

Characteristics, Treatments, and Outcomes of Hospitalized Heart Failure Patients Stratified by Etiologies of Cardiomyopathy



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ABSTRACT

OBJECTIVES The authors sought to describe characteristics, treatments, and in-hospital outcomes of hospitalized heart failure (HF) patients stratified by etiology.

BACKGROUND Whether characteristics and outcomes of HF patients differ by cardiomyopathy etiology is unknown.

METHODS The authors analyzed data on 156,013 hospitalized HF patients from 319 U.S. hospitals participating in Get With The Guidelines–HF between 2005 and 2013. Characteristics, treatments, and in-hospital outcomes were assessed by HF etiology. Standard regression techniques adjusted for site and patient-level characteristics were used to examine association between HF etiology and in-hospital outcomes.

RESULTS Median age was 75 years, 69.2% were white, and 49.5% were women. Overall, 92,361 patients (59.2%) had ischemic cardiomyopathy and 63,652 patients (40.8%) had nonischemic cardiomyopathy (NICM). Hypertensive (n = 28,141; 48.5%) and idiopathic (n = 17,808; 30.7%) cardiomyopathies accounted for the vast majority of NICM patients. Post-partum (n = 209; 0.4%), viral (n = 447; 0.8%), chemotherapy (n = 721; 1.2%), substance abuse (n = 2,653; 4.6%), familial (n = 556; 1.0%), and other (n = 7,523; 13.0%) etiologies were far less frequent. There were significant differences in baseline characteristics between those with ischemic cardiomyopathy compared with NICM with respect to age (76 years vs. 72 years), sex (44.4% vs. 56.9% women), and ejection fraction (38% vs. 45%). Risk-adjusted quality of care provided to eligible patients varied minimally by etiology. Similarly, in-hospital mortality did not differ among ischemic compared with NICM patients. However, among NICM patients, only hypertensive cardiomyopathy had a lower mortality rate compared with idiopathic NICM (adjusted odds ratio: 0.83; 95% confidence interval: 0.71 to 0.97).

CONCLUSIONS Characteristics of hospitalized HF patients vary by etiology. Both risk-adjusted quality of care and in-hospital outcomes did not differ by etiology. (J Am Coll Cardiol HF 2015;3:906–16)

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Although mortality due to heart failure (HF) is declining secondary to improved therapies, the prevalence of HF continues to increase (1,2). Whereas ischemic cardiomyopathy remains the most common etiology, over one-third of HF patients have nonischemic cardiomyopathy (NICM) (3). More recent studies in developed nations have suggested a shift in NICM epidemiology with a decline in hypertensive cardiomyopathy and increase in idiopathic NICM (1,4). Accordingly, contemporary etiologies and characteristics of HF patients need to be evaluated and can inform primary and secondary HF prevention strategies.

Furthermore, because the pathophysiology of NICM subtypes may vary, their prognosis may differ as well (5). However, previous studies have largely been limited to comparing outcomes among patients with ischemic cardiomyopathy and NICM. The association between specific NICM etiology and prognosis has not been well described. Identifying NICM etiologies associated with worse prognosis can help ensure that patients receive appropriate consideration for available therapies.

Accordingly, the objective of this study was to describe characteristics and in-hospital prognosis of hospitalized HF patients stratified by their etiology using a national, prospective HF registry. More specifically, we first examined the prevalence of ischemic cardiomyopathy, NICM, and NICM further characterized on the basis of specific etiologies, and assessed their temporal trends over the course of this study. Next, we described clinical characteristics and in-hospital treatment provided to HF patients by their etiology. Finally, we examined the association between HF etiologies and in-hospital outcomes.

METHODS

DATA SOURCE. Get With The Guidelines-Heart Failure (GWTG-HF) is an ongoing, prospective, in-hospital quality improvement program initiated in January 2005. Details and objectives of this American Heart Association-sponsored program have been

previously described (6). In brief, it enrolls adults hospitalized with a primary discharge diagnosis of HF. Participation is voluntary, and participating institutions submit data on consecutive, eligible patients in compliance with The Joint Commission and Centers for Medicare & Medicaid standards. Trained hospital personnel use standardized definitions to abstract extensive data from medical records on patient demographics, medical history, laboratory values, pharmacological and nonpharmacological interventions, HF performance measures, and outcomes at discharge. Data are submitted and assessed for completeness and quality using an Internet-based patient management tool (Get With The Guidelines-Heart Failure Patient Management Tool; Quintiles, Cambridge, Massachusetts). This Internet-based system performs checks to ensure data completeness. The data quality is also monitored for completeness and accuracy. Only fully participating hospitals and variables with a high degree of completeness (>95%) are used in analyses.

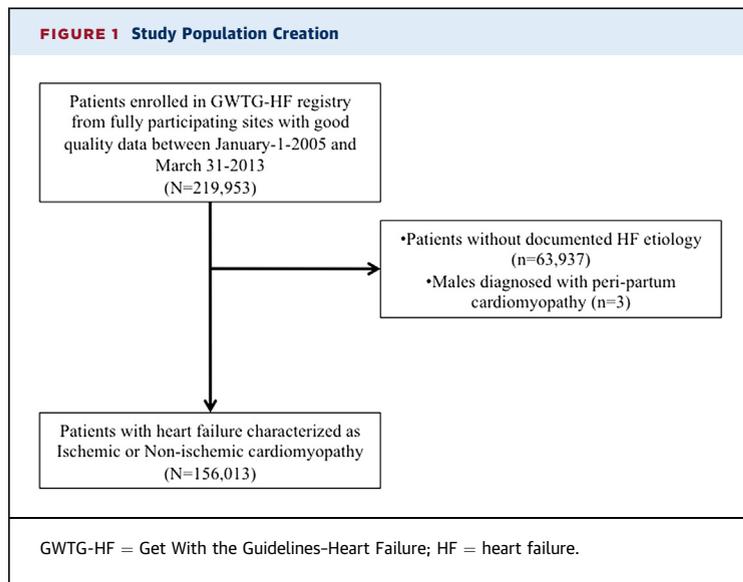
All participating institutions are required to comply with local regulatory and privacy guidelines, and to submit the program protocol for review and approval by their institutional review boards. Because data are used primarily at the local site for quality improvement, sites were granted a waiver of informed consent. The Duke Clinical Research Institute serves as the data center analysis and has an agreement to analyze the aggregate de-identified data for research purposes.

STUDY POPULATION. From January 1, 2005, to March 31, 2013, a total of 219,953 patients were enrolled in the GWTG-HF registry from 357 fully participating sites with a primary diagnosis of HF with good quality data. We excluded patients without documented HF etiology (n = 63,937) and men misclassified with post-partum cardiomyopathy (n = 3). Our final study population consisted of 156,013 patients with etiology documented as ischemic

ABBREVIATIONS AND ACRONYMS

CI	= confidence interval
CRT	= cardiac resynchronization therapy
EF	= ejection fraction
HF	= heart failure
IQR	= interquartile range
NICM	= nonischemic cardiomyopathy
OR	= odds ratio

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($n = 92,361$) versus nonischemic ($n = 63,652$) (Figure 1). In our analyses of NICM patients, we excluded patients without documented subtype of nonischemic etiology ($n = 5,594$). Our cohort of NICM patients with etiology further categorized included 58,058 patients.

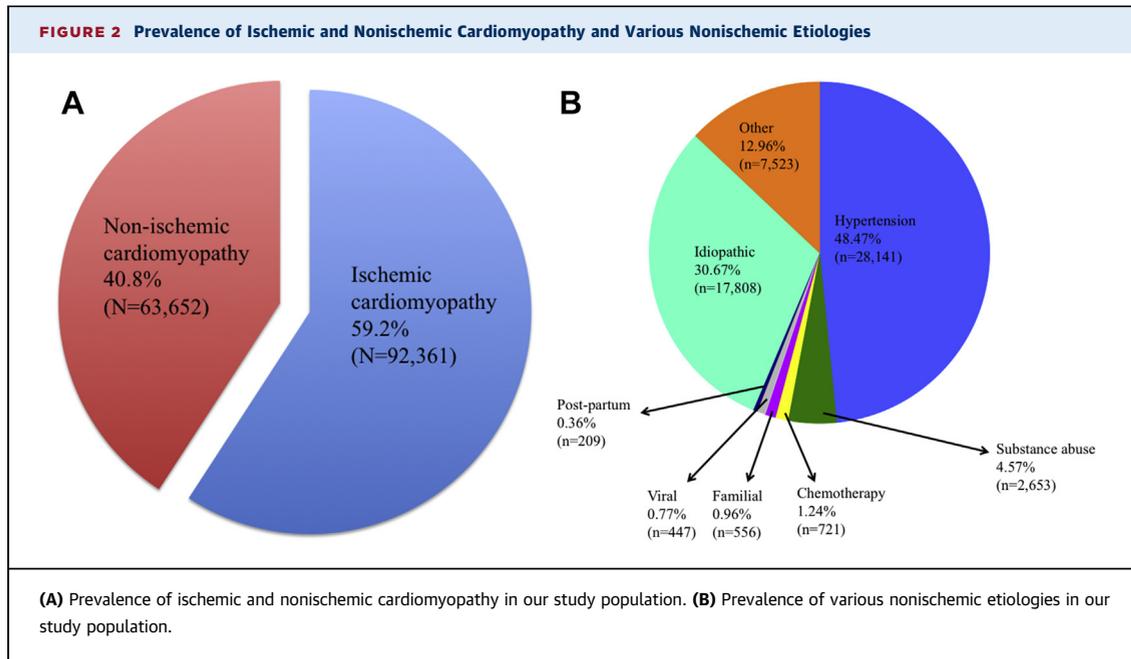
ETIOLOGY OF CARDIOMYOPATHY. HF etiology could be characterized as ischemic/nonischemic on the data collection form. In addition, all patients with a previous history of coronary artery disease, myocardial infarction, or coronary revascularization were characterized as having ischemic cardiomyopathy. The NICM etiology could be further characterized into pre-specified categories of hypertensive, alcohol/drug abuse, chemotherapy-induced, viral, post-partum, familial, unknown/idiopathic, or other. Trained personnel abstracted the cardiomyopathy etiology designated by treating physician through chart review. Coding instructions for the HF etiology in GWTG-HF registry are provided in Online Table 1.

OUTCOMES. We examined quality of care provided and in-hospital clinical outcomes for patients stratified by cardiomyopathy etiology as ischemic versus nonischemic, as well as NICM subcategory. For quality of care provided, we examined defect-free care that estimates provision of all appropriate interventions (pharmacological and nonpharmacological) to every patient. The GWTG-HF program uses similar criteria as Centers for Medicare & Medicaid Services and The Joint Commission to determine treatment eligibility for performance measures and American College of Cardiology/American Heart Association hospital performance measures.

In-hospital clinical outcomes assessed included mortality, length of stay longer than 4 days, discharge to home, and receipt of cardiac transplant.

COVARIATES. Covariates were included based on clinical rationale and/or previous studies. Demographic covariates included age, race/ethnicity, sex, insurance status (none/Medicare/Medicaid/other). Clinical covariates included history of diabetes, hyperlipidemia, hypertension, atrial fibrillation/flutter, chronic obstructive pulmonary disease/asthma, peripheral vascular disease, stroke/transient ischemic attack, renal insufficiency, depression, valve disease, and smoking status. Presentation variables included body mass index, systolic blood pressure, heart rate, and ejection fraction (EF) at admission. Hospital characteristics included in our models were region (Northeast/Midwest/South/East), location (rural vs. urban), number of beds, academic status (academic vs. nonacademic), and heart transplant capability.

STATISTICAL ANALYSIS. Baseline comparisons were made between patients stratified by cardiomyopathy etiology (i.e., ischemic vs. nonischemic) using chi-square tests for categorical variables and Kruskal-Wallis test for continuous variables. Similar analyses were also performed for NICM subgroups. To assess temporal trends in NICM etiology over the duration of this study, the study duration was stratified into yearly intervals, and patients were grouped by their respective etiologies into each year. Next, to examine the association between cardiomyopathy etiology and defect-free care, we constructed a logistic regression model using generalized estimating equation to account for in-hospital clustering, adjusted for the aforementioned covariates. The functional form of continuous variables was explored with restricted cubic splines and plots against the log odds ratios (ORs). Missing values were handled through simple imputation, to the most common category for categorical variables (<2% missing) and overall median for systolic blood pressure and heart rate (<4% missing), sex-specific median for body mass index (<14% missing), and EF (<5% missing). Hospital variables were not imputed, and observations with missing values were not included in the model. The associations between cardiomyopathy etiology and in-hospital clinical outcomes were examined using the same methodology. Additionally, analyses comparing patients with NICM stratified by their etiology were performed using the same methods described in the preceding text. All statistical analyses were performed at the Duke Clinical Research Institute (Durham, North Carolina) using SAS software (version 9.3, SAS Institute, Cary, North Carolina).



RESULTS

CARDIOMYOPATHY ETIOLOGY AND TEMPORAL TRENDS.

Overall, 92,361 patients (59.2%) had ischemic cardiomyopathy, and 63,652 patients (40.8%) had NICM (Figure 2A). Figure 2B shows the prevalence of various NICM etiologies in the study population. In our study population of 58,058 NICM patients with documented etiology subtype,

the most common etiology was hypertensive cardiomyopathy (n = 28,141; 48.5%). Prevalence of other etiologies was 4.6% for cardiomyopathy secondary to substance abuse (n = 2,653), 1.2% chemotherapy-induced (n = 721), 1.0% familial (n = 556), 0.8% viral (n = 447), 0.4% post-partum (n = 209), 30.7% idiopathic (n = 17,808), and 13.0% cardiomyopathy of other etiology (n = 7,523). Online Figure 1 shows the prevalence of various NICM etiologies in patients

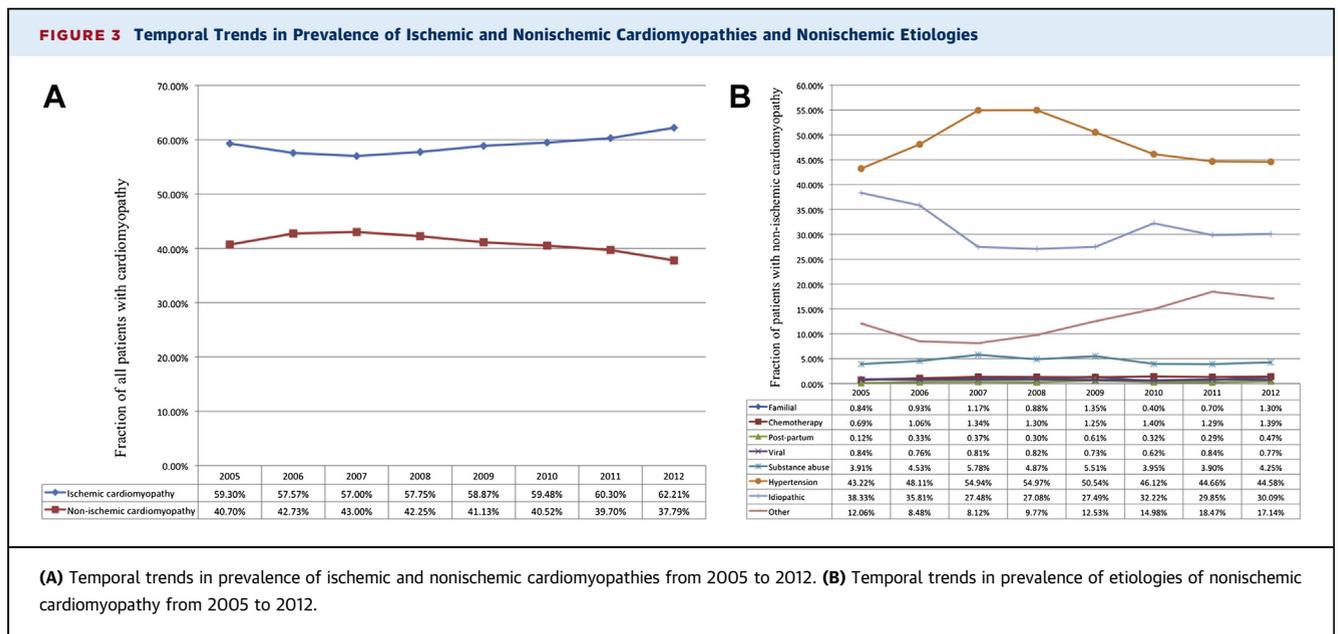


TABLE 1 Comparison of Baseline Characteristics of Patients With Ischemic and Nonischemic Cardiomyopathy

	Ischemic Cardiomyopathy (n = 92,361)	Nonischemic Cardiomyopathy* (n = 63,652)	p Value
Demographics			
Age, yrs	76 (66-84)	72 (57-84)	<0.0001
Race/ethnicity			<0.0001
White	68,633 (74.8)	38,639 (61.2)	
Black	12,789 (13.9)	16,384 (25.9)	
Hispanic	6,966 (7.6)	5,297 (8.4)	
Asian	1,097 (1.2)	941 (1.5)	
Other	2,296 (2.5)	1,906 (3.0)	
Women	41,040 (44.4)	36,186 (56.9)	<0.0001
Insurance			<0.0001
Medicare	53,595 (61.9)	30,830 (52.0)	
Medicaid	7,447 (8.6)	6,656 (11.2)	
Other	23,087 (26.6)	17,399 (29.3)	
None	2,469 (2.9)	4,461 (7.5)	
Medical history			
COPD/asthma	30,415 (33.1)	17,673 (28.3)	<0.0001
Atrial fibrillation	24,430 (36.2)	28,706 (33.0)	<0.0001
Diabetes	33,047 (36.0)	20,089 (32.1)	<0.0001
Hypertension	72,705 (79.1)	48,123 (77.0)	<0.0001
Hyperlipidemia	52,053 (56.6)	20,796 (33.3)	<0.0001
Stroke/TIA	16,215 (17.7)	7,398 (11.8)	<0.0001
PVD	15,809 (17.2)	4,183 (6.7)	<0.0001
Renal insufficiency	22,651 (24.7)	11,239 (18.0)	<0.0001
Anemia	20,301 (22.1)	11,298 (18.1)	<0.0001
Smoking	14,434 (15.8)	11,354 (18.0)	<0.0001
CRT-D	4,400 (4.8)	1,374 (2.2)	<0.0001
CRT-P	595 (0.7)	246 (0.4)	<0.0001
ICD only	12,472 (13.6)	3,940 (6.3)	<0.0001
Admission characteristics			
SBP, mm Hg	137 (118-158)	140 (120-163)	<0.0001
Heart rate, beats/min	80 (70-94)	86 (73-101)	<0.0001
BMI, kg/m ²	28 (24-33)	29 (24-36)	<0.0001
Ejection fraction, %	38 (25-52)	45 (25-56)	<0.0001
Ejection fraction <40%	45,350 (51.1)	25,474 (42.1)	<0.0001
BNP, pg/dl	850 (407-1,691)	725 (332-1,521)	<0.0001
Creatinine, mg/dl	1.4 (1.1-1.9)	1.2 (0.9-1.8)	<0.0001
Hospital characteristics			
Rural	4,965 (5.4)	3,035 (4.8)	<0.0001
Region			<0.0001
West	10,626 (11.5)	9,823 (15.4)	
South	31,073 (33.6)	21,057 (33.1)	
Midwest	23,362 (25.3)	15,595 (24.5)	
Northeast	27,300 (39.6)	17,177 (27.0)	
Academic hospitals	57,839 (62.7)	40,717 (64.0)	<0.0001
Number of beds	410 (250-593)	394 (251-566)	<0.0001

Values are median (interquartile range) or n (%). *Includes all patients with NICM irrespective of whether further etiology was classified.

BMI = body mass index; BNP = brain natriuretic peptide; COPD = chronic obstructive pulmonary disease; CRT-D = cardiac resynchronization therapy-defibrillator; CRT-P = cardiac resynchronization therapy-pacemaker; ICD = implantable cardioverter-defibrillator; NICM = nonischemic cardiomyopathy; PVD = peripheral vascular disease; SBP = systolic blood pressure; TIA = transient ischemic attack.

with an EF <40%. **Figure 3** shows the yearly prevalence of all these etiologies over the duration of this study period from 2005 to 2012. Overall, there were no significant changes in the yearly prevalence of various etiologies.

PATIENT CHARACTERISTICS BY CARDIOMYOPATHY ETIOLOGY.

Median age of the entire study population was 75 years (interquartile range [IQR]: 63 to 84 years), 69.2% were white, and 49.5% were women. **Table 1** shows demographic and clinical characteristics of patients with ischemic cardiomyopathy compared with NICM. Compared with patients with NICM, patients with ischemic cardiomyopathy were more likely to be older (median age 76 vs. 72 years), white (74.8% vs. 61.2%), and male (55.6% vs. 43.2%).

Table 2 shows characteristics of patients with NICM according to primary underlying etiology. As expected, patients with post-partum cardiomyopathy were the youngest, with a median age of 32 years (IQR: 25 to 38 years). For patients with post-partum and substance abuse cardiomyopathies, most were of black race (62.2% and 48.7%, respectively) in contrast to all other cardiomyopathies, in which patients were predominantly non-Hispanic white. Medical comorbidities were widely prevalent with 78% patients having hypertension, 37% having diabetes, 32% having atrial fibrillation/flutter, and 18% having renal insufficiency. The comorbidity burden was lowest in patients with post-partum cardiomyopathy, whereas patients with hypertensive cardiomyopathy had the highest prevalence of the most comorbidities. Furthermore, patients with hypertensive cardiomyopathy had the highest median EF (50%, IQR: 30% to 59%) and the largest proportion of patients with EF ≥40% (n = 16,658; 59.2%). Examination of hospital characteristics showed that the highest proportion of ischemic and NICM patients was seen in hospitals from the South and lowest in the West. Furthermore, the proportion of patients with hypertensive and substance abuse cardiomyopathies were highest in hospitals of the Northeast region, whereas all other NICM were most prevalent in hospitals of the South.

TREATMENT CHARACTERISTICS. **Table 3** lists various achievement and quality-of-care measures during index hospitalization among ischemic and NICM patients. Overall, a high proportion of patients met the achievement measures without clinically significant differences between ischemic patients compared with NICM patients. **Table 4** shows processes of care among patients with NICM stratified by etiology. There were again no clinically significant differences

TABLE 2 Baseline Characteristics of the Study Population Stratified by NICM Etiology

	NICM Etiology								p Value
	Hypertension (n = 28,141)	Idiopathic (n = 17,808)	Other (n = 7,523)	Substance Abuse (n = 2,653)	Chemotherapy (n = 721)	Familial (n = 556)	Viral (n = 447)	Post-Partum (n = 209)	
Demographics									
Age, yrs	73 (59-84)	73 (59-84)	73 (59-84)	52 (45-61)	66 (56-78)	62 (49-77.5)	50 (40-65)	32 (25-38)	<0.001
Race/ethnicity									<0.001
White	15,406 (54.8)	12,093 (67.9)	5,078 (67.5)	953 (35.9)	499 (69.2)	343 (61.7)	225 (50.3)	56 (26.8)	
Black	8,347 (29.7)	3,611 (20.3)	1,485 (19.7)	1,291 (48.7)	154 (21.4)	147 (26.4)	141 (31.5)	130 (62.2)	
Hispanic	2,783 (9.9)	1,351 (7.6)	527 (7.0)	230 (8.7)	39 (5.4)	45 (8.1)	46 (10.3)	10 (4.8)	
Other	1,381 (4.9)	683 (3.8)	360 (4.8)	139 (5.2)	26 (3.6)	10 (1.8)	31 (6.9)	13 (6.2)	
Women	16,530 (58.7)	10,297 (57.8)	4,289 (57.0)	552 (20.8)	488 (67.7)	277 (49.8)	187 (41.8)	209 (100)	<0.001
Insurance									<0.001
Medicare	14,174 (50.4)	8,767 (49.2)	4,040 (53.7)	555 (20.9)	316 (43.8)	187 (33.6)	113 (25.3)	23 (11.0)	
Medicaid	2,753 (9.8)	1,748 (9.8)	721 (9.6)	536 (20.2)	74 (10.3)	86 (15.5)	90 (20.1)	76 (36.4)	
Other	7,277 (25.9)	5,128 (28.8)	1,954 (26.0)	620 (23.4)	271 (37.6)	191 (34.4)	155 (34.7)	76 (36.7)	
None	2,067 (7.4)	1,006 (5.7)	349 (4.6)	716 (27.0)	22 (3.1)	60 (10.8)	52 (11.6)	18 (8.6)	
Medical history									
COPD/asthma	7,641 (27.7)	5,011 (28.6)	2,193 (29.5)	743 (29.2)	170 (24.2)	149 (27.2)	106 (24.5)	41 (20.0)	<0.001
Atrial fibrillation	8,314 (30.1)	5,896 (33.7)	2,901 (39.1)	494 (19.4)	158 (22.5)	146 (26.6)	88 (20.4)	8 (3.9)	<0.001
Diabetes	10,976 (39.7)	6,515 (37.2)	2,542 (34.2)	564 (22.1)	184 (26.2)	216 (39.4)	116 (26.9)	34 (16.6)	<0.001
Hypertension	25,504 (92.3)	11,957 (68.3)	4,183 (56.3)	1,775 (69.7)	419 (59.6)	365 (66.6)	216 (50.0)	114 (55.6)	<0.001
Hyperlipidemia	9,888 (35.8)	5,734 (32.8)	2,340 (31.5)	590 (23.2)	169 (24.0)	165 (30.1)	103 (23.8)	16 (7.8)	<0.001
Stroke/TIA	3,375 (12.2)	2,103 (12.0)	903 (12.2)	162 (6.4)	42 (6.0)	62 (11.3)	21 (4.9)	13 (6.3)	<0.001
PVD	1,846 (6.7)	1,259 (7.2)	522 (7.0)	95 (3.7)	31 (4.4)	35 (6.4)	12 (2.8)	4 (2.0)	<0.001
Renal insufficiency	5,550 (20.1)	2,561 (14.6)	1,405 (18.9)	345 (13.6)	89 (12.7)	82 (15.0)	59 (13.7)	10 (4.9)	<0.001
Anemia	5,099 (18.5)	3,066 (17.5)	1,483 (20.0)	339 (13.3)	180 (25.6)	62 (11.3)	62 (14.4)	40 (19.5)	<0.001
Smoking	4,435 (15.8)	2,900 (16.3)	1,103 (14.7)	1,656 (62.4)	108 (15.0)	134 (24.1)	138 (30.9)	76 (36.4)	<0.001
Admission characteristics									
SBP, mm Hg	147 (127-171)	138 (119-159)	132 (114-151)	138 (118-160)	128 (109-146)	134 (116-157)	124 (109-145)	124 (108-145)	<0.001
Heart rate, beats/min	85 (72-100)	86 (73-101)	86 (72-100)	96 (82-110)	92 (79-107)	86 (74-100)	95 (77-109)	99 (85-111)	<0.001
BMI, kg/m ²	29 (24-36)	29 (24-36)	28 (24-35)	28 (24-34)	27 (23-32)	30 (24-37)	28 (24-35)	32 (26-38)	<0.001
Ejection fraction, %	50 (30-59)	45 (25-55)	48 (28-57)	25 (16-40)	30 (20-50)	40 (25-55)	23 (15-35)	22 (16-30)	<0.001
Ejection fraction <40%	10,099 (35.9)	7,212 (40.5)	72,838 (37.7)	1,925 (72.6)	426 (59.1)	262 (47.1)	344 (77.0)	174 (83.3)	<0.001
BNP, pg/dl	694 (300-1,490)	697 (346-1,440)	768 (378-1,540)	1,010 (374-2,249)	834 (171-1,820)	667 (317-1,395)	878 (401-1,549)	690 (289-1,823)	<0.001
Creatinine, mg/dl	1.3 (1.0-1.8)	1.2 (0.9-1.7)	1.2 (0.9-1.7)	1.2 (1.0-1.6)	1.1 (0.8-1.5)	1.2 (0.9-1.5)	1.2 (0.9-1.6)	0.9 (0.7-1.1)	<0.001
Hospital characteristics									
Rural	1,205 (4.3)	945 (5.3)	423 (5.6)	43 (1.6)	34 (4.7)	47 (8.5)	7 (1.6)	4 (1.9)	<0.001
Region									<0.001
West	9,965 (35.4)	2,106 (11.8)	1,353 (18.0)	726 (27.4)	92 (12.8)	97 (17.5)	114 (25.5)	31 (14.8)	
South	7,967 (28.3)	7,138 (40.1)	2,970 (39.5)	619 (23.3)	219 (30.4)	331 (59.5)	137 (30.7)	86 (41.2)	
Midwest	4,520 (16.1)	5,504 (30.9)	1,597 (21.2)	505 (19.0)	184 (25.5)	69 (12.4)	99 (22.2)	45 (21.5)	
Northeast	5,689 (20.2)	3,060 (17.2)	1,603 (21.3)	803 (30.3)	226 (31.4)	59 (10.6)	97 (21.7)	47 (22.5)	
Academic hospitals	17,205 (61.1)	12,103 (68.0)	4,675 (62.1)	2,016 (76.0)	517 (71.7)	231 (41.6)	306 (68.5)	175 (83.7)	<0.001
Number of beds	372 (244-559)	431 (300-566)	372 (245-593)	425 (342-575)	438 (290-593)	395 (225-610)	431 (328-593)	555 (410-656)	<0.001

Values are median (interquartile range) or n (%).
 Abbreviations as in Table 1.

across various NICM etiology subtypes. Furthermore, the odds for receipt of 100% defect-free care remained similar across various NICM etiologies despite adjustment for aforementioned covariates. (Online Table 2).

IN-HOSPITAL CLINICAL OUTCOMES. Mortality. Table 5 shows rates of in-hospital mortality and other clinical outcomes in patients with ischemic cardiomyopathy compared with NICM patients. There were no significant differences in all-cause mortality rates between

	Ischemic Cardiomyopathy (n = 92,361)	Nonischemic Cardiomyopathy* (n = 63,652)	p Value
Achievement measures			
Discharged with appropriate instruction	65,065 (90.5)	45,115 (89.8)	<0.0001
LV function documented	82,102 (97.5)	56,896 (97.2)	0.0001
Patients with LVSD discharged on ACEI/ARB	28,863 (90.7)	18,862 (93.0)	<0.0001
Patients with LVSD discharged on beta-blockers	36,532 (94.9)	20,922 (93.9)	<0.0001
Smokers discharged with smoking cessation counseling	13,156 (95.8)	10,535 (96.3)	0.075
Composite performance measures			
100% defect-free care	72,586 (85.4)	50,438 (85.3)	0.63
Quality measures			
Patients with atrial fibrillation discharged on anticoagulation	18,494 (67.6)	12,477 (71.5)	<0.0001
Patients with LVSD discharged on aldosterone antagonist	11,440 (31.4)	7,458 (34.5)	<0.0001
Black patients with LVSD discharged on hydralazine/nitrate	1,911 (27.9)	1,849 (22.1)	<0.0001
DVT prophylaxis	16,567 (68.5)	10,889 (70.8)	<0.0001
Influenza vaccine during flu season	18,252 (45.4)	10,789 (39.0)	<0.0001
Pneumococcal vaccination	35,741 (45.5)	20,320 (37.9)	<0.0001
Procedures			
Cardiac resynchronization therapy-defibrillator	2,721 (3.1)	1,270 (2.1)	<0.0001
Implantable cardioverter defibrillator only	2,955 (3.4)	1,494 (2.5)	<0.0001

Values are n (%). *Includes all patients with NICM irrespective of whether further etiology was classified.
ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; DVT = deep vein thrombosis; LV = left ventricle; LVSD = left ventricular systolic dysfunction; NICM = nonischemic cardiomyopathy.

the 2 groups. **Table 6** shows unadjusted rates and multivariable-adjusted rates of in-hospital clinical outcomes among patients stratified by NICM etiologies. Overall, among NICM patients, there were 1,491 in-hospital deaths (2.6%) from 2005 to 2013.

The unadjusted rate of in-hospital deaths was lowest in patients with post-partum cardiomyopathy (1.0%, n = 2) and highest in patients with chemotherapy-induced NICM (3.7%, n = 27). Results of our multivariable analyses showed that compared

	NICM Etiology								p Value
	Hypertension (n = 28,141)	Idiopathic (n = 17,808)	Other (n = 7,523)	Substance Abuse (n = 2,653)	Chemotherapy (n = 721)	Familial (n = 556)	Viral (n = 447)	Post-Partum (n = 209)	
Achievement measures									
Discharged with appropriate instruction	20,288 (91)	12,043 (88)	5,239 (90)	2,237 (93)	554 (92)	438 (89)	367 (93)	196 (95)	<0.001
LV function documented	25,457 (97)	15,649 (97)	6,553 (97)	2,497 (99)	632 (98)	512 (98)	415 (99)	206 (100)	<0.001
Patients with LVSD discharged on ACEI/ARB	7,551 (93)	5,357 (92)	1,975 (93)	1,561 (95)	288 (91)	205 (95)	270 (96)	153 (96)	<0.001
Patients with LVSD discharged on beta-blockers	8,478 (94)	2,244 (95)	5,823 (93)	1,641 (96)	351 (96)	217 (95)	288 (96)	159 (98)	<0.001
Smokers discharged with smoking cessation counseling	4,140 (96)	2,654 (96)	1,009 (96)	1,559 (97)	101 (100)	121 (93)	130 (97)	75 (100)	0.01
Composite performance measures									
100% defect-free care	22,965 (86)	13,489 (81)	5,891 (86)	2,208 (86)	554 (84)	436 (82)	375 (88)	188 (91)	<0.001
Quality measures									
Patients with atrial fibrillation discharged on anticoagulation	5,128 (71)	3,713 (71)	1,739 (74)	289 (68)	82 (65)	103 (75)	65 (86)	8 (100)	0.003
Patients with LVSD discharged on aldosterone antagonist	2,650 (31)	2,034 (32)	909 (41)	747 (4)	128 (37)	96 (43)	149 (51)	93 (58)	<0.001
Black patients with LVSD discharged on hydralazine/nitrate	887 (23)	388 (20)	176 (25)	199 (22)	14 (16)	22 (29)	18 (20)	18 (16)	0.011
DVT prophylaxis	4,589 (71)	3,166 (71)	1,524 (74)	371 (73)	132 (76)	86 (68)	55 (60)	28 (67)	0.01
Influenza vaccine during flu season	4,947 (40)	2,862 (37)	1,434 (47)	389 (35)	123 (42)	110 (44)	66 (31)	25 (29)	<0.001
Pneumococcal vaccination	9,380 (39)	5,294 (36)	2,847 (47)	738 (32)	226 (40)	178 (38)	110 (28)	39 (21)	<0.001

Values are n (%).
Abbreviations as in **Table 3**.

TABLE 5 Comparison of In-Hospital Outcomes in Patients With Ischemic Compared With Nonischemic Cardiomyopathy

	Number of Events in Patients With Ischemic Cardiomyopathy (n = 92,361)	Number of Events in Patients With Nonischemic Cardiomyopathy* (n = 63,652)	Adjusted OR (95% CI) in Patients With Ischemic Cardiomyopathy†
In-hospital mortality	2,772 (3.0)	1,648 (2.6)	1.08 (1.00-1.15)
Median length of stay >4 days	36,488 (44.3)	25,321 (43.9)	0.97 (0.95-1.00)
Discharge home	69,660 (77.8)	49,123 (79.2)	1.08 (1.03-1.14)
Cardiac transplant	13 (0.01)	27 (0.04)	0.71 (0.40-1.23)
Defect-free care	72,586 (85.4)	50,438 (85.3)	1.04 (1.01-1.07)

Values are n (%), except as noted. *Includes all patients with NICM irrespective of whether further etiology was classified. †Patients with NICM were the reference group. Model was adjusted for demographics, including age, sex, race/ethnicity, insurance status, body mass index; medical history, including atrial arrhythmia, diabetes, hypertension, smoking, hyperlipidemia, hypertension, lung disease, stroke/transient ischemic attack, peripheral vascular disease, renal insufficiency, depression, valvular heart disease; presentation characteristics, including systolic blood pressure, ejection fraction, heart rate; and hospital characteristics, including region, urban versus rural location, number of beds, academic status.

CI = confidence interval; NICM = nonischemic cardiomyopathy; OR = odds ratio.

with idiopathic NICM, in-hospital mortality was lower only in patients with hypertensive cardiomyopathy (adjusted OR: 0.83; 95% confidence interval [CI]: 0.71 to 0.97).

Length of stay and hospital to home discharge rates. Compared with patients with NICM, patients with ischemic cardiomyopathy were as likely to have a median length of stay >4 days, but were more likely to be discharged home (Table 5). Median length of hospital stay was 4 days, without appreciable differences between various NICM etiologies (Table 6). The majority of post-partum (99.5%) and substance abuse (92.8%) cardiomyopathy patients were discharged home, with lower home discharge rates seen among patients with idiopathic (78.0%) and other (77.3%) cardiomyopathies.

In the multivariable-adjusted model, the odds for length of stay >4 days were similar to that of idiopathic NICM for all other etiologies. However, compared with idiopathic cardiomyopathy, only patients with chemotherapy-induced cardiomyopathy

had higher odds of being discharged home (adjusted OR: 1.45; 95% CI: 1.20 to 1.76).

Cardiac transplant. Cardiac transplant in our study population was performed in only 40 cases, of whom 13 patients had ischemic cardiomyopathy and 27 had NICM. Following multivariable adjustment, there were no statistically significant differences in the odds of receiving cardiac transplant between the 2 groups.

DISCUSSION

The objective of this study was to describe the prevalence of various etiologies of cardiomyopathy, including subtypes of NICM, their temporal trends, characteristics, and in-hospital outcomes in a contemporary population of hospitalized HF patients. We observed that the majority of patients had ischemic cardiomyopathy. The commonest cause of NICM was hypertension followed by idiopathic etiology, without significant differences in their

TABLE 6 Association Between In-Hospital Clinical Outcomes and NICM Etiology

	In-Hospital Mortality		Median Length of Stay >4 Days		Home to Hospital Discharge		
	Events	Adjusted OR* (95% CI)	Events	Adjusted OR* (95% CI)	Events	Adjusted OR* (95% CI)	Transplant Events
Hypertension	572 (2.0)	0.83 (0.71-0.97)	11,070 (39.3)	1.01 (0.95-1.07)	21,811 (79.1)	1.05 (0.96-1.15)	2 (0.01)
Idiopathic	556 (3.1)	1.00 (reference)	7,150 (40.2)	1.00 (reference)	13,450 (78.0)	1.00 (reference)	11 (0.1)
Other	258 (3.4)	0.98 (0.83-1.16)	3,011 (40.0)	1.03 (0.94-1.12)	5,615 (77.3)	1.04 (0.95-1.14)	7 (0.1)
Substance abuse	54 (2.0)	1.11 (0.78-1.56)	1,018 (38.4)	1.09 (0.99-1.20)	2,412 (92.8)	0.95 (0.77-1.16)	1 (0.04)
Chemotherapy	27 (3.7)	1.23 (0.86-1.77)	285 (39.5)	0.96 (0.81-1.14)	600 (86.5)	1.45 (1.20-1.76)	2 (0.3)
Familial	12 (2.2)	1.04 (0.63-1.71)	209 (37.6)	0.94 (0.79-1.13)	478 (87.9)	1.26 (0.77-2.06)	0
Viral	10 (2.2)	0.98 (0.50-1.91)	169 (37.8)	1.10 (0.89-1.35)	391 (89.5)	0.97 (0.66-1.41)	2 (0.5)
Post-partum	2 (1.0)	0.58 (0.12-2.91)	65 (31.1)	0.87 (0.67-1.14)	206 (99.5)	5.67 (0.66-49.04)	1 (0.5)

Values are n (%), except as noted. *Model was adjusted for demographics, including age, sex, race/ethnicity, insurance status, body mass index; medical history, including atrial arrhythmia, diabetes, hypertension, smoking, hyperlipidemia, hypertension, lung disease, stroke/transient ischemic attack, peripheral vascular disease, renal insufficiency, depression, valvular heart disease; presentation characteristics, including systolic blood pressure, ejection fraction, and heart rate; and hospital characteristics, including region, urban versus rural location, number of beds, and academic status.

Abbreviations as in Table 5.

prevalence over the duration of this study. Furthermore, as expected, there were significant differences in demographic and clinical characteristics of patients with ischemic as compared with NICM, as well as between various NICM etiologies. Patients with hypertensive cardiomyopathy had the highest EF, with a median EF of 47%, suggesting that the majority of these patients had HF with preserved ejection fraction. Additionally, the majority of NICM patients received guideline-concordant therapies, without significant differences between various etiologies following multivariable adjustment. Examination of in-hospital outcomes did not suggest significant differences, with the exception of a lower mortality rate in patients with hypertensive cardiomyopathy compared with those with idiopathic cardiomyopathy. Finally, comparison of treatment characteristics between patients with ischemic cardiomyopathy and NICM did not reveal clinically meaningful differences. Similarly, in-hospital mortality was similar between patients with ischemic cardiomyopathy and NICM; however, patients with ischemic cardiomyopathy were more likely to be discharged home.

PRIOR STUDIES. Traditionally, hypertension has been described as the most prevalent HF risk factor (7-10). Inasmuch as we know, previous studies have, however, reported idiopathic cardiomyopathy as the commonest NICM etiology, with the majority of hypertensive patients having ischemic cardiomyopathy (11-17). In the SOLVD (Studies Of Left Ventricular Dysfunction) registry, of a total of 6,273 patients with congestive HF between 1988 and 1989, the commonest NICM etiology was idiopathic cardiomyopathy, seen in 17% of the total population, followed by hypertensive cardiomyopathy in 7% of the entire cohort (11). In the Italian Network on HF registry established in 1995, the commonest NICM etiology was idiopathic cardiomyopathy, seen in 36%, followed by hypertension in 13% (4). Similarly, in a cohort of 220 patients with incident HF in London in 1995, the commonest NICM etiology was idiopathic cardiomyopathy (34%) followed by hypertension (14%) (16). [Online Table 3](#) summarizes other previous studies evaluating HF etiologies. Contrary to these previous observations, examination of NICM etiologies in our population of hospitalized HF patients showed that the most prevalent etiology was hypertensive cardiomyopathy.

Long-standing and uncontrolled hypertension is frequently associated with abnormalities of cardiac structure or function, including left ventricular hypertrophy and systolic and diastolic dysfunction, subsequently leading to overt HF (18). Hypertensive

heart disease has been excluded from various HF classification systems in a pragmatic attempt to refocus attention to primary genetic disorders (19-21). Unfavorable trends in awareness, treatment, and control of hypertension have been recently documented, potentially leading to an increase in the population-attributable risk of hypertension for HF (22,23). For example, in Olmsted County, there was no evidence of a change in the HF population-attributable risk with coronary artery disease, diabetes, or smoking. However, during the same time period, the HF population-attributable risk of hypertension increased from 15% in 1979 to 1984 to 29% in 1979 to 2002 (8).

In previous studies, estimates of idiopathic cardiomyopathy vary, ranging from 21% to 50%, as highlighted in [Online Table 3](#). In our cohort, it was the second most common etiology for NICM, with a prevalence of 30.67%. This likely reflects differences in the composition of our population compared with other studies that have predominantly focused on heart failure with reduced EF.

Among rarer causes of HF, we found a prevalence of 4.57% for substance abuse-induced cardiomyopathy. Two previous reports provide estimates similar to ours (15,24). Estimates of other rarer forms of cardiomyopathy, such as familial, are limited to subsets of HF patients and hence are difficult to extrapolate to our cohort of all patients with HF (25-27).

STUDY IMPLICATIONS. To the best of our knowledge, our study is one of the largest contemporary studies characterizing patients with ischemic cardiomyopathies and various etiologies of NICM with their in-hospital outcomes. Previous reports have been limited to small cohorts or patients enrolled in HF trials that typically enroll younger patients with systolic left ventricular dysfunction leading to limitations with their external validity ([Online Table 3](#)). Our study also highlights contemporary treatment practices in HF patients, demonstrating that over 90% of patients receive appropriate guideline-concordant therapies during hospitalization without any significant differences in treatment provided for various etiologies.

In addition, we found a lower adjusted in-hospital mortality among patients with hypertensive cardiomyopathy and comparable in-hospital outcomes among all other NICM etiologies. Accordingly, characterization of NICM etiology may help guide prognosis and help target higher-risk populations more aggressively. Furthermore, it may be postulated that due to the high rates of appropriate therapy use, in-hospital outcomes were similar across various etiologies.

STUDY LIMITATIONS. Our findings should be interpreted in the light of several considerations. First, generalizability of our results is limited to in-hospital patients and hospitals participating in the GWTG-HF registry. However, a previous study has shown that HF patients hospitalized at GWTG-HF hospitals have characteristics similar to hospitals nationwide (28). Second, we relied on HF etiology as extracted through chart review on the data collection form that was not available for all patients enrolled. This may introduce misclassification and selection bias. Nonetheless, detailed clinical information including laboratory, vital sign, and medication data not present in administrative billing data are recorded in this registry. Third, our classification of HF etiology does not conform to previously described classification systems. However, classification of HF etiology is currently evolving with several different systems being proposed by various societies (19,29). Furthermore, previous attempts to study HF etiologies have also not conformed to traditional classification systems. Fourth, as with all observational studies, there remains potential confounding by factors that we could not account for in our examination of in-hospital outcomes and treatment decisions made. Fifth, for certain etiologies, the sample size was small, requiring cautious interpretation of our regression estimates. Finally, lack of follow-up data after discharge and duration of heart failure therapy remain limitations in our study.

CONCLUSIONS

Using data from a large, national, prospective cohort of hospitalized HF patients, we identified that the most prevalent etiology for HF was ischemic

cardiomyopathy. Among patients with NICM, the commonest etiology was hypertensive cardiomyopathy, followed by idiopathic cardiomyopathy. Examination of temporal trends in etiology from 2005 to 2013 demonstrates no significant changes. Additionally, cardiomyopathy etiology did not influence physician decision making in terms of providing guideline concordant care. In-hospital mortality was similar by cardiomyopathy etiology with the exception that among NICM patients, hypertensive cardiomyopathy was associated with lower in-hospital risk-adjusted mortality compared with idiopathic cardiomyopathy.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The most common etiology for NICM in our study cohort was hypertensive heart disease followed by idiopathic. Evaluation of temporal trends showed no significant changes in their yearly prevalence. Furthermore, treatment characteristics and in-hospital outcomes were similar across various etiologies with the exception of hypertensive cardiomyopathy, which was associated with lowest rates of in-hospital mortality.

TRANSLATIONAL OUTLOOK: Further studies should evaluate whether differences exist in long-term outcomes across various NICM etiologies.

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KEY WORDS HF etiology, ischemic cardiomyopathy, nonischemic cardiomyopathy, outcome

APPENDIX For a supplemental figure and tables, please see the online version of this paper.