

# Explorative analysis of gender-specific characteristics in patients with heart failure in an Italian hospital

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**Abstract:** Sex-related differences have been shown to deeply affect health-related aspects of patients. However, the lack of gender-specific analysis makes it difficult to advance personalized medicine in terms of a gender-based approach. The aim of the present study was to describe gender-specific features of patients diagnosed with heart failure (HF), with a focus on the clinical presentation. Data were collected from a properly designed database and referred to an Italian hospital. Patients aged  $\geq 18$  years with a primary or secondary diagnosis of HF between 1 January 2012 and 31 December 2016 were included, and their demographic and clinical characteristics were analyzed according to gender. Of the 719 HF patients included, 317 (44.1%) were male and 402 (55.9%) were female. Women tended to be older compared to men ( $82.4 \pm 8.8$  years and  $77.1 \pm 10.6$  years, respectively). As for clinical presentation, 62.1% of female and 38.3% of male patients had preserved ejection fraction, and 56.1% of men and 58.2% of women suffered from atrial fibrillation. The left atrium was partially compromised in 62.4% of male and 63% of female patients, while right atrium dysfunction tended to be more frequent in male patients compared to female patients (29.1% and 25.5%, respectively). In conclusion, gender-specific features of a cohort of HF patients from a clinical setting were accurately described.

**Keywords:** gender, specific characteristics, heart failure, clinical setting

Sex-related differences have been shown to deeply affect health-related aspects of patients; for that reason, in recent years the approach to diagnosis, treatment, and prevention of diseases is becoming even more gender-specific.<sup>1</sup> Regarding the National Healthcare System, the attention on sex-related differences aims at increasing the appropriateness of prevention, diagnosis, and treatment as well as rehabilitation of patients, particularly for those diseases with major epidemiologic impact, such as cardiovascular diseases.<sup>1,2</sup> As also mentioned in a recent document released by the WHO entitled “Health 2020: European Policy for Health and Well-being”,<sup>3</sup> gender is identified as a crucial and fundamental issue as it affects health status, well-being and its perception, disease onset and progression, and pharmacological treatment approaches and their efficacy. However, the lack of gender-specific analysis makes it difficult to advance personalized medicine in terms of a gender-based approach.<sup>4</sup>

To this end, here we present an observational retrospective study whose aim was to describe gender-specific features of patients diagnosed with heart failure (HF), with a focus on the clinical presentation. The study was based on a designed

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database in which the selected data were previously extracted from medical records and hospitalization and laboratory test databases of the General Medicine Unit of the University Hospital of Verona (Italy); we included all patients aged  $\geq 18$  years with primary or secondary diagnosis of HF at hospital discharge (International Classification of Diseases, 9th Revision, Clinical Modification ICD-9-CM code 428) between 1 January 2012 and 31 December 2016. For all included patients we identified the index date (ID) as the date they met the inclusion criteria. As regards the presence of comorbidities, patients were classified as: a) HF only (ICD-9-CM code 428); and b) HF and diabetes mellitus (DM, ICD-9-CM codes 428 and 250). Demographic and clinical characteristics of patients at the ID were analyzed according to gender. We also analyzed the length of stay and costs related to the hospitalization index. All results were produced in an aggregate way. According to the Italian Guidelines regarding the conduction of observational studies,<sup>5</sup> this study has been notified to the competent local Ethics Committee (University Hospital of Verona). Informed consent was not required, since it is not required when using encrypted retrospective information for research purposes.

A total of 719 HF patients were included and, except for the cohort of HF patients with DM, the percentage of female patients was higher compared to male patients (Table 1). According to the mean age at the ID, women tended to be older compared to men ( $82.4 \pm 8.8$  years and  $77.1 \pm 10.6$  years, respectively; Table 1). Concerning the clinical presentation of patients at the time of HF diagnosis, a higher percentage of female patients had preserved ejection fraction compared to male patients (62.1% vs 38.3%, respectively), not only in the total study population but also when the single cohorts were considered (Table 1). 56.1% of men and 58.2% of women in the total study population of HF patients suffered from atrial fibrillation; this percentage is lower in both genders for the cohort of HF patients with DM compared to HF only patients (Table 1). The proportion of patients with NT-proBNP  $\geq 2,000$  pg/mL was higher in women compared to men in the HF cohort (70.6% and 60.8%, respectively), with this proportion inverted in the HF with DM cohort (53.1% and 76.1%, respectively; Table 1). The left atrium was mainly described as partially compromised except for female patients in the HF with DM cohort (Table 1). Right atrium dysfunction at the ID tended to be more frequent

in male patients compared to female patients (29.1% and 25.5%, respectively; Table 1).

The length of hospital stay for the hospitalization index was also analyzed; female patients stayed on average  $6.9 \pm 5.7$  days and male patients  $7.0 \pm 6.5$  days (Table 2). The percentage of male patients with subsequent HF-related hospitalization tended to be higher compared to female patients (89.0% and 92.5% of patients had no further hospitalization for HF, respectively; Table 2). Costs related to the hospitalization index were €3,374.27 for male and €3,386.12 for female patients (Table 2).

In the present study, gender-specific features of a cohort of HF patients from a clinical setting were accurately described. According to mean age, we found that women were older than men in all study populations and in all cohorts considered, consistent with a study reported in the literature.<sup>6</sup> Razzolini and Lin<sup>7</sup> reported that later-in-life HF is more prevalent in women than in men. In our study, age distribution analysis showed that the percentage of men was higher among age ranges up to 79 years, while this trend reverted after the age of 80 years. The higher percentage of preserved ejection fraction among women was in line with findings reported by Buonanno,<sup>8,9</sup> who pioneered the study of sex differences in the pathophysiology of HF, and is now widely observed in the literature.<sup>10</sup> To date, HF guidelines do not take into account gender-specific differences due also to the underrepresentation of women in clinical trials,<sup>11</sup> therefore analysis of data from the clinical setting can play an important role in improving the knowledge of gender-specific differences in the clinical presentation of HF. Similarly to data reported by Galvao et al's<sup>12</sup> and Stein et al's<sup>13</sup> studies, no differences were observed among genders for length of hospital stay.

Our cohort of patients reflected real clinical practice, and the results must be interpreted taking into account limitations mainly due to the observational nature of the study. Data were collected from a database properly designed for the study, in which only the variables herein described were reported. Moreover, patients diagnosed and managed by a general practitioner were not included, as the cohort consisted of patients discharged from hospital. The results and conclusions of this study are limited to the population analyzed; furthermore, studies with larger cohorts of HF patients are needed to confirm our results and to permit the application of relevant statistical methods.

**Table 1** Gender-specific demographic and clinical characteristics of HF patients

	Total study population (n=719)		HF only (n=566)		HF and DM (n=144)	
	Male	Female	Male	Female	Male	Female
Number of patients (%)	317 (44.1)	402 (55.9)	243 (42.9)	323 (57.1)	72 (50.0)	72 (50.0)
Mean (±SD) age (years)	77.1 (10.6)	82.4 (8.8)	77.8 (10.7)	82.8 (8.8)	74.6 (9.9)	80.2 (8.3)
Age distribution (%)						
40–49 years	1.6	n.i.	n.i.	n.i.	n.i.	0
50–59 years	5	1.2	4.1	1.5	8.3	0
60–69 years	15.5	8	15.2	6.8	16.7	13.9
70–79 years	32.5	18.4	31.7	17	36.1	26.4
80–89 years	36.3	53.2	37	54.5	34.7	47.2
>90 years	9.1	18.7	10.3	19.5	n.i.	12.5
Ventricular ejection fraction at ID <sup>a</sup> (%)						
>50%	38.3	62.1	42.0	61.3	26.4	66.0
41–50%	21.7	13.7	22.1	14.2	18.9	10.0
31–40%	22.1	13.7	19.9	13.3	30.2	16.0
≤30%	17.9	10.5	16.0	11.1	24.5	8.0
Atrial fibrillation at ID <sup>b</sup>	56.1	58.2	62.1	60.6	37.5	47.2
NT-proBNP at ID <sup>c</sup>						
<400 pg/mL	5.2	5.6	5.4	4.7	n.i.	10.2
400–2,000 pg/mL	30.5	27.3	33.7	24.8	19.6	36.7
≥2,000 pg/mL	64.3	67.0	60.8	70.6	76.1	53.1
Serum calcium level at ID <sup>d</sup> , mean (±SD)	2.2 (0.1)	2.2 (0.1)	2.2 (0.1)	2.2 (0.1)	2.2 (0.1)	2.2 (0.1)
Glycated hemoglobin at ID <sup>e</sup> , mean (±SD)	5.7 (1.9)	5.9 (1.8)	5.4 (1.5)	5.6 (1.4)	6.7 (2.9)	7.6 (2.4)
Left atrium description at ID <sup>f</sup> (%)						
Normal	8.5	8.7	9.4	7.6	n.i.	14.0
Reduced	11.5	13.8	11.7	11.2	11.3	26.0
Slightly compromised	17.1	14.5	17.8	13.4	15.1	18.0
Partially compromised	62.4	63.0	60.6	67.9	67.9	42.0
Totally compromised	n.i.	0	n.i.	0	0	0
Right atrium dysfunction at ID <sup>g</sup>	29.1	25.5	26.1	25.4	39.6	24.5

**Notes:** According to the Italian Regulation on protection of personal data (D.Lgs. 196/2003), results referring to a number of patients <4 cannot be presented as they are potentially reductible to single individuals. <sup>a</sup>Data available in 71.1% of patients. <sup>b</sup>Data available in 52.0% of patients. <sup>c</sup>Data available in 96.4% of patients. <sup>d</sup>Data available in 65.4% of patients. <sup>e</sup>Data available in 67.0% of patients. <sup>f</sup>Data available in 70.9% of patients. <sup>g</sup>Data available in 70.8% of patients.

**Abbreviations:** HF, heart failure; DM, diabetes mellitus; n.i., not issuable; ID, index date; NT-proBNP, NT-pro-brain natriuretic peptide.

**Table 2** Gender-specific characteristics of length of hospital stay, subsequent HF-related hospitalization and costs

	Total study population (n=719)		HF only (n=566)		HF and DM (n=144)	
	Male	Female	Male	Female	Male	Female
Number of patients (%)	317 (44.1)	402 (55.9)	243 (42.9)	323 (57.1)	72 (50.0)	72 (50.0)
Mean length of hospital stay (ID) (days), mean (±SD)	7.0 (6.5)	6.9 (5.7)	6.8 (6.3)	6.8 (5.6)	8.0 (7.2)	7.7 (6.5)
Number of subsequent HF-related hospitalizations (%)						
0	89.0	92.5	91.4	93.8	80.6	86.1
1	7.6	6.7	6.2	6.2	12.5	9.7
2	2.8	n.i.	2.1	0	5.6	n.i.
≥3	n.i.	0	n.i.	0	n.i.	0
Cost for hospitalization index (€)	3,348.01	3,395.72	3,374.27	3,386.12	3,303.97	3,449.53

**Notes:** According to the Italian Regulation on protection of personal data (D.Lgs. 196/2003), results referring to a number of patients <4 cannot be presented as they are potentially reductible to single individuals.

**Abbreviations:** HF, heart failure; DM, diabetes mellitus; ID, index date; n.i., not issuable.

## Disclosure

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