)	0	0.008[$]
No	72 (91.1)	79 (100.0)	

HF=heart failure, LVEF=left ventricular ejection fraction, NYHA=New York heart association, S.D.=standard deviation
[†]Paired samples test, [$]Wilcoxon signed rank test

in the multidisciplinary team likely improved medication adherence, facilitated GDMT optimization, and enhanced patient education. The benefits of optimizing GDMT[3,4] are shown to decrease significantly cardiovascular death, HF hospitalizations, and improve the quality of life in patients with HFrEF.

These findings are consistent with a systematic review demonstrating that pharmacist-led medication optimization can increase GDMT usage and potentially reduce hospitalizations and mortality[9]. Moreover, we found the rate of GDMT usage is still high, while we found the DRPs of adverse drug reactions were increased. It shows that pharmacists can detect and educate patients in order to prevent side effects.

This study has limitations. First, GDMT data could not be calculated at the individual level due to the large patient population and limited resources for data collection. Second, as a single-center, retrospective, observational study, confounding variables may influence the results. Future multicenter studies with larger sample sizes should verify these findings and adjust for potential confounders before broader implementation in other HF clinics.

Conclusion

The inclusion of a pharmacist in a multidisciplinary team in an HF clinic can optimize GDMT dose achievement, increase GDMT usage, and reduce DRPs, thereby improving therapeutic outcomes and quality of life for patients with HFrEF.

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Conflict of interest

There are no potential conflicts of interest to declare.

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