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ORIGINAL RESEARCH

HEART FAILURE AND CARDIOMYOPATHIES

Determinants of Guideline-Directed Medical Therapy Implementation During Heart Failure Hospitalization

Emily Margolin, MD,[a] Trina Huynh, PharmD,[b] Alison Brann, MD,[a,c] Barry Greenberg, MD[a,c]

ABSTRACT

BACKGROUND Despite evidence that guideline-directed medical therapies (GDMTs) improve outcomes in patients with heart failure (HF) with reduced ejection fraction (HFrEF), implementation remains suboptimal.

OBJECTIVES The purpose of this study was to measure GDMT implementation during acute HFrEF hospitalization, evaluate the association between socioeconomic factors and GDMT implementation, and assess the association of GDMT utilization with subsequent clinical events.

METHODS Retrospective determination of GDMT utilization using a modified optimal medical therapy (mOMT) score (which accounts for specific contraindications to drugs) during unplanned HF hospitalization of consecutive adult patients with new-onset or previously diagnosed HFrEF from 2017 to 2018. Outcomes included discharge mOMT score, association between socioeconomic factors and GDMT implementation (assessed using both the Mann-Whitney U test for binary variables and the Kruskall-Wallace for nonbinary variables), composite outcome 1-year all-cause mortality and 1-year HF readmission, and each component as a function of discharge mOMT score (assessed using univariate and multivariable Cox proportional hazards regression models).

RESULTS Of 391 patients fulfilling entry criteria (of which 152 [38.9%] had new-onset HFrEF), only 49 (12.5%) had a perfect or near-perfect discharge mOMT score. Black patients and those experiencing homelessness had significantly lower discharge mOMT scores. Higher discharge mOMT score is associated with a lower rate of composite endpoint events, particularly in patients with new-onset HFrEF. Overall, a 0.1-increase in the mOMT score resulted in a 9.2% reduction in the composite endpoint.

CONCLUSIONS Suboptimal implementation of GDMT during HF hospitalization is widespread and is associated with a worse outcome. Black patients and patients experiencing homelessness were less likely to have GDMT optimized. (JACC Adv 2024;3:100818) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

ACEI = angiotensin converting enzyme inhibitor

AHA/ACC = American Heart Association/American College of Cardiology

ARB = angiotensin receptor blockers

ARNI = angiotensin receptor-neprilysin inhibitor

GDMT = guideline-directed medical therapy

HF = heart failure

HFrEF = heart failure with reduced ejection fraction

LVEF = left ventricular ejection fraction

mOMT = modified optimal medical therapy score

SGLT2I = sodium-glucose co-transporter-2 inhibitor

Pharmacologic treatment of patients with heart failure (HF) with reduced ejection fraction (HFrEF) has evolved considerably since the initial publication of the American Heart Association (AHA)/American College of Cardiology (ACC) management guidelines in 1995.[1] In addition to diuretics, major guidelines[2-4] now provide Class I recommendations for use of beta-blockers, inhibitors of the renin angiotensin system [angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), angiotensin receptor-neprilysin inhibitors (ARNIs)], mineralocorticoid receptor antagonists, hydralazine with nitrate in Black patients, and most recently, sodium-glucose co-transporter-2 inhibitors (SGLT2Is), all of which improve outcomes in patients with HFrEF. The cumulative effects of these medications result in mortality reductions of up to 70 to 80%.[2] Unfortunately, guideline-directed medical therapies (GDMTs) are not optimally utilized in the HFrEF population.[5-10] Because socially vulnerable populations have particularly poor HF outcomes,[2,11-13] attention has focused on variability in GDMT utilization related to socioeconomic characteristics. Available information, however, is discordant with some studies finding evidence of discrepancies in treatment between racial and ethnic groups,[14,15] while others have failed to detect differences in GDMT utilization.[5,6,16-18]

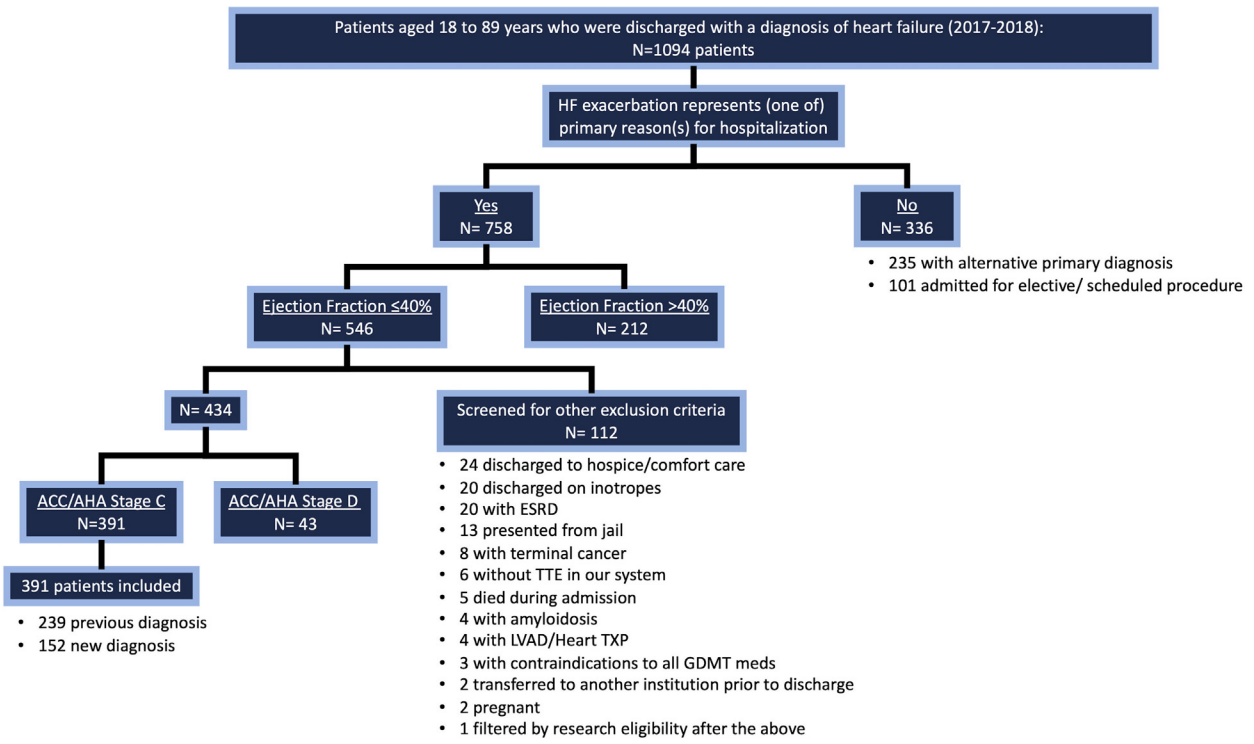
An important limitation of many prior studies of GDMT implementation is that medication classes were assessed individually,[5,6,14,15,17-19] without consideration of dose,[9,14-16,18,19] or accounting for contraindications to specific drug classes.[8-10,16,20,21] In clinical practice, however, avoidance of some GDMTs with continued use of others is determined on an individualized basis according to patient-specific contraindications. Thus, a measure that assesses GDMT for HFrEF in combination, while considering specific contraindications in individuals, would provide more accurate insights regarding GDMT utilization in clinical practice. Accordingly, we quantified GDMT optimization by modifying the Heart Failure Collaboratory's optimal medical therapy (OMT) score,[22] which considers the use of multiple agents in combination, to account for indications and contraindications of specific drugs used to treat an individual patient.

Hospitalization for HF provides an opportunity to initiate and uptitrate GDMT for chronic treatment. Aggressive implementation of GDMT in patients with HFrEF during hospitalization has recently been shown to substantially reduce subsequent morbidity and mortality.[23-25] The most recent guidelines therefore recommend inpatient initiation, continuation, and uptitration of GDMT toward optimal therapy in hospitalized patients with HFrEF who do not have a contraindication once they are hemodynamically stable.[2] Unfortunately, GDMT is rarely optimized in the inpatient setting.[9,10] Accordingly, we evaluated how GDMT was managed in patients hospitalized for decompensated HFrEF at our institution, whether socioeconomic factors were associated with optimization of therapy, and the impact of GDMT implementation on the patient's subsequent clinical course. We postulated that most patients were discharged on suboptimal GDMT, implementation was less robust in patients with lower socioeconomic status and in racial minorities, and that optimization of GDMT during hospitalization favorably impacts the subsequent clinical course of patients with HFrEF.

METHODS

The University of California-San Diego Institutional Review Board approved this study and granted a waiver of informed consent. This retrospective cohort study included adult patients with unplanned hospitalization with a primary discharge diagnosis of HF at our institution between January 1, 2017 and December 31, 2018. Patients were identified from the electronic health records (EHRs) according to the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM) or ICD-10-CM codes for this diagnosis. A retrospective review of the EHR was performed to confirm that patients met criteria for HF hospitalization, left ventricular ejection fraction (LVEF) was ≤40% during or proceeding current hospitalization, and patients were only included once (for multiple admissions, the first was used). If patients had multiple reasons for admission, the following inclusion criteria were used to determine if HF was a primary cause: 1) cardinal symptom(s) of HF (eg, edema, weight gain, shortness of breath) were present and not attributable to another cause (eg, pulmonary embolism, pneumonia); 2) documented HF diagnosis (previous or new diagnosis). Exclusion criteria included lack of documented LVEF ≤40%, admission in which HF was not a primary reason for hospitalization (alternative primary complaint or elective/scheduled admission), recipients of orthotopic heart transplantation, treatment with mechanical circulatory support, discharge to hospice/comfort care, discharge on inotropes, presence of end-stage renal disease, terminal cancer, cardiac amyloidosis, stage D HF, current pregnancy, incarceration in jail or

FIGURE 1 CONSORT Diagram of Patients Included in the Study



Patients with HFrEF who experienced an unplanned HF hospitalization during 2017 to 2018 were identified (n = 1,094) and screened for exclusion criteria. ACC/AHA = American Heart Association/American College of Cardiology; ESRD = end-stage renal disease; filtered by research eligibility = patients with reasons not to be exposed to research; GDMT = guideline-directed medical therapy; LVAD = left ventricular assist device; TTE = transthoracic echocardiogram; TXP = transplant.

prison, absence of documented EF in the EHR, and hospitalizations ending in death or transfer. **Figure 1** depicts selection of patients included in the analysis. The population was further subdivided according to whether HFrEF was newly diagnosed during index admission or had been previously diagnosed.

Review of each patient's EHR was performed to collect demographic, clinical, and socioeconomic information. Complete listing of the data collected including number of cases in which each variable was unavailable is provided in the Supplemental Appendix. Patients with pre-existing HF with EF >40% whose LVEF was found to be ≤40% during the current admission were classified as newly diagnosed HFrEF. Patients whose LVEF had improved from a previous value of ≤40% to a value >40% on the study most proximate to admission were also included in the study population, as guidelines recommend that these patients continue GDMT. The initial set of admission laboratory values and vital signs (including those obtained in the emergency department) and the last values obtained in-hospital were collected. Medical comorbidities and socioeconomic characteristics (summarized in the Supplemental Appendix) were obtained from the EHR. Dose of evidence-based beta blocker, ACEI, ARB, ARNI, mineralocorticoid receptor antagonist, and hydralazine/nitrate combination (for self-identified Black patients only) on admission and discharge were identified and converted to standardized class dose as described in Supplemental Table 1. SGLT2 inhibitors were not included, as specific recommendations for their use in patients with HFrEF had not yet appeared in HF guidelines.

To assess GDMT optimization, we modified the OMT score developed by the Heart Failure Collaboratory and the Academic Research Consortium[21,22] which considered a patient's eligibility for each class of drug and the dose prescribed. The method of calculating the score is detailed in the Supplemental Appendix and Supplemental Figure 1. It is reported as the fraction of total points earned out of the total points possible, with a maximum (perfectly optimized) score of 1.00 (100%) for all patients. This modified optimal medical therapy (mOMT) score was used to measure GDMT utilization on admission for

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TABLE 1 Baseline Characteristics

	All (N = 391)	New Diagnosis (n = 152)	Pre-Existing Diagnosis (n = 239)	*P* Value
Age on admission, y	62.4 ± 13.5	60.4 ± 13.2	63.7 ± 13.6	0.03
Sex				0.34
Male	290 (74.2%)	117 (77.0%)	173 (72.4%)	
Female	101 (25.8%)	35 (23.0%)	66 (27.6%)	
Race				0.65
White	200 (51.2%)	81 (53.3%)	119 (49.8%)	
Black	72 (18.4%)	30 (19.7%)	42 (17.6%)	
Mixed	93 (23.8%)	31 (20.4%)	62 (25.9%)	
Other	23 (5.9%)	10 (6.6%)	13 (5.4%)	
Unknown	3 (0.77%)	0 (0%)	3 (1.3%)	
Ethnicity				0.24
Non-Hispanic	302 (77.2%)	124 (81.6%)	178 (74.5%)	
Hispanic	84 (21.5%)	26 (17.1%)	58 (24.3%)	
Unknown	5 (1.3%)	2 (1.3%)	3 (1.3%)	
Primary language				0.07
English	340 (87.0%)	137 (90.1%)	203 (84.9%)	
Spanish	42 (10.7%)	10 (6.6%)	32 (13.4%)	
Other	9 (2.3%)	5 (3.3%)	4 (1.7%)	
Homelessness				0.63
Experiencing homelessness	95 (24.3%)	39 (25.7%)	56 (23.4%)	
Not experiencing homelessness	296 (75.7%)	113 (74.3%)	183 (76.6%)	
Distressed Community Index (DCI) quintile				0.24
Distressed	47 (12.0%)	16 (10.5%)	31 (13.0%)	
At-risk	70 (17.9%)	25 (16.4%)	45 (18.8%)	
Mid-tier	103 (26.3%)	38 (25.0%)	65 (27.2%)	
Comfortable	74 (18.9%)	27 (17.8%)	47 (19.7%)	
Prosperous	84 (21.5%)	43 (28.3%)	42 (17.6%)	
Unavailable	13 (3.3%)	3 (2.0%)	9 (3.8%)	
Employment status				0.06
Not employed	351 (89.8%)	131 (86.2%)	220 (92.1%)	
Employed	40 (10.2%)	21 (13.8%)	19 (7.9%)	
Marital status				0.52
Single	239 (61.1%)	96 (63.2%)	143 (59.8%)	
Not single	150 (38.4%)	55 (36.2%)	95 (39.7%)	
Not available	2 (0.5%)	1 (0.7%)	1 (0.4%)	
Insurance coverage				0.003
Commercial	177 (45.3%)	66 (43.4%)	111 (46.4%)	
Medicaid	58 (14.8%)	27 (17.8%)	31 (13%)	
Medicare	141 (36.1%)	47 (30.9%)	94 (39.3%)	
Self-pay	15 (3.8%)	12 (7.9%)	3 (1.3%)	
LVEF at closest proximity to admission	27 ± 9	27 ± 9	27 ± 9	0.52
Comorbidities				
Obstructive CAD	176 (45.0%)	58 (38.2%)	118 (49.4%)	0.03
Atrial fibrillation/flutter	165 (42.2%)	51 (33.6%)	114 (47.7%)	0.007
Hypertension	276 (70.6%)	101 (66.4%)	175 (73.2%)	0.17
Hyperlipidemia	141 (36.1%)	48 (31.6%)	93 (38.9%)	0.16
Diabetes mellitus	156 (39.9%)	53 (34.9%)	103 (43.1%)	0.11
Chronic kidney disease	120 (30.7%)	36 (23.7%)	84 (35.1%)	0.02
Obstructive lung disease	117 (29.9%)	34 (22.4%)	83 (34.7%)	0.009
Active cigarette smoking	112 (28.6%)	50 (32.9%)	62 (25.9%)	0.17
Days hospitalized	7.4 ± 5.6	8.1 ± 6.2	7.0 ± 5.1	0.02

Continued on the next page

TABLE 1 Continued

	All (N = 391)	New Diagnosis (n = 152)	Pre-Existing Diagnosis (n = 239)	*P* Value
Admission laboratory values				
Creatinine	1.3 ± 0.6	1.1 ± 0.5	1.3 ± 0.6	0.005
Potassium	4.3 ± 0.6	4.3 ± 0.6	4.3 ± 0.6	0.41
NT pro-BNP	8,793 ± 9122.1	8042.7 ± 9817.9	9,168 ± 8773.7	0.40
Discharge laboratory values				
Creatinine	1.3 ± 0.6	1.2 ± 0.5	1.3 ± 0.6	0.009
Potassium	4.2 ± 0.4	4.2 ± 0.4	4.3 ± 0.4	0.94
NT pro-BNP	4370.4 ± 5420.2	3635.7 ± 4930.8	4747.8 ± 5633.5	0.03
Admission vital signs				
Heart rate, beats/min	97.7 ± 22.7	104.3 ± 23.3	93.7 ± 21.4	<0.001
Systolic BP, mm Hg	132.1 ± 25.1	136.8 ± 26.6	129.3 ± 23.9	0.04
Discharge vital signs				
Heart rate, beats/min	83 ± 14.1	85.4 ± 15.2	81.4 ± 13.2	0.02
Systolic BP, mm Hg	115.9 ± 54	119.7 ± 84.2	113.4 ± 15.9	0.95

Values are mean ± SD or n (%).

BP = blood pressure; CAD = coronary artery disease; DCI = Distressed Communities Index; Dx = diagnosis; employed = employed, full time, part time, self-employed; HF = heart failure; LVEF = left ventricular ejection fraction; not employed = disabled, retired, not employed; not single = married, significant other; NS = not significant; NT pro-BNP = N-terminal pro-B-type natriuretic peptide; other language = Vietnamese, Mandarin, Tagalog, Arabic, Farsi, Greek, Other, Russian, Sign Language; other race = Asian, Native Hawaiian, Pacific Islander; single = divorced, separated, single, widowed.

patients with pre-existing HFrEF and on discharge for all patients. Outcomes of interest included discharge mOMT score, change in the mOMT score (in those with prior HF diagnosis) and percent of patients with perfect (1.00 or 100%) and near perfect (≥0.75 or 75% and <1.00 or 100%) discharge scores. Information regarding HF rehospitalization and all-cause mortality was extracted from the EHR.

Statistical analysis was performed using SPSS. Discharge and change in mOMT score were assessed as a function of socioeconomic characteristics, using both the Mann-Whitney U test for binary variables and the Kruskall-Wallace test for nonbinary variables. Patients were separated for analysis according to whether they had a new onset or previous diagnosis of HFrEF. Categorical variables were compared using chi-squared analysis. Continuous variables were compared using Spearman's correlation. These nonparametric tests were selected after the Kolmogorov-Smirnov test confirmed non-normal distributions of mOMT scores, changes in mOMT scores, and each clinical continuous variable. To minimize potential type I error due to multiple comparisons, adjusted alpha values based on the Benjamini-FDR 5% method were used to define statistical significance. Univariate and multivariable Cox proportional hazards regression models were used to assess the unadjusted and adjusted HR between the mOMT score as a continuous variable and all-cause mortality, subsequent HF hospitalization, and composite endpoint of either outcome. The rationale for model adjustments is described in the Supplemental Appendix. To facilitate interpretation of reported HRs, the mOMT score was transformed such that 1-U increase in HR corresponds to a 0.1 increase in score, where the score range was 0 to 1.0.

RESULTS

Of 1,094 adult patients hospitalized from 2017 to 2018, HF was a primary reason in 758 (**Figure 1**). Overall, 212 patients without documented LVEF ≤40% and 112 patients for reasons listed in **Figure 1** were excluded, leaving 391 patients for analysis. Of these, 152 (38.9%) had new onset, and 239 (61.1%) had a prior HFrEF diagnosis.

Patient socioeconomic characteristics, comorbid conditions, length of hospitalization, key laboratory variables, and vital signs on admission and discharge are summarized in **Table 1**. Patients averaged 62.4 ± 13.5 years of age; 290 (74.2%) were male, 200 (51.2%) were White, 93 (23.8%) classified themselves as mixed race, 72 (18.4%) were Black, and 84 patients (21.5%) were Hispanic. Almost one-quarter (n = 95, 24.3%) were experiencing homelessness at the time of hospitalization. Socioeconomic factors tended to be similar between patients with new-onset and previous HFrEF diagnoses. Comorbid conditions tended to be more common, and N-terminal pro-B-type natriuretic peptide levels were higher in patients with previously diagnosed HFrEF.

TABLE 2 Guideline-Directed Medical Therapy Optimization as a Function of Socioeconomic Characteristics

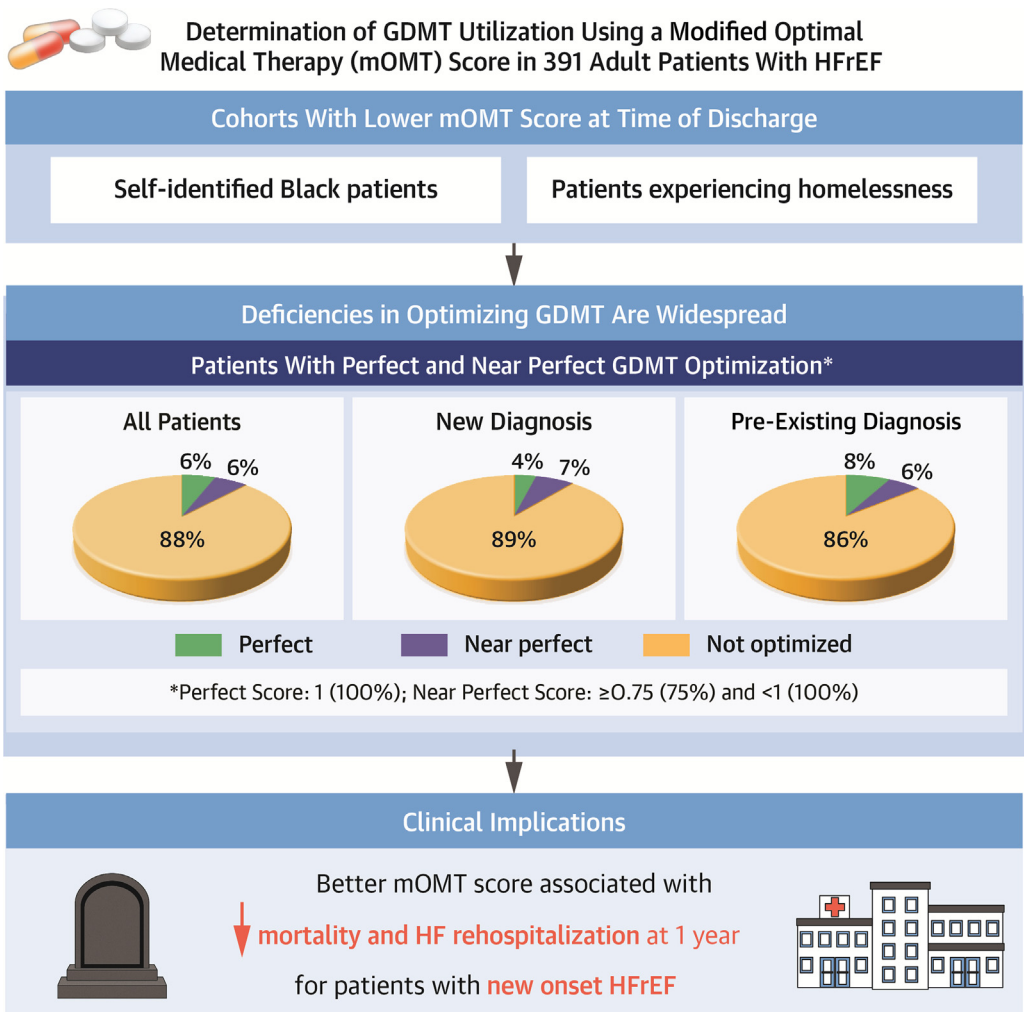
	All Patients (N = 391): mOMT Score	*P* Value	New Dx (n = 152): mOMT Score	*P* Value	Pre-Existing Dx (n = 239): Discharge mOMT Score	*P* Value	Pre-Existing Dx (n = 239): Change in Score	*P* Value
All included (n = 391)	0.470 ± 0.223	n/a	0.441 ± 0.214	n/a	0.488 ± 0.227	n/a	0.045 ± 0.237	n/a
Age (y)								
<65 (n = 221, 95, 126)	0.475 ± 0.222	0.65	0.438 ± 0.216	0.67	0.502 ± 0.224	0.22	0.038 ± 0.245	0.73
≥65 (n = 170, 57, 113)	0.464 ± 0.224		0.446 ± 0.212		0.473 ± 0.230		0.052 ± 0.229	
Sex								
Male (n = 290, 117, 173)	0.480 ± 0.226	0.19	0.456 ± 0.216	0.14	0.497 ± 0.231	0.48	0.038 ± 0.245	0.71
Female (n = 101, 35, 66)	0.440 ± 0.212		0.391 ± 0.203		0.465 ± 0.214		0.063 ± 0.216	
Marital status								
Single (n = 239, 96, 143)	0.458 ± 0.212	0.60	0.464 ± 0.230	0.80	0.479 ± 0.215	0.78	0.058 ± 0.209	0.34
Not single (n = 150, 55, 95)	0.488 ± 0.239		0.426 ± 0.205		0.503 ± 0.244		0.026 ± 0.274	
Ethnicity								
Non-Hispanic (n = 307, 126, 181)	0.461 ± 0.215	0.19	0.432 ± 0.197	0.27	0.481 ± 0.225	0.67	0.038 ± 0.232	0.68
Hispanic (n = 84, 26, 58)	0.503 ± 0.247		0.485 ± 0.281		0.511 ± 0.233		0.066 ± 0.252	
Race								
Black (n = 72, 30, 42)	0.416 ± 0.220	0.005*	0.356 ± 0.168	0.003*	0.458 ± 0.244	0.27	0.062 ± 0.190	0.72
Non-Black (n = 319, 122, 197)	0.482 ± 0.222		0.462 ± 0.219		0.495 ± 0.223		0.041 ± 0.246	
Primary language								
English (n = 340, 137, 203)	0.467 ± 0.220	0.91	0.439 ± 0.218	0.50	0.486 ± 0.219	0.56	0.048 ± 0.240	0.46
Not English (n = 51, 15, 36)	0.489 ± 0.245		0.460 ± 0.180		0.501 ± 0.269		0.026 ± 0.220	
Homelessness								
Not (n = 296, 113, 183)	0.486 ± 0.231	0.01*	0.454 ± 0.222	0.07	0.506 ± 0.235	0.07	0.045 ± 0.239	0.82
Experiencing homelessness (n = 95, 39, 56)	0.419 ± 0.187		0.402 ± 0.186		0.432 ± 0.188		0.043 ± 0.232	
Insurance								
Commercial (n = 177, 66, 111)	0.471 ± 0.218	0.85	0.448 ± 0.196	0.54	0.485 ± 0.230	0.94	0.016 ± 0.238	0.24
Medicaid (n = 58, 27, 31)	0.465 ± 0.216		0.415 ± 0.213		0.508 ± 0.213		0.119 ± 0.236	
Medicare (n = 141, 47, 94)	0.474 ± 0.228		0.449 ± 0.217		0.487 ± 0.233		0.053 ± 0.236	
Self-Pay (n = 15, 12, 3)	0.433 ± 0.276		0.425 ± 0.307		0.467 ± 0.115		0.067 ± 0.115	
DCI								
Distressed (n = 47, 31, 16)	0.503 ± 0.247	0.12	0.444 ± 0.253	0.72	0.511 ± 0.196	0.25	0.017 ± 0.220	0.45
At-risk (n = 70, 45, 25)	0.520 ± 0.242		0.472 ± 0.224		0.546 ± 0.250		0.085 ± 0.247	
Mid-tier (n = 103, 65, 28)	0.424 ± 0.203		0.386 ± 0.197		0.447 ± 0.204		0.047 ± 0.227	
Comfortable (n = 74, 47, 27)	0.458 ± 0.222		0.428 ± 0.177		0.475 ± 0.245		0.020 ± 0.222	
Prosperous (n = 84, 42, 43)	0.464 ± 0.213		0.461 ± 0.229		0.467 ± 0.120		0.044 ± 0.271	
Employment status								
Not employed (n = 351, 131, 220)	0.467 ± 0.220	0.58	0.58	NS	0.480 ± 0.223	0.08	0.039 ± 0.238	0.19
Employed (n = 40, 21, 19)	0.495 ± 0.251		0.416 ± 0.226		0.582 ± 0.254		0.118 ± 0.221	

Values are mean ± SD.
DCI = Distressed Communities Index; Dx = diagnosis; mOMT score = modified optimal medical therapy score; NS = not significant.

As shown in Table 2, the mOMT score for patients with either new-onset or previously diagnosed HFrEF tended to be low, averaging only 0.470 ± 0.223 for the entire population. As anticipated, the score was higher in previously diagnosed patients compared to newly diagnosed patients (0.488 ± 0.227 vs 0.441 ± 0.214; $P = 0.02$). In previously diagnosed patients, difference in mOMT score from admission to discharge averaged 0.045 ± 0.237, indicating little change in GDMT utilization during hospitalization. As shown in the Central Illustration, only 12.5% of patients received perfect (n = 24, 6.1%) or near-perfect (n = 25, 6.4%) mOMT scores at discharge, with little difference between the cohorts with new and pre-existing diagnoses.

The association between socioeconomic variables and GDMT optimization during HF hospitalization is summarized in Table 2. Although there were small differences in mOMT score according to sex, marital status, ethnicity, primary language, type of insurance, and economic status (assessed by the distressed communities index quintile), differences in GDMT utilization at discharge were not significant when testing for multiple comparisons was taken into

CENTRAL ILLUSTRATION **Patients With Perfect and Near-Perfect GDMT Optimization on Discharge After HF Hospitalization**



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Most patients hospitalized for HF were discharged on suboptimal GDMT, with only 12.5% receiving either perfect or near-perfect mOMT scores at discharge. mOMT = modified optimal medical therapy score.

account. Black patients had significantly lower discharge mOMT scores compared to non-Black patients (0.42, 95% CI: 0.36-0.47 vs 0.48, 95% CI: 0.46-0.51; $P = 0.005$), due predominantly to worse mOMT scores for those with a new diagnosis of HFrEF (0.36, 95% CI: 0.30-0.42 vs 0.46, 95% CI: 0.42-0.50; $P = 0.003$). Post-hoc sensitivity analysis (excluding hydralazine/nitrate in the calculation of mOMT scores) showed no significant difference in mOMT scores between Black and non-Black patients, regardless of whether HFrEF was new-onset or pre-existing. Patients experiencing homelessness also had significantly lower discharge mOMT scores (0.42, 95% CI: 0.38-0.46 vs 0.48, 95% CI: 0.46-0.51; $P = 0.01$), with values trending toward significance in both patients with new and pre-existing diagnoses. Post hoc stratification (described in detail in Part 3 of Supplemental Methods) was utilized to confirm that neither Black race nor homelessness confounded each's respective association with lower mOMT scores (Supplemental Tables 4 to 7). Unemployed patients with pre-existing HFrEF diagnosis had

TABLE 3 Multivariable Cox Regression Analysis for All Outcomes by mOMT Score

	All Patients (N = 391)	*P* Value	New Diagnosis (n = 152)	*P* Value	Pre-Existing Diagnosis (n = 239)	*P* Value
1-y mortality &/or heart failure rehospitalization						
Unadjusted	0.908 (0.829-0.995)	0.04*	0.746 (0.613-0.906)	0.003*	0.938 (0.847-1.040)	0.22
Age-sex-adjusted	0.910 (0.830-0.997)	0.04*	0.732 (0.600-0.894)	0.002*	0.947 (0.853-1.051)	0.30
Fully adjusted	0.946 (0.862-1.039)	0.25	0.768 (0.613-0.962)	0.02*	0.975 (0.877-1.084)	0.64
1-y heart failure readmission						
Unadjusted	0.924 (0.838-1.020)	0.12	0.757 (0.618-0.928)	0.007*	0.965 (0.862-1.079)	0.53
Age-sex-adjusted	0.920 (0.833-1.016)	0.10	0.739 (0.600-0.911)	0.005*	0.978 (0.871-1.099)	0.49
Fully adjusted	0.954 (0.863-1.055)	0.36	0.808 (0.643-1.014)	0.07	0.978 (0.871-1.099)	0.71
1-y all-cause mortality						
Unadjusted	0.868 (0.731-1.031)	0.11	0.555 (0.330-0.932)	0.03*	0.891 (0.742-1.070)	0.22
Age-sex-adjusted	0.884 (0.740-1.057)	0.18	0.595 (0.350-1.011)	0.06	0.942 (0.779-1.140)	0.54
Fully adjusted	0.936 (0.779-1.125)	0.48	0.552 (0.291-1.045)	0.07	1.010 (0.840-1.213)	0.92

Values are HR (95% CI). All patients: Fully adjusted = age, sex, discharge heart rate, admission systolic blood pressure, admission NT pro-BNP (N-terminal pro-B-type natriuretic peptide), obstructive lung disease, hyperlipidemia, and chronic kidney disease. Pre-existing Diagnosis: Fully adjusted = age, sex, hyperlipidemia, chronic kidney disease, obstructive lung disease, length of stay, admission NT-pro BNP, discharge heart rate. New diagnosis: Fully adjusted = age, sex, homeless, discharge heart rate, chronic kidney disease, Black race.

borderline significantly lower discharge mOMT scores compared to employed patients (0.48, 95% CI: 0.45-0.51 vs 0.58, 95% CI: 0.47-0.70; $P = 0.08$). When analyzed as a continuous variable, worse mOMT scores were modestly associated with increasing age only in patients with a pre-existing HFrEF diagnosis ($r^2 = 0.096$, $P = 0.10$).

Over a median time of 1 year (IQR: 120-365 days), patients with a pre-existing diagnosis of HFrEF had higher rates of combined 1-year mortality or HF rehospitalization (33.5% vs 15.8%; $P < 0.001$), HF rehospitalization (27.2% vs 14.5%; $P = 0.003$), and all-cause mortality (10.9% vs 2.63%; $P = 0.003$) than patients with new-onset HFrEF (Supplemental Table 2).

Unadjusted analysis assessing the relationship between mOMT score as a continuous variable (**Table 3**) and the composite clinical endpoint of combined 1-year mortality or HF rehospitalization at 1 year showed that greater optimization of therapy was associated with lower rates of the composite endpoint at 1 year (HR: 0.908; 95% CI: 0.829-0.995; $P = 0.04$), with a 9.2% reduction in combined composite outcome for every 0.1 increase in mOMT score. This finding was largely driven by effects in patients with new-onset HFrEF who experienced a 25.4% reduction in combined composite outcome for every 0.1 increase in their mOMT score (HR: 0.746; 95% CI: 0.613-0.906); $P = 0.003$). There was also a significant association between mOMT score and HF rehospitalization at 1 year and 1-year all-cause mortality in patients with new onset but not in patients with previously diagnosed HFrEF. For the entire population, the mOMT remained significantly associated with the composite after adjustment for age and sex but not after multivariable analysis. For patients with new diagnosis of HFrEF, the association continued to be significant after adjustment and tended toward significance after adjustment for both rehospitalization and mortality. For patients with pre-existing diagnosis, mOMT was not significantly associated with either the composite endpoint or either component.

DISCUSSION

In patients with HFrEF hospitalized at an academic medical center, we found that implementation of GDMT was suboptimal. While deficiencies were widespread with no patient group achieving a high rate of GDMT optimization, implementation was significantly less in Black patients compared to patients of other races and in patients experiencing homelessness. Failure to implement optimized medical therapy was not due to either contraindications to specific therapies (ie, elevated creatinine, hyperkalemia, or bradycardia) or lack of an indication in certain populations (ie, hydralazine/isosorbide combination in non-Black patients), as the mOMT score accounts for these factors. Suboptimal implementation of GDMT was associated with a higher likelihood of postdischarge events, particularly in patients with newly diagnosed HFrEF. These findings demonstrate a need for greater attention to the implementation of GDMT during HF hospitalization, particularly in vulnerable populations and in patients with new-onset HFrEF, in order to improve outcomes and reduce disparities in health care.

HF management guidelines provide strong recommendations for medication classes that improve

outcomes in patients with HFrEF.[2-4] In clinical practice, however, these agents are often not initiated or uptitrated to recommended target doses.[5-10] Hospitalization for HF represents a 'watershed event,' identifying a cohort of patients at substantially higher risk of death or rehospitalization postdischarge than are nonhospitalized patients. Moreover, hospitalization offers an opportunity to optimize GDMT at a time when patients can be closely observed for intolerance or side effects. Guidelines recommend that GDMT be "initiated or increased toward target doses" during HF hospitalization once adequate diuresis and hemodynamic stability have been established.[2-4] Results from STRONG-HF suggest that rapid uptitration of GDMT to target doses after an acute HF admission reduces mortality and HF readmission while improving symptoms and quality of life.[23] The PIONEER-HF[24] and SOLOIST[25] trials have shown that initiation of individual GDMT medications during hospitalization for decompensated HF can be accomplished safely and improve postdischarge outcomes.

This study evaluated implementation of GDMT in patients with HFrEF who were hospitalized for decompensated HF at an academic institution between 2018 and 2019, a period that was selected to ensure a 1-year follow-up period that avoided the 2020 COVID-19 pandemic, which impacted both clinic visits and hospital admissions.[26] Implementation of GDMT was assessed using a mOMT score, which takes contraindications to specific therapies into account and allows GDMT utilization to be quantified when patients are simultaneously receiving several classes of medications. The mOMT score accounts for dose of medication and is sensitive to uptitration of GDMT. By recognizing specific contraindications to specific drugs, it does not penalize the score when a drug is appropriately withheld. Thus, unlike prior studies characterizing GDMT in patients with HFrEF, contraindications were accounted for rather than excluded[21] or overlooked.[8-10,16,20] Additionally, in this study, patients were stratified according to new onset vs pre-existing diagnosis of HFrEF to account for lower doses prescribed to those with a new HFrEF diagnosis in the early stages of GDMT initiation.

Consistent with previous work,[5-10] we found that the majority of patients hospitalized for HF were discharged on suboptimal GDMT with only ~12% receiving perfect or near-perfect mOMT scores. Importantly, the use of the mOMT score allowed us to determine that suboptimal GDMT utilization was not due to contraindications or lack of indication for their use. Moreover, there was minimal change in mOMT score during hospitalization in patients with previously diagnosed HFrEF.

A variety of socioeconomic factors influence health care delivery in the United States. When the association between socioeconomic characteristics and GDMT utilization was analyzed, mOMT scores did not differ significantly according to age (as a dichotomized variable), sex, ethnicity, language, distressed communities index, or insurance coverage. Since prior studies had reported that GDMT utilization was related to patient age,[5,6,14,19] we also considered age as a continuous rather than dichotomous variable and found that increasing age had only a modest impact of borderline significance on optimal GDMT utilization. Although men have been reported to be more likely to receive GDMT than women,[20] we found no difference in GDMT optimization between sexes during hospitalization for acute HFrEF. This discrepancy may be related to the fact that the mOMT takes into account contradictions to medication classes that might differ between men and women. The lack of association between insurance coverage and optimization of GDMT seen in the present study also differs from previous reports of decreased GDMT optimization in patients lacking private insurance,[6] although this finding could have been influenced by imperfect categorization of insurance into a single class in the present study, a strategy necessitated by electronic medical record coding, which lists multiple classes of insurance for a single encounter.

Black patients had significantly lower mOMT scores upon discharge compared to non-Black patients, with differences seen both for patients with new-onset and pre-existing HFrEF. Underutilization of GDMT in Black patients is similar to some[14,15] but not all[5,6,15-17] previous studies. Although racial differences in GDMT optimization were not apparent when hydralazine/nitrate was removed from the mOMT score equation, our findings point out an important deficiency in the management of Black patients with HFrEF, as this drug combination was shown to have striking benefits on outcomes including a reduction in mortality when it was added to other therapies.[27] Notably, the hydralazine/nitrate combination has a Class 1 recommendation for Black patients in HF management guidelines[2] and was included in the original OMT score created by the Heart Failure Collaboratory and the Academic Research Consortium.[21]

Our study included patients living in both affluent locations and underserved communities, thereby allowing us to sample across a spectrum of socioeconomic strata. A unique aspect of the population studied is that almost one-fourth of patients were experiencing homelessness at the time of index hospitalization. Compared to patients with permanent shelter, these patients had significantly lower mOMT

scores upon discharge with values trending toward significance in both patients with new and pre-existing diagnoses. While perhaps not unexpected, this is, to our knowledge, a novel finding that has not been previously reported. Attention to this discrepancy in GDMT optimization may present an opportunity to improve outcomes for patients experiencing homelessness, who often have disproportionally worse cardiovascular outcomes.[28,29] Finally, we found that unemployed patients had lower mOMT scores upon discharge. Although this finding only approached statistical significance, it is consistent with previous findings.[6]

To determine the clinical implications of GDMT implementation, the association between mOMT scores at discharge with outcomes at 1 year was evaluated. Overall, patients with pre-existing HFrEF had higher rates of the composite outcome of 1-year all-cause mortality and HF readmission, in addition to higher rates of each of the individual components compared to patients with new-onset HF (Supplemental Table 2). Interestingly, higher mOMT scores were associated with reduced 1-year HF readmission and 1-year all-cause mortality in patients with a new HFrEF diagnosis, whereas outcomes of patients with a previous HFrEF diagnosis were less influenced by their mOMT scores. This finding suggests that patients with newly diagnosed HFrEF are particularly vulnerable to the consequences of failure to optimize their GDMT during their initial HFrEF hospitalization, while the trajectories of patients with a pre-existing HFrEF diagnosis may be less influenced, at least over a 1-year period, by changes in drug treatment during hospitalization.

The etiologies of institutional inertia in GDMT optimization during hospitalization for HF are likely multifactorial but can be postulated to reflect those of the broader health care system. Our finding that implementation was significantly lower in patients experiencing homelessness than in those with home security suggests that there may have been concerns on the part of the provider about the availability of these patients for follow-up assessment, which is needed to ensure that changes in medical therapy are not associated with significant side effects. The reason for lower use of GDMT in Black patients is uncertain. The fact that the difference observed based on race was no longer significant when the mOMT was calculated without including the hydralazine/nitrate combination suggests that, despite a Class I recommendation in the AHA/ACC/HFSA guidelines, providers were not motivated to implement this therapy due to either unfamiliarity with the guideline recommendation for its use, limited prior experience with the combination, concerns about potential side effects, or patient reluctance to accept an additional drug. For the entire population, failure to implement GDMT might be due to similar reasons as well as provider reluctance to initiate and uptitrate multiple drugs while patients remain hospitalized. Although our data doesn't allow us to determine which of these possibilities were responsible for the low rate of implementation of GDMT in either specific cohorts or the study population at large, it does emphasize the need for a better understanding of the factors involved and the initiation of remedial approaches for their correction.

STUDY LIMITATIONS. Patients included were followed at a single academic medical center, and our results may not be generalizable to other populations. However, the patients who are followed at our institution are quite diverse, encompassing a broad spectrum of the population, both in regard to socioeconomic status and race/ethnicity. Sample size was relatively small and included relatively few women, so conclusions in this subgroup should be made with caution. Medication regimens were analyzed based on what the provider documented in the medical record and could be inaccurate in some cases. This analysis did not include SGLT2 inhibitors, as guidelines had not yet included these drugs during the study time frame (2017-2018). Since our analysis focused only on drug classes that were given Class I recommendations in the AHA/ACC guidelines, we did not include other drugs such as ivabradine or digoxin that received lower levels of recommendations. We recognize that ARNIs are now the preferred drugs for renin angiotensin system blockade and that SGLT2 inhibitors now have a Class I recommendation, so it would be important to determine their utilization and impact on outcomes in future studies. Also, when evaluating the hydralazine/nitrate combination, we did not consider whether a patient was first fully maximized on ARNI/ACE/ARB prior to hydralazine/nitrate initiation, as this was not considered in the calculation of the original OMT score and such information was rarely available in patients' records. This may have been a factor in limiting the implementation of hydralazine/nitrate in the study population. Additionally, we did not define a time window for LVEF measurements that proceeded hospitalization. Therefore, some LVEFs obtained from years preceding hospitalization were accepted.

CONCLUSIONS

As guidelines strongly recommend HF hospitalization as an opportunity to implement GDMT, we sought to determine the extent to which this occurred in

patients who were nonelectively hospitalized for HFrEF and if specific socioeconomic factors were associated with deficiencies in GDMT implementation. Using a mOMT score, we found that most patients hospitalized for HFrEF, whether new-onset or pre-existing, are discharged on suboptimal GDMT. While Black patients and those experiencing homelessness had lower rates of GDMT optimization, the overall picture of treatment demonstrates widespread marked deficiencies in implementation. Recognition of this fact, as well as insights into which populations are at particularly high risk for insufficient treatment, should help provide both the impetus and direction for the development of novel strategies using interventions aimed at improving patient care and outcomes through optimization of therapy.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE: Most patients in our population, with both new onset and pre-existing HFrEF, were discharged on suboptimal GDMT. While deficiencies in GDMT implementation were widespread, we found that Black patients and patients experiencing homelessness were less likely to have drug therapy optimized during a HF hospitalization.

COMPETENCY IN MEDICAL KNOWLEDGE: More complete optimization of GDMT during hospitalization was independently associated with a more favorable postdischarge course, particularly in patients with new-onset HF.

TRANSLATIONAL OUTLOOK 1: Our findings indicate that better implementation of GDMT during hospitalization, particularly in vulnerable populations and in patients with newly diagnosed HF, is needed to avoid missing an opportunity to favorably affect the subsequent clinical course of patients with HFrEF.

TRANSLATIONAL OUTLOOK 2: Future efforts focused on improving outcomes in patients with HF and reducing disparities in health care should take these findings into account in devising new treatment strategies to improve outcomes in patients with HFrEF.

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APPENDIX For supplemental methods, tables, and figures, please see the online version of this paper.