Clinical Characteristics of Young Patients With Heart Failure With Reduced Ejection Fraction in a Racially Diverse Cohort

Ignacio Zepeda, MD,* Dan L. Li, MD, PhD,* Renato Quispe, MD, MHS,* and Cynthia C. Taub, MD†

Background: Information on the clinical and echocardiographic characteristics of young patients with heart failure with reduced ejection fraction is scant, especially among racially diverse populations.

Methods: Patients admitted to Montefiore Medical Center between 2000 and 2016 with heart failure and ejection fraction of <40% were categorized as young (18–39 years), middle-aged (40–64 years), and elderly (≥65 years). Multivariable Cox regression models were used to evaluate mortality risk.

Results: A total of 1032 young, 8336 middle-aged, and 13,315 elderly patients were included. Median follow-up was 36 (14–69) months. The young group had more black individuals, lower socioeconomic scores, larger left ventricular chambers, but lower N-terminal pro B-type natriuretic peptide levels (P < 0.001). Better survival outcomes were observed in the young compared to the middle-aged [hazard ratio (HR), 1.52; 95% confidence interval (CI), 1.31–1.77] and elderly (HR, 3.19; 95% CI, 2.75–3.70). After multivariable adjustments, only β-blockers were associated with a significant reduction of mortality in young patients (HR, 0.33; 95% CI, 0.22–0.51).

Conclusion: In conclusion, young patients with heart failure with reduced ejection fraction have distinct demographic, clinical, and echocardiographic characteristics. They had lower socioeconomic status yet received more aggressive treatments and had lower mortality rates. Only β-blockers were associated with improved survival in young patients from our cohort.

Key Words: echocardiography, HFrEF, mortality, race

Although heart failure (HF) with reduced ejection fraction (HFrEF) is well described in the elderly, there is a paucity of information regarding the characteristics of HF in the young, likely due to its lower prevalence in patients younger than 40 years of age.1 To date, 3 post hoc analyses of clinical trials have focused on young patients with HFrEF;2-4 which showed that young patients have milder symptoms, less remarkable clinical and radiological signs, but more severe left ventricular (LV) dysfunction. Readmission rates in young patients are similar to those of older patients,1 but survival rates are higher;2,4 These 3 studies, however, offered little information on racial and socioeconomic background of young patients with HFrEF. There were only 14 young patients in the Coronary Artery Risk Development in Young Adults (CARDIA) cohort2 and 84 in the Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity (CHARM) trial,3 the latter consisting of mostly white patients.1

Although the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) study included 718 young patients with HFrEF, it did not assess racial differences.4 In addition, none reported N-terminal pro B-type natriuretic peptide (NT-proBNP) levels or echocardiographic data beyond ejection fraction (EF) and LV mass index. Furthermore, therapeutic decisions for young patients with HF are currently extrapolated from landmark clinical trials for HF that mostly included older patients (mean age, ≈50–60 years old),5-13 who may have different primary etiologies and pathophysiological mechanisms. Therefore, we aim to describe the clinical and echocardiographic characteristics of the largest cohort to date of racially diverse patients with HFrEF younger than 40 years, in addition to the association between HF therapies and outcomes.

METHODS

This is a retrospective cohort study of patients hospitalized in Montefiore Medical Center, Bronx, NY. The study was reviewed and approved by the Institutional Review Board of Montefiore Medical Center and Albert Einstein College of Medicine. There were no financial sponsors for this study.

We included adult patients (age ≥18 years) with a diagnosis of HF (by International Classification of Diseases [ICD]-9 codes) upon inpatient discharge from the Montefiore Health System, Bronx, NY, between January 1, 2000, and December 31, 2016, with an echocardiogram showing an EF of less than 40% at the time of diagnosis. For patients who had multiple hospitalizations during that period, the first admission was selected. The cohort was divided into 3 age groups, the young (18–39 years), the middle-aged (40–64 years), and the elderly (≥65 years).

Demographic and clinical information was collected from electronic medical record via Clinical Looking Glass, a clinical analytic system used at Montefiore Health System. Baseline demographic data included age, sex, self-reported race/ethnicity, and socioeconomic status (SES). SES was a summary Z-score that combined wealth, income, and education level; it was presented as above (positive) or below (negative) mean SES in New York State. Other clinical data included reported cardiac diseases (eg, ischemic heart disease, dilated cardiomyopathy, valvular heart disease, alcoholic and peripartum cardiomyopathy), chronic comorbidities (eg, hypertension, diabetes, atrial fibrillation, chronic kidney disease, etc), additional diagnostic tests (NT-proBNP and echocardiographic measurements), and treatments such as guideline-directed medications prescribed within 6 months of discharge of the index admission, automatic implantable cardioverter defibrillator placement, LV assist device, and heart transplantation within 5 years of the index admission.

The end of the follow-up period was December 31, 2017. Median follow-up was 36 (14–69) months. The outcome was all-cause mortality.

Clinical characteristics were summarized in descriptive statistics. Continuous variables were shown either as mean ± SD for normally distributed data or median with interquartile range for data following non-normal distribution. Categorical variables were presented as number of patients and frequencies (%). Comparisons were conducted among groups using 1-way analysis of variance test for continuous variables and Pearson χ² test for categorical variables.
Kaplan-Meier curves were used to analyze the cumulative probabilities of all-cause mortality. Unadjusted Cox proportional models were performed to compare risk of all-cause mortality among different age groups, and multivariable Cox regression models were constructed to assess the predictors of mortality in the 3 age groups. A 2-sided \( P \) value \( \leq 0.05 \) was considered statistically significant. Analyses were conducted using STATA 13 (StataCorp, College Station, TX).

RESULTS

Of the 22,683 patients included, 1032 (4.6%) were in the young age group, 8336 (36.7%) in the middle-age group, and 13,315 (58.7%) in the elderly group. The baseline clinical characteristics are shown in Table 1. The proportions of Hispanic (25.9%) and non-Hispanic black (43.7%) patients were significantly higher in the young group compared with their counterparts. On the other hand, the proportion of white patients was significantly higher in the elderly group compared to young and middle-age groups. The young group had a significantly lower SES score than older age groups (Table 1).

Ischemic heart disease in young patients was not as common as it was in middle-aged or elderly patients: 14.1% vs. 43.7% and 59%, respectively \((P < 0.001)\). In contrast, a significantly larger proportion of young patients had dilated cardiomyopathy (36% vs. 24.8% and 15.7% in middle-age and elderly patients, respectively; \( P < 0.001 \). HF was attributable to alcoholic cardiomyopathy (1.65%) and peripartum cardiomyopathy (7.8% of female patients) in a small but significantly larger proportion of young patients than that of the older groups (Table 1). The presence of hypertension was remarkably high in the young group (40.8%) albeit lower than the middle-aged (63.4%) and elderly (73.3%) groups. Cocaine abuse was highest in the middle-age group (8.7%), followed by the young group (5.5%), and lowest in the elderly group. Other chronic comorbidities, including diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, malignancy, peripheral vascular disease, and valvular heart disease, were significantly lower among the young patients compared to other age groups (Table 1).

### TABLE 1. Baseline Patient Characteristics by Age Group

|                   | Young (\( n = 1032 \)) | Middle-aged (\( n = 8336 \)) | Elderly (\( n = 13,315 \)) | \( P \)   |
|-------------------|------------------------|-------------------------------|----------------------------|---------|
| Percentage of total | 4.55%                  | 36.7%                         | 58.7%                      | <0.001  |
| Age (mean ± SD)    | 32.5 ± 5.5             | 54.9 ± 6.5                    | 77.8 ± 8.3                 | <0.001  |
| Male, n (%)        | 624 (60.5)             | 5323 (63.9)                   | 6848 (51.4)                | <0.001  |
| Race, n (%)        |                        |                               |                            | <0.001  |
| White              | 72 (6.9%)              | 1160 (13.9%)                  | 4179 (31.3%)               |         |
| Non-Hispanic black | 451 (43.7%)            | 3095 (37.1%)                  | 3655 (27.4%)               |         |
| Hispanic           | 268 (25.9%)            | 2035 (24.4%)                  | 2667 (20.0%)               |         |
| Other races        | 241 (23.3%)            | 2046 (24.5%)                  | 2814 (21.1%)               |         |
| SES score, median* (interquartile ratio) | -3.2 (-6.4 to -1.25) | -2.7 (-6.17 to -1.09) | -1.9 (-5.2 to -0.7) | <0.001  |
| Comorbidities, n (%) |                       |                               |                            |         |
| MI                 | 104 (10.0%)            | 2146 (25.7%)                  | 4264 (32.0%)               | <0.001  |
| PVD                | 46 (4.4%)              | 884 (10.6%)                   | 2276 (17.0)                | <0.001  |
| Stroke             | 61 (5.9%)              | 797 (9.5%)                    | 2046 (15.3%)               | <0.001  |
| COPD               | 275 (26.5%)            | 2617 (31.3%)                  | 4582 (34.3%)               | <0.001  |
| Malignancy         | 39 (3.7%)              | 465 (5.5%)                    | 1313 (9.8%)                | <0.001  |
| IHD                | 146 (14.1%)            | 3648 (43.7%)                  | 7868 (59.0%)               | <0.001  |
| DCM                | 372 (36.0%)            | 2070 (24.8%)                  | 2089 (15.7%)               | <0.001  |
| VHD                | 191 (18.5%)            | 1659 (19.9%)                  | 3682 (27.6%)               | <0.001  |
| Alcoholic CM       | 17 (1.6%)              | 121 (1.4%)                    | 44 (0.3%)                  | <0.001  |
| Peripartum CM      | 32 (7.8%)†             | 3 (0.04%)                     | 0 (0%)                     | <0.001  |
| Cocaine abuse      | 57 (5.5%)              | 728 (8.7%)                    | 131 (0.9%)                 | <0.001  |
| AF                 | 114 (11.0%)            | 1844 (22.1%)                  | 5322 (40.0%)               | <0.001  |
| HTN                | 422 (40.8%)            | 5290 (63.4%)                  | 9765 (73.3%)               | <0.001  |
| DM                 | 171 (16.5%)            | 3400 (40.7%)                  | 5646 (42.4%)               | <0.001  |
| CKD                | 199 (19.2%)            | 2170 (26.0%)                  | 4445 (33.3%)               | <0.001  |
| HIV                | 137 (4.9%)             | 662 (4.1%)                    | 101 (0.5%)                 | <0.001  |
| NT-proBNP, median* (interquartile ratio) | 2840 (888 to 7436) | 3137 (1109 to 9173) | 5616 (2074 to 14890) | <0.001  |

*By Kruskal-Wallis method.
†Percentage of females only.

AF indicates atrial fibrillation; alcoholic CM, alcoholic cardiomyopathy; CKD, chronic kidney disease; DCM, dilated cardiomyopathy; DM, diabetes mellitus; HIV, human immunodeficiency virus; HTN, hypertension; IHD, ischemic heart disease; MI, myocardial infarction; peripartum CM, peripartum cardiomyopathy; PVD, peripheral vascular disease; VHD, valvular heart disease.
diuretics, β-blockers, angiotensin-converting enzyme inhibitors (ACEI), aldosterone receptor blockers (ARB), and combination hydralazine/isosorbide were similar among the young and middle-aged groups and higher than the elderly group (Table 3; Fig. 1). Only mineralocorticoid receptor antagonists were prescribed in a significantly higher proportion of young patients (28.4% vs. 20.7% and 11.5% in the middle-aged and elderly groups, respectively, Table 3).

The same trend between age groups was seen when comparing patients receiving automatic implantable cardioverter defibrillator. Young patients were more likely to receive LV assist device and heart transplantation than middle-aged and elderly patients (Table 3).

In a median follow-up time of 36 months (interquartile range, 14–69 months), there were 7620 deaths overall. Middle-aged [HR, 1.52; 95% confidence interval (CI), 1.31–1.77] and elderly patients (HR, 3.19; 95% CI, 2.75–3.70) had significantly higher risk of mortality compared with the young group (Fig. 2).

In multivariable analysis, use of a β-blocker was associated with significantly lower risk of mortality in the young group (HR, 0.33; 95% CI, 0.22–0.51) as well as in the middle-age (HR, 0.65; 95% CI, 0.57–0.74) and elderly groups (HR, 0.76; 95% CI, 0.70–0.82). In contrast, the use of an ACEI or ARB portended a significantly reduced risk of mortality in middle-age (HR, 0.76; 95% CI, 0.67–0.85) and elderly individuals (HR, 0.81; 95% CI, 0.76–0.87) but not in the young group (HR, 1.39; 95% CI, 0.92–2.11; Table 4).

## DISCUSSION

We present an observational retrospective analysis of young patients with HFrEF in a single tertiary care center with a racially diverse population. Our data provide valuable clinical and epidemiologic information derived from the largest number of young patients with HFrEF in the literature. Our study had several important findings. First, we found that young patients with HFrEF were more likely non-Hispanic black and Hispanic rather than white and had lower SES compared with older age groups. Second, our data revealed that young patients had lower NT-proBNP than older populations despite worse LV dilatation. Last, we showed remarkable differences with regards to HF medications and risk of mortality: β-blockers were associated with significantly reduced mortality in comparison to older groups, whereas the use of ACEI/ARB was associated with reduced mortality in older groups but not in young patients.

In our cohort, young patients with HFrEF were more often male and black, consistent with previous studies. Notably, the proportion of white patients with HFrEF increased with age, the proportion of black patients with HFrEF decreased with age, whereas the proportion of Hispanic patients remained stable across age groups. This distribution may be partly explained by the higher prevalence of idiopathic dilated cardiomyopathy in black patients although it could also be due to higher survival rates in white HF patients compared to other races as previously reported. In addition, the term “Hispanic” refers to a place of origin and can include white, black, and native Americans. The racial heterogeneity in this denomination

---

**TABLE 2. Echocardiographic Measurements**

|                    | Young (n = 1032) | Middle-aged (n = 8336) | Elderly (n = 13,315) | P     |
|--------------------|------------------|------------------------|----------------------|-------|
| Echocardiography, median (IQR) |                   |                        |                      |       |
| EF (%)             | 30 (20–35)       | 30 (20–35)             | 31 (25–35.5)         | <0.001|
| LVESD (mm)         | 48 (39–57)       | 45 (37–53)             | 40 (33–48)           | <0.001|
| Missing data, n (%)| 246 (23)         | 1937 (23)              | 3546 (26)            |       |
| LVEDD (mm)         | 59 (52–66)       | 56 (50–62)             | 52 (46–58)           | <0.001|
| Missing data, n (%)| 108 (10)         | 835 (10)               | 1551 (11)            |       |
| LAV (mL)           | 76 (55.8–105)    | 73.8 (54.7–96.2)       | 72 (55.8–93.4)       | <0.05 |
| Missing data, n (%)| 605 (58)         | 4979 (59)              | 8086 (60)            |       |

IQR indicates interquartile range; LAV, left atrial volume; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter.

---

**TABLE 3. Comparison of Heart Failure Treatments Between Age Groups**

|                    | Young (n = 1032) | Mid-Aged (n = 8336) | Elderly (n = 13,315) | P     |
|--------------------|------------------|---------------------|----------------------|-------|
| HF therapies, n (%)|                   |                      |                      |       |
| Diuretics          | 489 (47.3%)      | 4153 (49.8%)        | 6172 (46.3%)         | <0.001|
| β-blockers         | 690 (66.8%)      | 5603 (67.2%)        | 7597 (57.0%)         | <0.001|
| ACEI/ARB           | 605 (58.6%)      | 4898 (58.7%)        | 6146 (46.1%)         | <0.001|
| H/I                | 196 (18.9%)      | 1417 (17.0%)        | 1654 (12.4%)         | <0.001|
| MRA                | 294 (28.4%)      | 1731 (20.7%)        | 1531 (11.5%)         | <0.001|
| AICD (in 10 years) | 196 (19.0%)      | 1795 (21.5%)        | 1892 (14.2%)         | <0.001|
| LVAD               | 25 (2.4%)        | 83 (1%)             | 25 (0.2%)            | <0.001|
| Heart transplant (in 10 years) | 55 (5.3%) | 200 (2.4%)         | 49 (0.37%)           | <0.001|
| Other therapies, n (%)|                |                      |                      |       |
| ASA                | 336 (32.5%)      | 4526 (54.2%)        | 6396 (48.0%)         | <0.001|
| Statins            | 241 (23.3%)      | 4192 (50.2%)        | 6409 (48.1%)         | <0.001|
| Anticoagulation    | 222 (21.5%)      | 2019 (24.2%)        | 3108 (23.3%)         | 0.04  |

AICD indicates automated implantable cardioverter defibrillator; ASA, acetylsalicylic acid; H/I, hydralazine/isosorbide; LVAD, left ventricular assist device.

© 2018 Wolters Kluwer Health, Inc. All rights reserved.
may explain the stable proportion of Hispanic patients across age groups. Young patients had significantly lower SES than other age groups. This might reflect lower educational levels, poorer lifestyle choices, and more limited access to medical resources in these patients and therefore highlights the need for different approaches in real-world practice to prevent and treat HF in the young. Emphasis could be placed on increasing adherence and decreasing health care utilization through health-related technology applications for chronic disease self-management. Younger patients could benefit more from these approaches compared with older patients given that younger patients are more likely to be familiarized with electronic devices and online platforms and less likely to have cognitive or physical impairment.17 In addition, the lower SES in the young may be a result of limited employment opportunities and/or lost work days due to illness.

Echocardiographic parameters and NT-proBNP values appear paradoxical at first glance. Young patients had significantly larger LV end-diastolic diameter and LV end-systolic diameter, which may be partly explained by the higher prevalence of dilated cardiomyopathy. This may suggest the presence of other pathophysiology in HFrEF of the young that account for these echocardiographic findings. Moreover, despite a worse ventricular dilatation phenotype on echocardiography, our analysis showed that younger patients tend to have lower levels of NT-proBNP. It is reported that NT-proBNP levels increase with advancing age,18,19 and that black individuals tend to have lower NT-proBNP levels compared with white patients.20 These observations might explain the lower NT-proBNP we found in our young HF group, which consisted of a large proportion of black patients. Furthermore, our study might help to strengthen the relationship between NT-proBNP levels and age because prior studies included few patients below the age of 40.18–20

Special consideration should be given to the analysis of medical therapy. Young patients were more often receiving guideline-directed treatments, which may reflect the presence of fewer comorbidities, contraindications for cardiac medications, or interactions with other noncardiac medications compared with older groups. The higher proportion of young patients receiving a combination of hydralazine/nitrates likely represent the higher proportion of black patients in the young group. Patients younger than 40 years old are a minority of the cohorts for the trials that provided the evidence of mortality benefit in HFrEF.5–13 Therefore, it is less clear whether the benefits of these medications are comparable to that in older populations. Our data showed that β blockers were associated with ≈60% reduction of mortality risk in the young group, whereas they portended about ≈20% reduced mortality in the 2 older groups with no overlap between HR 95% CIs between young and elderly groups. The substantial benefit seen in the young population might suggest a significant impact of adrenergic blockade in reversing LV remodeling, which might be greater at earlier ages.21 It also has implications for daily practice, it underscores the importance of medication adherence, and it should prompt additional efforts by clinicians to discuss common side effects of β-blockers such as depression and impotence that may significantly hinder the quality of life of young patients and lead to discontinuation of life prolonging therapy.

Although the use of ACEI/ARB was associated with decreased mortality risk in the older populations, it failed to reduce mortality in the young group. This finding highlights the possible differences in the mechanisms for the development of HFrEF in the young compared with older patients. It suggests a lesser role of an altered renin-angiotensin-aldosterone system in the pathophysiology of HFrEF in the young. It has also been postulated that black patients, which the young group was mainly comprised of, respond less well to ACEI than white patients.16 This finding, however, may also be explained, in part, by the smaller sample size in the young group leading to limited power of the test. Nonetheless, although these findings might have clinical importance, they are hypothesis-generating and further studies with randomized clinical trials are needed to confirm these findings.
TABLE 4. Multivariable Analysis of Prediction of Mortality Between Age Groups

| Comorbidities HR (95% CI) | Young (n = 986) | Middle-aged (n = 7966) | Elderly (n = 11,898) |
|---------------------------|-----------------|------------------------|----------------------|
| HTN | 1.10 (0.80–1.51) | 1.18 (1.07–1.30) | 1.12 (1.05–1.19) |
| DM | 1.08 (0.72–1.62) | 1.36 (1.24–1.49) | 1.10 (1.04–1.17) |
| MI | 1.14 (0.72–1.82) | 1.04 (0.94–1.15) | 1.17 (1.10–1.24) |
| Stroke | 1.59 (0.93–2.70) | 1.31 (1.15–1.50) | 1.23 (1.15–1.33) |
| COPD | 2.32 (1.32–4.06) | 1.45 (1.27–1.64) | 1.23 (1.14–1.32) |
| CKD | 1.33 (0.96–1.83) | 1.16 (1.06–1.28) | 1.09 (1.03–1.16) |
| PVD | 2.53 (1.77–3.61) | 2.01 (1.82–2.23) | 1.36 (1.28–1.45) |
| Malignancy | 2.15 (1.10–4.18) | 1.96 (1.66–2.31) | 1.36 (1.24–1.49) |
| Atrial Fibrillation | 1.23 (0.78–1.95) | 1.12 (1.01–1.24) | 1.00 (0.99–1.00) |
| EF HR (95% CI) | 0.98 (0.97–1.00) | 0.99 (0.99–1.00) | 1.00 (0.99–1.00) |

DISCLOSURES

Nothing to declare.

REFERENCES

1. Benjamin EJ, Virani SS, Callaway CW, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2018 Update: a report from the American Heart Association. Circulation. 2018;137:e67–e492.

2. Bibbins-Domingo K, Pletcher MJ, Lin F, et al. Racial differences in incident heart failure among young adults. N Engl J Med. 2009;360:1179–1190.

3. Wong CM, Hawkins NM, Jhund PS, et al. Clinical characteristics and outcomes of young and very young adults with heart failure: the CHARM programme (Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity). J Am Coll Cardiol. 2013;62:1845–1854.

4. Wong CM, Hawkins NM, Petrie MC, et al; MAGGIC Investigators. Heart failure in younger patients: the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). Eur Heart J. 2013;35:2714–2721.

5. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). Lancet 1999;353:2001–2007.

6. Young JB, Dunlap ME, Pfeffer MA, et al; Candesartan in Heart Failure Assessment of Reduction in Mortality and morbidity (CHARM) Investigators and Committees. Mortality and morbidity reduction with Candesartan in patients with chronic heart failure and left ventricular systolic dysfunction: results of the CHARM low-left ventricular ejection fraction trials. Circulation. 2004;110:2618–2626.

7. Cohn JN, Tognoni G; Valsartan Heart Failure Trial Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. N Engl J Med. 2001;345:1667–1675.

© 2018 Wolters Kluwer Health, Inc. All rights reserved.
8. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *N Engl J Med* 1987;316:1429–1435.

9. Pitt B, Poole-Wilson PA, Segal R, et al. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial—the Losartan Heart Failure Survival Study ELITE II. *Lancet*. 2000;355:1582–1587.

10. Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med*. 1999;341:709–717.

11. Zannad F, McMurray JJ, Krum H, et al; EMPHASIS-HF Study Group. Eplerenone in patients with systolic heart failure and mild symptoms. *N Engl J Med*. 2011;364:11–21.

12. Yusuf S, Pitt B, Davis CE, et al. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991;325:293–302.

13. Pfeffer MA, Braunwald E, Moyé LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. *N Engl J Med*. 1992;327:669–677.

14. Coughlin SS, Labenberg JR, Tefft MC. Black-white differences in idiopathic dilated cardiomyopathy: the Washington DC dilated Cardiomyopathy Study. *Epidemiology*. 1993;4:165–172.

15. Coughlin SS, Szkl{6} M, Baughman K, et al. The epidemiology of idiopathic dilated cardiomyopathy in a biracial community. *Am J Epidemiol*. 1990;131:48–56.

16. Dries DL, Exner DV, Gerh{9} BJ, et al. Racial differences in the outcome of left ventricular dysfunction. *N Engl J Med*. 1999;340:609–616.

17. Archer N, Keshavjee K, Demers C, et al. Online self-management interventions for chronically ill patients: cognitive impairment and technology issues. *Int J Med Inform*. 2014;83:264–272.

18. Hogenhuis J, Voors AA, Jaarsma T, et al. Influence of age on natriuretic peptides in patients with chronic heart failure: a comparison between ANP/NT-ANP and BNP/NT-proBNP. *Eur J Heart Fail*. 2005;7:81–86.

19. Frankenstein L, Clark AL, Ribeiro JP. Influence of sex on treatment and outcome in chronic heart failure. *Cardiovasc Ther*. 2012;30:182–192.

20. Bajaj NS, Gutierrez OM, Arora G, et al. Racial differences in plasma levels of N-terminal pro-B-type natriuretic peptide and outcomes: the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. *JAMA Cardiol*. 2018;3:11–17.

21. Groenning BA, Nilsson JC, Sondgaard L, et al. Antiremodeling effects on the left ventricle during beta-blockade with metoprolol in the treatment of chronic heart failure. *J Am Coll Cardiol*. 2000;36:2072–2080.

22. Levitan EB, Van Dyke MK, Chen L, et al. Medical therapy following hospitalization for heart failure with reduced ejection fraction and association with discharge to long-term care: a cross-sectional analysis of the REasons for Geographic And Racial Differences in Stroke (REGARDS) population. *BMC Cardiovasc Disord*. 2017;17:249.

23. DiMartino LD, Shea AM, Hernandez AF, et al. Use of guideline-recommended therapies for heart failure in the Medicare population. *Clin Cardiol*. 2010;33:400–405.

24. Santana C, Shaines M, Choi P, et al. Designing a comprehensive strategy to improve one core measure: discharge of patients with myocardial infarction or heart failure on ACE inhibitors/ARBs. *Am J Med Qual*. 2012;27:398–405.