

# Management of patients with heart failure in clinical practice: differences between men and women

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## ABSTRACT

**Objectives:** This study evaluated gender differences in clinical characteristics, treatment and outcome among patients with heart failure, and to what extent these differences are due to age and differences in left ventricular (LV) function. Although gender differences are observed among heart failure patients, few studies have been adequately powered to investigate these differences.

**Methods:** A total of 8914 (out of 10 701) patients (47% women) from the Euro Heart Survey on Heart Failure with confirmed diagnosis of heart failure were included in the analyses.

**Results:** Women were older (74.7 vs 68.3 years,  $p < 0.001$ ), and less often had evidence of coronary artery disease (56% vs 66%, age-adjusted odds ratio (OR) 0.62; 95% CI 0.57 to 0.68). Women were more likely to have hypertension, diabetes, or valvular heart disease. Fewer women had an investigation of LV function (59% vs 74%, age-adjusted OR 0.67; 95% CI 0.61 to 0.74), and, among those investigated, fewer had moderate/severe left ventricular systolic dysfunction (44% vs 71%, age-adjusted OR 0.35; 95% CI 0.32 to 0.39). Drugs with a documented impact on survival, that is ACE-inhibitors and  $\beta$ -blockers, were given less often to women, even in the adjusted analysis (OR 0.72; 95% CI 0.61 to 0.86 and OR 0.76; 95% CI 0.65 to 0.89, respectively). 12-week mortality was similar for men and women.

**Conclusions:** Fewer women had an assessment of LV function, but, when investigated, women had better ventricular function. Women were less often treated with evidence-based drugs, even after adjustment for age and important clinical characteristics. Clinicians need to be aware of deficiencies in the treatment of women with heart failure and measures should be taken to rectify them.

Chronic heart failure is a major cause of morbidity and mortality, and the reason for at least 20% of all hospital admissions in patients older than 65 years.<sup>1,2</sup> Major advances over the last two decades in the diagnosis and treatment of heart failure have proven highly effective in reducing morbidity and mortality among both men and women. However, survival is still poor among both men and women, and the absolute number of women dying of heart failure each year still increases.<sup>3</sup> Men and women with heart failure have different clinical characteristics, in that women are older and have more hypertension but less evidence of coronary heart disease and better ventricular function than men with heart failure.<sup>3</sup> Few studies have been adequately powered to investigate how many of these known differences

between men and women are due to gender alone, and how many are due to known other differences such as the discrepancies in age, ventricular function, or cause of heart failure. The large number of both men and women enrolled in the Euro Heart Survey on Heart Failure (EHS-HF) and the extensive data collection of patient characteristics, investigations and treatment provide a unique opportunity to analyse gender differences in patients with confirmed or suspected heart failure.

## METHODS

We performed a comparison of men and women who were enrolled in the EHS-HF. The design details of this observational study, which was undertaken between March 2000 and May 2001, were published previously.<sup>4,5</sup> Briefly, the case notes of consecutive discharges and deaths in the departments of cardiology, cardiovascular surgery, general internal medicine, non-vascular surgery and geriatrics were reviewed over a 6-week period to screen patients for:

1. a clinical diagnosis of heart failure recorded during the admission;
2. a diagnosis of heart failure recorded in the hospital notes at any time in the last 3 years;
3. administration of a loop diuretic for any reason other than renal failure within 24 h of death or discharge;
4. pharmacological treatment for heart failure or ventricular dysfunction within 24 h of death or discharge (investigators were asked to review any prescription of ACE-inhibitors,  $\beta$ -blockers, diuretics, digitalis or spironolactone to determine the reason for their administration).

All patients who fulfilled at least one of these criteria had a detailed record of the events precipitating their admission, cardiovascular investigation, cardiovascular and non-cardiovascular disease and therapy completed by an investigator at each site. Surviving patients were contacted and asked to attend an interview at 12 weeks, at which time any further clinical events, investigations and treatment were recorded and a brief examination was performed. Median (quartiles) follow-up was 12 (11–14) weeks.

From a total of 46 788 deaths and discharges from 115 hospitals in 24 ESC member countries, 10 701 patients with suspected or confirmed heart failure were enrolled in the EHS-HF. As we acknowledge the fact that the validity of heart failure diagnosis in all included patients may be challenged, we restricted the analyses to patients with a clinical diagnosis of heart failure during the

current admission or diagnosed within the past 3 years ( $n = 8953$ ). After exclusion of 39 patients with missing data for age and gender, the total study population consisted of 8914 patients.

CAD was defined as a history of coronary revascularisation procedure, myocardial infarction or angina pectoris. Patients were considered to have left ventricular systolic dysfunction (LVSD) if they had a left ventricular ejection fraction of  $<40\%$ , or moderate or severe impairment of left ventricular (LV) systolic function on echocardiography. Patients with an ejection fraction of  $\geq 40\%$ , as well as patients with a normal or only mildly depressed LV systolic function, were classified as having preserved LV function (PLVF).

### Statistical analysis

Continuous variables are described as mean values with their corresponding standard deviation (SD), and dichotomous variables are described as counts and percentages. To evaluate the differences in clinical characteristics between men and women,  $\chi^2$  tests and Student *t* tests were applied as appropriate. In addition, univariate and multivariate analyses were performed to study the association in clinical variables and outcome between men and women. In the multivariate analyses we adjusted for age and a number of clinical variables with a *p* value of  $<0.10$ . These variables included history of hypertension, diabetes, stroke or transient ischaemic attack (TIA), respiratory disease, coronary artery disease, cardiomyopathy, and atrial fibrillation. We report odds ratios (OR) and corresponding 95% confidence intervals (CI). For all tests, a *p* value of  $<0.05$  (two-sided) was considered statistically significant. All calculations were performed using the SPSS 12.0.1 software package.

### RESULTS

In table 1, the baseline characteristics of the 8914 patients (47% women) with suspected or confirmed heart failure are summarised. Women were significantly older than men (74.7 versus 68.3 years,  $p < 0.001$ ) with more patients aged  $>80$  years (36% versus 18%,  $p < 0.001$ ). A history of hypertension and diabetes was more prevalent among women, whereas men more often were smokers and heavy alcohol drinkers. Fifty-six per cent of the women but 66% of the men had known CAD ( $p < 0.001$ ), and corresponding figures for coronary revascularisation were 17% and 35% ( $p < 0.001$ ), respectively. Older patients ( $\geq 70$  years) had more co-morbid conditions such as stroke (19% versus 12%,  $p < 0.001$ ), a history of renal dysfunction (serum creatinine  $>150$  mmol/l) (22% versus 15%,  $p < 0.001$ ), or atrial fibrillation (49% versus 37%,  $p < 0.001$ ).

Table 2 shows that women were admitted to a cardiology ward less often than men (36% versus 53%,  $p < 0.001$ ). Left ventricular function was measured less often in women (59% versus 74%,  $p < 0.001$ ), and, when it was measured, fewer women had left ventricular systolic dysfunction (44% versus 71%,  $p < 0.001$ ). In a subgroup of patients who had an echocardiogram, valvular heart disease was seen more often in women (42% versus 36%,  $p < 0.001$ ). The most frequently observed valvular heart disease was mitral regurgitation (31% and 29% for men and women, respectively ( $p = 0.05$ )). In addition to these gender differences, it is also important to note that younger patients were more likely to be admitted to cardiology wards (64% versus 34%,  $p < 0.001$ ), and more often had an assessment of the LV function (81% versus 60%,  $p < 0.001$ ).

After adjustment for age, most of the observed gender differences remained statistically significant (table 3); however, gender differences with respect to stroke or TIA, atrial fibrillation and aortic regurgitation did not persist after adjustment for age. Irrespective of left ventricular function, women were more likely to have hypertension but less often a history of an ischaemic heart disease (table 4).

Men and women differed with respect to pharmacological treatment (table 5). Fewer women with evidence of LVSD ( $n = 3584$ ) were treated with drugs with a documented impact on survival (ACE-inhibitors (OR 0.71; 95% CI 0.60 to 0.84),  $\beta$ -blockers (OR 0.66; 95% CI 0.57 to 0.77), and spironolactone (OR 0.69; 95% CI 0.59 to 0.81), whereas they were more often treated with cardiac glycosides (OR 1.16; 95% CI 1.05 to 1.28). In addition, women were also less likely to be treated with antithrombotic drugs (OR 0.66; 95% CI 0.59 to 0.75). After adjustment for age and clinical characteristics including CAD, these observed gender differences remained significant. We repeated the analyses in a subgroup of patients who had PLVF ( $n = 2396$ ). In this subgroup of patients no significant gender differences were observed with respect to ACE-inhibitors,  $\beta$ -blockers, and spironolactone. Conversely, gender differences were observed regarding the administration of diuretics, cardiac glycosides, and antithrombotic agents.

Patients with evidence of LVSD, admitted to cardiology wards (including cardiovascular surgery), were treated more often with ACE-inhibitors (81%),  $\beta$ -blockers (55%), and spironolactone (32%) than patients admitted to general internal medicine wards (75%, 30%, and 27% respectively) or patients admitted on non-vascular surgery or geriatric wards (66%, 32%, and 21% respectively).

No substantial gender differences could be demonstrated with respect to 12-week mortality and readmission within 12 weeks (table 6). Although the percentage of women who died during the observation period was slightly higher (15.2% versus 12.7%), gender was not an independent predictor of mortality (OR 1.10; 95% CI 0.88 to 1.38 for patients with LVSD, and OR 1.23; 95% CI 0.93 to 1.64 for patients with PLVF).

### DISCUSSION

This study confirms earlier reports that women with heart failure have a different clinical profile from that seen in men, and more often have a preserved left ventricular function.<sup>3-6</sup> These differences remained significant after adjustment for age. In addition, women were less often admitted to cardiology wards, or had an assessment of left ventricular function, and were also less often treated with evidence-based drugs. The observed differences were still evident after adjustment for age and other clinical variables. Despite the fact that women had better left ventricular systolic function and less often had CAD, outcomes with respect to in-hospital and total 12-week mortality were similar in men and women.

Consistent with previous reports, women were older, more often had hypertension, diabetes, cerebrovascular disease, and valvular heart disease, but had a lower prevalence of CAD and LVSD.<sup>3-6,9</sup> Because women were less likely to undergo assessment of the left ventricular function a substantial proportion could not be identified as having depressed or preserved left ventricular function. Although this gender difference with respect to lack of information on ventricular function confirms results from other studies,<sup>10,11</sup> the fact that women were less likely than men to undergo qualitative or quantitative assessment of left ventricular function causes concern, because this information is critical to confirm heart failure, to provide

**Table 1** Baseline characteristics by sex and age

	Total (n = 8914)	All patients (n = 8914)			Patients <70 years (n = 3520)			Patients ≥70 years (n = 5394)		
		Men (%) (n = 4748)	Women (%) (n = 4166)	p Value	Men (%) (n = 2368)	Women (%) (n = 1152)	p Value	Men (%) (n = 2380)	Women (%) (n = 3014)	p Value
Age (mean, SD)	71.3 (12.7)	68.3 (12.7)	74.7 (11.9)	<0.001	58.3 (9.0)	59.8 (9.1)	<0.001	78.3 (6.4)	80.5 (6.7)	<0.001
Age group										
<60	1523	23	11	<0.001	47	36	<0.001	–	–	
60–69	1997	27	18	<0.001	53	64	<0.001	–	–	
70–79	3014	32	36	<0.001	–	–		64	50	<0.001
>80	2380	18	36	<0.001	–	–		36	50	<0.001
Current smoker	1068	18	6	<0.001	24	10	<0.001	11	4	<0.001
Heavy alcohol drinker, ever	564	11	1	<0.001	15	2	<0.001	7	1	<0.001
History of hypertension	4771	49	59	<0.001	48	58	<0.001	49	60	<0.001
Diabetes	2457	26	29	<0.001	26	30	0.006	26	29	0.02
Stroke or transient ischaemic attack (TIA)	1468	16	18	0.02	11	14	0.05	20	19	0.38
History of renal dysfunction	1688	21	17	<0.001	15	14	0.18	26	18	<0.001
Respiratory disease	2833	33	31	0.06	27	30	0.11	38	31	<0.001
Cumulative evidence for CAD†	5451	66	56	<0.001	65	55	<0.001	67	56	<0.001
Myocardial infarction, ever	3510	71	55	<0.001	74	55	<0.001	69	55	<0.001
History of angina, ever	3865	70	73	0.01	71	78	0.002	68	71	0.06
Revascularisation (PCI or CABG), ever	1484	35	17	<0.001	44	28	<0.001	26	13	<0.001
Dilated cardiomyopathy	240	4	2	<0.001	5	3	0.008	2	1	<0.001
Atrial fibrillation (AF), ever	3932	42	46	<0.001	36	37	0.63	48	50	0.21
Chronic AF	2202	24	26	0.01	19	20	0.41	29	28	0.80

†CAD (coronary artery disease): myocardial infarction, angina, or revascularisation.

optimal treatment and to estimate prognosis.<sup>12</sup> Although our study did not identify reasons for the observed diagnostic deficiency, we were able to exclude age and a number of clinical characteristics as important confounders.

As discussed in previous reports, recommended drugs in patients who were enrolled in the EHS-HF were underused.<sup>13 14</sup> The current study adds another dimension to this observation, namely that men and women were treated differently.

Univariate analyses revealed that women were less likely to be treated with drugs that have a proven effect on reducing mortality (ACE-I,  $\beta$ -blockers, and spironolactone), but were treated more often with cardiac glycosides and diuretics. Although the observed differences decreased after adjustment for age and a number of clinical characteristics, drugs with a proven effect on reducing mortality were still prescribed to women less often than to men. This indicates that older age and

**Table 2** Clinical characteristics by sex and age

	Total (n = 8914)	All patients (n = 8914)			Patients <70 years (n = 3520)			Patients ≥70 years (n = 5394)		
		Men (%) (n = 4748)	Women (%) (n = 4166)	p Value	Men (%) (n = 2368)	Women (%) (n = 1152)	p Value	Men (%) (n = 2380)	Women (%) (n = 3014)	p Value
Ward of admission:										
Cardiology (incl. cardiovascular surgery)	4041	53	36	<0.001	67	56	<0.001	39	29	<0.001
General internal medicine	5165	40	55	<0.001	28	40	<0.001	51	60	<0.001
Non-vascular surgery or geriatrics	708	7	9	<0.001	4	4	<0.001	10	11	<0.001
Assessment of left ventricular (LV) function	5980	74	59	<0.001	84	76	<0.001	65	53	<0.001
LVSD‡	3584	71	44	<0.001	74	48	<0.001	66	42	<0.001
LVEF measured, ever	5532	69	54	<0.001	80	71	<0.001	58	48	<0.001
Ejection fraction <40%	2089	47	24	<0.001	52	27	<0.001	42	22	<0.001
Echocardiography performed:	6023	73	61	<0.001	82	76	<0.001	65	56	<0.001
Normal/mild LV systolic function	2560	33	55	<0.001	30	53	<0.001	37	57	<0.001
Moderate/severe LV systolic dysfunction	2861	58	33	<0.001	62	38	<0.001	53	31	<0.001
LV dilatation	1597	35	14	<0.001	41	18	<0.001	28	13	<0.001
Moderate/severe diastolic dysfunction	759	15	10	<0.001	16	9	<0.001	13	10	0.002
Mitral stenosis	185	2	5	<0.001	2	6	<0.001	1	5	<0.001
Aortic stenosis	444	6	9	<0.001	4	6	0.18	8	11	0.001
Mitral regurgitation	1778	29	31	0.05	30	26	0.06	27	33	<0.001
Aortic regurgitation	448	7	8	0.01	6	6	0.55	8	10	0.13

‡LVSD = ejection fraction <40% or moderate to severe LV systolic dysfunction.

**Table 3** Unadjusted and adjusted ORs for the association in clinical characteristics between men and women (total population, n = 8914)

	Gender differences (reference group is men)	
	Unadjusted OR* (95% CI)	OR* adjusted for age (95% CI)
Current smoker	0.28 (0.24 to 0.33)	0.36 (0.31 to 0.42)
Heavy alcohol drinker, ever	0.10 (0.07 to 0.13)	0.12 (0.09 to 0.16)
History of hypertension	1.55 (1.42 to 1.69)	1.51 (1.39 to 1.65)
Diabetes	1.18 (1.09 to 1.30)	1.17 (1.06 to 1.29)
Stroke or transient ischaemic attack (TIA)	1.15 (1.03 to 1.28)	0.98 (0.87 to 1.10)
History of renal dysfunction	0.79 (0.71 to 0.87)	0.67 (0.60 to 0.75)
Respiratory disease	0.92 (0.84 to 1.00)	0.84 (0.77 to 0.93)
Cumulative evidence for CAD†	0.65 (0.60 to 0.71)	0.62 (0.57 to 0.68)
Dilated cardiomyopathy	0.40 (0.30 to 0.53)	0.57 (0.42 to 0.77)
Atrial fibrillation, ever	1.18 (1.09 to 1.29)	1.03 (0.95 to 1.13)
Ward of admission:		
Cardiology	0.50 (0.46 to 0.54)	0.66 (0.61 to 0.73)
General internal medicine	1.85 (1.70 to 2.01)	1.47 (1.35 to 1.61)
Other ward	1.30 (1.11 to 1.51)	1.01 (0.86 to 1.18)
Assessment of LV function:		
LVSD‡	0.51 (0.47 to 0.56)	0.67 (0.61 to 0.74)
Echocardiography performed:		
Mitral stenosis	0.57 (0.52 to 0.62)	0.74 (0.67 to 0.81)
Aortic stenosis	3.54 (2.57 to 4.89)	3.89 (2.79 to 5.41)
Aortic regurgitation	1.66 (1.37 to 2.01)	1.39 (1.14 to 1.70)
Mitral regurgitation	1.12 (1.00 to 1.25)	1.12 (1.00 to 1.25)
Aortic regurgitation	1.28 (1.05 to 1.55)	1.17 (0.96 to 1.42)

\*OR >1 correlates with a higher prevalence in women.

†CAD (coronary artery disease): myocardial infarction, angina, or revascularisation.

‡LVSD = EF < 40% or moderate to severe LV systolic dysfunction.

a different clinical profile in women do not altogether explain the observed gender differences in pharmacological treatment between men and women. It is in this context important to

**Table 5** Pharmacological treatment by gender, including unadjusted and adjusted ORs for the association with treatment (incl. total population and stratified to patients with depressed and preserved left ventricular function)

	Gender differences		
	Unadjusted OR* (95% CI)	OR* adjusted for age (95% CI)	Adjusted OR* (95% CI)†
<i>Total population (n = 8914)</i>	<i>Men (n = 4748) (%)</i>	<i>Women (n = 4166) (%)</i>	
ACE-inhibitors	69	60	0.67 (0.62 to 0.74)
β-Blockers	41	32	0.70 (0.65 to 0.77)
Spironolactone	26	19	0.67 (0.61 to 0.75)
Diuretics	85	88	1.25 (1.11 to 1.42)
Cardiac glycosides	38	40	1.12 (1.03 to 1.22)
Antithrombotic agents	82	75	0.65 (0.58 to 0.71)
<i>Patients with LVSD (n = 3584)</i>	<i>Men (n = 2490) (%)</i>	<i>Women (n = 1094) (%)</i>	
ACE-inhibitors	80	74	0.71 (0.60 to 0.84)
β-Blockers	49	39	0.66 (0.57 to 0.77)
Spironolactone	32	25	0.69 (0.59 to 0.81)
Diuretics	88	89	1.18 (0.94 to 1.47)
Cardiac glycosides	41	45	1.16 (1.05 to 1.28)
Antithrombotic agents	87	83	0.66 (0.59 to 0.75)
<i>Patients with PLVF (n = 2396)</i>	<i>Men (n = 4082) (%)</i>	<i>Women (n = 2904) (%)</i>	
ACE-inhibitors	60	58	0.91 (0.77 to 1.07)
β-Blockers	40	36	0.85 (0.72 to 1.00)
Spironolactone	17	20	1.22 (0.99 to 1.50)
Diuretics	78	88	2.03 (1.63 to 2.53)
Cardiac glycosides	28	37	1.45 (1.22 to 1.73)
Antithrombotic agents	83	77	0.72 (0.59 to 0.88)

LVSD, left ventricular systolic dysfunction; PLVF, preserved left ventricular function.

\*OR >1 correlates with a higher prevalence in women.

†Adjusted for age, hypertension, diabetes, stroke or transient ischaemic attack (TIA), renal failure, respiratory disease, coronary artery disease, cardiomyopathy, and atrial fibrillation.

**Table 4** Age, hypertension and CAD by gender and left ventricular function among patients with known LV function (n = 5980)

	Men (n = 3513)	Women (n = 2467)	OR* adjusted for age (95% CI)
Left ventricular systolic dysfunction (n)	2490	1094	
Mean age (SD)	65.7 (12.4)	71.1 (12.6)	
History of hypertension (%)	1179 (47)	628 (57)	1.50 (1.30 to 1.73)
Myocardial infarction, ever (%)	1383 (56)	528 (48)	0.67 (0.58 to 0.78)
History of angina (%)	1191 (48)	500 (46)	0.85 (0.74 to 0.99)
Revascularisation (PCI, CABG) (%)	687 (28)	175 (16)	0.53 (0.44 to 0.63)
Cumulative evidence for CAD† (%)	1754 (70)	720 (66)	0.68 (0.58 to 0.80)
Preserved left ventricular function (n)	1023	1373	
Mean age (SD)	68.3 (12.6)	72.9 (11.6)	
History of hypertension (%)	559 (55)	880 (64)	1.42 (1.20 to 1.67)
Myocardial infarction, ever (%)	377 (37)	311 (23)	0.49 (0.41 to 0.59)
History of angina (%)	499 (48)	547 (40)	0.69 (0.58 to 0.81)
Revascularisation (PCI, CABG) (%)	238 (23)	146 (11)	0.42 (0.34 to 0.53)
Cumulative evidence for CAD† (%)	656 (64)	726 (53)	0.61 (0.51 to 0.72)

\*OR >1 correlates with a higher prevalence in women.

†CAD (coronary artery disease): myocardial infarction, angina, or revascularisation. PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

note that guidelines do not discriminate between men and women, and treatment with evidence-based drugs is advocated in all patients with heart failure and left ventricular dysfunction.<sup>12</sup> However, women are known to have more side effects when treated with ACE-I,<sup>15 16</sup> and the use of cardiac glycosides may even be associated with an increased mortality among women, but not men, with LVSD.<sup>17</sup>

In our study, no differences were observed in the adjusted analyses regarding in-hospital and 12-week mortality despite the fact that women were less likely to be diagnosed with CAD or LVSD, both markers of increased risk. The lack of a sex difference in mortality is consistent with a large Italian

**Table 6** Unadjusted and adjusted ORs for outcome (mortality and readmission) among women compared with men

	Men/Women (%)	Gender differences			
		Unadjusted OR (95% CI)	OR adjusted for age (95% CI)	Adjusted OR, patients with LVSD only, n = 3584 (95% CI)†	Adjusted OR, patients with PLVF only, n = 2396 (95% CI)†
12-week mortality	12.7/15.2	1.24 (1.10 to 1.39)	0.97 (0.86 to 1.10)	1.10 (0.88 to 1.38)	1.23 (0.93 to 1.64)
Readmissions during 12-week follow-up period	20.3/18.9	0.92 (0.83 to 1.02)	0.92 (0.82 to 1.02)	1.03 (0.86 to 1.23)	0.86 (0.70 to 1.05)

\*OR >1 correlates with a higher prevalence in women.

†Adjusted for age, hypertension, diabetes, stroke or transient ischaemic attack (TIA), renal failure, respiratory disease, coronary artery disease, cardiomyopathy, and atrial fibrillation.

registry,<sup>18</sup> but contrasts with others.<sup>19–21</sup> However, our data are limited by short-term (12-week) follow-up and lack of certainty about the preceding duration of heart failure. Studies suggest that LVEF and CAD are stronger predictors of prognosis in women, as for every 1% increase of LVEF the decrease in mortality was 4% in women versus 1% in men, and women with CAD and heart failure have a 2.5-fold increase in the risk of mortality as compared with a 1.5-fold increase in men.<sup>7</sup> Potentially, fewer investigations in women might have led to prognostically important information being missed.

The limitations of this study are those inherent to observational studies involving voluntarily participating hospitals for a clinical syndrome that does not have a clear, simple objective definition. Although we attempted to include a wide spectrum of hospitals in many European countries, the results will almost certainly be biased towards better than average practices. However, a high proportion of relevant patients at each centre were included (approximately 16 patients each week per centre), suggesting that the population was relatively unselected and likely to be representative of clinical practice. One of the strengths of the survey was that it included a large number of unselected and consecutively enrolled patients from multiple hospitals across Europe with both suspected and confirmed diagnosis of heart failure. We were able to perform multivariate analyses in which we could adjust for age and a number of relevant clinical characteristics.

In conclusion, in this large population of patients with a diagnosis of heart failure who were enrolled in the Euro Heart Survey on Heart Failure, we confirmed that, compared with men, women are older and more likely to have preserved left ventricular function, hypertension, diabetes, and valvular heart disease, but less likely to have a diagnosis of CAD. Women were also less likely to be admitted to cardiology wards, or have an assessment of left ventricular function, and, in addition, were treated with guideline recommended drugs to a lesser extent than men. After adjustment for age and important clinical characteristics, the observed differences decreased, but remained statistically significant for ACE-I,  $\beta$ -blockers and spironolactone. Despite better left ventricular function and less CAD, women and men had similar age-adjusted 12-week mortality. There is no evidence-based justification for treating women with heart failure less intensively than men. As it is a challenge for all clinicians to ensure equal treatment for men and women, it is important that clinicians are aware of these deficiencies in the management of women with heart failure and measures should be taken to rectify them.

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## REFERENCES

- Jessup M, Brozena S. Heart Failure. *N Engl J Med* 2003;**348**:2007–18.
- Khand A, Gemmel I, Clark AL, et al. Is the prognosis of heart failure improving? *J Am Coll Cardiol* 2000;**36**:2284–6.
- Bello N, Mosca L. Epidemiology of coronary heart disease in women. *Prog Cardiovasc Dis* 2004;**46**:287–95.
- Cleland JGF, Swedberg K, Cohen-Solal A, et al. The Euro Heart Failure Survey of The EUROHEART Survey Programme: A survey on the quality of care among patients with heart failure in Europe. *Eur J Heart Fail* 2000;**2**:123–32.
- Cleland JGF, Swedberg K, Follath F, et al. The EuroHeart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe. Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003;**24**:442–63.
- Stromberg A, Martensson J. Gender differences in patients with heart failure. *Eur J Cardiovasc Nurs* 2003;**2**:7–18.
- Ghali JK, Krause-Steinrauf HJ, Adams KF, et al. Gender differences in advanced heart failure: insights from the BEST study. *J Am Coll Cardiol* 2003;**42**:2128–34.
- Jessup M, Pina IL. Is it important to examine gender differences in the epidemiology and outcome of severe heart failure? *J Thorac Cardiovasc Surg* 2004;**127**:1247–52.
- McDonagh TA, Morrison CE, Lawrence A, et al. Symptomatic and asymptomatic left-ventricular systolic dysfunction in an urban population. *Lancet* 1997;**350**:829–33.
- Mejert M, Holmgren J, Wandell P, et al. Diagnostic tests, treatment and follow-up in heart failure patients—is there a gender bias in the coherence to guidelines? *Eur J Heart Fail* 1999;**1**:407–10.
- Burns RB, McCarthy EP, Moskowitz MA, et al. Outcomes for older men and women with congestive heart failure. *J Am Geriatr Soc* 1997;**45**:276–80.
- Swedberg K, Cleland J, Dargie H, et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. *Eur Heart J* 2005;**26**:1115–40.
- Komajda M, Follath F, Swedberg K, et al. The EuroHeart Failure Survey programme—a survey on the quality of care among patients with heart failure in Europe: Part 2: treatment. *Eur Heart J* 2003;**24**:464–74.
- Lenzen MJ, Boersma E, Scholte Op Reimer WJ, et al. Under-utilization of evidence-based drug treatment in patients with heart failure is only partially explained by dissimilarity to patients enrolled in landmark trials: a report from the Euro Heart Survey on Heart Failure. *Eur Heart J* 2005;**26**:2706–13.
- Shah MR, Granger CB, Bart BA, et al. Sex-related differences in the use and adverse effects of angiotensin-converting enzyme inhibitors in heart failure: the study of patients intolerant of converting enzyme inhibitors registry. *Am J Med* 2000;**109**:489–92.
- Kostis JB, Shelton B, Gosselin G, et al. Adverse effects of enalapril in the Studies of Left Ventricular Dysfunction (SOLVD). SOLVD Investigators. *Am Heart J* 1996;**131**:350–5.
- Rathore SS, Wang Y, Krumholz HM. Sex-based differences in the effect of digoxin for the treatment of heart failure. *N Engl J Med* 2002;**347**:1403–11.
- Opasich C, Tavazzi L, Lucci D, et al. Comparison of one-year outcome in women versus men with chronic congestive heart failure. *Am J Cardiol* 2000;**86**:353–7.
- Ho KK, Anderson KM, Kannel WB, et al. Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circulation* 1993;**88**:107–15.
- Schocken DD, Arrieta MI, Leaverton PE, et al. Prevalence and mortality rate of congestive heart failure in the United States. *J Am Coll Cardiol* 1992;**20**:301–6.
- Bourassa MG, Gurne O, Bangdiwala SI, et al. Natural history and patterns of current practice in heart failure. The Studies of Left Ventricular Dysfunction (SOLVD) Investigators. *J Am Coll Cardiol* 1993;**22**:14A–19A.