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Racial/Ethnic and Gender Disparities in Heart Failure with Reduced Ejection Fraction

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Abstract

Purpose of review: This review highlights variability in prescribing of non-pharmacologic heart failure with reduced ejection fraction (HFrEF) therapies by race, ethnicity, and gender. The review also explores the evidence underlying these inequalities as well as potential mitigation strategies.

Recent findings: There have been major advances in HF therapies that have led to improved overall survival of HF patients. However, racial, and ethnic groups of color and women have not received equitable access to these therapies.

Summary: Patients of color and women are less likely to receive non-pharmacologic therapies for HFrEF than Whites and men. Therapies including exercise rehabilitation, percutaneous transcatheter mitral valve repair, cardiac resynchronization therapy, heart transplant, and ventricular assist devices all have proven efficacy in patients of color and women but remain under-prescribed. Outcomes with most non-pharmacologic therapy are similar or better among patients of color and women than White patients and men. System-level changes are urgently needed to achieve equity in access to non-pharmacologic HFrEF therapies by race, ethnicity, and gender.

Keywords

Heart failure; health disparities; race; ethnicity; women’s health; outcomes

INTRODUCTION

Racial, ethnic, and gender disparities in heart failure (HF) outcomes persist [1]. African Americans and Hispanics have higher prevalence of HF than Whites, and African American women have the highest prevalence of all racial and ethnic groups [1]. Despite advances in HF therapy and notable improvement in HF survival, African Americans have the highest 5-

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year mortality risk after HF diagnosis, highest hospitalization rate for HF with reduced ejection fraction (HFrEF) and have poorer health status compared to Whites [1, 2]. Notably, there is a dearth of data on non-pharmacologic HFrEF therapies and outcomes among American Indians. In parallel to racial and ethnic disparities, women and men have unequal HF outcomes [3, 4]. While women with HFrEF live longer than their male counterparts, they have a higher burden of HF symptoms, psychological morbidity, and poorer quality of life [1, 3]. HF with preserved ejection fraction (HFpEF) is the predominant HF phenotype in women overall, but HFrEF is more prevalent in African American women and is a common cause of HF hospitalization [1, 5].

Racial and ethnic groups of color and women are undertreated with HF therapies. Despite deriving similar benefits from guideline directed therapy, African Americans are less likely than Whites to receive cardiac resynchronization therapy (CRT) [6, 7]. African Americans, Hispanics, and Asians receive fewer physician referrals for cardiac exercise training and participate less in cardiac rehabilitation than Whites [8, 9, 10]. African Americans are also less likely than Whites to receive in-hospital care by a cardiologist for treatment of HF [11, 12]. Finally, African Americans receive lower rates of ventricular assist devices (VADs) and heart transplants than expected [1, 13, 14]. Likewise, women with HFrEF including races and ethnicities of color, derive comparable therapeutic benefits from cardiac rehabilitation [15], VAD implantation and cardiac transplantation [1, 4] and benefit more from CRT [6, 16] than men, but are undertreated. Women are also more likely than men to die while on transplant waitlists post VAD [17].

While social determinants of health contribute to the observed disparities in HF outcomes, race and gender biases influence decisions on advanced HF therapy including transplantation [18, 19] which can adversely affect patient outcomes. HF contributed to US $30.7 billion in health care costs in 2012 as well as lost productivity years; these are projected to rise with an increasingly older US population. Therefore, it is important to identify etiologies of these inequalities in HF outcomes to mitigate health and economic costs [1, 20]. This review examines access and outcomes with non-pharmacologic HFrEF therapy [exercise rehabilitation, percutaneous transcatheter mitral valve repair (TMVr), cardiac resynchronization therapy, heart transplant/ventricular assist devices (VAD)] by race/ethnicity and gender, examines etiologies of disparities, and strategies for equity.

RACIAL/ETHNIC AND GENDER DISPARITIES IN HFrEF OUTCOMES

Exercise Rehabilitation

Exercise intolerance, or dyspnea and fatigue-limited physical activity is one of the cardinal presenting symptoms of HF [21]. In patients with HF, exercise training in the form of prescriptive cardiac rehabilitation (CR) improves metrics of maximal and submaximal exercise performance including peak oxygen consumption (peak VO2) [22, 23] and the ventilatory threshold [22, 24]. Exercise training in HF patients is safe and is associated with improved clinical outcomes [15], decreased mortality [25], reduced hospitalizations [25], and improved quality of life [26]. Both the U.S. (American College of Cardiology Foundation/American Heart Association) [27] and European (European Society of

Cardiology) [28] guidelines provide Class I recommendations for exercise training in stable HF patients.

Despite the preponderance of evidence of beneficial effects of CR, racial and ethnic patients of color are less likely to receive referrals to CR for qualifying diagnoses. Analysis of the American Heart Association Get with the Guidelines Coronary Artery Disease (CAD) registry from 2003 to 2009 showed that African American, Hispanic, and Asian eligible patients were 20%, 36%, and 50% less likely to receive referral for CR than White patients [10] (Table 1). Improved survival at 3 years was noted in individuals referred to CR, and patients of color referred to CR at hospital discharge had lower mortality at follow up in comparison to patients of color that did not receive CR referrals [10]. The authors concluded that the mortality disparity gap could be narrowed with equitable CR referral across racial and ethnic groups. Though HF patients were a minority of the overall study population (HF patients with CAD 28.4%), this study demonstrated that CR is significantly underutilized across all eligible cardiac diagnoses, as seen previously [29, 30, 31]. A study of Medicare claims data across three different geographic regions to assess CR underutilization in racial/ethnic patients of color observed a consistent 7–11% gap in CR utilization in patients of color compared to White eligible patients. This difference was even more profound in the post-coronary artery bypass graft population (less than 9% in patients of color versus more than 26% in Whites) [32], and mandates attention and action to health equity in CR usage.

Factors contributing to lower CR utilization among racial and ethnic patients of color include geographic limitations to access of CR sites, inadequate reimbursement of CR services, underinsurance of patients with cost-prohibitive co-payments, clinician perceptions regarding patient interest in CR, and low referral rates [30, 31, 32]. Other contributing factors to underutilization of CR include logistical barriers of inflexible patient work hours and incongruent CR program hours, lack of transportation and social support, language barriers, and home responsibilities which may disproportionately affect racial and ethnic patients of color and women [30]. Women are less likely to be referred than men [33] and less likely to enroll or complete the program once initiated given higher likelihood of conflicting caregiving responsibilities [31].

Percutaneous Edge to Edge Mitral Valve Repair

Mitral regurgitation (MR) often complicates HFrEF and is associated with excess mortality, hospitalization, and a higher burden of HF symptoms [34]. MR is categorized as primary, degenerative, when related to abnormalities of the anatomical structures of the mitral valve versus secondary, functional mitral regurgitation (FMR) when related to adverse left ventricular remodeling and dilatation. The exact prevalence of MR is unknown but increases with age and HFrEF severity [1, 34].

TMVr has emerged as an efficacious therapeutic intervention in patients with moderate to severe MR with NYHA class III/IV symptoms despite GMDT [34]. TMVr is also a viable therapeutic option for primary MR patients with NYHA class III/IV symptoms who have a prohibitive surgical risk [35]. TMVr is associated with improvements in the severity of MR, NYHA functional class, hospitalization rates, and all-cause mortality in appropriately selected HFrEF [35, 36].

Despite recent demonstration of efficacy and the addition of TMVr to the HF therapeutic armamentarium, racial/ethnic and gender differences are present with this therapy. For example, the adoption of TMVr in the US has been increasing; however, the proportion of African Americans receiving interventions has remained unchanged [37]. This occurs in the background of demonstrable benefit in outcomes among this racial group.

Inequalities in the access to TMVr among women have also been reported even in the face of increasing adoption of this therapy. Although women derive benefit from TMVr and have comparable in-hospital mortality and other procedure-related complications, evidence suggests that they have fewer implantations compared to men [38]. When considering the interaction of race and gender, African American women were more likely to receive TMVr than African American men [38].

It is noteworthy that women are less likely to be referred for surgical evaluation of severe MR, and when referred, it is often later in the disease process [35, 39]. Potential reasons for these lingering disparities besides the known structural social determinants of health include physician referral bias [40], and underestimation of the severity of MR due to the use of metrics that do not account for body surface areas. For example, the American College of Cardiology guidelines of echocardiographic left ventricular end systolic dimension >40mm indicate operable MR but does not correct for body surface area [36]. Others have proposed that the different manifestation of symptoms between men and women could lead to differential triggers in cardiac evaluation. For example, women may present with more insidious symptoms such as fatigue rather than shortness of breath [41].

Cardiac Resynchronization Therapy

Among patients with HF, left bundle branch block (LBBB) contributes to LV dyssynchrony and dysfunction, maladaptive cardiac remodeling, and increased sudden cardiac death and all-cause mortality [42]. CRT restores ventricular synchrony via biventricular pacing and is an effective therapeutic intervention that reduces risk of death, hospitalization, and HF symptom burden [43]. CRT also reverse remodels the left ventricle, reduces mitral regurgitation, and improves exercise tolerance and quality of life [44, 45, 46]. Current HF guidelines strongly recommend CRT in appropriately selected HF patients [27]. Nonetheless, notable disparities in CRT usage have emerged and persist in racial and ethnic patients of color and women.

In late 2005, Centers for Medicare and Medicaid Services expanded coverage of implanted devices, including implanted cardiac defibrillators (ICD) and CRT combined with a defibrillator (CRT-D), but disparities persisted [7]. Initial evaluation of the National Cardiovascular Data Registry (NCDR) for CRT-D usage across demographic groups between 2005–2007 demonstrated that CRT-eligible African American and Hispanic patients were less likely to receive CRT-D than White patients [7]. Persistent and pervasive disparities in CRT utilization were further corroborated by analysis of hospitalized patients in the Nationwide Inpatient Sample (NIS), one of the largest all-payer inpatient care databases. Between 2002 and 2010, nearly 375,000 de novo CRT devices were implanted, and White patients accounted for 79.6% of device recipients. Conversely, African American patients and patients identified in other racial/ethnic groups were 9.9 and 10.4%, respectively [6]. Adjustment for differences in HF incidence and hospitalizations across demographic groups, reinforced significantly higher CRT utilization in Whites and men, compared to African Americans and women [6], which has also been observed in multiple studies of ICD utilization among patients of color and women.

Most landmark CRT trials had underrepresented racial and ethnic patients of color due to underreporting or under-enrolling population-reflective proportions of African Americans, Hispanics, and American Indians [47]. This underrepresentation levied uncertainty regarding the efficacy of CRT benefit among patients of color. Real-world clinical practice data provided by Registry to Improve the Use of Evidence-Based HF Therapies in the Outpatient Setting (IMPROVE-HF) has definitively demonstrated similar 24-month mortality benefit from CRT across racial/ethnic groups, disproving assumptions of uncertainty of benefit in racial/ethnic patients of color [48]. The AHA's Get with the Guidelines (GWTG) HF registry of hospitalized patients similarly showed that CRT use was more common in White patients compared to African American patients and those identified as other races. The GWTG-HF registry also highlighted important differences in CRT usage at the intersectionality of race and gender, noting that African American women were more likely to receive CRT than African American men [49]. Within other racial/ethnic groups, men were noted to have higher CRT use than women. Implantation of new CRT devices was notably lowest in African Americans within this cohort [49]. Underutilization of CRT remains a challenge and likely contributor to disproportionately high mortality rates, particularly in African Americans [6].

Gender-based disparities in CRT utilization have emerged and persisted over the past twenty years [16]. Women are underrepresented in CRT trials and observational studies, often accounting for less than 35% of the study population [16, 50]. Female sex has been associated with greater reverse cardiac remodeling, more HF symptom improvement, more efficacious CRT response, and improved survival; however, women are consistently less likely to receive CRT implantation than men [6, 51]. Women are more likely to have LBBB [52] and are more likely to benefit from CRT at a narrower QRS [52, 53]. Notably, sex-based differences in CRT utilization are increasing, despite the higher likelihood of clinical characteristics predictive of a favorable CRT response [54]. Older women (age>80) and/or those with significant comorbidities e.g., CKD are also less likely than men to receive CRT [54]. Factors contributing to the persistent and widening sex disparity in CRT use in women remain poorly understood, though differences in physician referral and patient consideration of CRT implantation possibly contribute [16, 54].

Heart Transplant & VAD

Racial/ethnic patients of color and women are inequitably allocated to advanced HF therapies, heart transplants and VAD. Approximately 3800 heart transplants [14] and 2600 VAD [55] are performed per year in the US. Although racial/ethnic patients of color have higher prevalence of HF than Whites [1] and African Americans have the highest mortality from HF [56], racial/ethnic patients of color receive 38% of heart transplants [14] and less than a third of VAD [13]. Among patients awaiting heart transplant with VAD, African Americans and women have higher waitlist mortality and are less likely to receive heart transplants than patients of other races and ethnicities and men [17, 57]. Women have similar prevalence of HF as men, but African American women have the highest prevalence of HF of all races/ethnicities and sexes [1]. Women are allocated to less than a third of heart transplants and VAD in the US [14, 17].

HF phenotype does not explain the differences in allocation. Women have higher incidence of hospitalized HFpEF, which is not typically an indication for advanced therapies, than men, but the incidence of hospitalized HFrEF is higher than HFpEF among African American women [1, 5]. Among high-risk patients with recurrent hospitalized HF, incidence of HFrEF and HFpEF is similar in White women and remains higher among African American women [56].

Advanced HF therapies unequivocally improve mortality and quality of life, but outcomes vary somewhat by race/ethnicity and sex. Compared to Whites, 5-year survival post heart transplant is lower for most patients of color [14]. However, comprehensive multi-disciplinary care post heart transplant has eliminated racial disparities in survival post-transplant in at least one major transplant center [58]. Survival post heart transplant is similar across sexes [14]. Among Medicare beneficiaries, survival post VAD is similar and at times better for racial/ethnic patients of color and women than for Whites and men [58].

FACTORS ASSOCIATED WITH DISPARITIES

Factors Associated with Racial/Ethnic Disparities in HFrEF

Etiologies of racial and ethnic disparities in HF outcomes are complex and multifaceted (Table 2). Broadly, some of the factors cited to underpin these disparities include historical racial/ethnic injustices against patients of color as well as the larger systemic socioeconomic inequalities that when taken together have negative adverse impact on cardiovascular outcomes [59]. A disproportionately higher number of African Americans and other patients of color are of low socioeconomic position leading to underinsurance and limited access to specialist care [59, 60]. Low socioeconomic position is also associated with living in disadvantaged neighborhoods and poor social networks which both contribute to limited access to care [61].

Further, low socioeconomic position is closely tied to low education (high school diploma and below) and low health literacy, and both are associated with increased mortality after HF hospitalization [62]. Low health literacy contributes to communication challenges between health care professionals and an ethnically and culturally diverse patient population resulting in poor quality patient care, nonadherence to therapy, and unequal HF outcomes.

Implicit and explicit racial/ethnic biases influence physician decision-making [19, 63] contributing to suboptimal advanced HF care for African Americans and other patients of color. African American men with HF are usually perceived as being sicker and less adherent to therapy than Whites, which may contribute to more LVAD implantations and fewer heart transplant allocations [18, 64] among African Americans. These racial/ethnic biases also may explain why African Americans and Hispanic patients with HF are less likely than Whites to be cared for by a cardiologist [11, 12]. Such practices can lead to under-recognition of advanced HF in racial/ethnic patients of color, delayed institution of advanced HF therapy, and adverse clinical outcomes including higher mortality and readmission rates.

Racial/ethnic biases also affect patient-physician interaction and communication, which contribute to poor health literacy and adverse HF outcomes [40]. More than 52% of African Americans and 6% of Hispanics (vs 6% for non-Hispanic Whites) have reported biased treatment [65]. These racial biases contribute to less trust of the health care system, and may lead to low adherence to therapy, self-care, participation in medical research, and low uptake of currently available advanced HF therapies [66, 67].

In addition, patients of color are underrepresented in HF clinical trials, which contributes to poor understanding of HF in these patients [67], and potentially poor outcomes. African Americans have been observed to have increased immunosuppressant metabolism and immune/inflammatory dysregulation that heighten allograft failure and reduce post heart transplant survival [68]. The role of genetics in HFrEF treatment, albeit lesser than social determinants of health, has not been comprehensively studied and may lead to appropriately tailored precision medicine in HF [68, 69].

Factors Associated with Gender Disparities in HFrEF

Multiple factors contributed to gender disparities in HFrEF (Table 2). Social determinants of health intertwined with gender and sociocultural factors likely contribute to these disproportionate adverse HF outcomes in women. Women with HF have disproportionate HF symptoms, anxiety, depression, and poorer quality of life than men [3]. Women's predominant home care giving responsibilities may prevent their enrollment and participation, if enrolled, in exercise training [30] and other HF management programs due to conflicting care giving responsibilities.

Clinician bias may contribute to underutilization of advanced HF therapies in women, particularly given persistent disparities after adjustment for age and socioeconomic factors [4, 13]. African American women are perceived as having more financial challenges and inadequate social support compared to Whites and men [18, 64] which may impact clinician decisions on advanced HF therapies. Women have higher heart transplant waitlist mortality and are less likely than men to be transplanted urgently [17]. Gender bias is supported by evidence that male physicians are more likely than female physicians to use suboptimal HF therapy when treating women with HF [70]. A recent study revealed that cardiologists, particularly male cardiologists, believe that women are not risk-takers [71]. This bias could also contribute to low enrollment of women in advanced HF clinical trials [67] due to thoughts that the patient would not want the risk associated with participating in a study.

The intersection of race and gender heighten social determinants of health including structural racism. This results in a larger proportion of women, particularly African Americans and Hispanics, having low socioeconomic position, which is associated with adverse HF outcomes [59, 60]. Low socioeconomic position is inextricably tied to underinsurance, limited health care access, low health literacy, and poor family and social support, which negatively impact HF outcomes.

Women with HF are generally older than men and have a larger burden of concurrent comorbidities (hypertension, anemia, diabetes, anxiety, depression, and cognitive impairment). Clinician perceived frailty likely leads to suboptimal HF therapy including exercise therapy [72, 73]. Mental morbidity is particularly prevalent among women with HF. Under-recognition of this by clinicians probably contributes to inadequate referrals to psychiatry and psychology, leading to poor quality of life.

STRATEGIES TO ACHIEVE EQUITY

There is need to strengthen existing public policies to address etiologies of racial/ethnic and gender differences in HF outcomes (Table 2). Underinsurance can be addressed by adoption of health policies that promote universal health coverage especially for vulnerable groups such as those with advanced HF. The ACA has been associated with improved access to heart transplants among African Americans [74]. Although it has not been associated with improved access to VAD, the ACA has been associated with increased access to quality healthcare [75]. Broader [76] state approval may narrow disparities in access to care.

Given the geographical maldistribution of the cardiologist workforce in the US, leveraging use of information technology including telemedicine, to improve access to cardiologists can aid timely cardiology care and potentially improve outcomes. Physician incentives can also be introduced to promote retention of cardiologists and improve access to care.

Alternative models to traditional hospital or outpatient clinic-based cardiac rehabilitation, such as home-based and internet-based prescriptive exercise training have been endorsed by guideline agencies to address barriers to this efficacious therapy for patients with qualifying cardiac diagnoses [30]. Further data is needed to determine the benefits and shortfalls of these alternative methods in narrowing the disparity gap for racial/ethnic patients of color and women. The higher likelihood of limited digital access and community and home-based resources among some populations may diminish the success of these programs.

Implementation of ongoing screening measures to evaluate patients for low health literacy and empowering them with specific interventions to improve health literacy is also important. Financial and other resource support to improve heart transplant outcomes in worse performing transplant centers would potentially reduce regional variation in HF outcomes by building capacity in these health care facilities. It is often the case that socioeconomically disadvantaged populations, particularly African Americans and Hispanics, receive care in underperforming health care centers [77].

HF disparities may be improved through equitable representation of women and racial/ethnic groups of color in HF clinical trials. This may be improved by diversifying leadership of clinical trials to include more women, racial/ethnic groups of color, and patients [78]. Race is a social construct and should be examined as such when considering new technology. Efforts to equitably disseminate technology are as important as establishing efficacy and effectiveness of therapies for HF. These issues may be more appropriately addressed by a diverse HF trial leadership team.

System-wide interventions are required to dismantle structural racism and racial and gender biases that hinder equitable access to care. Health care professionals need sensitization on the existence of structural racism, explicit and implicit racial and gender biases, and their negative impact on health care outcomes. Health care professionals may benefit from implicit racial and gender bias mitigation training as well as education on race, diversity, and culture since acquisition of these competencies can potentially improve patient-provider communication, health literacy, trust, and quality of health care [79].

Loan forgiveness programs may diversify the cardiovascular workforce. Incentivizing medical training of racial/ethnic physicians of color and women may increase the pipeline of diverse cardiologists. This can help offset existing biases through eradication of patient-physician racial/ethnic and gender discordance. Racial/ethnic and gender concordance may enhance health care, particularly among patients of color who tend to be more trusting of physicians they can self-identify with given unethical treatment of patients of color by healthcare [79, 80].

Timely management of patient comorbidities may reduce gender disparities. Since women often have more comorbidities, checklists and routine use of evidence-based quality metrics such as Kansas City Cardiomyopathy Questionnaire [81] may help clinicians make appropriate referrals to specialists. Ultimately, early management of comorbidities may improve quality of life of women with HF.

SUMMARY

Racial/ethnic groups of color and women are less likely to receive non-pharmacologic therapies for HFrEF than Whites and men. Outcomes post exercise rehabilitation, TMVr, CRT, and VAD are similar and in some case better for racial/ethnic groups of color and women than White patients and men. Survival is lower at 5-years for most patients of color compared to White patients, but specialized multidisciplinary care has mitigated differences in survival.

Equitable access to HFrEF therapies will require strategies that deploy changes at the system-level. Major etiologies for racial/ethnic and gender disparities include system-level problems such as social determinants of health, bias, and structural racism. Policies that expand access to quality insurance and provide social resource support for patients are deftly needed. Evidence-based bias reduction and antiracism training should be regularly disseminated. In addition, implementation research is needed to identify successful strategies to actively replace policies that support structural racism. Finally, diversity in leadership and enrollment of marginalized racial/ethnic groups including American Indians and women for HF trials is needed. In whole, this will contribute to better HF outcomes across patient race/ethnicity and gender.

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Abbreviations:

HF	Heart Failure
HFrEF	Heart Failure with reduced Ejection Fraction
HFpEF	Heart Failure with Preserved Ejection Fraction
CRT	Cardiac Resynchronization Therapy
LV	Left ventricle/ventricular
LVAD	Left Ventricular Assist Device
MR	Mitral Regurgitation
TMVr	Transcutaneous Mitral Valve repair
GDMT	Guideline Directed Medical Therapy
GWTG	American Heart Association's Get with The Guidelines Registry
ACA	Affordable Care Act
FDA	U.S. Food and Drug Administration
CMS	Centers for Medicare and Medicaid Services

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Table 1:

Data on Outcomes of HFrEF by Race and Gender

	Demographics	Outcomes
Exercise training (cardiac rehabilitation)		
Race/Ethnicity, and Gender	HF-ACTION (2003–2007) multicenter clinical trial: Median age of enrolled patients, 59 years (28% female and 32% African Americans) [15].	After adjustment for prognostic factors, exercise training demonstrated modest significant reductions in all-cause mortality, cardiovascular mortality, and HF hospitalization; subgroup post hoc analysis demonstrated greater benefits in women than men [15].
Transcatheter Mitral Valve Repair (TMVr/Mitraclip)		
Race	NIS database (2012–2016) analysis of TMVr utilization and outcomes in the US: Of 7940 TMVr performed, only 8.6% were performed in African Americans [37]. Compared to African Americans, White recipients of Mitraclip were older (77.7±10.8 vs 67.2±14.28, p<0.001) and less likely to be women (45.3% vs 60.3%, p < 0.001) [37].	Whites had higher in-hospital mortality than African Americans [4.7% vs 1.6%; OR: 3.10 (95% CI:1.61–5.97); p<0.001] [37] Whites also had higher in-hospital cardiac arrest and pacemaker implantation compared to African Americans [37].
Gender	In the NIS database (2012–2016), White women were less likely than African American women to receive Mitraclip (45.3% vs 60.3%, p<0.001) [37, 38].	Women and men had similar in-hospital survival except for lower incidence of ventricular arrhythmias (4.1% vs 7.2%; p=0.01) in women and higher incidence of pacemaker implantation in women (1.7% vs 0.4%; p=0.01) [38].
Cardiac Resynchronization Therapy (CRT)		
Race/Ethnicity and Gender	NIS database (2002–2010) analysis of CRT utilization trends in the US: Of the 374 202 CRT procedures recorded, Whites received 79.6% of which 71.4% were male recipients [6]. Predominant age group of CRT recipients was 64–84 years which accounted for 64.6% of procedures recorded) [6].	Women, particularly age<85, have slightly better in-hospital mortality than men (0.71% vs 0.93%) [6]. Women have more adverse outcomes with CRT-D compared to men including hemothorax and pneumothorax (4.4% vs 0.9%) and infection requiring reoperation (2.5% vs 0.6%), and fewer appropriate shocks [4, 6]. Gender disparities in utilization are widening despite greater benefit in women [82].
VAD/Transplant		
Race/Ethnicity	Analysis of the UNOS registry (2008–2018) for trends on LVAD implantation as a bridge to heart transplant in the US: 14 324 patients (64% Whites; 26% African Americans; 7% Hispanics; and 3% other races) received cLVAD as a bridge to heart transplant [57].	African Americans had the lowest incidence of heart transplantation, and African American race was a predictor of waitlist mortality and delisting for worsening clinical status post VAD [57]. VAD survival and hospitalization benefits are similar across race and ethnicity [83].
	OPTN/SRTR 2018 heart transplant waitlist composition (as of December 2018): Whites (61.1%), African Americans (26.5%), Hispanics (8.9%), Asians (2.7%) [14]. In 2018, Whites received 64.2% versus 22.0% (African Americans), 8.8% (Hispanics), 4.1% (Asian), and 0.8% (other/unknown) of heart transplants, respectively [14].	African Americans have worst 5-year post heart transplant mortality across race/ethnicity [14].
Gender	NIS database (2004–2016) analysis on temporal trends in LVAD utilization and post-LVAD mortality by sex demonstrated a decrease in LVAD implantation from 25.8% (2004) to 21.9% (2016) [84]. Men comprise 80% of the destination VAD population [84].	With contemporary cLVAD, women have similar complications (post cVAD in-hospital mortality, time to infection, bleeding, and device malfunction) to men [17, 84]. Stroke risk post VAD is greater in women than men [adjusted hazard's ratio: 1.44(95% CI: 1.05–1.96); p=0.002]) [17].
	Men comprise 75.8% of patients on heart transplant waitlist and 71.7% of heart transplant recipients [14].	Women receiving cLVAD while listed had lower chances of heart transplant than men, increased risk of waitlist mortality, and delisting for worsening clinical status at 2-years post implantation. Women have higher adjusted waitlist mortality & are less likely than men to be transplanted urgently (UNOS status1A) [14].

HFrEF indicates heart failure with reduced ejection fraction; NIS, National Inpatient Sample; INTERMACS, Interagency Registry of Mechanically Assisted Circulatory Support; HF-ACTION, UNOS, United Network for Organ Sharing; OPTN/SRTR, US Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients; Heart Failure- A Controlled Trial Investigating Outcomes of Exercise Training; cVAD, continuous flow ventricular assist device; LVAD, left ventricular assist device; CRT-D, cardiac resynchronization therapy- defibrillator; CMS, Centers for Medicare and Medicaid Services.

Table 2:

Seeking Equity- HFrEF Data by Race and Gender

	Reasons for Disparities	Strategies for Equity
Exercise training (cardiac rehabilitation)		
Race/Ethnicity and Gender	Patient level factors older age (62–83 years), low socioeconomic position, limited access (underinsurance, prohibitive co-pays, and proximity to rehab center), greater comorbidity burden (COPD, CVA, CKD, cognitive dysfunction), and race, ethnicity and female sex are associated with less participation in exercise training [72, 73].	System-wide interventions to broaden insurance coverage and decrease copays. Expansion of exercise training services to include community, home- and internet-based cardiac rehabilitation. Government programs aimed at improving residential environments to enhance green space and facilities for physical activity to promote exercise outside of formal rehab centers.
	Language barriers and low health literacy [59].	Hospital support to widen use of interpreter services including video/audio services. Ongoing screening measures to identify communication barriers e.g., low health literacy and implementation of timely targeted interventions. Patient education to improve awareness on the importance of exercise training may result in improved adherence.
	Physician perceptions of patient interest and ability to tolerate exercise training (association of patient referral and physician presumed patient frailty) [32].	Physician education and awareness programs to address biases and gaps in disease management including referrals for exercise training and mental health support especially for women. Shared decision-making.
	Gender biases contribute to less disease management program referrals including exercise and mental health [10].	Mandatory gender bias mitigation training; mandatory and automated referrals for hospitalized HFrEF patients at discharge.
	Lack of and/or inadequate social support (e.g., larger proportion of older women live alone) [85].	Enhance home health care for patients of color and women with HF Leverage use of information technology
Device therapy: Cardiac Resynchronization Therapy (CRT) and Mitraclip		
Race/Ethnicity and Gender	Underrepresentation of racial/ethnic patients of color and women in HF clinical trials [67].	Make clinical trials more inclusive for better understanding of HF and to ensure generalizability of trial outcomes to underrepresented HFrEF populations via extension of NIH policy mandating inclusion of racial/ethnic patients of color and women to industry sponsored HF clinical trials. Prioritize areas with a high proportion of patients of color and women during clinical trial site selection [67]. Racial/ethnic and gender diversification of investigators to allay participate mistrust. Education, awareness campaigns, and local community leadership involvement to allay research mistrust and improve recruitment Incentivize clinical trial participation (e.g., compensation for time, transportation, etc.).
	Underinsurance [59] and limited access to specialist care.	Broaden insurance coverage and reduce copays for HF therapies. Advocacy and resource allocation to address limitation in access related to unequal geographical distribution of cardiologist workforce. Leverage use of information systems technology including telemedicine.
	Lack of social support (intertwined with low socioeconomic position and neighborhood deprivation) [59].	Expand home-based care for patients of color and women with HF. Leverage use of information technologies to improve social support.
	Racial, ethnic, and gender biases [63, 64].	Mandatory evidence-based clinician training on bias reduction and anti-racism therapy.
	Patient mistrust of health system (related to racial, ethnic, and gender biases) contributes to avoidance and refusal of HF therapy [66].	Patient education and advocacy. Loan forgiveness programs and medical grants/scholarships to recruit more racial/ethnic people of color and women physicians to improve patient-physician racial/ethnic and gender concordance.
VAD/Transplant		

	Reasons for Disparities	Strategies for Equity
Race/Ethnicity, and Gender	Racial biases [63, 64] and structural racism.	Funding to support evidence-based Implicit racial/gender bias reduction and structural racism policy changes. Implementation research to test strategies that reduce bias and structural racism. Hospital funding support.
	Biologic factors such as genes likely responsible for increased immunosuppressant metabolism (CYP3A5*1 – associated with higher clearance and lower bioavailability of tacrolimus in African Americans) and immune and inflammatory dysregulation (partially explains higher odds of allograft failure and lower post heart transplant survival among African Americans) [69]. African Americans are most likely to receive HLA-mismatched and race-mismatched grafts, but this accounts for only a small portion of racial disparity in outcomes [69].	Funding of genetic/molecular studies to understand the role of genetics, including immunologic factors in graft failure and heart transplant survival in high-risk racial/ethnic populations of color (African Americans and Hispanics) to individualize immunosuppressive regimens [68, 86]. Recognition and incorporation of pharmacogenetics in post heart transplant immunosuppressive algorithms. Mandating and implementing uniform guidelines across transplant centers.
	Underinsurance [74] (African Americans and Hispanics are disproportionately uninsured [87])	Broaden health care insurance coverage for racial/ethnic groups of color including coverage for immunosuppressive regimens and heart transplant care.
	Listing in low volume transplant centers, particularly Hispanics [88], and transplantation at transplant centers with higher-than-expected mortality [77].	Financial and other resource support for improved transplant center performance. Incentivizing outcomes to improve quality of care in worse performing transplant centers.
	Low socioeconomic position, limited access to care and being a patient of color are associated with low likelihood of heart transplantation, death, retransplant, higher risk of transplant rejection and loss, and other adverse post heart transplant outcomes (poorer adherence, hospitalization, and infection) [77, 86, 89].	Broadening insurance coverage for heart transplant recipients including coverage for immunosuppressive regimens and heart transplant care. Strengthening existing transplant counselling and education programs to offset nonadherence resulting from financial strain and low health literacy. Early referral for transplant listing.
	Social support and marital status [90].	Strengthen home and community-based care for high-risk patients of color and women with HF. Leverage technology to improve social support.
	VAD implantation refusal by women [91].	Offer patient education to improve awareness on the benefits of advanced HF therapies.

HFrEF indicates heart failure with reduced ejection fraction; VAD, ventricular assist device; COPD, Chronic pulmonary lung disease; CVA, Cerebrovascular disease; CKD, Chronic kidney disease; NIH, National Institutes of Health.