The heart failure in Internal Medicine in Tuscany: the SMIT Study

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ABSTRACT

The incidence and prevalence associated with the growing age of population have made heart failure (HF) a new epidemic. In Italy most of HF patients are admitted to Internal Medicine Departments (IMD). We conducted a 30-day cross-sectional study involving patients with HF admitted to IMD of Tuscany. The aim of the study was to provide an updated snapshot of in-hospital management of HF in Tuscany and to analyze the differences in relation to the most recent guidelines. We have recruited 770 patients (M=45.4%) with a mean age of 82.5±8.9 years. Only 16.1% had a *de novo* HF. Most of them were re-admitted for decompensated HF. Hypertension and ischemic disease are the prevailing etiologies. *HF alone* was in less than 2%. 71.5% of patients had more than two comorbidities and 40.6% more than three concomitant diseases. The mean hospital stay (overall 8.6±5.5 days) correlated with the number of comorbidity. About 25% of patients had a creatinine clearance <30 mL/min. Nearly 50% of patients had atrial fibrillation but only the half was anti-coagulated. β-blockers, angiotensin converting enzyme-inhibitors (ACE-I) or angiotensin receptor blockers (ARB) were prescribed in about two-thirds of the subjects. Echocardiography was performed in 64.1% of patients. BNP or NT-pro BNP was tested in 67% at the hospital admission and in 18.3% at the discharge. At the discharge 50.1% of patients had loss of autonomy, 57% a polypharmacy prescription (≥8 classes of medicines) and 21.2% needed domiciliary oxygen therapy, but despite these critical points only 8% of the patients were transferred to long-term/intermediate care settings. In conclusion, the main characteristics of patients with HF admitted to IMD in Tuscany are the advanced age (the patients are old and very old) and the presence of multiple comorbidities (HF *alone is a rarity indeed*). The use of echocardiography and the pharmacological therapy with ACE-I, ARB, β-blocker and anti-aldosterone agents is wider than previous surveys, but some diagnostic, therapeutic and prognostic aspects are not similar to that recommended by the most recent HF guidelines. This survey underscores again some differences between *HF trials world* and *HF real world*, where the management is probably also driven by a clinical holistic approach.

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Key words: Heart failure; Tuscany.

See online Appendix for Centers participating in the SMIT (*Scompenso Cardiaco in Medicina Interna in Toscana*) Study Group.

Received for publication: 22 October 2014.
Revision received: 19 January 2015.
Accepted for publication: 19 October 2015.

Italian Journal of Medicine 2015; 9:349-355
doi:10.4081/itjm.2015.554

Introduction

Chronic heart failure (CHF) develops as a result of left ventricular (LV) systolic and/or diastolic dysfunction.[1] The ageing of the global population and the availability of effective treatments in patients with acute coronary syndromes prolong survival, so the incidence of CHF is increasing[2,3] and the number of patients at risk of developing this condition is expected to grow.[4,5] In Italy it is estimated that in 2050 life expectancy for 65-year-old people will be about 30 years more[6] and we know that CHF is a predictor of mortality also in the elderly and very elderly patients.[7]

Until a few years ago epidemiological data on CHF came from observational or registry studies in settings of Cardiology Departments.[8-11] The characteristics of these patients in many ways are similar to those of the HF trials designed for younger subjects without comorbidities.[12,13]

It is about a decade that in Italy we have data of the HF impact within Internal Medicine Departments (IMD). In Italy, most of the patients hospitalized for HF is discharged by these Departments[14] and it is pos-

sible to ascertain that they are similar to the so-called *real world*, *i.e.*, old or very old patients, most often frail, with multiple comorbidities. Their management is often different from that of the trials and it is not always possible to fully apply the recommendations of HF guidelines.

We performed an observational study in IMD of Tuscany, an Italian region characterized by a mean age of population higher than the mean of Italy.[15] With the aim to record the epidemiological and clinical data and to analyze the differences of the HF management in relation to the most recent guidelines.

Materials and Methods

Most of Tuscany IMD (32 of 36) took part in the study. We enrolled patients who were discharged by departments in a period of 30 days (30th January-28th February 2014) with the main diagnosis of HF. Diagnosis was performed on the ground of clinical/instrumental/laboratory data.[16] For each patient had to be filled a data sheet consisting of separate sections: in the first section in addition to the personal demographic data it was defined the Department of origin (Emergency room, Intensive Brief Observation, Coronary Intensive Care Unit, Intensive Therapy Departments), if it was a *de novo* HF, if the patient was admitted within 30 days and/or within 1 year with the same diagnosis; in the second section were recorded clinical data, HF etiology, the New York Heart Association (NYHA) class at admission; in the third one were recorded the instrumental and laboratory data such as BNP-NT-pro BNP (admission and discharge), echocardiography (no. of examinations performed), if the examination had been carried out by the internist or cardiologist, stratification of left ventricular ejection fraction (LVEF) computed by Simpson method;[17] in the fourth section was recorded the therapy generically defined in classes of drugs [angiotensin converting enzyme-inhibitors (ACE-I), angiotensin receptor blockers (ARBs), β-blockers, calcium antagonists, ivabradin, digoxin, anti-aldosterone agents, warfarin, new oral anticoagulants (NOA), antiplatelet drugs, statins]; in the fifth were analyzed the comorbidities (number, prevalence and severity); in particular we studied chronic renal failure (stratified according to the glomerular filtration rate calculated by the Cockroft-Gault formula), diabetes mellitus (defined as previous diagnosis, or specific therapy, or blood glucose greater than 126 mg/dL), arterial hypertension regardless of severity, clinically defined chronic obstructive pulmonary disease, active cancer (if cancer was a relevant part of the clinic at the time of recruitment), anemia defined according to the criteria of the World Health Organization (WHO)[18] and in particular moderate/severe anemia defined as anemia with hemoglobin (Hb) <10 g/dL; in the sixth section were taken into consideration: outcome, hospital mortality, critical situation at the discharge (loss of autonomy, need of domiciliary oxygen therapy, discharge at long-term care, geriatric wards/intermediate care, prescription of more than 7 classes of medicines), definition of follow-up programs (cardiac rehabilitation units, designed home care program, in-hospital follow-up program).

Statistics

The data were analyzed by calculating averages (mean+standard deviation) of continuous numeric variables or percentages for not-continuous ones. In some cases, a transformation was applied in not-continuous variable in order to define a clinical severity (mild, moderate and severe) score.

Numeric variables were compared by Student's *t* test. Discrete variables were summarized by frequency percent and compared by the chi-square test.

Linear regression analysis using the least square method was employed to correlate the length of staying and the number of comorbidities. A P value <0.05 was considered statistically significant.

Statistical analyses were carried out by using SAS software (version 9.1; SAS Institute, Cary, NC, USA).

Results

We have taken into consideration 770 patients (341 males =45.4%. P<0.001) aged 82.5±8.9 years, including 708 (91.7%) over 70 years old. Near 70% (68.3%) are over 80 and nonagenarians are over 15% (M=50 *vs* F=103; P<001).

The admission to IMD of the patients came from emergency settings in almost all cases (91.7%), in 4.2% from intensive coronary care unit, in the remaining 4.1% from other departments. Only 121 cases represented *de novo* HF (16.1%), the others were admitted due to worsening of HF. One hundred and seventy patients (22.6%) had another admission for the same cause during the previous 30 days.

The etiology of the HF is for the most part ischemic and/or hypertensive (Figure 1).

At admission to hospital, over eighty-three percent of the subjects were in NYHA class III/IV (mean NYHA class was 3.1±0.74).

The clinical and the most significant instrumental and laboratory data (Hb, creatinine, BNP/NT pro-BNP and echocardiography) are shown in Table 1. More in detail echocardiography was performed in 64.1% of the patients. Preserved LVEF (>50%) was present in 40.2%, a marked depressed ventricular ejection fraction (LVEF <35%) in 28.6% of the population studied.

BNP or NT pro-BNP was tested in 516 patients (67%) at admission (mean value: BNP 1197±2436

pg/mL; NT pro-BNP 8776±9474 pg/mL) and in 133 (18.3%) at discharge (mean value: BNP 1103±1757 pg/mL; NT pro-BNP 7416±8818 pg/mL). In only 114 patients (15.7%) BNP or NT pro-BNP was measured both at admission and at discharge.

Atrial fibrillation (AF) was present in 423 (47%) of patients (M=244 *vs* F=179; P<0.01).

The prevalence and the number of comorbidities is shown in Table 2.[17,19] HF *alone* was present in less than 2%; 71.5% of patients had more than two comorbidities and as much as 40.6% more than three concomitant diseases; a previous transient ischemic attack or stroke or a symptomatic peripheral vascular disease were recorded in 29% of cases.

The cardiovascular therapy is resumed in Table 3.

Overall mean hospital stay was 8.63±5.5 days and average length of staying (LOS) in IMD was 7.92±4.8. The length of staying (Table 4) showed a gradual increase according to the number of comorbidities both in hospital and in IMD (Figure 2); this was particularly evident in those who had more than four comorbidities for which they had a significant higher LOS both in hospital and in IMD than the other patients who had a lower number of concomitant diseases.

In-hospital mortality was 5.9% (45 patients), more in detail 21 males (5.4%) and 24 females (7.8%) (P; not significant) died. 58 patients (8%) were transferred to long-term care settings, more in detail 36 males (9.7%) and 22 females (6.7%) (P; not significant).

The most important criticalities at the discharge are summarized in Table 5.[20]

Discussion

Heart failure is a real problem in western countries: life expectancy is progressively rising and this goes pari passu with the reduction of mortality related to acute ischemic heart disease. So we may expect that over the next years the overall burden of HF (economic, social) will increase.

Our survey was performed in an Italian Region, Tuscany, characterized by a higher prevalence of elderly than the rest of Italy (mean age 45.45 *vs* 43.50 years, respectively).[18]

In our study the population is old, the mean age being over 82 years old, three female patients were over 100. Compared with precedent studies in Italy[21-23] we may notice that from 2002 the mean age of the patients with HF has increased over 5 years.

According to the most recent guidelines,[16,24] echocardiography had a more wider use than that of previous surveys in IMD,[21,23] irrespective of the fact that the examination is performed from an internist or a cardiologist.

Our data confirm that in an old population the form of HF with preserved systolic function is prevalent.[25,26]

We considered the cardiovascular treatment in relation to the adherence to the International guidelines suggestions: about two-thirds of the subjects were in therapy with ACE-I or ARB, a figure not so high like that of recent cardiologic surveys[27,28] but higher enough, taken into account the age of our population, and the well-known problems linked to their tolerance in this age group.

Moreover 25% of our subjects presented a marked reduction in creatinine clearance (<30 mL/min) and this may have conditioned a wider use of this class of drugs.

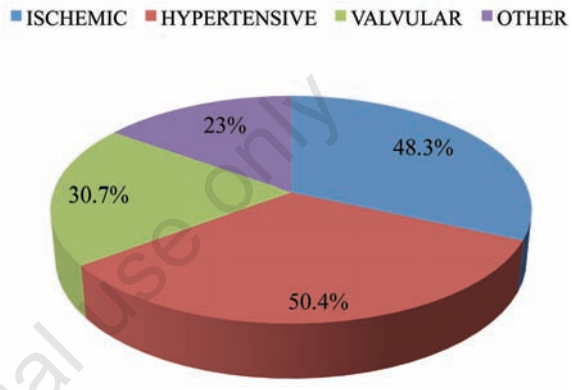

Figure 1. Etiology of heart failure. Note that percent is over one hundred since in many cases the etiology of heart failure is multiple.

Table 1. Clinical, instrumental and laboratory characteristics of the patients admitted to Internal Medicine Departments.

Parameter	Value
NYHA class	3.1±0.74
NYHA 2	14.9%
NYHA 3	46.8%
NYHA 4	32.2%
Creatinine	46.64±24.34
Creatinine/clearance <30 mL min	25.3%
Hb g/dL	11.98±2.0
Hb <10 g/dL	14.6%
Beats/min	77.47±12.71
LVEF	44.09±12.25
LVEF >50%	38.6%
LVEF <35%	18.3%
BNP pg/mL	1197+2436
NT pro-BNP pg/mL	8776+9474

NYHA, New York Heart Association; Hb, hemoglobin; LVEF, left ventricular ejection fraction.

More patients than before[21,23] are treated β-blockers, especially the patients with reduced systolic function, in fact about three out of four patients with LVEF <40% are in β-blocker treatment. This is in good accord with the most recent suggestion of International guidelines:[24] taking into account the characteristics of our population this means that internist are now more trained to use these drugs in patients in which their safety (*i.e.*, the therapeutic range) may be reduced.[29]

One in two patients with LVEF <35% was treated with anti-aldosterone agents: this figure can be explained by the concomitant use ACE-I/ARBs in an old patient which could lead to life-threatening hyperkalemia as previously reported.[30] Ivabradine was prescribed in only 17.6% of the patients in sinus rhythm. We suppose that this low figure may depend first on the low heart rate of our patients (secondary to the widened use of β-blockers?) and on the fact that this drug is a

Table 2. Comorbidities and differences by gender.

Comorbidities	No.	%	M%	F%	X
Arterial hypertension	559	72.6	30.1	41.6	ns
Diabetes mellitus	269	35.8	17.5	17.5	ns
COPD	269	35.8	18.7	16.7	ns
Moderate/severe renal dysfunction (creatinine/clearance <60 mL/min)	554	71.9	41.1	30.7	ns
Cognitive impairment*	236	31.4	10.2	20.6	0.05
Anemia°	425	44.2	26.3	28.9	ns
Anemia with Hb <10 g/dL	110	14.6	7.9	6.3	ns
Active cancer	50	6.6	3.6	3.5	ns

ns, not significant; COPD, chronic obstructive pulmonary disease; Hb, hemoglobin. *Cognitive impairment=Pfeiffer test<7;[19] °M<13 g/dL F<12 g/dL.[17]

Table 3. Medications list at admission and at discharge.

	Admission N=770 %	Discharge N=721 %	P
ACE-I	43.6	49.4	0.05
ARB	19.8	15.0	0.01
ACE or ARB in <40% LVEF	71	67.7	ns
β-blockers	51.7	67.8	0.001
β-blockers in <40% LVEF	61	76.7	0.001
Diuretics	78.0	91.4	0.001
Ivrabradine	2.5	5.4	0.005
Anti-aldosterone agents	21.4	37.5	0.001
Anti-aldosterone agents in LVEF <35%	32.1	25.0	ns
Digoxin	13	14.7	ns
Warfarin	26.6	27.4	ns
Warfarin in aa ff	40.9	42.0	ns
NOA	4.0	4.4	ns
Anti-platelet	45.5	51.2	0.001
Anti-platelet in aa ff	35.6	37.2	ns
Statins	28	31	ns
Ca-blockers	16	14.4	ns
No. of other drugs	3.2	4.1	ns

ACE-I, angiotensin converting enzyme-inhibitors; ARB, angiotensin receptor blockers; ns, not significant; LVEF, left ventricular ejection fraction; aa ff, atrial fibrillation; NOA, new oral anticoagulants.

relative new entry in the therapeutic scenario of HF treatment. Digoxin use is almost exclusive (90%) in patients with AF. Near one out of two patients has AF.

CHA_2DS_2-VASc score[31] identifies our patients at high risk of thromboembolism but anticoagulant therapy is present only in half of the cases of the patients with AF. It is possible that the age factor, other comorbidities such as cognitive impairment or active cancer or, on the whole, high HAS-BLED score[32] may have played a role even though the characteristic of the subjects of our study should have suggested a more extended use. NOA are still marginally used.

Our patients have many comorbidities, their prevalence is similar to that of previous surveys, and from our data the number of comorbidities is correlated with the mean hospital stay. Our study was not retailed to define the prognostic impact of each comorbidity but it is well known that renal failure, anemia and cognitive deficit are the worse prognostic factors of HF in an elderly population.[21,23]

Also BNP or NT pro-BNP are powerful prognostic markers: above all their discharge values are good predictors of hospital readmission,[33-35] but their determination was uncommon in our study.

Concerning the patients discharged from the wards we found many critical elements. First of all about one third of population has cognitive impairment and one half is not self-sufficient: this makes difficult to take care of them. And this is especially true if we consider that more than a half of patients must take over 8 drugs a day, a marker of multiple pathologies, and over 20% need oxygen. It is probable that the percentage of patients temporary assigned to lower intense settings of care is still minimal for the needs of this population.

Another admission for the same cause during the previous 30 days was present in 22.6% of patients. Although our aim was not to define the most used and useful follow up program, we have registered that 40% of patients were discharged with a well-stated one and this could contribute to lower the *rolling doors phenomenon*.

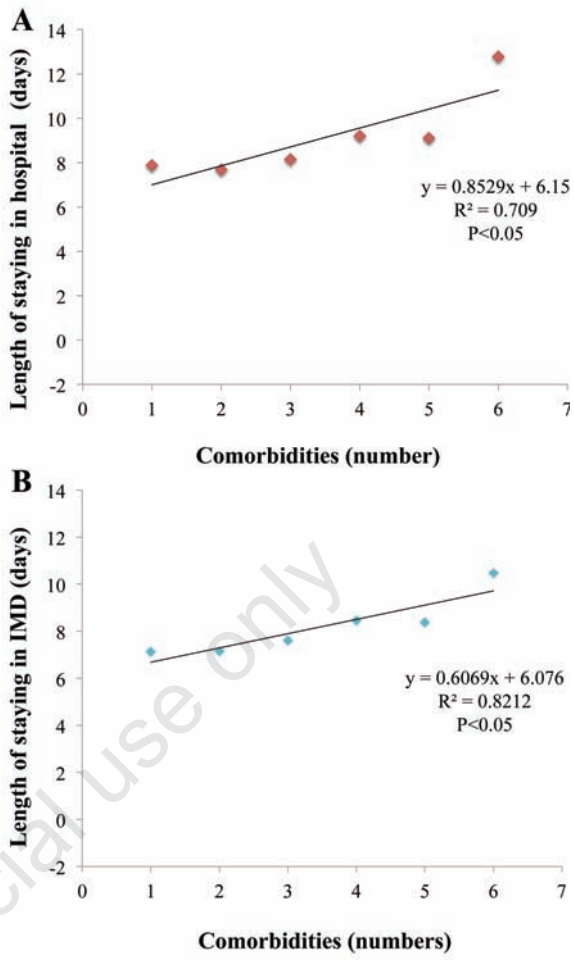

Figure 2. A) Length of staying (LOS) in hospital according to the number of comorbidities in patients admitted for heart failure. The LOS in hospital was statistically longer in patients with more than 4 comorbidities (9.46+6.05 days *vs* 8.60+5.53 days, respectively; P<0.05); B) LOS in Internal Medicine Departments (IMD) according to the number of comorbidities in patients admitted for heart failure. The LOS to IMD was statistically longer in patients with more than 4 comorbidities (8.62+4.99 *vs* 7.96+4.91 days; P<0.05).

Table 4. Number of comorbidities and length of staying in hospital and in the Internal Medicine Departments. Two patients had more than 6 comorbidities so they were not calculated.

No. of comorbidities	No. of patients	LOS in hospital (mean+SD)	LOS in IMD (mean+SD)
0	8	10.25±5.73	7.5±5.02
1	61	7.88±4.10	7.13±3.95
2	151	7.68±5.26	7.15±4.64
3	240	8.15±5.20	7.89±4.93
4	198	9.21±4.97	8.46±4.56
5	98	9.11±6.38	8.38±5.06
6	19	12.78±10.86	10.47±7.08

LOS, length of staying; SD, standard deviation; IMD, Internal Medicine Departments.

Table 5. Critical situations at discharge.

Criticality	Total number (%)
Loss of autonomy*	354 (50.1)
Domiciliary oxygen therapy°	150 (21.2)
Prescription of more than >7 drugs	403 (57.0)

*Loss of autonomy means a Barthel index score of 40 or less;[20] °Need of oxygen for more than two hours a day.

Conclusions

Our study represents a snapshot of HF in IMD in Tuscany; it shows that the patients admitted for HF to IM wards have become older and have many comorbidities. The number of comorbidities is correlated with the mean hospital stay.

The use of echocardiography and the pharmacological therapy with ACE-I, ARB, β-blocker and anti-aldosterone agents is wider than previous surveys in similar population and settings, but some diagnostic, therapeutic, prognostic elements are not still similar to that recommended by the most recent HF guidelines.

We must take into account that no trial has been made and no guidelines have been drawn up in the very old patients and that the treatment of HF in complex patients like those admitted to IMD is often driven by a clinical holistic approach. We are confident that surveys concerning *real world* of HF patients admitted to IMD will contribute to improve their care.

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