ORIGINAL ARTICLE

Usage of Guideline-directed Medical Therapy in Patients with Heart Failure and Reduced Ejection Fraction in a Tertiary Care Hospital

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Abstract

Objective: To assess the prevalence of guideline-directed medical therapy (GDMT) and identify reasons for nonprescription and dose optimization in heart failure patients with reduced ejection fraction (HFrEF) in a tertiary care hospital in southern India.

Methods: A cross-sectional study was conducted in a tertiary care hospital involving HFrEF patients. Patients with heart failure were categorized based on GDMT prescriptions. Reasons for nonprescription and suboptimal dosing were identified.

Results: The study included 102 HFrEF patients with a mean age of 54 ± 11.7 years, predominantly male (89%). Only 10.8% of patients received GDMT at optimal doses. Although 62% were on triple therapy, many had one or more medications at suboptimal doses. Additionally, 26% of patients were not prescribed all recommended drug classes. Notably, the majority of patients with renal impairment fail to receive triple therapy. Barriers identified included hemodynamic issues and renal dysfunction.

Conclusion: GDMT adherence in HFrEF patients is significantly lower than expected, with only 10.8% receiving therapy at recommended doses. Key issues include suboptimal dosing and incomplete prescription of drug classes, influenced by patient-specific factors and systemic barriers.

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Introduction

Heart failure (HF) is a common and serious health condition that significantly impacts morbidity and mortality worldwide. With >64 million individuals affected globally and an increasing incidence in India, estimated between 0.5 and 1.7 per 1,000 persons annually and a prevalence of 1.3–4.6 million, the burden of HF is substantial.[1–3]

For individuals with heart failure with reduced ejection fraction (HFrEF), clinical guidelines from both the American Heart Association (AHA) and the European Society of Cardiology (ESC) advocate for the use of guideline-directed medical therapy (GDMT). This typically includes angiotensin receptor–neprilysin inhibitors (ARNIs), angiotensin-converting enzyme inhibitors (ACEi), or angiotensin receptor blockers (ARBs), along with beta-blockers and mineralocorticoid receptor antagonists (MRAs).[4,5] More recently, sodium-glucose cotransporter-2 (SGLT2) inhibitors have been added to the GDMT regimen due to their proven effectiveness in managing heart failure.[6] Following these clinical guidelines is essential, as individuals who do not receive GDMT face a 37% higher risk of death compared to those who do.[6] Additionally, not initiating GDMT prior to the placement of a primary prevention implantable cardioverter-defibrillator (ICD) has been linked to notably reduced survival rates within the 1st year.[7]

Despite well-established evidence supporting GDMT for improving outcomes and minimizing hospital admissions,[8] many HFrEF patients remain undertreated or do not attain the recommended therapeutic doses. Studies indicate that only 25–50% of HF patients reach target dosages.[9] The reasons for nonprescription and suboptimal dosing of GDMT are not well understood, highlighting the need for further investigation into these gaps. This study aims to assess the prevalence of GDMT prescriptions, evaluate adherence to recommended dosages, and identify potential factors contributing to GDMT nonprescription and suboptimal dosing in a tertiary care hospital setting.

By analyzing these factors, the study seeks to provide insights into improving GDMT adherence and optimizing patient outcomes in HFrEF management.

Methods

A cross-sectional study was carried out at a tertiary care hospital in southern India, which included HFrEF patients attending the cardiology OPD over a 2-month period (December 2023–January 2024).

Study Procedure

The investigator identified patients meeting the inclusion and exclusion criteria from those attending the cardiology OPD. Information collected from case sheets and electronic medical records included are mentioned below.

Patient parameters such as age, gender, hospital number, pulse rate, blood pressure, serum creatinine, serum potassium, cause of HF, duration of treatment, ejection fraction, and comorbidities.

Drugs prescribed along with dosages.

Based on the drugs prescribed, patients were categorized into three groups:

1. Category 1: HFrEF patients receiving all 3 recommended drug classes (ACEi/ARBs/ARNIs, beta-blockers, MRAs) at ≥50% of the target dose (optimal dose).
2. Category 2: HFrEF patients receiving all 3 recommended drug classes, but 1 or more drugs prescribed at <50% of the target dose.
3. Category 3: HFrEF patients not receiving all 3 recommended drug classes.

Target doses for the drugs were based on the effective dose as studied in major clinical trials. The target doses used for the different drugs are listed in Table 1.

The patient categories were later analyzed in terms of potential factors to determine their role in GDMT prescription and dose optimization.

Inclusion Criteria

Patients aged 18 years and above diagnosed with symptomatic heart failure and reduced

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ejection fraction (≤40%) (HFrEF) attending the cardiology outpatient department (OPD).

Patients who had been on treatment for heart failure for at least 3 months from the cardiology OPD.

Exclusion Criteria

Heart failure patients classified as NYHA class IV.

Sample Size Calculation

Assuming that 40% of HFrEF patients are prescribed all recommended drugs at optimal doses, the study required a sample size of 102 patients to estimate the proportion with 8% absolute precision and 90% confidence.

Statistical Analysis

Categorical variables were presented as frequencies and percentages, while continuous variables were described as mean and standard deviation or median and interquartile range (IQR), depending on the data distribution. The Chi-squared test (or Fisher's exact test for expected cell counts <5) was used to compare categorical variables. A two-tailed significance level of $p < 0.05$ was considered statistically significant. All statistical analyses were performed using STATA version 16.1 (Stata Corporation, College Station, TX, USA).

Table 1: Target dose for the heart failure drugs

Drug	*Target dose*
ACEi	
Enalapril	10 mg BID
Lisinopril	20 mg OD
Ramipril	10 mg OD
ARNi	
Sacubitril/valsartan	97/103 mg BID
ARB	
Losartan	50 mg OD
Valsartan	160 mg BID
Beta-blockers	
Bisoprolol	10 mg OD
Carvedilol	25 mg BID
Metoprolol succinate	200 mg OD
Nebivolol	10 mg OD
Mineralocorticoid receptor antagonist	
Spironolactone	25 mg OD
Eplerenone	50 mg OD
SGLT2i	
Dapagliflozin	10 mg OD
Empagliflozin	10 mg OD

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; BID, bis in die (twice daily); GDMT, guideline-directed medical therapy; OD, omne in die (once daily); SGLT2i, sodium glucose cotransporter 2 inhibitor; TID, ter in die (three times a day)

Ethics Approval

This cross-sectional study did not include any invasive procedures or clinical trials. Informed consent was obtained from all participants, and their personal information was kept confidential. The study received approval from the institute ethics committee prior to initiation and adhered to widely recognized ethical guidelines for human research.

Results

A total of 102 HFrEF patients who had been on treatment for at least 3 months were recruited from the cardiology outpatient department (OPD) during the course of the study. The baseline demographics of the study participants are detailed in Table 2. The average age of participants was 54 ± 11.7 years, with males comprising 89.2% of the sample. Most patients had heart failure due to ischemic causes (84.3%). The average left ventricular ejection fraction was 32.8 ± 5.6%.

Prevalence of Guideline-directed Medical Therapy

Among the 102 patients, 11 (10.8%) were receiving all 3 recommended classes of medications at optimal dosages (≥50% of target dose), classified as category 1. In contrast, 64 patients (62.7%) were on all 3 classes but with 1 or more medications at suboptimal dosages (<50% of target dose), categorized as category 2. Additionally, 27 patients (26.5%) did not receive all 3 recommended classes of medications, falling into category 3 (Fig. 1).

GDMT distribution by patient subgroups is presented in Table 3. The majority of patients with renal impairment (creatinine ≥1.5 mg/dL) failed to receive all 3 classes of medications (category 3). Patients with low blood pressure (<100/60 mm Hg) and abnormal potassium levels (<3.5 and >5.1 mmol/L) were either on suboptimal dosing (category 2) or did not receive all 3 classes of drugs (category 3). Of the 102 patients, 64 (62.7%) had been on treatment for 1 year or more. Patients in Category 1 were more likely to have been on treatment for >1 year compared to those in categories 2 or 3.

Table 2: Baseline characteristics of patient

Parameter		*Values*
Age		54 ± 11.7
Sex	Males	91 (89.2%)
	Females	11 (10.7%)
Cause of heart failure	Ischemic	86 (84.3%)
	Nonischemic	16 (15.7%)
Ejection fraction (%)		32.8 ± 5.6

Treatment Patterns

The prescription rates for ACEi/ARBs/ARNi, beta-blockers, and MRAs were 94 (92.1%), 95 (93.1%), and 85 (83.3%), respectively. Optimal dosing was achieved in 43 (45.7%) for ACE inhibitors/ARBs/ARNi, 19 (20%) for beta-blockers, and 85 (100%) for MRAs (Fig. 2). Among ACE inhibitors/ARBs/ARNi, enalapril and losartan were prescribed in 94.7 and 5.3% of cases, respectively. Metoprolol was the most commonly prescribed beta-blocker (75.8%), followed by carvedilol (22.1%) and bisoprolol (2.1%). Spironolactone was prescribed to all patients receiving MRAs. However, 5 patients (4.9%) were prescribed atenolol, a beta-blocker not recommended under GDMT guidelines.

SGLT2 inhibitors, recently introduced into clinical practice, were prescribed to 36 patients (35.3%). Of these, 5 patients received all drugs at optimal dosage, while 27 patients were on quadruple therapy with 1 or more drugs at suboptimal dosages.

Discussion

This study aimed to assess the prevalence and adequacy of GDMT in patients with HFrEF in a tertiary care setting in southern India and to explore reasons behind nonprescription and suboptimal dosing. The results highlight notable discrepancies between guideline recommendations and real-world clinical practice.

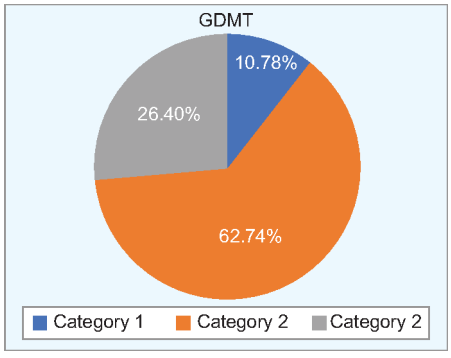

Fig. 1: Prevalence of GDMT in HFrEF patients. 10.78% of patients received all three drug classes at optimum dose (category 1) compared to 62.74% of patients who received all three classes with one or more drugs at suboptimum dose (category 2). 26.4% of patients were not on triple therapy (category 3). GDMT, guideline-directed medical therapy; HFrEF, heart failure with reduced ejection fraction

Table 3: GDMT with respect to patient subgroups

Subgroups		*Overall (n = 102)*	*Category 1 and 2 (n = 75)*	*Category 3 (n = 27)*	*p-value*
Duration of treatment (≥1 year)		64	46	18	0.623
Diabetes mellitus		48	37	11	0.443
Renal impairment (creatinine level ≥1.5mg/dL)		13	5	8	0.001
Blood pressure	High (≥140/90 mm Hg)	43	32	11	0.862
	Low (<100/60 mm Hg)	5	3	2	0.606
Potassium levels	High (>5.1 mmol/L)	6	3	3	0.146
	Low (<3.5 mmol/L)	4	3	1	1.000

mm Hg, millimeters of mercury; mmol/L, millimole per liter;

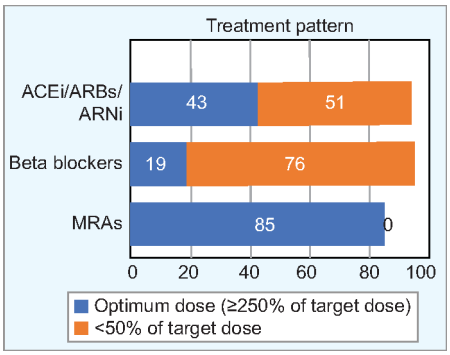

Fig. 2: Prescription rates and optimal dosing of heart failure medications. The prescription rates for ACEi/ARBs/ARNi, beta-blockers, and mineralocorticoid receptor antagonists (MRAs) were 94 (92.1%), 95 (93.1%), and 85 (83.3%), respectively. Optimal dosing was achieved in 43 (45.7%) patients for ACEi/ARBs/ARNi, 19 (20%) for beta-blockers, and 85 (100%) for MRAs. ACEi, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; ARNis, angiotensin receptor neprilysin inhibitors; MRAs, mineralocorticoid receptor antagonists

Prevalence and Adequacy of Guideline-directed Medical Therapy

Our study observed that only 10.8% of HFrEF patients received all three recommended classes of drugs (ACEi/ARBs/ARNi, beta-blockers, and MRAs) at optimal dosages. This figure is notably lower than the optimal adherence rates seen in some international studies, such as the 22.1% reported by the CHAMP-HF study and the 39.2% observed in the CHECK-HF registry.[10,11] This discrepancy highlights a substantial gap in adhering to GDMT, indicating that only a minority of patients receive treatment according to guideline recommendations. The setting was a cardiology OPD in a tertiary care center. GDMT rates may be lower in patients not treated in a specialist OPD in other centers.

In our cohort, 62.7% of patients were prescribed all 3 classes of recommended medications, though at suboptimal doses, aligning with results from other studies that also report high levels of under-dosing.[12–14] This under-dosing can have significant implications for patient outcomes, as inadequate dosing is associated with poorer clinical results and increased mortality risk.[6] Furthermore, 26.5% of patients failed to receive all recommended classes of drugs, a situation observed in other studies and indicative of systemic issues in achieving comprehensive GDMT coverage.[15]

Factors Influencing Guideline-directed Medical Therapy Prescription

Several patient-specific factors were identified as barriers to achieving optimal GDMT. Notably, patients with renal impairment and those with blood pressure abnormalities were less likely to receive all 3 classes of drugs, and when they did, the dosing was often suboptimal. This aligns with other research indicating that medical conditions, particularly renal dysfunction and hypotension, frequently lead to reluctance or limitations in prescribing certain GDMT agents.[13,15]

The duration of treatment was another important factor, with patients who had been on treatment for over 1 year more likely to achieve optimal dosing. This suggests that longer treatment duration may be associated with better optimization of therapy, possibly due to increased familiarity with the patient's condition and ongoing adjustments to therapy.

Treatment Patterns and Medication Adherence

Our study found high prescription rates for ACEi/ARBs/ARNi, beta-blockers, and MRAs, but only a minority of these prescriptions were at optimal doses. This reflects a broader issue observed in other research where, despite high prescription rates, target doses are often not achieved.[11,16,17] The choice of specific medications also varied, with enalapril and losartan being the most commonly prescribed ACEi/ARBs and metoprolol being the predominant beta-blocker, reflecting typical prescribing patterns observed in practice.

The introduction of SGLT2 inhibitors in a small percentage of patients indicates a gradual incorporation of newer therapies into practice. However, their limited use suggests potential barriers to their widespread adoption, such as cost or lack of familiarity.

This study has a few limitations:

- Only the prevalence of GDMT prescription at the physician or health facility level was assessed; patient adherence to GDMT and its impact on clinical outcomes were not evaluated. Further prospective studies on these patients will provide a better understanding of GDMT prevalence and other potential factors influencing patient adherence.
- The sample size of patients in this study was small. Further studies with larger sample sizes are required.
- Recently introduced SGLT2 inhibitors were not included while categorizing the patients due to their nonavailability from the hospital pharmacy. However, they were still prescribed to some patients; hence, further prospective studies involving quadruple therapy can be conducted to analyze their enhanced role in HFrEF patients.

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