Journal of Cardiac Failure 00 (2026) 1–5

JCF
Journal of Cardiac Failure

Brief Report

Practical Guideline-Directed Medical Therapy (PGDMT) in Heart Failure With Reduced and Mildly Reduced Ejection Fraction—Real World Multicenter Cross-sectional Interim Analysis at Enrollment: Data from Associates for Cardiology Education and Research Chronic Heart Failure (ACERT CHEF) Registry

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Heart failure (HF) is classified based on the left ventricular ejection fraction (LVEF) in reduced ejection fraction (HFrEF), mildly reduced ejection fraction (HFmrEF) and preserved ejection fraction (HFpEF) when the LVEF is ≤40%, 41% to 49%, and ≥50%, respectively.[1] Most HF registries have enlisted persons who have been admitted for acute decompensated HF. There are limited contemporary chronic outpatient HF registries in India.

Conventional guideline-directed medical therapy (GDMT) comprises beta blockers (BBs), angiotensin receptor blocker and neprilysin inhibitor (ARNIs), mineralocorticoid receptor antagonists (MRAs) and sodium glucose cotransporter inhibitors (SGLT2i). Ivabradine is recommended when a heart rate of ≤70/minute is not achieved despite a maximally tolerated dose of BB or when BBs are contraindicated.[2] Addressing real-world cost constraints and patient tolerance, the present registry used practical guideline directed medical therapy (PGDMT), defined as a prescription of BB or ivabradine, any renin angiotensinogen aldosterone system inhibitor (RAASi; angiotensin converting enzyme inhibitors [ACEi], angiotensin II receptor blocker [ARB] or ARNI), MRA, and SGLT2i. All medications in the PGDMT are off patent and are affordable in India.

The registry also included a mandatory period of at least 2 months following hospitalization to provide time to initiate GDMT.

Study Design

The ACERT CHEF registry is a multicenter prospective observational study of consecutive adults (age ≥18 years) with an LVEF ≤50%. A minimum of 2 months and at least 2 visits following acute HF hospitalization were mandatory

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Manuscript received January 28, 2026; revised manuscript received February 14, 2026; revised manuscript accepted March 20, 2026.

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1071-9164/$ - see front matter

https://doi.org/10.1016/j.cardfail.2026.03.021

to allow adequate time for the physician to initiate GDMT. The registry was approved by the ethics committees in 7 centers and registered with the clinical trials registry of India (CTRI): CTRI/2023/10/058641.

Baseline demographics, clinical characteristics, comorbidities, and pharmacotherapy were captured through a web-based platform. Patients were categorized as HFrEF and HFmrEF. This article reports the cross-sectional prescription pattern of the registry at enrollment. Conventional GDMT and the more pragmatic PGDMT defined in the introduction were also assessed.

Baseline characteristics were summarized as descriptive statistics, categorized into HFrEF and HFmrEF, and analyzed. A multivariable binomial logistic regression was conducted to evaluate the predictors of PGDMT.

Results

Among 2033 registered patients during the study period from October 2023 to October 2025, 2013 patients were included after data cleansing. The mean age was 61.3 ± 11 years. HFrEF was present in 1164 patients and HFmrEF in 849 patients. The baseline demographic data, etiology, risk factors, and hemodynamic features for this study are given in Table 1.

Statistically significant higher systolic blood pressure and lower pulse rates were noted in patients with HFmrEF compared with patients with HFrEF. Among the comorbidities, a statistically significant higher intake of alcohol was noted in patients with HFrEF, whereas dyslipidemia, chronic kidney disease, and obesity were noted more often in patients with HFmrEF. Etiology was ischemic in about 65% of both categories. Coronary angiography was performed in 69.3% of the patients.

Conventional GDMT prescription patterns were BB, 81%; ARNI, 58%; MRA, 50%; and SGLT2i, 53%. Combining BB and ivabradine, the prescription rate increased to 85% and changing ARNI to any RAASi to 74% (Table 2). Conventional GDMT was prescribed in 24.6%, which improved modestly to 28.2% when PGDMT was applied.

Conventional 3-drug GDMT without SGLT2i was prescribed for 40% of the patients. Analysis of PGDMT revealed none, any of 1, 2, 3, or all 4 PGDMTs were prescribed in 4%, 16%, 24%, 28%, and 28%, respectively (Figure 1). PGDMT was prescribed at the rate of ≥2 and ≥3 drugs in 80% and 56%, respectively.

Several covariates emerged as statistically significant predictors of PGDMT use. Obesity (odds ratio [OR], 1.62; 95% confidence interval [CI], 1.15−1.81; $P = .004$) was associated with an increased likelihood of receiving PGDMT. In contrast, ischemic etiology (OR, 0.53; 95% CI, 0.40−0.88; $P < .001$), chronic kidney disease (OR, 0.49; 95% CI, 0.20−0.81; $P = .007$), and female sex (OR, 0.71; 95% CI, 0.54−0.94; $P = .020$) were significantly associated with decreased odds of PGDMT prescription. Higher systolic blood pressure (OR, 0.99 per mm Hg; $P < .001$) and heart rate (OR, 0.98 per bpm; $P < .001$) were also associated with a lower likelihood of PGDMT implementation. Type 2 diabetes mellitus showed a nonsignificant trend toward lower PGDMT use (OR, 0.82; $P = .099$).

Discussion

The present multicentric registry recorded a high percentage of individual drug prescriptions, whereas the overall

Table 1 Baseline demographic data and clinical profiles of patients.

Characteristic	HFmrEF (n = 849)	HFrEF (n = 1164)	Total (N = 2013)	*P* value
Age, mean in years (SD)	61.1 (11.5)	61.5 (11.8)	61.3 (11.7)	.470*
Women	171.0 (20.1%)	229.0 (19.7%)	400.0 (19.9%)	.795†
Systolic BP	123.8 (20.8)	120.1 (20.8)	121.7 (20.9)	< .001*
Pulse rate (per minute)	77.8 (12.8)	81.3 (21.8)	79.8 (18.6)	< .001*
BMI value	25.9 (4.4)	25.4 (4.5)	25.6 (4.5)	.022*
Smoking	54.0 (6.4%)	98.0 (8.4%)	152.0 (7.6%)	.084†
Chewing tobacco	2.0 (0.2%)	6.0 (0.5%)	8.0 (0.4%)	.324†
Alcohol intake	25.0 (2.9%)	73.0 (6.3%)	98.0 (4.9%)	< .001†
Type2 diabetes mellitus	519.0 (61.1%)	676.0 (58.1%)	1195.0 (59.4%)	.168†
Systemic hypertension	389.0 (45.8%)	515.0 (44.2%)	904.0 (44.9%)	.483†
Dyslipidemia	230.0 (27.1%)	190.0 (16.3%)	420.0 (20.9%)	< .001†
Chronic kidney disease	47.0 (5.5%)	116.0 (10.0%)	163.0 (8.1%)	< .001†
Atrial fibrillation	29.0 (3.4%)	46.0 (4.0%)	75.0 (3.7%)	.531†
Coronary angiography	609.0 (71.7%)	786.0 (67.5%)	1395.0 (69.3%)	.043*
Etiology				
Ischemic	553.0 (65.1%)	767.0 (65.9%)	1320.0 (65.6%)	.7242
Valve_disease-induced_heart failure	19.0 (2.2%)	31.0 (2.7%)	50.0 (2.5%)	.5452

BMI, body mass index; BP, blood pressure; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; SD, standard deviation.

*Linear model analysis of variance

†Pearson's chi-squared test

Table 2 Drug use and combination drug use in the registry.

	HFmrEF (n = 849)	HFrEF (n = 1164)	Total (N = 2013)	*P* value*
Beta blocker	707.0 (83.3%)	922.0 (79.2%)	1629.0 (80.9%)	.022[1]
Ivabradine	151.0 (17.8%)	196.0 (16.8%)	347.0 (17.2%)	.578[1]
Beta blocker or ivabradine	741.0 (87.3%)	973.0 (83.6%)	1714.0 (85.1%)	.022[1]
ACEi	134.0 (15.8%)	103.0 (8.8%)	237.0 (11.8%)	< .013[1]
ARB	110.0 (13.0%)	110.0 (9.5%)	220.0 (10.9%)	< .001[1]
ARNI	465.0 (54.8%)	703.0 (60.4%)	1168.0 (58.0%)	.012[1]
Any RAASi[†]	638.0 (75.1%)	853.0 (73.3%)	1491.0 (74.1%)	.346[1]
MRA	397.0 (46.8%)	601.0 (51.6%)	998.0 (49.6%)	.031[1]
SGLT2i	437.0 (51.5%)	625.0 (53.7%)	1062.0 (52.8%)	.324[1]
Vericiguat	50.0 (5.9%)	115.0 (9.9%)	165.0 (8.2%)	.001[1]
Digoxin	50.0 (5.9%)	112.0 (9.6%)	162.0 (8.0%)	.002[1]
Diuretic	351.0 (41.3%)	738.0 (63.4%)	1089.0 (54.1%)	< .001[1]
Hydralazine and nitrate	55.0 (6.5%)	80.0 (6.9%)	135.0 (6.7%)	.727[1]
Multidrug therapy implementation				
GDMT3 (without SGLT2i)	326.0 (38.4%)	478.0 (41.1%)	804.0 (39.9%)	.228[1]
Conventional GDMT	204 (24.0%)	292 (25.1%)	496 (24.6%)	.587[1]
Practical GDMT	239.0 (28.2%)	329.0 (28.3%)	568.0 (28.2%)	.955[1]

ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor and neprilysin inhibitor; GDMT, guideline-directed medical therapy; HFmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; RAASi, renin angiotensin aldosterone system inhibitors; SGLT2i, sodium glucose cotransporter 2 inhibitor.

*Pearson's Chi-squared test

[†]114 patients received various combinations of ARB, ACEi and ARNI.

conventional quadruple therapy use was 25%. There was a modest improvement to 28% when PGDMT was incorporated. However, PGDMT is not a proven outcome measure and long-term outcome data are still to come. PGDMT is intended as a pragmatic operational metric of foundational therapy implementation and does not replace guideline-directed quadruple therapy. The OPTIPHARM-HF registry from Italy showed that BB (90%),

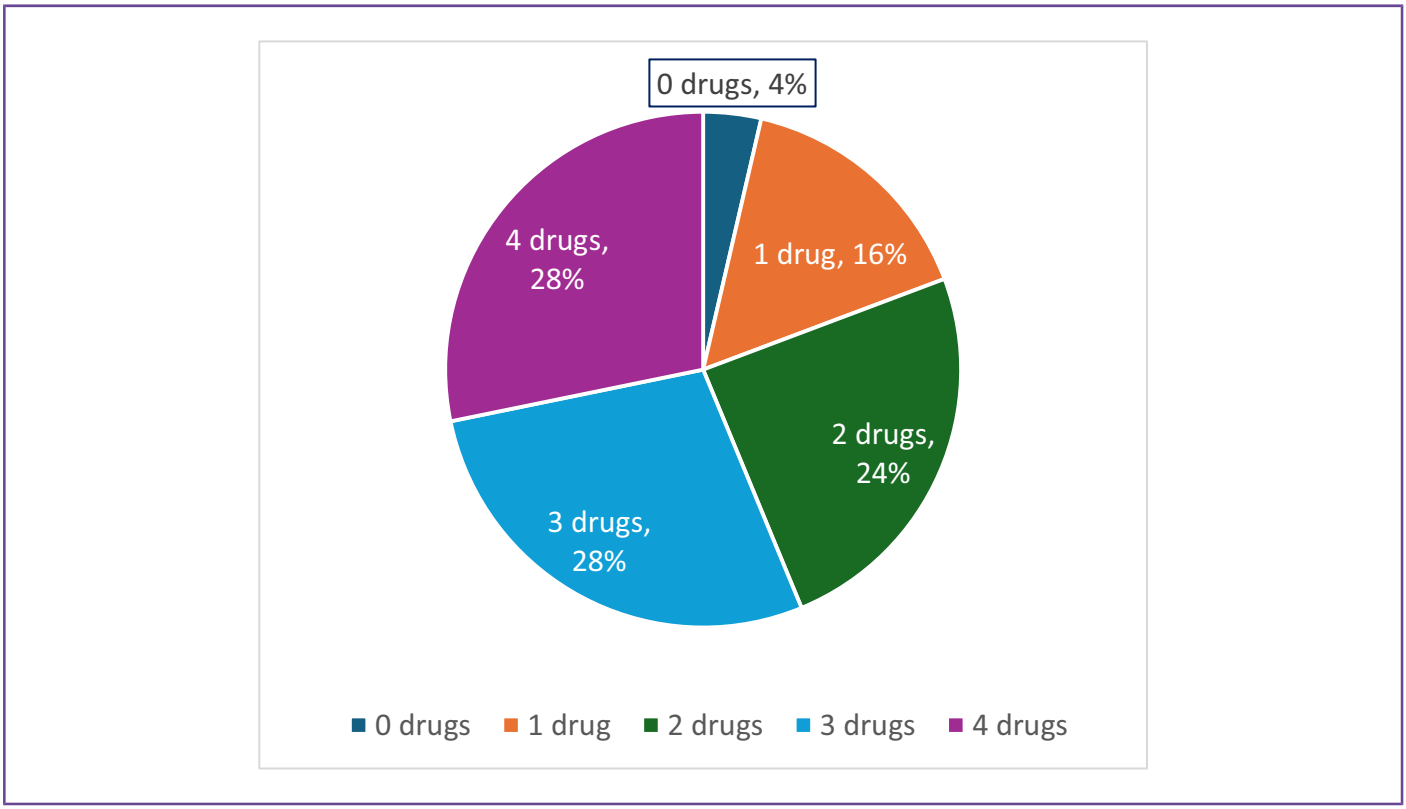


Figure 1. Percentage of patients on practical guideline-directed medical therapy (PGDMT). Practical GDMT was a beta blocker or ivabradine, a RAAS inhibitor (can be angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker/angiotensin receptor–neprilysin inhibitor), mineralocorticoid receptor antagonists, and sodium glucose co-transporter-2 inhibitors.

RAASi (81%), MRA (70%), SGLT2i (67%), and quadruple drug use (44%) is higher than other registries, including the present registry.[3]

Previous Indian registries predated SGLT2i being standard therapy. GDMT with RAASi, BB, and MRA use in the other Indian registries was 25% to 47%, whereas the present registry had 40% on the same 3 drugs. The other registries also included patients with HFpEF.[4–6]

The ACERT-CHEF registry had 4% of patients on none of the GDMT drugs, and all were on a combination of isosorbide dinitrate and hydralazine. Patients receiving hydralazine–nitrate therapy without foundational GDMT did not uniformly have advanced renal dysfunction, suggesting that incomplete GDMT implementation may reflect real-world prescribing complexity rather than strict contraindication. Ongoing registry follow-up will clarify clinical drivers and longitudinal outcomes in this subgroup. The OPTIPHARM study recorded 2% of patients in whom none of the drugs was administered.[3]

The association between obesity and higher PGDMT use may reflect clustering of metabolic comorbidities that facilitate the adoption of contemporary therapies, including SGLT2 inhibitors. Conversely, lower PGDMT use with higher systolic blood pressure and heart rate may suggest therapeutic inertia or incomplete treatment optimization. Given the cross-sectional design of the study, these findings should be considered hypothesis generating rather than causal.

HFrEF and HFmrEF have shown no etiologic and modest pharmacotherapeutic differences. However, the larger picture is the significant underutilization of GDMT despite the removal of cost constraints. Since this is a real-world registry, the reasons for nonprescription were not ascertained.

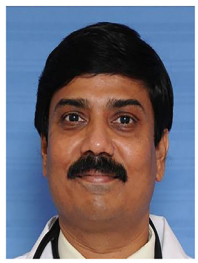
Conclusion

In this first contemporary multicenter outpatient HF registry from India, we found that although individual components of GDMT—particularly beta blockers, RAAS inhibitors, ARNI, and SGLT2 inhibitors—are prescribed at comparatively high rates in this affordable era, full implementation of quadruple therapy remains suboptimal, with only 28% of patients receiving all 4 pillars of PGDMT. Redefining GDMT in a pragmatic, patient-centered manner as PGDMT is an operational metric and not a replacement for the guideline-endorsed conventional GDMT.

The ACERT-CHEF registry underscores the urgent need for structured physician-education programs, systematic treatment pathways, and follow-up mechanisms to improve GDMT uptake. As follow-up data mature, this registry will provide critical insight into whether a practical, flexible definition of GDMT can achieve better real-world outcomes in chronic HF management.

Limitations of the Study

This is an interim, cross-sectional evaluation of baseline treatment patterns. Longitudinal outcomes, dose optimization, and changes in therapy over time are not yet reported. The outpatient design of at least 2 months following hospitalization may introduce survivor bias in the follow-up and limit the generalizability of the findings. Medication adherence, persistence, and reasons for nonprescription of GDMT could not be systematically analyzed owing to the real-world nature of the study.



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CRediT authorship contribution statement

PRABHAKAR DORAIRAJ: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **ILAYARAJA UTHIRAPATHI:** Visualization, Validation, Supervision. **KARTHIKEYAN B:** Visualization, Validation, Supervision. **EZHILAN JANAKIRAMAN:** Validation, Supervision, Resources, Investigation, Conceptualization. **PARTHASARATHY THIRUVENKADAM:** Visualization, Validation, Supervision, Investigation. **SARJUN BASHA KHADHAR MOHAMMED:** Validation, Supervision, Methodology, Investigation. **SAMA AKBER:** Visualization, Validation, Supervision, Formal analysis, Data curation. **SENGOTTUVELU G:** Supervision, Investigation. **SIVAKADAKSHAM NATARAJAN:** Validation, Supervision, Investigation. **SUNDAR RH:** Supervision, Methodology, Investigation. **ABRAHAM OOMMAN:** Writing – review & editing, Visualization, Validation, Supervision, Investigation, Formal analysis, Conceptualization. **SHANMUGA SUNDARAM RATHAKRISHNAN:** Visualization, Validation, Supervision, Investigation. **DHAMODARAN KALIYAMURTHY:** Visualization, Validation, Supervision, Methodology, Investigation. **HARIKRISHNAN PARTHASARATHY:** Validation, Supervision, Investigation, Data curation. **SATHYAMURTHY IMMANENI:** Validation, Supervision, Methodology, Data curation. **REFAI SHOWKATHALI:** Supervision, Methodology, Investigation, Data curation. **SHANMUGASUNDARAM SOMASUNDARAM:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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