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ORIGINAL ARTICLE

Heart failure with preserved systolic function: prevalence and clinical features in a cohort of patients admitted to internal medicine units. The study PRESYF-HF Tuscany

Scompenso cardiaco con funzione sistolica conservata: prevalenza e presentazione clinica in una coorte di pazienti ricoverati in reparti di medicina interna. Lo studio PRESYF-HF Toscana

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ABSTRACT: ***Heart failure with preserved systolic function: prevalence and clinical features in a cohort of patients admitted to internal medicine units. The study PRESYF-HF Tuscany. P. Biagi, L. Abate, M. Alessandri, S. Bocchini, V. Verdiani, G. Pettinà, C. Nozzoli.***

Background. **There is uncertainty about the prevalence and clinical characteristics of heart failure (HF) patients with preserved systolic function (PRESYF).**

Aim. **To analyze the prevalence and clinical characteristics of patients with PRESYF in an unselected cohort of subjects consecutively hospitalized for HF.**

Methods. **The study cohort included 338 patients consecutively admitted for HF at 24 Internal Medicine units homogeneously settled in Tuscany area (Italy). We did not have any criteria for exclusion. All patients had an echocardiographic measure of left ventricular ejection fraction (LVEF) within 72 hours from hospital admission. Patients with LVEF ≥ 50% were considered to have PRESYF.**

Results. **The patients with PRESYF were 112 (33,1%), those with depressed systolic function (DESYF) 226 (66,9%). In the group PRESYF were prevalent female sex, hypertensive etiology, and elevated BMI. The distribution for classes of age shows a great frequency of PRESYF in the elderly.**

Conclusion. **About one third of patients admitted for HF have a PRESYF. They are different compared to those with DESYF. A correct identification of this form of HF may be important in clinical practice for more targeted therapeutic options and for prognostic implications.**

Keywords: heart failure, preserved left ventricular ejection fraction, prevalence, clinical features.

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1. Introduction

Heart failure (HF) with preserved systolic function (PRESYF) is a growing remarkable clinical problem [1, 2]. This condition is generally considered to be primarily due to diastolic dysfunction [3]. The most accurate evaluation of the diastole is obtainable through cardiac catheterism [4, 5], but it is not routinely employed in clinical setting for practical reasons (invasive method, not available in all hospitals). Although Doppler echocardiography is a widely accepted tool for identifying left ventricular ejection fraction (LVEF) [6-10] a non-invasive gold standard for assessing left ventricular diastolic function does not exist [3].

Controversy exists on many key elements of this entity, including prevalence and clinical characteristics. In a recent metanalysis, its prevalence ranged between 13 to 74% [11]. That was primarily due to difference in the populations studied and the definition of PRESYF.

In the past, only few studies have been conducted in unselected populations [12,13], and the definition of preserved LVEF ranged from ≥40% to ≥55% [3].

Recently, it has been underlined that PRESYF is defined as LVEF greater than or equal to 50% and to date this is the most widely accepted cut off [14, 15].

Furthermore, the timing of echo examination (within 72 hours from admission) seems important for the proper definition of HF with preserved LVEF [16, 17].

The aim of our study was to analyze the prevalence and clinical characteristics of patients with PRESYF in an unselected cohort of subjects consecutively hospitalized for symptoms of HF in Internal Medicine Units of Tuscany, a region of central Italy.

2. Methods

The study cohort included 338 patients consecutively admitted at 24 Internal Medicine units homogeneously settled in Tuscany area (Italy).

Criteria for inclusion were exacerbation of previously documented HF or new onset of HF using standard Framingham criteria [18]. We did not have any criteria for exclusion.

All patients had an echocardiographic measure of LVEF within 72 hours from hospital admission, and performed according to guidelines of the European Society of Cardiology [19]. Patients with clinical diagnosis of HF and LVEF ≥ 50% measured with Simpson method [20] were considered to have PRESYF HF. Demographic features, clinical and laboratory data were also recorded.

2.1. Statisical analysis

Data are presented as mean ± 1 standard deviation (SD) or absolute number or percentages. Statistic analysis has been effected applying the chi-square test or Fisher test when appropriate. After testing data for normality (Kolmogorov-Smirnov test associated to the index of Lilliefors), analysis of variance (ANOVA) has been applied and a p value < 0.05 was considered statistically significant. Statistic analysis has been performed with "Epi Info 6.0" by the Centers for Disease Control and Prevention (CDC) and with "Statistica", version 6.0, by the StatSoft Inc. (2001).

3. Results

Of the 40 Internal Medicine units of Tuscany, 24 (60%) have participated in the study. Their regional distribution was homogeneous (Figure 1).

The cohort of patients consecutively admitted with HF included 338 subjects, mean age 81± 9 yrs, males 156 (46,2%), females 182 (53,8%).

The patients with PRESYF (LVEF≥ 50%) were 112 (33,1%), those with depressed systolic function (DESYF) (LVEF <50%) 226 (66,9%).

In the group PRESYF were prevalent female sex, hypertensive etiology, and elevated body mass index (BMI) (Table 1).

Table 1. - Characteristics and clinical and laboratory data of the population and comparison between patient with preserved systolic function – heart failure (PRESYF-HF) and depressed systolic function – heart failure (DESYF-HF) – in parenthesis the number of the cases

	Overall	**DESYF (LVEF < 50%)**	**PRESYF (LVEF ≥ 50%)**	**P value**
Number of Cases	338	226 (66.9%)	112 (33.1%)	
Age	81.9 ± 7.8	80.8 ± 7.1	81.3 ± 9.1	NS
Male	156 (46.2%)	53.1%	31.3%	0.002
Etiology				
Ischemic	178 (52.7%)	148 (65.4%)	30 (26.8%)	P<0.001
Hypertensive	146 (43.2%)	84 (37.2%)	62 (55.4%)	P<0.001
Valvular	57 (16.9%)	37 (16.4%)	20 (17.9%)	P<0.001
Idiopathic	12 (3.6%)	8 (3.5%)	4 (3.6%)	NS
Atrial Fibrillation	134 (39.6%)	89 (39.3%)	45 (40.2%)	NS
Comorbidities				
Diabetes	94 (27.8%)	60 (26.6%)	34 (30.4%)	NS
Chronic renal failure	33 (9.8%)	25 (11.1%)	8 (7.1%)	NS
Hypertension	135 (39.9%)	81 (35.8%)	54 (48.2%)	P<0.001
Depression	33 (9.8%)	22 (9.7%)	11 (9.8%)	NS
		Laboratory data		
BMI	(205) 25.8 ± 5.0	(141) 24.9 ± 3.7	(64) 27.6 ± 6.6	P<0.001
Heart rate(beats/min)	(327) 93.4 ± 22.7	(118) 95.1 ± 22.7	(109) 90.0 ± 22.5	NS
Atrial Fibrillation	134 (39.6%)	89 (39.3%)	45 (40.2%)	NS
Systolic Blood pressure (mmHg)	(335) 142.0 ± 27.8	(223) 139.0 ± 27.9	(112) 148.2 ± 26.7	P<0.01
Creatinine (mg%).	(332) 1.4 ± 0.9	(221) 1.5 ± 1.0	(111) 1.3 ± 0.7	P<0.05
Creatinine >2,5 mg%	29 (8.6%)	23 (10.2%)	6 (5.4%)	NS
Hemoglobin (g/dL)	(338) 12.3 ± 2.0	(226) 12.4 ± 2.0	(112) 12.1 ± 2.1	NS
Na^+ (mEq/L)	(338) 138.6 ± 5.1	(226) 138.3 ± 5.5	(112) 139.2 ± 4.2	NS
BNP (microU/ml)	(22) 840.0 ± 810.4	(10) 1112.9 ± 901.1	(12) 512.4 ± 566.9	NS
NTproBNP (microU/ml)	(32) 10304.6 ± 14870.6	(28) 10901.6 ± 15711.3	(4) 6125.3 ± 6069.5	NS
Ca125 (microU/ml)	(89) 82.6 ± 114.0	(59) 89.7 ± 127.7	(30) 68.7 ± 80.5	NS

The distribution for classes of age shows a great frequency of PRESYF in the elderly (Table 2).

Among the causes of in hospital admission hypertensive crisis and atrial fibrillation were more frequent in PRESYF HF than in DESYF HF subjects (Table 3).

The number of HF patients with New York Heart Association (NYHA) classes III-IV was greater in the DESYF group both at admission and at hospital discharge, while we did not find any difference about lenght of hospital staying and intrahospital mortality (Table 4).

4. Discussion

In our cohort of unselected consecutive HF patients, the prevalence of PRESYF HF is 33,1%.

Retrospective hospital based studies have shown a prevalence ranging from 40 to 53%. The reasons for such difference may be due to differences in age [21, 22], gender [23-25], or race [26]; in other cases methods for measuring ventricular dysfunction [6, 7] or a lower threshold for LVEF (> 40%) [13, 27-29] may account for different results. Furthermore, the time of execution of the echo is reported in few studies.

In a perspective analysis of about one decade of patients admitted to a HF Clinic the echo performed within 2 weeks from the entry, has individualized a prevalence of almost 40% [30].

In a cohort study [31] on 328 patients admitted in the hospital with HF (Framingham criteria) with echo effected within 48 hours, the prevalence of PRESYF has been of 41,5%, individualizing a predominantly female population and slightly more elderly in comparison to the subjects with LVEF <40%. However, that cohort was younger than our population (65 yrs of average) and also included patients with modestly DESYF (LVEF ≥40%).

In another perspective study echo was performed within 72 hours from admission in over 70% of patients and the prevalence of PRESYF was 48%, identifying a population of elderly, hypertensive with several comorbidities and showing a trend to a precocious re-hospitalization; however also in that population the cut off value for preserved LVEF was ≥40% [32].

Although the timing of the echo seems not to modify the prevalence of the PRESYF induced by hypertensive HF [17] it is not clear if the same can be said for the forms induced by ischemic cause. It is reasonable to suppose that HF induced by ischemic heart disease may have a depressed ventricular function during and immediately after the event. We argue that if the echo is performed early after the admission we might measure the real burden of the PRESYF HF phenomenon irrespective of the etiology. Therefore, in our study, echocardiogram was performed within 72 hours from the admission in all patients, included those with ischemic heart disease (who represented about 30% of the whole cohort).

The demographic characteristics of our cohort are similar to data of observational studies performed in the same setting and territory [33, 34]. Patients were

Table 2. Distribution of the population in three classes of age. The differences are not statistically significant

Years Age Classes	Number of Patients (%)		
	All (338)	LVEF<50% (226)	LVEF>50% (112)
<60	9 (2,7%)	5 (2,2%)	4 (3,6%)
61-80	127 (37,5%)	91 (40,2%)	36 (32,1%)
>80	202 (59,7%)	130 (57,5%)	72 (64,2%)

Table 3. - Causes of admission

Cause of admission	LVEF< 50% N° of cases	LVEF > 50% N° of cases	P value
Progressive worsening *	179 (53%)	56 (50%)	NS
Hypertensive crisis §	44 (13%)	29 (26%)	<0.05
Atrial fibrillation	27 (8%)	21 (19%)	<0.05
Infection	30 (9%)	15 (13%)	NS
Low compliance	20 (6%)	12 (11%)	NS
Anemia	24 (7%)	6 (5%)	NS
Myocardial infarction	7 (2%)	3 (3%)	NS
Tyreotoxicosis	3 (1%)	2 (2%)	NS
Emotionall Stress	7 (2%)	2 (2%)	NS
Pulmonary embolism	3 (1%)	1 (1%)	NS
Not defined	41 (12%)	13 (12%)	NS

(*) The term progressive "worsening" points out the progressive worsening of HF irrespective of the etiology and not induced by any evident recognizable cause which altered a relatively stable disease.
(§) Hypertensive crisis means any increase of systolic blood pressure above 179 mmHg and/or any increase of systodiastolic blood pressure above 179/110 mmHg.

Table 4. - Frequency of the most compromised heart failure (HF) functional classes at entry and of the less severe at discharge from hospital, mean lenght of stay (+ 1 SD) and mortality. Length in hospital staying of the patients with preserved systolic function-heart failure (PRESYF-HF) and depressed systolic function – heart failure (DESYF-HF)

NYHA Class	LVEF ≥ 50% N° of cases	LVEF < 50% N° of cases	P value
III-IV class at admission	83 (74%)	202 (90%)	P< 0.05
I-II classe at discharge	85 (75%)	134 (59%)	P< 0.05
mortality	3 (2.6%)	9 (4%)	n.s.
	Lenght of stay		
(days± SD)	8.82 + 5.18	8.60 + 5.65	n.s.

those consecutively admitted for HF, without any criterium of exclusion. They could be so considered very representative of the "real world" of HF [27, 35, 36].

In our study, subjects with PRESYF HF are prevalently female, and older than patients with DESYF HF (age>80 years in 64,2% vs. 57,5%). These characteristics are consistent with results of a study on a community cohort in Olmsted County, Minnesota [15], where HF with preserved LVEF had a prevalence of 55% and was associated with older age, female sex, and no history of myocardial infarction. The higher prevalence may be due to the fact that the population study included outpatients.

In our cohort, hypertensive heart disease is prevalent in patients with PRESYF HF (54,1% vs 37,4; p <0,001) and systolic blood pressure (SBP) values were significantly higher in this group. On the contrary, the ischemic heart disease prevails in the DESYF HF (65,3% vs 27,5%; p <0,001). Body mass index (BMI) was higher in the PRESYF HF subjects, consistently with published data [42, 43], while comorbidity was similar in patients with HF and preserved or reduced LVEF, as elsewhere reported [15, 32, 37, 38].

Atrial fibrillation (AF) was more frequent in subjects with PRESYF than in those with DESYF but the difference was not statistically significant: overall AF frequency was elevated (over 1/3 of all the patients) and advanced age of our population has probably contributed to attenuate the differences of the two groups taking into account that AF is an age dependent phenomenon [39].

Hypertensive crisis and arrhythmia more frequently induced hospital admission in PRESYF HF than in DESYF HF subjects.

Length of in hospital staying was similar in the two groups but the severity of symptoms at discharge was different: 23 patients with PRESYF-HF and 74 with DESYF-HF were in NYHA class III-IV (21% vs 29%; OR 0,5 CI 95% 0,3-0,89). This could underline that DESYF HF patients are more serious or that they improve slower. In-hospital deaths were 3 in the group PRESYF and 9 in the group DESYF ((2,6% vs 4%; ns).

The Brain natriuretic peptide (BNP) and N-terminal-probrain natriuretic peptide (NT- proBNP) data are numerically limited and therefore not suitable for statistic definition; nevertheless, BNP and NT-proBNP values are lower in the PRESYF HF patients in comparison to those with DESYF HF. Since such markers are powerful predictors of new cardiovascular events [40, 41], it is probable that PRESYF-HF patients may have a better prognosis [32].

In conclusion, our data suggest that about one third of patients admitted for HF has a PRESYF. This result comes from a cohort very similar to "real world" of HF patients and that we have studied according to accurate diagnostic criteria (echocardiogram performed within 72 hours from the admission and LVEF ≥50%). Patients with HF and PRESYF are different compared to those with DESYF. Particularly, they are older, primarily female, obese and with arterial hypertension. A correct identification of this form of HF may be important in clinical practice for more targeted therapeutic options and for prognostic implications.

Riassunto

Premesse. *Vi è incertezza sulla prevalenza e sulle caratteristiche cliniche dello scompenso cardiaco (HF) con funzione sistolica conservata (PRESYF).*

Scopo del lavoro. *Analizzare la prevalenza e le caratteristiche cliniche di pazienti con PRESYF in una popolazione non selezionata di pazienti ricoverati consecutivamente per HF.*

Metodi. *La popolazione era composta da 338 pazienti ricoverati consecutivamente per HF in 24 reparti di Medicina Interna della Toscana, senza nessuna esclusione. In tutti i pazienti fu eseguito un ecocardiogramma con misura della FEVS entro 72 ore dal ricovero. Furono considerati pazienti con PRESYF quelli con FEVS ≥ 50%.*

Risultati. *I pazienti con PRESYF erano 112 (33,1%), quelli con funzione VS depressa (DESYF) 226 (66,9%). Nel gruppo PRESYF erano prevalenti sesso femminile, ipertensione arteriosa, elevato BMI,, ed età avanzata.*

Conclusioni. *Circa un terzo dei pazienti ricoverati per HF appartengono al gruppo PRESYF e possiedono differenti caratteristiche cliniche rispetto al gruppo DESYF. Una corretta identificazione di questa forma di HF è importante nella pratica clinica per un più appropriato indirizzo terapeutico e per una migliore caratterizzazione prognostica.*

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Appendix

Partecipating centers

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