Influence of patient age and sex on delivery of guideline-recommended heart failure care in the outpatient cardiology practice setting: Findings from IMPROVE HF

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Background The influence of patient age and sex on delivery of guideline-recommended heart failure (HF) therapies in contemporary outpatient settings has not been well studied. The Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) is a prospective cohort study designed to characterize current management of outpatients with chronic HF and left ventricular ejection fraction ≤35%.

Methods Baseline data for eligible patients with systolic HF in a national registry of 167 US outpatient cardiology practices were collected by trained chart abstractors. Data were stratified and analyzed as male/female and by age tertiles with generalized estimating equation models constructed for 7 care measures.

Results A total of 15,381 patients were enrolled, with 8,770 (71.1%) of these male. Median age of female patients was 72.0 and 70.0 for males. Use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, aldosterone inhibitors, and cardiac resynchronization therapy was not significantly different between male and female patients, but rates for implantable cardioverter defibrillators, anticoagulation therapy for atrial fibrillation, and HF education were significantly lower for females. After adjusting for patient and practice characteristics, 3 of 7 measures significantly differed by patient sex, and 6 of 7 measures by age. Older patients, particularly older women, were significantly less likely to receive guideline-indicated HF therapies.

Conclusions Patient age and sex were independently associated with reduced rates of some, but not all, HF therapies in outpatient cardiology practices. Older women are especially at risk. Further research is needed to understand the causes and consequences of these age- and sex-related differences in care. (Am Heart J 2009;157:754-762.e2.)

Heart failure (HF) causes substantial morbidity and mortality. The incidence of HF rises sharply with advancing age, and in community-based studies, the mean age of patients with HF is >70 years.[1-3] Women comprise 52% of inpatient HF populations, although among HF patients with left ventricular systolic dysfunction (LVSD), only 25% to 40% are female.[4]

Numerous clinical trials have established that pharmacologic therapies, including angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB), β-adrenergic receptor blockers, aldosterone antagonists, and isosorbide dinitrate/hydralazine, as well as implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy (CRT) devices with defibrillation (CRT-D), significantly reduce morbidity and mortality in patients with HF and LVSD.[5-9] Current national guidelines recommend administration of these therapies for all eligible patients with HF, regardless of

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sex and age.[5] Despite such recommendations, prior studies demonstrate age- and sex-related differences in use of evidence-based therapies, and clinical outcomes for female and older patients with HF have not improved at rates equivalent to those reported for male and younger patients with HF.[10-16] These findings largely emanate from inpatient registries and observational experiences prior to the most contemporary HF guidelines and thus may not capture the full extent of use of HF therapies as a function of patient age and sex.

The Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF) is a national registry and performance improvement program for patients with HF receiving care in outpatient cardiology practices. Analysis of baseline data from IMPROVE HF was performed to assess the association of age and sex with use of evidence-based care for patients with HF and determine whether patient age or sex is independently associated with care in a contemporary, national cohort of patients with HF.

Methods

IMPROVE HF is a prospective cohort study designed to characterize current management of patients with diagnosed HF and LVSD or prior myocardial infarction (MI) along with LVSD in outpatient cardiology practices. The methods, design, and study objectives of IMPROVE HF have been previously reported in detail.[17] Community and academic cardiology or multispecialty outpatient practices throughout the United States were invited to participate. Eligible patients included those with a clinical diagnosis of HF documented by a cardiologist on at least 2 separate visits and LVSD demonstrated by a quantitative left ventricular ejection fraction (LVEF) ≤35% measured by the most recent echocardiogram, nuclear multiple-gated acquisition scan, contrast ventriculogram, or magnetic resonance imaging scan. Patients with preserved systolic function or without LVEF quantified were not included. The IMPROVE HF registry and this study are sponsored by Medtronic, Inc (Minneapolis, MN). The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

Baseline data collected by 34 chart abstractors included patient demographic and clinical characteristics, medical history, previous treatments, laboratories, diagnostic tests, current treatments for HF, and contraindications, intolerance, or other documented reasons (including economic, social, and religious reasons, noncompliance, and other reasons for refusal) for not prescribing evidence-based HF therapies. A representative sample of medical records were screened to yield an average of 90 eligible patients from each practice for each study assessment period using the methodology described in the design paper.[17] The present analysis of baseline care by patient age and sex was prespecified in the study protocol.

All practices participating in IMPROVE HF were approved by local institutional review boards (IRBs) and central IRB or received IRB waivers. Data quality was addressed through use of highly trained, centralized chart abstractors who participated in ongoing training and testing to maintain accuracy in data abstraction. The average interrater reliability was substantial ($\kappa = 0.82$). To further ensure the accuracy and completeness of data, we performed 1.7 automated data quality checks for each data field, and data quality was monitored and reports generated monthly. The registry coordinating center was Outcome Sciences, Inc (Cambridge, MA).

Guideline-recommended care measures

Seven care measures were prospectively selected by the IMPROVE HF Steering Committee, independent of the study sponsor.[17] The selection of these 7 measures predated the 2005 American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the treatment of chronic HF and the ACC/AHA Performance Measures for HF in outpatient settings.[5] A potential set of 16 metrics were developed and ranked based on their impact on patient outcomes, precision of definition, construct and content validity, and feasibility.[18,19] The 7 highest-rated measures were selected for the quality improvement intervention that will be administered to practices enrolled in IMPROVE HF. Further details about the selection process for these measures are described in greater detail in an earlier publication, and the measures are presented in Appendix A.[17] Four of the measures selected were ACC/AHA outpatient HF performance measures, whereas 3 were not, including use of aldosterone antagonists, ICD/CRT-D, and CRT therapies. Documentation of New York Heart Association (NYHA) functional class is a prerequisite for eligibility for ICD, CRT, and aldosterone antagonist treatment, and analyses including these measures excluded patients who did not meet the quantitative or qualitative documentation of NYHA functional class established for each metric.[17] Patients eligible for inclusion in an individual care measure calculation included only those who met the criteria for a given therapy for whom there were no contraindications, intolerance, or other documented rationale explaining why the therapy should not be provided.

Statistical methods

All statistical analyses were performed by an independent biostatistician contracted by Outcome Sciences, Inc. This analysis was based on all baseline data entered in the registry between 2005 and 2007 including 167 cardiology practices and 15,381 patients. The proportion of patients receiving specific therapies among those eligible for each therapy was stratified by practice and reported with 95% confidence intervals (CIs). Descriptive statistics for patient and practice characteristics by tertiles of patient age (≤64, 65-76, and >76) and sex were calculated, and each of the 7 care measures was evaluated separately. The primary analyses assessed associations between patient age (10-year increments) and sex and each care metric. Univariate and multivariate generalized estimating equations (GEE) regression models were developed for each metric. The multivariate analyses of age and sex were adjusted for practice and patient characteristics including HF etiology, LVEF, diabetes, prior MI, coronary bypass, percutaneous coronary intervention, systolic blood pressure, and all practice characteristics in Table II. Analysis of the interaction of age and sex for each care measure was performed by including the age-by-sex interaction in GEE models for each care metric. The interaction term was excluded from the model if the *P* value exceeded .10. Care metrics with a significant age-by-sex interaction were further

Table I. Comparison of baseline patient characteristics by age and sex

Patient characteristic	Age* (y) ≤64 (n = 5307)	65-76 (n = 5176)	>76 (n = 4791)	P	Sex* Male (n = 10,925)	Female (n = 4446)	P
Age, median (IQR)					70.0 (60, 78)	72 (61, 80)	<.001
≤64 (%)					35.5	32.2	
65-76 (%)					34.6	31.2	
>76 (%)					29.3	35.8	
Male, %	73.0	73.1	66.8	<.001			
Race (%)				<.001			<.001
White	36.8	44.2	43.2		41.7	40.6	
African American	16.6	6.2	3.9		7.8	12.1	
Not documented/missing	44.4	48.0	51.5		48.7	45.7	
HF etiology (%)				<.001			<.001
Ischemic	52.6	71.1	72.9		70.0	53.4	
Nonischemic	25.2	12.2	9.7		13.6	21.8	
Valvular	2.0	1.7	2.3		1.6	3.0	
Other	12.7	7.7	7.2		7.9	12.8	
Not documented	7.2	7.3	7.8		6.9	9.0	
Hx atrial fibrillation (%)	19.9	32.2	41.4	<.001	32.5	26.6	<.001
Hx diabetes (%)	35.0	38.2	28.5	<.001	34.2	33.5	.378
Hx hypertension (%)	57.5	63.9	63.7	<.001	61.1	63.0	.032
Prior MI (%)	34.3	42.8	41.5	<.001	42.4	32.1	<.001
Hx COPD (%)	12.5	19.8	17.3	<.001	16.9	15.5	.032
Hx CABG (%)	21.5	36.7	35.0	<.001	35.7	19.1	<.001
Hx PVD (%)	7.8	13.5	12.7	<.001	11.8	10.1	.003
Hx depression (%)	10.4	8.0	7.9	<.001	7.8	11.2	<.001
LVEF, median (IQR)	25 (20, 30)	25 (20, 30)	25 (20, 30)	<.001	25 (20, 30)	25 (20, 30)	.599
SBP, median (IQR)	119.5 (107, 130)	120 (109, 131)	120 (110, 132)	<.001	120 (108, 130)	120 (110, 133)	<.001
Resting HR, median (IQR), beat/min	72 (65, 80)	70 (64, 78)	70 (64, 77)	<.001	70 (64, 78)	72 (65, 80)	<.001
Sodium, median (IQR), mEq/L	139 (137, 141)	140 (137, 142)	140 (138, 142)	<.001	140 (137, 141)	140 (137, 142)	.932
BUN, median (IQR), mg/dL	18 (14, 25)	22 (17, 31)	26 (19, 35)	<.001	22 (17, 30)	21.0 (15, 31)	<.001
Creatinine, median (IQR), mg/dL	1.1 (0.9, 1.4)	1.2 (1.0, 1.6)	1.3 (1.1, 1.7)	<.001	1.3 (1.1, 1.6)	1.1 (0.9, 1.4)	<.001
BNP, median (IQR), pg/mL	254 (91.3, 668.5)	383 (168, 871)	546.5 (261, 1080)	<.001	384 (156, 866)	382.5 (161, 907)	.462
QRS duration, median (IQR), ms	110 (96, 144)	130 (104, 160)	136 (106, 162)	<.001	124 (102, 158)	122 (96, 152)	<.001
NYHA classification (%)				.022			<.001
Class I	21.2	20.7	18.3		21.0	18.0	
Class II	27.9	25.0	25.8		25.8	27.0	
Class III	18.4	17.2	17.7		16.9	19.5	
Class IV	2.2	2.5	2.8		2.7	2.0	
Not documented	30.3	34.6	35.4		33.6	33.5	

IQR, Interquartile range; *Hx*, history; *SBP*, systolic blood pressure; *HR*, heart rate; *BUN*, blood urea nitrogen; *BNP*, brain natriuretic peptide.
*Age was missing in 107 (0.7%) patients, and sex was missing in 10 (0.07%) patients.

analyzed by stratifying the data by sex and age group. All analyses were performed with SAS statistical software, version 9.1 (SAS Institute, Cary, NC) using 2-side statistical inference testing. Results were considered statistically significant if the *P* value was less than .05.

Results

Baseline patient and practice characteristics

The medical records of 15,381 patients at 167 outpatient cardiology practices in the United States were included in this analysis. A median of 90 patients (25th to 75th percentile, 58 to 107) were enrolled per practice. Mean and median patient ages were 68.7 and 70 years, respectively, and 71.0% of patients were male. The NYHA functional class was documented in 66.6% of patients, with 20.1% class I, 26.3% class II, 17.7% class III, and 2.5% class IV. The QRS duration was available for 67.2% of patients with mean QRS duration of 129.2 ± 40.11 milliseconds and QRS duration ≥120 milliseconds documented for 52.0% of patients. Both NYHA functional class and QRS duration were documented in only 46.2% of patients. Demographic and clinical characteristics for total patients enrolled, those with NYHA functional class documented, and those with both NYHA class and QRS duration were similar (see Appendix B).

Baseline patient characteristics stratified by age and sex are shown in Table I. Male patients were younger compared with female patients (70 vs 72 years, $P < .001$).

Table II. Comparison of baseline practice characteristics by patient age and sex

Practice characteristic	Age (y)				Sex		
	≤64 (n = 5307)	65-76 (n = 5176)	>76 (n = 4791)	*P*	Male (n = 10,925)	Female (n = 4446)	*P*
Region (%)				<.001			.055
South	44.2	42.5	37.8		41.5	42.1	
Northeast	25.9	28.1	29.7		27.8	27.8	
Central	17.6	17.0	17.0		17.0	18.0	
West	11.4	11.8	14.7		13.0	11.5	
Multispecialty (%)	25.0	22.5	22.1	<.001	23.3	23.1	.788
Hospital based (%)	32.2	25.3	24.2	<.001	27.4	26.8	.503
Transplant center (%)	19.0	11.2	9.0	<.001	12.7	14.1	.025
Outpatient practice setting* (%)				<.001			.902
University-teaching	13.1	7.3	5.3		8.6	8.5	
Non–university-teaching	24.3	21.6	21.1		22.3	22.2	
Nonuniversity, nonteaching	57.8	66.0	69.3		64.1	64.7	
No. of physicians (%)				.398			.272
1-10	42.2	43.4	44.0		43.0	43.6	
11-20	30.4	29.8	29.5		29.6	30.5	
>20	22.6	21.6	22.0		22.3	21.3	
Interventionalist in practice (%)	91.5	90.6	91.1	.013	90.9	91.4	.230
EP part of practice (%)	70.9	68.5	67.1	<.001	68.4	69.7	.214
No. of patients with HF managed annually				<.001			.415
n	4380	4293	4024		9080	3694	
Median, (IQR)	2250 (600, 4578)	2250 (679, 5000)	2319 (800, 5000)		2250 (679, 5000)	2300 (750, 5000)	
Suburban (%)	68.2	72.8	76.0	<.001	72.1	72.4	.952
HF clinic (%)	52.2	45.1	43.1	<.001	46.8	47.1	.764
Medical records (%)				.210			.061
EHR only/mixed	46.5	47.4	45.6		46.1	47.7	
Paper only	53.5	52.6	54.4		53.9	52.3	
HF nurses >1 FTE (%)	40.4	39.5	39.4	.750	40.2	38.6	.162
Device clinic (%)	81.3	81.0	81.1	.676	80.4	82.8	<.001

EP, Electrophysiology; *IQR*, interquartile range; *EHR*, electronic health record; *FTE*, full-time equivalent.
*Outpatient practice setting was missing for 10 practice sites.

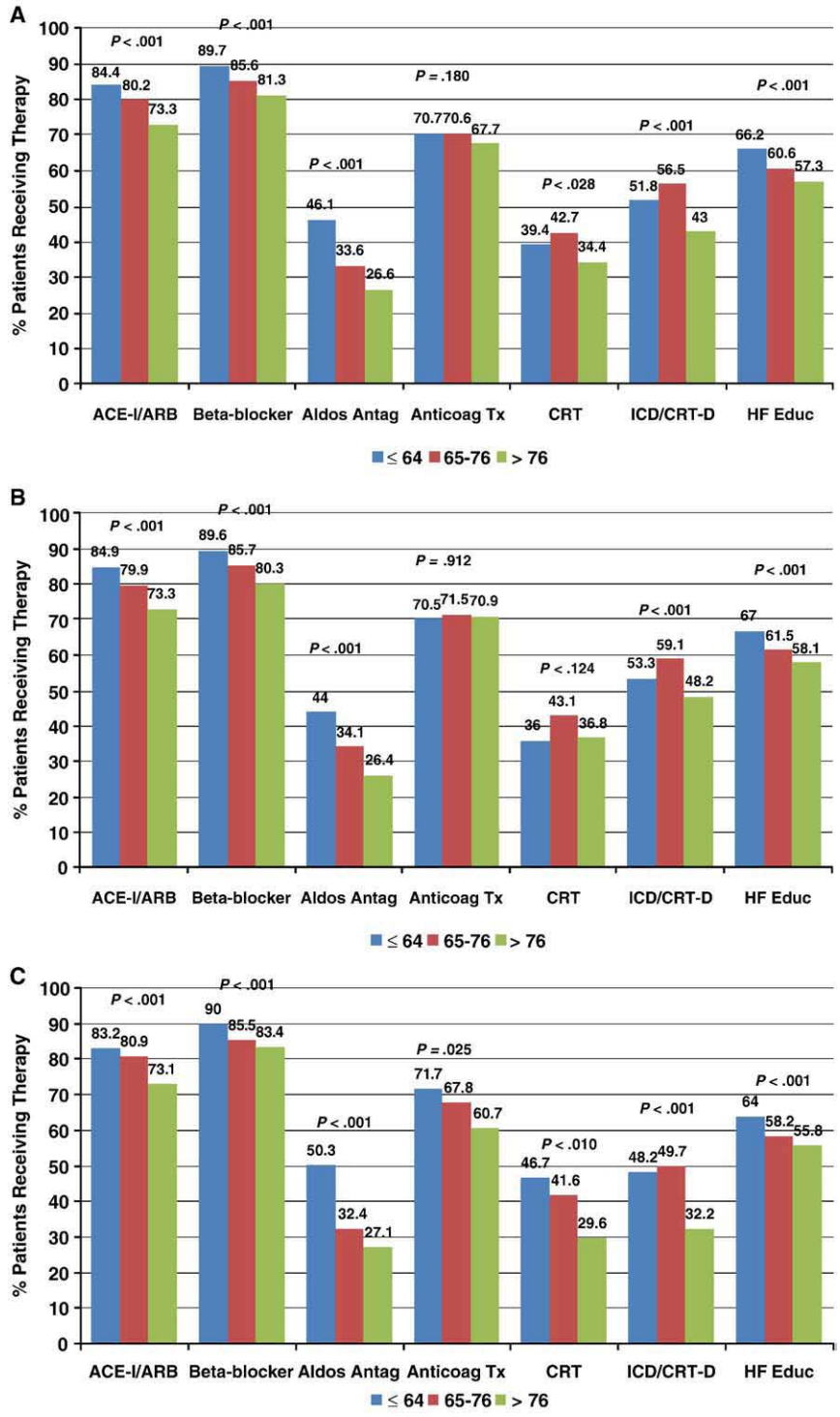
There was also a significant sex difference in HF etiology, with 70.0% of men affected by ischemic disease compared with 53.4% of women ($P < .001$). Age was associated with significant differences in HF etiology, with ischemic disease reported for 52.6% of patients ≤64 years compared with 71.1% of those aged 65 to 76 years and 72.9% of patients >76 years ($P < .001$). Significantly higher rates of atrial flutter, hypertension, prior MI, history of chronic obstructive pulmonary disease (COPD), coronary artery bypass graft (CABG), and peripheral vascular disease (PVD) were evident for older patients. Significant age differences were also reported for all laboratory assessments and QRS duration ($P < .001$ for all comparisons).

Baseline practice characteristics stratified by age and sex are shown in Table II. There were significant differences in practice characteristics associated with patient sex including higher rates of women (14.1%) compared with men (12.7%) receiving care at outpatient facilities affiliated with a transplant center ($P < .025$) and more women attending practices with a device clinic (82.8% of women vs 80.4% of men; $P < .001$). Analysis of practice characteristics by age tertiles revealed that younger patients were significantly more likely to attend multispecialty, hospital-based, and transplant-affiliated outpatient practices as well as those with dedicated HF clinics and electrophysiology cardiologists on staff ($P < .001$ for all comparisons).

Provision of guideline-recommended care

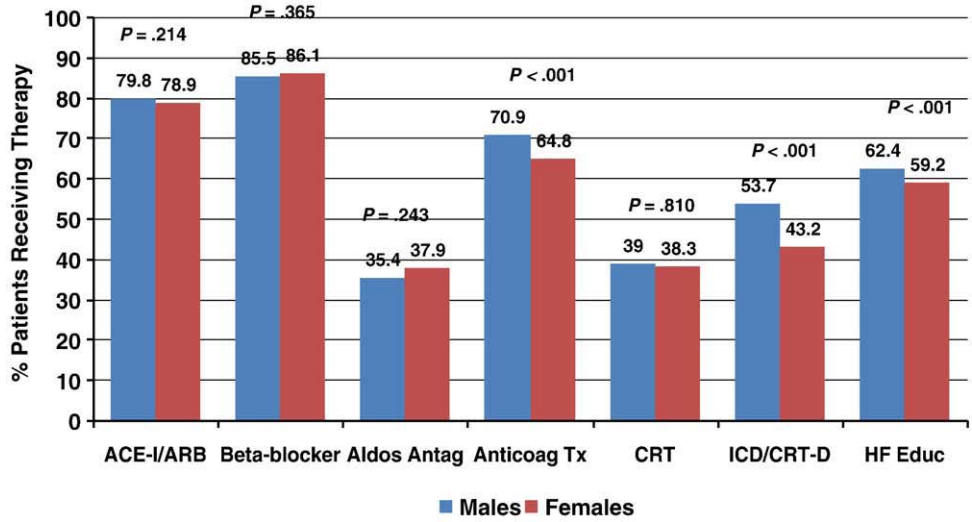
Among patients eligible for each care metric, ACEI or ARB was prescribed for 11,271 (80%) of 14,167 patients; β-blockers were prescribed for 12,039 (86%) of 14,058 patients; and aldosterone antagonists were administered to 905 (36%) of 2,505 patients. Anticoagulants were received by 2,450 (69%) of 3,533 patients with permanent, persistent, or paroxysmal atrial fibrillation or flutter. Of 1,361 patients eligible for device therapy, 528 (39%) patients received CRT, including CRT-D or CRT with pacemaker; whereas ICD/CRT-D therapy was provided to 3,630 (51%) of 7,169 eligible patients. Heart failure education was provided to 9,459 (61%) of all patients.

Figure 1



A, Patients receiving recommended HF therapies by age tertiles. IMPROVE HF care measures at baseline. Aldosterone antagonist, CRT, or ICD therapy care metrics are not ACC/AHA outpatient HF performance measures. **B**, Men receiving recommended HF therapies by age tertiles. IMPROVE HF care measures at baseline. Aldosterone antagonist, CRT, or ICD therapy care metrics are not ACC/AHA outpatient HF performance measures. **C**, Women receiving recommended HF therapies by age tertiles. IMPROVE HF care measures at baseline. Aldosterone antagonist, CRT, or ICD therapy care metrics are not ACC/AHA outpatient HF performance measures.

Figure 2



Patients receiving recommended HF therapies by sex. IMPROVE HF care measures at baseline. Aldosterone antagonist, CRT, or ICD therapy care metrics are not ACC/AHA outpatient HF performance measures.

Table III. Estimated unadjusted and adjusted odds ratio for conformity to IMPROVE HF care measures based on increasing age

	Unadjusted odds ratio estimates					Adjusted odds ratio estimates				
Care measure	**Point estimate**	**95% CI**	**95% CI**	**Wald χ^2**	***P***	**Point estimate**	**95% CI**	**95% CI**	**Wald χ^2**	***P***
ACEI/ARB	0.844	0.817	0.871	106.78	<.0001	0.869	0.835	0.903	50.25	<.0001
β-Blocker	0.861	0.829	0.894	61.92	<.0001	0.846	0.808	0.886	50.80	<.0001
Aldosterone antagonist	0.756	0.711	0.803	81.49	<.0001	0.811	0.753	0.874	30.35	<.0001
Anticoagulation for atrial fibrillation*	0.953	0.897	1.012	2.48	.1149	0.990	0.922	1.063	0.08	.7767
CRT*	0.903	0.825	0.989	4.83	.0279	0.883	0.794	0.983	5.15	.0233
ICD/CRT-D*	0.938	0.906	0.970	13.89	.0002	0.938	0.900	0.977	9.28	<.0023
HF education	0.910	0.888	0.932	57.64	<.0001	0.927	0.900	0.955	24.61	<.0001

Age (per 10 years) was a continuous variable.
* An age-sex interaction was significant for these care measures.

Analysis of treatment rates by patient age revealed significant differences for 6 of the 7 care measures (Figure 1, *A*). Patients in the oldest age group were less likely to receive recommended interventions compared with their younger counterparts. The largest absolute difference by patient age group was 19.5% for use of aldosterone antagonists.

Significant differences by sex were observed for anticoagulant therapy, ICD/CRT-D therapy, and HF education, with higher rates evident for men ($P < .001$ for all comparisons) (Figure 2). The largest absolute difference was 10.5% for ICD/CRT-D use. Stratification of the care measures by age and sex revealed the most striking differences for aldosterone antagonist, CRT, and ICD/CRT-D therapy for older females (Figure 1, *B* and *C*).

To determine the independent contribution of age and sex on the provision of guideline-recommended therapies, a series of GEE analyses were performed adjusting for practice and other patient characteristics. Tables III and IV present the unadjusted and adjusted odds ratio estimates for the 7 care measures by age and sex. Increasing age was independently associated with 6 of 7 measures, whereas sex was predictive of 5 of 7 measures. Significant age × gender interactions were evident for 3 of the 7 care measures including anticoagulation therapy, CRT, and ICD/CRT-D implantation. When stratified by age tertiles, there were no significant differences between males and females receiving CRT or anticoagulation therapy for atrial fibrillation; however, males aged between 65 and 76 years and >76 years were

Table IV. Estimated unadjusted and adjusted odds ratio for conformity to IMPROVE HF care measures based on sex (male vs female)

	Unadjusted odds ratio estimates					Adjusted odds ratio estimates				
Care measure	**Point estimate**	**95% CIs**	**95% CI**	**Wald χ^2**	***P***	**Point estimate**	**95% CI**	**95% CI**	**Wald χ^2**	***P***
ACEI/ARB	1.059	0.968	1.158	1.55	.2128	1.136	1.020	1.264	5.42	.0199
β-Blocker	0.951	0.856	1.056	0.88	.3487	0.927	0.816	1.052	1.38	.2400
Aldosterone antagonist	0.898	0.753	1.069	1.46	.2268	0.793	0.639	0.985	4.41	.0358
Anticoagulation for atrial fibrillation*	1.322	1.126	1.554	11.57	.0007	1.439	1.192	1.736	14.41	.0001
CRT*	1.032	0.814	1.308	0.07	.7945	1.042	0.790	1.375	0.09	.7702
ICD/CRT-D*	1.524	1.376	1.689	65.30	<.0001	1.422	1.260	1.606	32.37	<.0001
HF education	1.145	1.066	1.229	13.85	.0002	1.156	1.060	1.260	10.77	.0010

An odds ratio <1 indicates the performance measure was more likely for female patients.
*An age-sex interaction was significant for these care measures.

significantly more likely than females to receive ICD/CRT-D devices (Appendix C).

Discussion

This study evaluates the influence of age and sex on delivery of guideline-recommended HF therapies within IMPROVE HF, a registry of patients with HF and LVSD receiving care in outpatient cardiology practices. The ACC/AHA HF guidelines assign a class I recommendation that groups of patients including women and elderly persons, even if underrepresented in clinical trials, should, in the absence of specific evidence to treat otherwise, have clinical screening and therapy in a manner identical to that provided to the broader HF population. It is also specifically recommended that evidence-based therapy for HF be provided to elderly patients, with individualized consideration of the possibility that older patients may have an altered ability to metabolize or tolerate standard medications. It is therefore recommended in the national guidelines that all eligible patients with HF in the absence of contraindications or intolerance receive recommended therapies, irrespective of patient age and sex.

Age, gender, and HF care

The IMPROVE HF data reveal that based on information as documented in the medical record, the use of ACEI or ARB, and β-blockers was remarkably similar for men and women. Prior studies in the usual care setting have consistently shown lower HF treatment rates in women. A retrospective survey of 9,387 hospital admissions with HF from October 2005 to March 2006 in England, Wales, and Northern Ireland revealed that women were significantly less likely to be prescribed HF medications on discharge compared with men (ACEI/ARB 66.5% vs 73.4%, β-blocker 31.3% vs 37.5%, and aldosterone antagonists 23.4% vs 30.1%, all $P < .001$).[20] The IMPROVE HF data may differ from other published literature because the data were collected for outpatients, there was a greater awareness of guideline-based HF medical therapies, or there was selection bias in the 167 participating practices. However, the IMPROVE HF data confirm other differences in HF care associated with patient sex with women less likely to receive anticoagulation therapy, ICD/CRT-D implantation, and HF education.

Increasing age was also a significant predictor of lower adherence rates for all therapies except anticoagulation therapy for atrial fibrillation. These findings are consistent with results from prior studies such as the Enhanced Feedback for Effective Cardiac Treatment study, which reported significant age disparities in treatment with ACEI/ARB and β-blockers 90 days after hospital discharge. Specifically, among eligible, older, higher-risk patients with HF, only 68% received ACEI/ARB and 27% β-blockers, which was substantially lower than treatment rates for the same pharmacotherapies administered to eligible, younger, lower-risk patients.[21] Increasing age has also been shown to be an independent factor associated with lower ICD implantation rates among eligible patients who have survived cardiac arrest.[22]

Some of these variations may reflect quality-of-care issues, patient preferences, and other nonmedical considerations such as access to care or other comorbidities.

The lower rates of provision of guideline-recommended therapies in older patients in IMPROVE HF may also reflect differences in training, guideline familiarity, and implementation of tools and systems to ensure that recommended care is provided to all eligible patients. There may be uncertainty about risks versus benefits in treating elderly patients who are underrepresented in randomized controlled trials. Misperceptions regarding contraindications and lack of tolerability in elderly patients may also contribute to age-related treatment gaps and disparities in care. The increased difficulty experienced by older patients as they attempt to comply with the demands of multiple medications, coupled with the desire to avoid side effects and adverse drug interactions, may also contribute to limitations in the types of HF treatment administered to older patients. Importantly,

elderly patients may be more reluctant to undergo a surgical procedure, such as device implantation. These challenges may make physicians more reluctant to provide optimal HF pharmacotherapy and/or device therapy to older patients with HF.

The differences in care associated with age and sex in IMPROVE HF may also reflect differences in documentation of care that was actually provided. Information in medical records may have suggested that patients were eligible for treatment. However, decisions to administer device therapy often require multiple, in-depth discussions that resulted in appropriate decision to withhold specific interventions. These discussions may not have been fully documented in patients' medical records. Furthermore, differences in documentation of current HF symptoms, contraindications, intolerances, patient reasons, and physician reasons for not providing guideline-recommended therapies may have varied by patient age and sex.

Limitations

Certain limitations inherent in the design of IMPROVE HF should be considered when interpreting these findings. Data were collected by medical chart review, including age and gender, and depend upon the accuracy and completeness of documentation. As such, a proportion of patients reported to be eligible for treatment who did not receive recommended treatments may have had contraindications or intolerance to specific interventions that were present but not documented. Residual measured or unmeasured confounding variables may account for some of the observations. These findings demonstrate associations rather than cause-and-effect relationships between patient age and sex with delivery of guideline-recommended care for HF. Aldosterone antagonist, CRT, and ICD therapy for eligible patients are class I recommendations in the ACC/AHA guidelines. However, the ACC/AHA performance measures for outpatients with HF do not include measures for these therapies, optimal treatment rates have not been defined, and some experts question whether such measures are appropriate for quality assessment and improvement.[18,19] These findings may not apply to practices that differ in patient characteristics or care patterns from the outpatient cardiology practices enrolled in IMPROVE HF. The patients seen in the IMPROVE HF practices may not be representative of the general outpatient population of individuals with HF, as these patients were followed in cardiology practices and ascertainment bias may be related to this point of care.

Conclusions

Patients with HF who are female and those who are elderly are at increased risk for morbidity and mortality. Despite less favorable outcomes, these patients were less likely to receive certain guideline-recommended evidence-based treatments in the outpatient arena. Older patients with HF receive less pharmacologic and device therapy as well as less HF education than younger patients in outpatient cardiology practices. Women received less HF education and less device therapy in the outpatient cardiology setting than their male counterparts with HF, and sex is independently associated with differences in the use of anticoagulation therapy for atrial fibrillation, ICD/CRT-D placement, and HF education. Additional research is needed to identify the full complement of explanations for these apparent differences in adherence to guideline-driven, evidence-based care for older and female patients with HF.

Disclosures

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Appendix A. IMPROVE HF care measures

Use of ACEI and/or angiotensin receptor blocker in eligible patients with LVSD and without documented contraindications or intolerance
Use of β-blocker in eligible patients with LVSD and without documented contraindications or intolerance
Use of aldosterone receptor antagonist in eligible patients with LVSD and NYHA Functional Class III or IV HF and without documented contraindications or intolerance*
Use of anticoagulation therapy in eligible patients with atrial fibrillation without documented contraindications
Use of an ICD in eligible patients with LVEF ≤35%, NYHA Class II or III HF without documented contraindications or medical, patient, or other reason for not implanting device*
Use of CRT in eligible patients with LVEF ≤35%, QRS duration ≥120 milliseconds, and NYHA Class III or ambulatory Class IV HF without documented contraindications or medical, patient, or other reason for not implanting device*
Documentation that HF education (including discussion of salt-restricted diet, monitoring of daily weight, warning signs of worsened HF, and activity recommendations) was provided to eligible patients

* These metrics are not ACC/AHA performance measures for outpatients with HF.

Appendix B. Baseline characteristics of overall patient population, patients with NYHA class documented, and patients with both NYHA Class and QRS duration documented

Characteristic	Overall	Documented NYHA class	Documented NYHA class and QRS duration
Age, median (IQR)	70.0 (60, 79)	70.0 (59, 78)	70.0 (59, 78)
≤64 (%)	34.5	36.2	36.9
65–76 (%)	33.7	33.1	32.6
>76 (%)	31.1	30.3	30.2
Male (%)			
Race (%)			
White	41.4	43.5	44.9
African American	9.1	10.2	10.8
Not documented/missing	47.8	44.3	42.4
HF etiology (%)			
Ischemic	65.2	64.8	64.5
Nonischemic	16.0	18.9	19.4
Valvular	2.0	1.9	1.8
Other	9.3	8.6	8.7
Not documented	6.7	5.2	5.2
Hx atrial fibrillation (%)	30.8	30.9	31.9
Hx diabetes (%)	34.0	34.0	34.2
Hx hypertension (%)	61.7	61.5	62.7
Prior MI (%)	39.4	38.0	38.0
Hx COPD (%)	16.4	15.9	16.3
Hx CABG (%)	30.9	30.2	30.6
Hx PVD (%)	11.3	11.1	11.2
Hx depression (%)	8.8	9.2	9.2
LVEF, median (IQR)	25.0 (20, 30)	25.0 (20, 30)	25.0 (20, 30)
SBP, median (IQR)	120.0 (108, 130)	120.0 (108, 130)	120.0 (108, 130)
DBP, median (IQR)	70.0 (60, 80)	70.0 (60, 78)	70.0 (60, 78)
Resting HR beat/min, median (IQR)	71.0 (64, 80)	72.0 (64, 80)	72.0 (64, 80)
Rales on most recent examination (%)	3.7	4.0	4.0
Edema on most recent examination (%)	19.7	20.6	20.9
Sodium, median (IQR), mEq/L	140.0 (137, 141)	139.0 (137, 141)	139.0 (137, 141)
BUN, median (IQR), mg/dL	22.0 (16, 30)	22.0 (16, 30)	22.0 (16, 31)
Creatinine, median (IQR), mg/dL	1.2 (1.0, 1.6)	1.2 (1.0, 1.6)	1.2 (1.0, 1.6)
BNP, median (IQR), pg/mL	383.7 (158, 877)	376.0 (150, 863)	376.0 (150, 834)
QRS duration, median (IQR), ms	124.0 (100, 156)	126.0 (100, 158)	126.0 (100, 158)
NYHA classification (%)			
Class I	20.1	30.3	29.5
Class II	26.1	39.3	39.3
Class III	17.7	26.6	27.6
Class IV	2.5	3.7	3.7
Not documented	46.2	69.5	–

IQR, Interquartile range; *Hx*, history; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *HR*, heart rate; *BUN*, blood urea nitrogen; *BNP*, brain natriuretic peptide.
*Age was missing in 107 (0.7%) patients, and sex was missing in 10 (0.07%) patients.

Appendix C. Adjusted odds ratio for conformity to IMPROVE HF care measures stratified analyses of age and sex

	Adjusted odds ratio estimates			
Care measure	**Point estimate**	**95% Wald confidence limits**		***P***
Analysis of age within gender group				
Anticoagulation for atrial fibrillation				
Male	1.065	0.984	1.154	.1208
Female	0.764	0.650	0.899	.0011
CRT				
Male	0.918	0.806	1.046	.2002
Female	0.759	0.617	0.934	.0093
ICD/CRT-D				
Male	0.986	0.938	1.037	.5795
Female	0.841	0.780	0.906	<.0001
Analysis of gender within age group				
Anticoagulation for atrial fibrillation				
Age ≤64	0.899	0.543	1.489	.6788
64< age ≤76	1.255	0.897	1.756	.1842
Age >76	1.884	1.439	2.468	<.001
CRT				
Age ≤64	0.565	0.324	0.987	.0449
64< age ≤76	1.298	0.804	2.096	.2865
Age >76	1.515	0.914	2.512	.1074
ICD/CRT-D				
Age ≤64	1.154	0.941	1.416	.1675
64< age ≤76	1.325	1.066	1.648	.0113
Age >76	1.943	1.553	2.432	<.0001

GEE model analyses adjusting for other patient and practice characteristics. Age (per 10 years) was analyzed as a continuous variable.