

# Caring at Cardiology Clinic versus Heart Failure Clinic: Impact of Implementation of Guideline-Directed Medical Therapy in Heart Failure with Reduced Ejection Fraction in Outcomes of Death and Heart Failure Readmission

Supaphong Eiamakarawit<sup>1</sup> MD<sup>1</sup>, Wichada Hunsakunachai<sup>1</sup> MD<sup>1</sup>

<sup>1</sup> Division of Cardiovascular, Department of Medicine, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok 10300, Thailand

## ABSTRACT

**OBJECTIVE:** This study aimed to determine whether the heart failure (HF) clinic setting can improve guideline-directed medical therapy (GDMT) use and reduce HF readmission and mortality rates in patients with heart failure with reduced ejection fraction (HFrEF).

**METHODS:** This was a retrospective cohort study including patients with HFrEF admitted to Vajira Hospital between May 2016 and December 2021. Data were collected from electronic medical records to compare the usage of GDMT, including beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs)/ angiotensin receptor blockers (ARBs)/ angiotensin receptor-neprilysin inhibitors (ARNIs), mineralocorticoid receptor antagonists (MRAs), and sodium glucose transporter 2 inhibitors (SGLT2s), after discharge from the inpatient department at 1-, 3-, 6-, and 12-month follow-up between the HF clinic and general cardiology clinic groups. Moreover, readmission, mortality rates and composite endpoint of mortality and HF admission rate at the 1-year follow-up were recorded.

**RESULTS:** In total, 234 patients with HFrEF were included in this study (88 in the HF clinic group and 146 in the general cardiology clinic group). After 1-year follow-up, the incidence rates of mortality in the HF clinic and general cardiology clinic groups were 3.45 and 11.66 per 100 person-years, respectively ( $p = 0.040$ ), and the incidence rates of readmission were 23.77 and 79.01 per 100 person-years, respectively ( $p < 0.001$ ). The HF clinic group showed reduced risk for the composite outcome of readmission and mortality (0.37, 95% confidence interval (CI): 0.23–0.60) ( $p < 0.001$ ), mortality (0.30, 95% CI: 0.09–1.02) ( $p = 0.054$ ), and readmission (0.33, 95% CI: 0.21–0.53) ( $p < 0.001$ ) than the general cardiology clinic group. At the 12-month follow-up, the HF clinic could up-titrate GDMT to target doses higher than the general cardiology clinic (beta-blockers 68.20% vs. 32.90% ( $p < 0.001$ ), ACEIs/ARBs/ARNIs 12.50% vs. 3.40% ( $p = 0.003$ ), MRAs 9.10% vs. 4.10% ( $p = 0.001$ ), and SGLT2s 4.50% vs. 7.50% ( $p = 0.648$ )).

**CONCLUSION:** Patients in the HF clinic showed a significant improvement in survival and HF readmission rates and had a higher use of GDMT with a shorter duration to achieve the target doses.

## KEYWORDS:

guideline-directed medical therapy, heart failure clinic, heart failure reduced ejection fraction, readmission

## INTRODUCTION

Heart failure (HF) is a growing public health concern. Heart failure with reduced ejection fraction (HFrEF), defined as left ventricular ejection of less than 40%, has been reported to account for more than half of the HF cases; its incidence continues to increase<sup>1</sup>. Many global guidelines from various associations, including the American College of Cardiology, the European Society of Cardiology, and the Thai Heart Association, provide cardiologists with information on best practices for managing patients with HFrEF<sup>2-5</sup>. Appropriate use and titration of drugs, including beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), angiotensin receptor-neprilysin inhibitors (ARNIs), mineralocorticoid receptor antagonists (MRAs), and sodium glucose transporter 2 inhibitors (SGLT2s), have been reported to improve left ventricular function, reduce HF rehospitalization, and decrease mortality<sup>6-8</sup>. However, titration of these drugs in real-world clinical practice is often insufficient<sup>9</sup> due to various factors, including doctor inertia and overcrowding of patients at outpatient departments<sup>10-14</sup>. This can increase the risk of adverse outcomes, including readmission and mortality, which cause disability and increase treatment costs<sup>15</sup>.

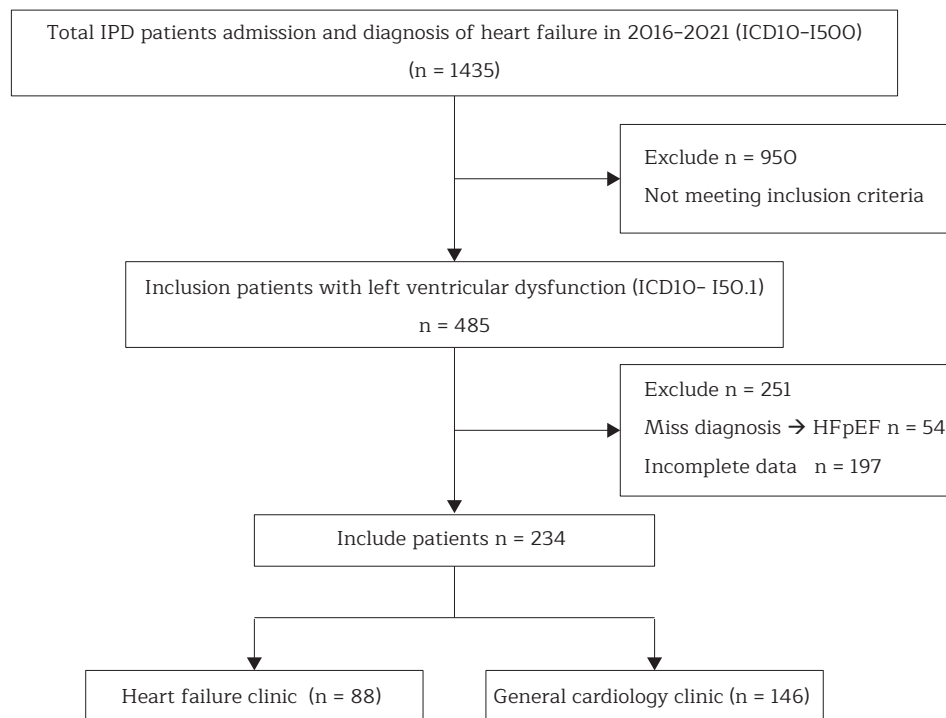
In Thailand has not HF clinic in every hospital. Benefits of HF clinic compared to general cardiology clinic can include comprehensive management of HF patients including sophisticated medical and device therapies ,patients centered education, cardiac rehabilitation, adequate monitoring. To address this problem, HF clinics have been established to improve treatment quality<sup>16</sup>. These clinics provide intensive care and a multimodal approach, resulting in decreased readmission and mortality<sup>17</sup>. However, data on the drug profile in HF clinics are limited. Thus, this study aimed to fill the gap in knowledge focusing on guideline-directed medical therapy (GDMT) usage in HF clinics and general cardiology

clinics, specifically the rate of GDMT dose escalation. Additionally, this study aimed to compare the 1-year readmission rates, mortality and composite of mortality and readmission of HF outcomes between the HF clinic and general cardiology clinic groups to confirm that the HF clinics can improve outcomes.

## METHODS

This was a retrospective cohort study including patients with HFrEF who were admitted to the Internal Medicine Department, Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand, between May 2016 and December 2021. The inclusion criteria included patients aged  $\geq 18$  years and those with a first diagnosis of HFrEF with evidence of left ventricular ejection fraction ( $< 40\%$ ) as indicated by echocardiography. The exclusion criterion was patients with incomplete data, such as less than 1-year follow-up or no echocardiogram data. All patients were considered eligible for participation in the study and were selected based on the criteria in the database of the inpatient department's electronic medical record summary discharge record form (figure 1). In Vajira Hospital, inclusion of patients for HF clinic is HFrEF (ejection fraction  $< 40\%$ ) with at least 1 condition of the following: rehospitalization 2 times within a year, poor compliance, many comorbidities, difficult medication titration. This study was approved by the Institutional Review Board of the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University (COA 014/2565).

Data were collected from electronic medical records to compare the use of GDMT, including beta-blockers, ACE inhibitors/ARBs/ARNIs, MRAs, and SGLT2s, after discharge from inpatient care at 1-, 3-, 6-, and 12-month follow-ups between the HF clinic and general cardiology clinic groups. The primary outcomes were the 1-year readmission rate for HF, mortality, composite outcome of readmission and mortality and the secondary outcomes were the pattern of GDMT use and



Abbreviations: HFpEF, heart failure preserved ejection fraction; ICD 10, international classification of disease 10th revision; IPD, inpatient department

**Figure 1** Study patients selection

the time to escalate to the target doses at 1-, 3-, 6-, and 12-month follow-ups. Sample size was calculated based on cohort study for binary data formula of Bernard<sup>18</sup> and use the percentage of rehospitalization and mortality between general cardiology clinic group and HF clinic group reference from Howlett et al.<sup>17</sup> for calculated the sample size.

Baseline characteristics and categorical variables were presented as numbers and percentages. Continuous variables were presented as means and standard deviations if normally distributed and median and interquartile range if not normally distributed. We use Kolmogorov-Smirnov test or Shapiro-Wilk test to test the normality of quantitative variables. Categorical variables were compared using Chi-square or Fisher's exact tests, and continuous variables were compared using the independent samples t-test if normally distributed or the Mann-Whitney U test if not normally distributed. The primary outcomes, 1-year readmission and mortality, were analyzed using Cox proportional hazards models or Kaplan-Meier curves, with

a significance level of  $p < 0.05$  and a power of 90%. At first, we use univariate analysis to explain the association between each variable (including practice in 2 clinics and all other factors) and outcomes. After that, the variables associated with outcomes ( $p < 0.05$ ) or trend closely associate with outcomes ( $p < 0.1$ ) were include in multivariate analysis. Then we check the multicollinearity assumption of the Cox regression in our multivariate analysis the factor that correlate with other factors were excluded and choose factor that they correlate to represent the factor that we exclude. Data analysis was performed using the Statistical Package for the Social Sciences version 24 (IBM Corporation, Somers, NY, USA).

## RESULTS

A total of 234 patients with HFrEF were included in this study (88 in the HF clinic group and 146 in the general cardiology clinic group). The baseline characteristics of patients in both groups are shown in [Table 1](#).

**Table 1** Baseline and clinical characteristics of study patients in heart failure clinic and general cardio clinic

Variables	Heart failure clinic (N = 88)	General cardio clinic (N = 146)	P-value
Sex			0.290 <sup>c</sup>
Male	62 (70.50)	93 (63.70)	
Female	26 (29.50)	53 (36.30)	
Age (years)	60.31 ± 13.30	66.21 ± 13.48	0.001 <sup>t</sup>
Weight (kg)	67.00 ± 16.40	64.02 ± 14.36	0.146 <sup>t</sup>
Body mass index (kg/m <sup>2</sup> )	24.82 ± 5.14	23.89 ± 4.46	0.145 <sup>t</sup>
At 1 <sup>st</sup> time			
Systolic blood pressure (mmHg)	125.33 ± 23.06	137.62 ± 23.88	< 0.001 <sup>t</sup>
Heart rate (bpm)	88.92 ± 21.14	93.53 ± 21.25	0.109 <sup>t</sup>
Left ventricular ejection fraction (%)	27.25 ± 5.72	28.21 ± 6.69	0.263 <sup>t</sup>
At 12 months			
Systolic blood pressure (mmHg)	122.09 ± 18.67	125.33 ± 22.87	0.278 <sup>t</sup>
Heart rate (bpm)	73.72 ± 13.85	78.71 ± 17.03	0.025 <sup>t</sup>
Smoking	13 (14.80)	14 (9.60)	0.229 <sup>c</sup>
Alcohol	14 (15.90)	6 (4.10)	0.002 <sup>c</sup>
Comorbidities			
Diabetes mellitus type 2	29 (33.00)	70 (47.90)	0.025 <sup>c</sup>
Hypertension	86 (97.70)	131 (89.70)	0.022 <sup>c</sup>
Dyslipidemia	75 (85.2)	120 (82.20)	0.546 <sup>c</sup>
Coronary artery disease	39 (44.30)	70 (47.90)	0.590 <sup>c</sup>
Stroke	6 (6.80)	19 (13.00)	0.137 <sup>c</sup>
Asthma/Chronic obstructive pulmonary disease	0 (0.0)	2 (1.40)	0.529 <sup>c</sup>
Atrial fibrillation	18 (20.50)	36 (24.70)	0.460 <sup>c</sup>
Hyperthyroid	2 (2.30)	1 (0.70)	0.558 <sup>c</sup>
Chronic kidney disease	15 (17.00)	51 (34.90)	0.003 <sup>c</sup>
Medication drug			
Antiplatelet	64 (72.70)	104 (71.20)	0.806 <sup>c</sup>
Anticoagulant	23 (26.10)	44 (30.10)	0.512 <sup>c</sup>
Statins	77 (87.50)	127 (87.00)	0.909 <sup>c</sup>
Furosemide dose			0.655 <sup>c</sup>
< 40 mg	30 (34.10)	54 (37.00)	
≥ 40 mg	58 (65.90)	92 (63.00)	
Cause of heart failure			0.941 <sup>c</sup>
Ischemic	36 (40.90)	62 (42.46)	
Non ischemic	49 (55.68)	80 (54.79)	
Unknown	3 (3.4)	4 (2.73)	
Reimbursement scheme			0.644 <sup>c</sup>
Universal coverage	57 (64.77)	89 (60.95)	
Social security	26 (29.54)	45 (30.82)	
Government or state enterprise officer	5 (5.68)	12 (8.21)	

Abbreviations: bpm, beats per minute; kg/m<sup>2</sup>, kilogram per square meter; mg, milligram; mmHg, millimeters of mercury; n, number

Data are presented as number (%), mean ± standard deviation or median (interquartile range). P-value corresponds to <sup>t</sup>Independent samples t-test, <sup>m</sup>Mann-Whitney U test, <sup>c</sup>Chi-square test or <sup>f</sup>Fisher's exact test.

Differences in patient gender (70.50% vs. 63.70% males, respectively) and age (average age 60.31 vs. 66.21 years, respectively) were observed between the HF and general cardiology groups. The baseline systolic blood pressure was lower in the HF group (systolic blood pressure = 125.33 vs. 137.62 mmHg,  $p < 0.001$ ). No significant difference in the baseline left ventricular ejection fraction was observed between the two groups. The HF group had a higher alcohol consumption and lower prevalence of diabetes and chronic kidney disease than the general cardiology group. Cause of heart failure in both HF group and general cardiology group was more common in non ischemic caused. No significant differences in other cardiovascular diseases, such as coronary artery disease, atrial fibrillation, and cerebrovascular disease, were observed between the two groups. Furthermore, no significant difference in the baseline use of other drugs apart from GDMT such as antiplatelets, anticoagulants, and diuretics (furosemide dose), was observed between the two groups.

**Table 2** shows the primary outcomes. The results showed that the mortality rate was 3.45 events/100 person-years in the HF clinic group and was 11.66 events/100 person-years ( $p = 0.040$ ) in the general cardiology clinic group, respectively. The readmission rate was 26.37 events/100 person-years in the HF clinic group, and was 79.01 events/100 person-years ( $p < 0.001$ ) in the general cardiology clinic group, respectively. The composite outcome rate of mortality and readmission was 28.74 events/100 person-years in the HF clinic group, whereas it was 91.79 events/100 person-years in the general cardiology clinic group ( $p < 0.001$ ).

**Table 3** shows the results of the multivariate Cox regression analysis. The HF clinic group had adjusted hazard ratios versus general cardiology clinic for mortality (0.27, 95% confidence interval (95% CI) 0.07–0.99,  $p = 0.048$ ), readmission (0.40, 95% CI 0.24–0.67,  $p = 0.001$ ), and composite outcome of mortality or readmission (0.37, 95% CI 0.23–0.60,  $p < 0.001$ ). The Kaplan–Meier analysis was showed in **Figures 2, 3, and 4**.

**Table 2** Incidence rate of one-year outcomes for heart failure clinic versus general cardio clinic

1-year outcome	Heart failure clinic (n = 88)	General cardio clinic (n = 146)	P-value
	Incidence rate/ 100 person years	Incidence rate/ 100 person years	
Mortality	3.45	11.66	0.040
Readmission	26.37	79.01	< 0.001
Composite (mortality/readmission)	28.74	91.79	< 0.001

Abbreviations: n, number

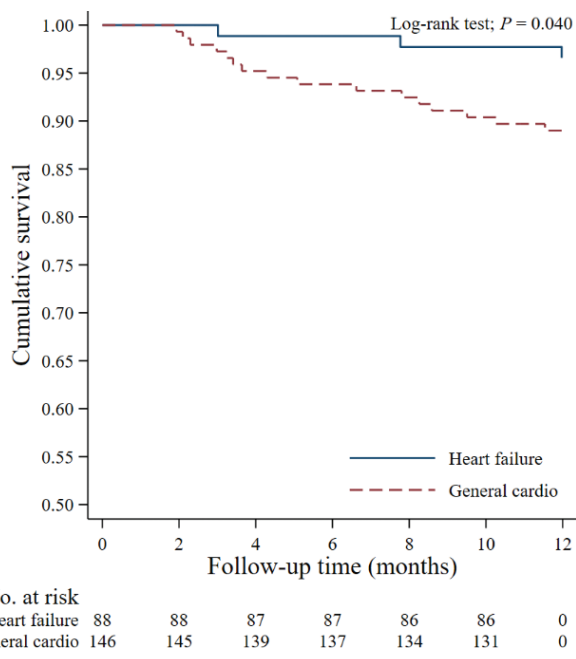
**Table 3** Multivariable Cox regression analysis for adjusted one-year outcomes for heart failure clinic versus general cardio clinic

1-year outcome	Univariable analysis			Multivariable analysis		
	HR	95%CI	P-value	HR <sub>adj</sub> *	95%CI	P-value
Mortality	0.30	(0.09 - 1.02)	0.054	0.27	(0.07 - 0.99)	0.048
Readmission	0.33	(0.21 - 0.53)	< 0.001	0.40	(0.24 - 0.67)	0.001
Composite (mortality/readmission)	0.31	(0.20 - 0.48)	< 0.001	0.37	(0.23 - 0.60)	< 0.001

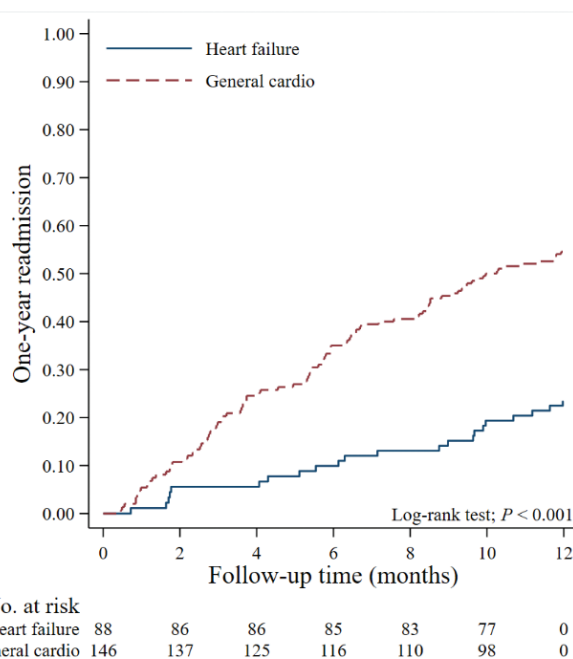
Abbreviations: CI, confident interval; HR, hazard ratio; HR<sub>adj</sub>, adjusted hazard ratio

\*Adjusted for age, weight, BMI, SBP baseline, stroke, asthma, AF, and CKD

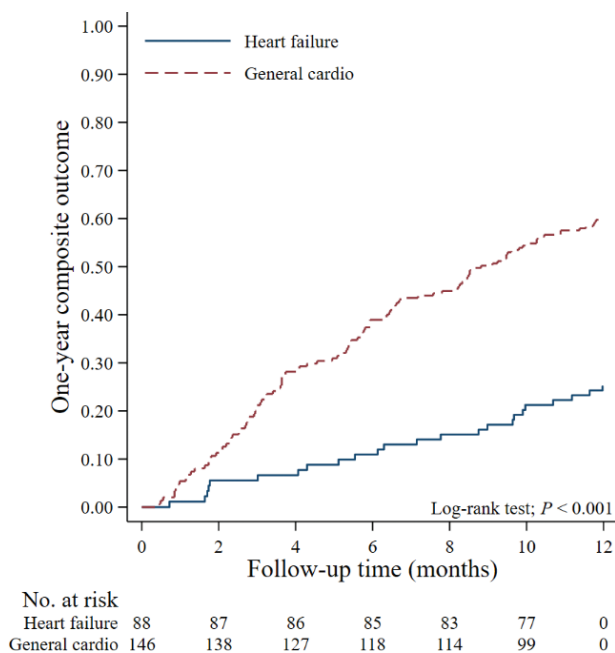
\*\*For heartrate at 12 months, alcohol, DM, and HT that have a statistical significant at baseline do not include in the multivariate analysis because they don't have any association with any outcomes in the univariate analysis.



**Figure 2** Cumulative survival and follow up time



**Figure 4** 1 year readmission and follow up time



**Figure 3** 1 year composite outcome of mortality and HF admission and follow up time

Regarding the secondary outcomes were pattern of GDMT use and the time to escalate to the target doses at 1-, 3-, 6-, and 12-month follow-ups. The results of pattern of GDMT was showed that in the HF group with use of beta blocker dosage < 50.00% at 1-, 3-, 6-, and 12-month follow-ups was 42.00% (n = 37), 15.90% (n = 14), 14.80% (n = 13), 8.00% (n = 7), respectively and group use of beta blocker ≥ 50% at 1-, 3-, 6-, and 12-month follow-ups was 34.10% (n = 30), 27.30% (n = 24), 19.30% (n = 17), 19.30% (n = 17), respectively. In cardiology clinic group with use of beta blocker dosage < 50.00% at 1-, 3-, 6-, and 12-month follow-ups was 58.90% (n = 86), 34.90% (n = 51), 30.10% (n = 44), 27.40% (n = 40), respectively and group use of beta blocker ≥ 50.00% at 1-, 3-, 6-, and 12-month follow-ups was 17.80% (n = 26), 25.30% (n = 37), 21.90% (n = 32), 21.20% (n = 31), respectively. In use of ACEI/ARB/ARNI with dosage < 50% in HF clinic groups at 1-, 3-, 6-, and 12-month follow-ups was 69.30% (n = 61), 61.40% (n = 54), 53.40% (n = 47), 45.50% (n = 40), respectively and group use of ACEI/ARB/ARNI with dosage ≥ 50% at 1-, 3-, 6-, and 12-month follow-ups was 17.00% (n = 15), 18.20% (n = 16), 22.70% (n = 20), 25.00% (n = 22),

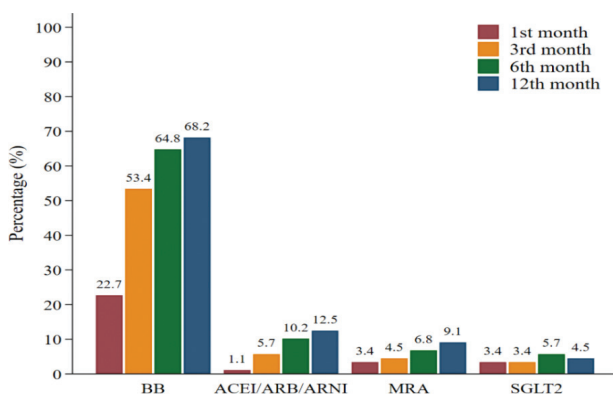
respectively. In use of ACEI/ARB/ARNI with dosage < 50.00% in cardiology clinic groups at 1-, 3-, 6-, and 12-month follow-ups was 43.20% (n = 63), 41.80% (n = 61), 39.70% (n = 58), 36.30% (n = 53), respectively and group group use of

ACEI/ARB/ARNI with dosage ≥ 50% at 1-, 3-, 6-, and 12-month follow-ups was 15.80% (n = 23), 17.10% (n = 25), 18.50% (n = 27), 19.90% (n = 29), respectively. Other drug were showed in Table 4 and Figures 5 and 6.

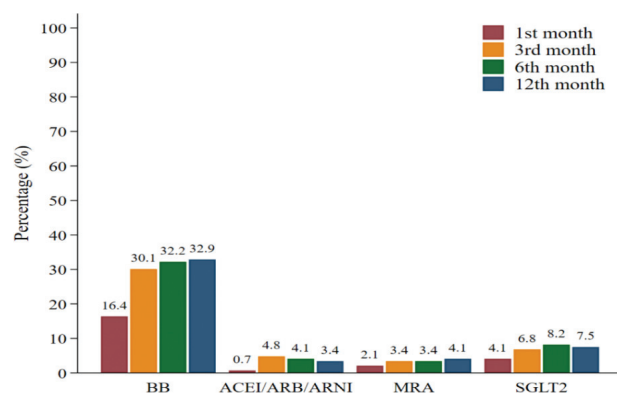
**Table 4** Percentage of target doses achieved by the drugs in heart failure clinic and general cardio clinic

Dosage used	Heart failure clinic (n = 88)				General cardio clinic (n = 146)			
	Baseline	3 months	6 months	12 months	Baseline	3 months	6 months	12 months
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
<b>Beta blocker</b>								
none	1 (1.10)	3 (3.40)	1 (1.10)	4 (4.50)	10 (6.80)	14 (9.60)	23 (15.80)	27 (18.50)
< 50%	37 (42.0)	14 (15.90)	13 (14.80)	7 (8.0)	86 (58.90)	51 (34.90)	44 (30.10)	40 (27.40)
≥ 50%	30 (34.10)	24 (27.30)	17 (19.30)	17 (19.30)	26 (17.80)	37 (25.30)	32 (21.90)	31 (21.20)
100%	20 (22.70)	47 (53.40)	57 (64.80)	60 (68.20)	24 (16.40)	44 (30.10)	47 (32.20)	48 (32.90)
<b>ACEI/ARB/ARNI</b>								
none	11 (12.50)	13 (14.80)	12 (13.60)	15 (17.0)	59 (40.40)	53 (36.30)	55 (37.70)	59 (40.40)
< 50%	61 (69.30)	54 (61.40)	47 (53.40)	40 (45.50)	63 (43.20)	61 (41.80)	58 (39.70)	53 (36.30)
≥ 50%	15 (17.0)	16 (18.20)	20 (22.70)	22 (25.0)	23 (15.80)	25 (17.10)	27 (18.50)	29 (19.90)
100%	1 (1.10)	5 (5.70)	9 (10.20)	11 (12.50)	1 (0.70)	7 (4.80)	6 (4.10)	5 (3.40)
<b>MRA</b>								
none	31 (35.20)	26 (29.50)	24 (27.30)	25 (28.40)	88 (60.30)	75 (51.40)	71 (48.60)	74 (50.70)
< 50%	39 (44.30)	31 (35.20)	30 (34.10)	22 (25.0)	38 (26.0)	43 (29.50)	41 (28.10)	40 (27.40)
≥ 50%	15 (17.0)	27 (30.70)	28 (31.80)	33 (37.50)	17 (11.60)	23 (15.80)	29 (19.90)	26 (17.80)
100%	3 (3.40)	4 (4.50)	6 (6.80)	8 (9.10)	3 (2.10)	5 (3.40)	5 (3.40)	6 (4.10)
<b>SGLT2</b>								
none	83 (94.30)	85 (96.60)	80 (90.90)	83 (94.30)	137 (93.80)	132 (90.40)	131 (89.70)	132 (90.40)
< 50%	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
≥ 50%	2 (2.30)	0 (0.0)	3 (3.40)	1 (1.10)	3 (2.10)	4 (2.70)	3 (2.10)	3 (2.10)
100%	3 (3.40)	3 (3.40)	5 (5.70)	4 (4.50)	6 (4.10)	10 (6.80)	12 (8.20)	11 (7.50)

Abbreviations: ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor neprilysin inhibitor; BB, beta blockers; MRA, mineralocorticoid receptor antagonist; n, number; SGLT2 I, sodium -cotransporter2 inhibitors



**Figure 5** Time to achieve target drug dose in heart failure clinic



**Figure 6** Time to achieve target drug dose in general cardio clinic



## DISCUSSION

With the rise of digital technology and widespread internet usage, global evidence-based guidelines for GDMT use in HFrEF management have become easily accessible to practicing cardiologists, thereby removing potential barriers to guideline information and improving HFrEF management. However, the implementation of these guidelines in real-world clinical practice, particularly percentage usage and drug titration, is often inadequate. Thus, in this study, we compared the prescription of GDMT between the two groups, with the focus on evaluating the implementation of management and medication adjustment, to determine whether HF clinics can improve the implementation of GDMT and lead to improved outcomes in terms of mortality and readmission.

In this study, the primary outcomes confirmed that the setting of HF clinics had a statistically significant impact on reducing HF readmission and mortality rates compared with the traditional approach of general cardiology care. HF clinics offer several advantages, including improved patient education and self-management skills, better medication adherence, and more effective monitoring and management of symptoms. In this study, drug profiles and the time frame for dose escalation were analyzed to provide new insights into the success of HF clinics in improving patient outcomes. The study results showed that general cardiology clinics had a plateau phase in up-titrating the GDMT dose, with the majority of the dose increase occurring in the first 3 months and little to no additional increase in the subsequent follow-up visits at 6 and 12 months. In contrast, the HF clinic showed a more steady increase in the GDMT dose throughout the 12-month follow-up period, potentially contributing to the better outcomes observed in this group. But the rate of SGLT-2 inhibitor usage in the general cardiology clinic is higher than HF clinic due to patients in general cardiology clinic group have higher underlying DM than HF clinic group and in general cardiology clinic group many patients have background in government or state enterprise officer.

The study findings suggest that the general cardiology clinic group had lower adherence to the management of HF than the HF clinic group. At baseline, the systolic blood pressure was lower in the HF clinic group, and at the 12-month follow-up, the heart rate was higher in the general cardiology clinic group. This finding suggests that there was more room for increasing the dose of medication, but there was a plateau in the management of the disease. The more aggressive approach used in the HF clinic may have led to improved outcomes, such as reduced rehospitalization and mortality rates, compared with the general cardiology clinic.

Furthermore, patients in the HF clinic group were generally younger, whereas those in the general cardiology clinic group had a higher incidence of comorbidities such as chronic kidney disease and diabetes. The decrease in the estimated glomerular filtration rate may have limited clinicians' ability to add and up-titrate drug doses according to guidelines, which could have resulted in suboptimal patient management. This may have contributed to decreased efficacy in treating patients in the general cardiology clinic group, leading to higher readmission and mortality rates than those in the HF clinic group.

Patients in the HF clinic group may experience significant improvements in their quality of life because they are not recurrently admitted to hospitals and are able to stay at home and maintain their normal daily activities. Reducing hospital readmissions can also be cost-effective for patients and the healthcare system. Hospital stays and readmissions can be costly for patients, especially for those who have to pay out of pocket for any part of their care, and the healthcare system. Reducing the need for readmissions can reduce the burden on the healthcare system, allowing for the allocation of resources to other critical areas.

This study emphasizes the crucial role of following treatment guidelines in improving clinical outcomes in patients with HF. The Eliminate Coronary Artery Disease (ECAD) trial showed that simply closely monitoring patients and providing



follow-up care may not be sufficient to achieve optimal results if the drug profile is not optimized<sup>19</sup>. Therefore, it is necessary to ensure that patients receive appropriate medications at appropriate doses according to the current guidelines. This study showed that the rapid up-titration of GDMT could be a safe and well-tolerated approach that leads to improved clinical outcomes in patients with acute HF. These findings are consistent with those of the STRONG-HF trial<sup>20</sup>, which emphasized the importance of intensively titrating GDMT in patients with HF. However, it is important to note that drug up-titration should be performed under close medical supervision and with personalized treatment plans based on each patient's unique needs and health status. HF clinics can play a critical role in this process by providing specialized care and monitoring to ensure that patients receive the appropriate GDMT at the optimal dose. This can lead to improved clinical outcomes, including reduced mortality and HF rehospitalization, while minimizing the risk of adverse effects from medication titration.

This study has some limitations. First, this was a retrospective, not randomized study. Thus, other unknown variables may have affected the results. Second, patient allocation to HF clinic care was not randomized, which raises the possibility of referral bias. Third, in this study, only patients who were able to visit HF clinics or those believed to benefit from increased testing were referred, whereas patients in the nonclinic group may have been less willing to undergo such testing for various reasons. Thus, this study may have the potential for selection bias. Further studies are needed to address these limitations.

## CONCLUSION

The study results showed that the HF clinic setting had a significant impact on patient outcomes. HF clinics showed better results in reducing readmission and mortality rates. The results showed that HF clinics could steadily increase drug doses throughout the 12-month follow-up period. These findings highlight the importance of guideline adherence in improving patient outcomes in HF

treatment and identifying barriers to optimal HF management in general cardiology clinics.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

## ACKNOWLEDGEMENT

The author would like to acknowledge the participants for their information. Our research was funded by the Navamindrathiraj University Research Fund.

## DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## REFERENCES

1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation* 2020;141(9):e139-596.
2. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013;128(16):e240-327.
3. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;37(27):2129-200.
4. Yingchoncharoen T, Kanjanavanich R. Heart Failure Council of Thailand (HFCT) heart failure guideline: pharmacologic treatment of chronic heart failure - part II. *J Med Assoc Thai* 2019;102(3):368-72.

5. Buakhamsri A, Chirakarnjanakorn S, Sanguanwong S, Porapakham P, Kanjanavanich R. Heart Failure Council of Thailand (HFCT) 2019 heart failure guideline: pharmacologic treatment of chronic heart failure - part I. *J Med Assoc Thai* 2019;102(2): 240-4.
6. Konstam MA, Neaton JD, Dickstein K, Drexler H, Komajda M, Martinez FA, et al. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): a randomised, double-blind trial. *Lancet* 2009;374(9704):1840-8.
7. Packer M, Poole-Wilson PA, Armstrong PW, Cleland JG, Horowitz JD, Massie BM, et al. Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. ATLAS Study Group. *Circulation* 1999;100(23):2312-8.
8. Bristow MR, Gilbert EM, Abraham WT, Adams KF, Fowler MB, Hershberger RE, et al. Carvedilol produces dose-related improvements in left ventricular function and survival in subjects with chronic heart failure. MOCHA Investigators. *Circulation* 1996;94(11):2807-16.
9. Balakumaran K, Patil A, Marsh S, Ingrassia J, Kuo CL, Jacoby DL, et al. Evaluation of a guideline directed medical therapy titration program in patients with heart failure with reduced ejection fraction. *Int J Cardiol Heart Vasc* 2018;22:1-5.
10. Greene SJ, Fonarow GC, DeVore AD, Sharma PP, Vaduganathan M, Albert NM, et al. Titration of medical therapy for heart failure with reduced ejection fraction. *J Am Coll Cardiol* 2019;73(19):2365-83.
11. Phillips SM, Marton RL, Tofler GH. Barriers to diagnosing and managing heart failure in primary care. *Med J Aust* 2004;181(2):78-81.
12. Bhatt AS, DeVore AD, DeWald TA, Swedberg K, Mentz RJ. Achieving a maximally tolerated  $\beta$ -blocker dose in heart failure patients: Is there room for improvement? *J Am Coll Cardiol* 2017;69(20):2542-50.
13. Fonarow GC, Ziaeian B. Gaps in adherence to guideline-directed medical therapy before defibrillator implantation. *J Am Coll Cardiol* 2016;67(9):1070-3.
14. Komajda M, Anker SD, Cowie MR, Filippatos GS, Mengelle B, Ponikowski P, et al. Physicians' adherence to guideline-recommended medications in heart failure with reduced ejection fraction: data from the QUALIFY global survey. *Eur J Heart Fail* 2016;18(5): 514-22.
15. Cheng RK, Cox M, Neely ML, Heidenreich PA, Bhatt DL, Eapen ZJ, et al. Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population. *Am Heart J* 2014; 168(5):721-30.
16. Jain A, Mills P, Nunn LM, Butler J, Luddington L, Ross V, et al. Success of a multidisciplinary heart failure clinic for initiation and up-titration of key therapeutic agents. *Eur J Heart Fail* 2005;7(3):405-10.
17. Howlett JG, Mann OE, Baillie R, Hatheway R, Svendsen A, Benoit R, et al. Heart failure clinics are associated with clinical benefit in both tertiary and community care settings: data from the improving cardiovascular outcomes in Nova Scotia (ICONS) registry. *Can J Cardiol* 2009;25(9):e306-11.
18. Bernard R. Hypothesis testing: categorical data. Bernard R, editor. *Fundamentals of biostatistics*. Boston: Cengage learning; 2010. P. 384-5.
19. Logeart D, Berthelot E, Bihry N, Eschalier R, Salvat M, Garcon P, et al. Early and short-term intensive management after discharge for patients hospitalized with acute heart failure: a randomized study (ECAD-HF). *Eur J Heart Fail* 2021;24(1):219-26.
20. Mebazaa A, Davison B, Chioncel O, Cohen-Solal A, Diaz R, Filippatos G, et al. Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial. *Lancet* 2022; 400(10367):1938-52.