Intern Emerg Med
DOI 10.1007/s11739-015-1336-z

EM - ORIGINAL

Acute heart failure in the emergency department: a follow-up study

Andrea Fabbri[1] · Giulio Marchesini[2] · Giorgio Carbone[3] · Roberto Cosentini[4] · Annamaria Ferrari[5] · Mauro Chiesa[6] · Alessio Bertini[7] · Federico Rea[8]

Received: 26 May 2015 / Accepted: 30 September 2015

Abstract Acute heart failure (AHF) is a major public health issue due to high incidence and poor prognosis. Only a few studies are available on the long-term prognosis and on outcome predictors in the unselected population attending the emergency department (ED) for AHF. We carried out a 1-year follow-up analysis of 1234 consecutive patients from selected Italian EDs from January 2011 to June 2012 for an episode of AHF. Their prognosis and outcome-associated factors were tested by Cox proportional hazard model. Patients' mean age was 84, with 66.0 % over 80 years and 56.2 % females. Comorbidities were present in over 50 % of cases, principally a history of acute coronary syndrome, chronic obstructive pulmonary disease, diabetes, chronic kidney disease, valvular heart disease. Death occurred within 6 h in 24 cases (1.9 %). At 30-day follow-up, death was registered in 123 cases (10.0 %): 110 cases (89.4 %) died of cardiovascular events and 13 (10.6 %) of non-cardiovascular causes (cancer, gastrointestinal hemorrhages, sepsis, trauma). At 1-year follow-up, all-cause death was recorded in 50.1 % (over 3 out of 4 cases for cardiovascular origin). Six variables (older age, diabetes, systolic arterial pressure <110 mm/Hg, high NT pro-BNP, high troponin levels and impaired cognitive status) were selected as outcome predictors, but with limited discriminant capacity (AUC = 0.649; SE 0.015). Recurrence of AHF was registered in 31.0 %. The study identifies a cluster of variables associated with 1-year mortality in AHF, but their predictive capacity is low. Old age and the presence of comorbidities, in particular diabetes are likely to play a major role in dictating the prognosis.

Keywords Acute heart failure · Emergency department · Clinical characteristics · Epidemiology · Follow-up

✉ Andrea Fabbri
andrea.fabbri@auslromagna.it

[1] Department of Emergency Medicine, Presidio Ospedaliero Morgagni-Pierantonio, AUSL della Romagna - Forlì, Via Forlanini 34, 47121 Forlì, Italy

[2] Department of Medical and Surgical Sciences, Clinical Dietetics, University of Bologna, S. Orsola-Malpighi Hospital, via Massarenti 9, 40138 Bologna, Italy

[3] Department of Emergency Medicine, Gradenigo Hospital, Corso Regina Margherita 8/10, 10100 Torino, Italy

[4] Department of Emergency Medicine, Osp. Maggiore Policlinico, fondazione Cà Granda, via F. Sforza 35, 20122 Milan, Italy

[5] Department of Emergency Medicine, Ospedale S. Maria Nuova, via Risorgimento 80, 4100 Reggio Emilia, Italy

[6] Department of Emergency Medicine, Ospedale S. Antonio, Azienda Ospedaliera, via Facciolati 71, 36124 Padua, Italy

[7] Department of Emergency Medicine, Azienda Ospedaliera Universitaria Pisana, via Roma 67, 56126 Pisa, Italy

[8] Department of Statistics and Quantitative Methods, University of Milano-Bicocca, via Bicocca degli Arcimboldi 8, 20126 Milan, Italy

Introduction

AHF is a global public health issue characterized by high rates of complications, unfavorable outcome and significant economic burden for National Health Systems [1]. Recent reviews report that the total number of AHF incidents exceeds 20 million patients/year in Europe and in the United States, with an incidence of over 1.5 million cases/year [1–4]. Nearly 50 % of patients with AHF are re-hospitalized within 6 months after discharge, with 70 % of hospital admissions due to recurrent episodes [5, 6].

Published online: 27 October 2015

Several prognostic models have been proposed and validated to predict recurrence and outcome [7–10].

In a US population-based study derived from medical records, the long-term prognosis of hospitalized patients with AHF is poor, despite improvement in survival in the last decades, as less than 1 in 3 hospitalized patients treated in the year 2004 survived more than 5 years [8]. By 2050, it is estimated that 20 % of the US population will be aged over 65, with 80 % at risk of being hospitalized for AHF [11].

The majority of studies on predictors of morbidity and mortality in AHF are derived from in-patient settings, and only a few studies considered all cases presenting in the emergency departments (EDs). Compared with in-patient settings, the ED represents a high-yield area to identify symptomatic patients eligible for enrollment in AHF studies in their early treatment phase. Exclusion of the ED cohorts has been indicated as a selection bias and a potential source of error in AHF outcome studies [12].

We used the database of the SAFE-SIMEU Study (Screening of Acute Heart Failure in the Emergency Department) to perform a secondary analysis on predictors of short- and long-term outcome of subjects visited in the ED for AHF.

Methods

Data collection

In 2012, the Study and Research Center of the Italian Society of Emergency Medicine (SIMEU) launched a study on patients presenting to EDs for an AHF episode between January 2011 and December 2012. The words "acute heart failure" were used as search terms to retrieve the cases from databases, with reference to the definition of the working group of European Society of Cardiology [13]. An expert emergency physician was designed as independent abstractor in all centers; abstractors, blinded to the study protocol, retrieved electronic medical records following a standardized training program organized by the coordinating center. During the study period, the principal investigator actively monitored abstractors on chart reviews. Quality control was performed by an independent physician for all cases to ensure the accuracy and validity of the data retrieved in the Case Report Form (CRF), by centrally random checking of the original records.

In the present analysis the main characteristics of 1234/2683 subjects from 3 out of 6 participating centers of the original database (Forlì, Reggio Emilia and Padua) were considered for 1-year follow-up. The centers were included in the analysis provided that the ED was the sole district hospital admitting subjects with recurrent AHF or other significant events.

The CRF included demographic characteristics (age, gender, race), medical history and clinical presentation (comorbidities, precipitating factors and time of first occurrence of symptoms to initial registration in ED). The main precipitating factors of the AHF episode were grouped into the following categories: insufficient compliance with therapy, uncontrolled hypertension, new-onset dysrhythmias, worsening renal failure, ischemic cardiac disease, fever, acute respiratory diseases, anemia, other causes, and undefined causes.

Cardiovascular comorbidities included dysrhythmias (atrial fibrillation, atrial flutter) valvular heart disease, any diagnosis of prior coronary artery disease, and the presence of pacemaker or implantable cardioverter defibrillator. In particular, the abstractors checked the patients' histories for the presence of previous episodes of AHF. Non-cardiac comorbidities included chronic kidney, cerebrovascular and obstructive pulmonary disease, diabetes mellitus, cognitive defects and poor nutritional status.

The prescription of drugs acting on the cardiovascular system before the ED admission was also registered, in particular: ACE inhibitors (ACE-Is) or angiotensin renin blockers (ARBs), furosemide, mineralocorticoid receptor antagonists (MRA), anticoagulants, or antithrombotic agents. The type of pharmacological intervention during treatment in the ED was also considered (oxygen, non-invasive mechanical ventilation, diuretics, nitro-glycerine and opiates).

Biochemical data were registered for risk stratification analysis: plasma sodium concentration (high risk <135 mEq/L) [1], NT pro-BNP concentration (high-risk cut-off values >5000 ng/L) [14], troponin-T or I concentration at admission (predefined cut-off, ≥50 μg/L for troponin-T (Roche Elecsys® assay) [15]) and ≥0.5 ng/L for troponin-I (Siemens Healthcare Global® assay) [16] systolic blood pressure (high risk, <110 mm/Hg) [17]. Mean glomerular filtration rate at baseline was estimated by the CKD-EPI equation [18]. Left ventricular ejection fraction value was measured by trans-thoracic echocardiography in 1174 out of 1234 (95.1 %) subjects before hospital admission.

Disposition was categorized as (1) referral to general practitioners (GPs) after 3–6 h of ED treatment; (2) short-term (<24 h) intensive observation before referral to GP; (3) admission to hospital (internal medicine or any specialty); (4) admission to intensive care units.

The main outcome measure was all-cause death at 1-year follow-up. Secondary outcomes were 30-day and 1-year death for definite cardiac causes, unfavorable outcome (death for cardiac origin, non-fatal myocardial infarction, non-fatal stroke), and AHF recurrence.

Other causes of readmission to the ED of reference (trauma, COPD, digestive hemorrhages, sepsis, etc.) were

registered. In the follow-up analyses, we assumed that patients not re-admitted, either did not have events or died from acute events before admission (in which case they were traced in the health district administrative database). In order to determine the patients' statuses, the death certificates and the medical and administrative databases of individual local health districts through 1 year were systematically searched. The search was carried out by crossing family name, address, birth date, district health code, and coded reasons for visit/admittance of all index cases as identification source. Any of the following events were considered and censored on 31 December 2012 for cases enrolled between January and December 2011 and on 31 December 2013 for cases enrolled between January and December 2012.

Exclusion criteria were: (1) renal failure needing haemodialysis, because of different AHF pathophysiology and treatment (55 cases); (2) non-cardiac pulmonary oedema, including suspected sepsis (23 cases); (3) terminal status, i.e., death expected within weeks from chronic, non-cardiac diseases (78 cases). All cases with AHF as a secondary diagnosis were not considered.

The ethics committee of the coordinating center of Forlì CEAV-AVR Romagna approved the study (1112/2014/O/OssN, February 19, 2014), and the approval was for all participating centers.

Data analysis

The population was described as the number of cases and percentages (categorical variables) or as the means with standard deviation (SD) and median with interquartile range (IQR) (continuous variables). We then tabulated data of main comorbidities in relation to new-onset AHF or recurrent AHF presentation. Differences between groups were analyzed by χ^2 test as crude odds ratios (ORs) and corresponding 95 % confidence interval (CI).

Multivariable analysis was developed with a Cox proportional hazard models by stepwise analysis (backward and forward) of factors considered significant in univariable analysis (entered into the model if $p < 0.15$) and according to clinically relevant parameters (e.g., history of acute coronary syndrome, diabetes) [19, 20]. Prognostic models were performed to define factors associated with all-cause mortality, cardiovascular mortality and any recurrence of AHF. The assumption of proportional hazard was checked with analytical and graphical methods (log minus log plot of the cumulative hazard function). In the multivariate model, variables were selected on the basis of previous reports and a reasonable relevance for association with main outcome measures.

Variables tested for multivariable analyses were: age sex, cardiac comorbidities, in particular new-onset dysrhythmias, cardiac valvular diseases, any previous diagnosis of coronary artery disease (CAD), the presence of Pacemaker (PM) or implantable cardioverter defibrillator (ICD), and history of AHF. Non-cardiac comorbidities included the presence of chronic kidney disease (CKD) (any type), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), cerebrovascular disease (CVD), cognitive defects and poor nutritional status. Other variables tested were compliance with pharmacology prescriptions before ED admission for AHF (ACE-Is, ARBs, β-Blockers, loop diuretics, MRA, anticoagulants, antithrombotic agents) in subjects with a history of AHF, and biochemical markers of severity [plasma sodium concentration (high risk <135 mEq/L), NT pro-BNP concentration (high-risk cut-off values >5000 ng/L), troponin-T or I concentration at admission (cut-off, ≥50 μg/L for troponin-T and ≥0.5 ng/L for troponin-I), systolic blood pressure (<110 mm/Hg), estimated mean glomerular filtration rate at baseline <30 mL/min/1.73 m^2] [1, 14, 16, 17].

Persons-time estimates were calculated using an actuarial method. For all-cause mortality, Cox proportional hazard model was performed. The estimates were reported with 95 % CI. p values < 0.05 were considered statistically significant. Analyses were performed using SPSS software, version 20 (SPSS Inc., Chicago, IL, USA).

Results

Clinical characteristics

A total of 1234 out of 1806 AHF patients (68.3 %) of 3 centers were included in the analyses; 671 patients presented to the EDs for a first episode of (54.4 %) AHF. Demographic characteristics and comorbidities are reported in Table 1. The median age was 84 [21] (range 27–103), with 818 subjects (66.3 %) over 80 years and 693 females (56.2 %). The time from onset of symptoms to ED presentation was <12 h in 382 cases (31.0 %) and <24 h in 610 (49.4 %); no relationship was observed between time from the occurrence of symptoms and age, gender, or comorbidity.

Acute respiratory disease (25.2 %), uncontrolled hypertension (12.0 %) and new-onset dysrhythmias (13.2 %) were the main precipitating factors. A total of 841 subjects (68.1 %) had 3 or more comorbidities and a previous episode of AHF was registered in nearly 50 % of cases (Table 1). 223 cases (39.6 %) were being treated with ACE-Is/ARBs and β-blockers, 204 (36.2 %) with a combination with ACE-Is-ARBs, β-blockers and furosemide.

Type and number of cardiac and non-cardiac comorbidities were more represented in the subjects with history

Table 1 Demographic and clinical characteristics of patients admitted to ED for AHF

Characteristics	No. of cases 1234
Demographic	
Female	693 (56.2)
Age, years[a]	84.0 [41]
Comorbidity	
History of acute heart failure	563 (45.6)
Valvular heart diseases	459 (37.2)
Chronic arrhythmias	647 (52.4)
History of acute coronary syndrome	639 (23.8)
Intra-cardiac devices (PM and/or ICD)	152 (12.3)
Chronic obstructive pulmonary disease	446 (36.1)
Chronic kidney disease	715 (26.6)
Diabetes mellitus	325 (26.3)
Cerebral-vascular disease	363 (29.4)
Impaired cognitive status	385 (31.2)
Nutritional deficit	136 (11.0)
Number of comorbidities	
$N = 0$	50 (4.1)
$N = 1$	134 (10.9)
$N = 2$	209 (16.9)
$N = 3$	248 (20.1)
$N = 4$	250 (20.3)
$N = \geq 5$	343 (28.8)

Data reported as number of cases and %. Data are reported as number of cases and percentage

ACS acute coronary syndrome, *PM* pacemaker, *ICD* implantable cardioverter defibrillator

[a] Variable described as median [42]

of AHF than in the subjects presenting with new-onset AHF (Table 2).

Clinical and laboratory data

At first evaluation in the ED, median systolic blood pressure was 130 (37) mm/Hg, with 24.7 % of cases with values <110 mm/Hg. The mean estimated glomerular filtration rate (eGFR; CKD-EPI method [18]) was 45.3 (33.6) mL/min/1.73 m^2. Severe renal dysfunction (eGFR <30 mL/min/1.73 m^2) was present in 284 (24.2 %) subjects, mainly in cases with a history of recurrent AHF. The median values of N-terminal pro-brain natriuretic peptide (NT pro-BNP) or BNP were 3,610 [22], with 440 cases (35.7 %) with values over >5000 pg/mL. Troponin-T or I, registered in 1025 cases (83.1 % of cases), were over cut-off levels in 278 cases (22.5 %).

Trans-thoracic echocardiography was available in most cases (1,223, 99.1 % of enrolled subjects). The median LVEF was 45 % (IQR 4), with 335 values (27.4 %) under 40 %.

Disposition and follow-up

A disposition was recorded in 1,234 cases (100 % of cases). Of these, 24 subjects (1.9 %) died within 6 h from cardiogenic shock. In this group, low-sodium concentration, hypotension, and a high number of prior drug prescriptions were associated with mortality. After visit and ED treatment, 79 subjects (16.8 %) were admitted to intensive care units and 887 patients (71.9 %) to ordinary wards in different medical departments, according to different hospital configurations. Only 67 patients (5.4 %) were referred to their GPs within a few hours, whereas 177 patients (14.3 %) underwent a short-term (<24 h) intensive observation.

At 30-day follow-up, 123 cases (10.0 %) had died: 110 of the 123 cases (89.4 %) from cardiovascular events, and 13 (10.6 %) from non-cardiovascular conditions (cancer, gastrointestinal hemorrhages, sepsis, trauma). In a Cox proportional hazard model, only hypotension and poor nutritional status were selected as significant predictors of all-cause death, accounting for 20 % total mortality. These predictor variables were also confirmed when death from definite cardiac origin, or unfavorable outcome (death from cardiac origin, non-fatal myocardial infarction, non-fatal stroke) were selected as outcome measures. The recurrence rate of ED presentation for AHF was as high as 4.5 % at 30 days.

At 1-year follow-up, death was recorded in 618 subjects (50.1 %): 486 subjects (39.4 %) from cardiovascular events, 132 (10.7 %) from non-cardiovascular causes (hemorrhage, cachexia, sepsis, worsening respiratory diseases, trauma). A group of 6 items, out of the 22 tested in the model, were selected as significant outcome predictors (Table 3). Analytical and graphical methods show that the proportionality assumption of the model is not violated (not reported in detail) and the final model shows an overall accuracy (area under the curve) of 0.649 ± SE 0.015. These results are confirmed when either cardiovascular mortality or the combined unfavorable outcome are tested. One-year recurrence rate is as high as 31.0 %, and the mortality of recurrent AHF (306 cases; 49.5 %) is higher compared to that registered in new-onset AHF (257 cases; 41.7 %) (OR 1.37, 95 % CI 1.09–1.71; $p < 0.006$). The hazard model confirmed an increased risk of mortality in older subjects (over 80 years, 473 cases; 76.5 %) vs. subjects under 80 (145 cases, 23.5 %; OR 2.0, 95 % CI 1.57–2.58; $p < 0.001$) and in subjects with diabetes (232 (37.5 %) vs. those without diabetes (174 cases, 28.2 %; OR 1.52, 95 % CI 1.20–1.94; $p < 0.001$) (Fig. 1).

Table 2 Comorbidity of patients attending the ED for AHF in relation to main clinical characteristics: subjects with history of AHF were compared with subjects with new-onset AHF

	History of AHF 563 (45.6 %)	New-onset AHF 671 (54.4 %)	Odds ratio (95 % CI)	*p* value
Comorbidity				
Valvular heart disease	257 (56.0)	202 (44.0)	1.9 (1.5–2.5)	<0.001
Chronic arrhythmias	313 (48.4)	334 (51.6)	1.3 (1.0–1.6)	0.045
History of ACS	204 (51.1)	195 (48.9)	1.4 (1.1–1.8)	0.009
Intra-cardiac devices (PM and/or ICD)	74 (48.7)	78 (51.3)	1.1 (0.8–1.6)	0.435
Chronic obstructive pulmonary disease	253 (56.7)	193 (43.3)	2.0 (1.6–2.6)	<0.001
Chronic kidney disease	197 (60.6)	128 (39.4)	2.3 (1.8–3.0)	<0.001
Diabetes mellitus	211 (52.0)	195 (48.0)	1.5 (1.2–1.9)	0.002
Cerebral-vascular disease	177 (48.8)	186 (51.2)	1.2 (0.9–1.5)	0.168
Impaired cognitive status	216 (56.1)	169 (43.9)	1.8 (1.4–2.4)	<0.001
Nutritional deficit	78 (57.4)	58 (42.6)	1.7 (1.2–2.4)	0.005

Data reported as number of cases and %. Data are reported as number of cases and percentage

PM pacemaker, *ICD* implantable cardioverter defibrillator, *ACS* acute coronary syndrome

p for significance <0.05

Table 3 Cox proportional hazard model for all-cause mortality in patients attending the ED for AHF at 1-year follow-up

Cox proportional hazard model	Hazard ratio	95 % CI	*p* value
Age (for decades)	1.09	1.02–1.16	0.006
NT pro-BNP >5000 pg/mL	1.25	1.10–1.41	<0.001
SBP <110 mm/Hg	1.22	1.07–1.40	0.004
Diabetes mellitus	1.21	1.07–1.37	0.003
Troponin	1.21	1.05–1.39	0.008
Impaired cognitive status	1.15	1.01–1.31	0.036

Variables tested but not included in the final model were: sex, valvular diseases, chronic obstructive pulmonary disease, history of acute coronary syndrome, chronic kidney disease, diabetes mellitus, chronic arrhythmias, history of AHF, obstructive cardiomyopathy, implantable cardioverter defibrillator, history of cerebrovascular diseases, nutritional deficits, sodium concentration, left ventricular ejection fraction, eGFR value, adherence to pharmacology prescription before ED admission in subjects with history of AHF

ACS coronary artery syndrome, *SBP* systolic blood pressure, *NT pro-BNP* N-terminal pro-hormone of brain natriuretic peptide >5000 pg/mL, *troponin-I or T cut-off levels* Forlì and Reggio Emilia, Tn T > 0.50 μg/L; Padova, Tn I < 0.5 ng/L

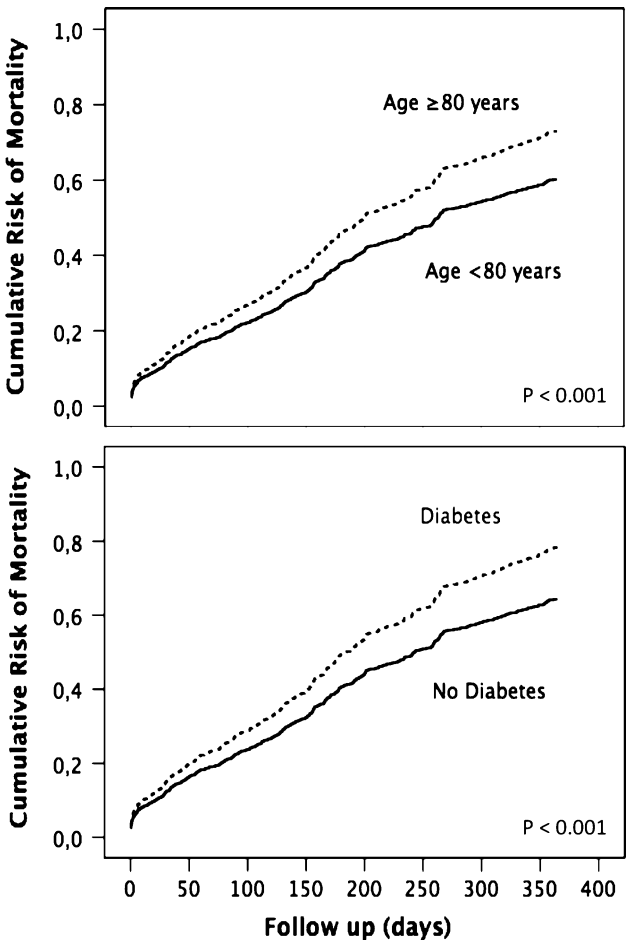

Fig. 1 Cox proportional hazard model for all-cause mortality at 1-year follow-up in subjects attending the ED for acute heart failure, stratified by age (cut-off, 80 years) (*upper panel*) and the presence of diabetes (*lower panel*) (*p* for significance ≤0.005)

Discussion

This follow-up study, derived from an unselected, real-life population, shows that subjects admitted to the participating Italian EDs with a diagnosis of AHF are different from subjects included in most international registries or in large clinical trials [1]. Our subjects are older, have a higher percentage of cardiac and non-cardiac comorbidities, a much poorer prognosis (50 % mortality at 1-year follow-up), and high rates of recurrent AHF associated with mortality.

In the last 10 years, many predictors of morbidity and mortality with high discriminant capacity have been proposed in selected settings, but the majority of them have limited external validity. A few studies including unselected ED patients have been reported, but the selected variables had only a marginal discriminant capacity [23]. Also in our series, the model selected a group of 6 out of 19 tested variables, but the discriminant capacity is low (AUC 0.65), and older age remained the main predictor variable.

Age represents a pivotal risk factor; in most international large registries, the mean age of patients ranges from 70 to 75 years, with an SD of 15 [1]. Regional variations in age are likely to be explained by different prevalence of underlying risk factors as well as the mean age of the population. In particular, patients included in North American registries tend to be older than patients enrolled in countries with developing economies [1, 24]. We find that 66 % of our subjects were over 80. This proportion is higher than that reported in European registries (Euro Heart Failure Survey), with 26 % [25] and 21 % [26] over 80. Our proportion of elderly patients is also higher than that reported in a recent French national registry (53 % of cases admitted for the first episode of AHF) [27].

Also the standard of living, calculated by the human development index, a composite measure including life expectancy, adult literacy, and educational level, may contribute to further increasing the prevalence of risk factors associated with an unfavorable outcome [24]. Older age per se is expected to drive the prevalence of risk factors, and, given the heterogeneous nature of AHF population, the "one size fits all" strategy in diagnosis and treatment may not be appropriate [28]. In a large, unselected sample of patients enrolled in 26 Spanish EDs, age was again the main prognostic factor [22]. All these data provide important information on the process of care in the ED for elderly patients with AHF, potentially useful for social welfare planners and health policy makers.

Inclusion rate is important too, since large clinical trials reportedly enroll only approximately 40 % of observed patients [29–31]. Inclusion criteria may introduce a selection bias in centers with low enrollment rate [32]. Finally, over 55 % of the patients in our series were women, a proportion similar to that observed in the US registries, but not in most clinical trials of hospitalized subjects, which include only 40–50 % females [24, 33]. This is a noteworthy observation, as female patients are unique in that they tend to be older at the time of initial diagnosis, and are more likely to have acute HF with preserved ejection fraction [34].

Cardiac and non-cardiac comorbidities are both highly prevalent among hospitalized patients in most large trials, and dictate the management of AHF across Europe, according to the guidelines on diagnosis and treatment of AHF published by the European Society of Cardiology (ESC) [1, 35]. In our series more than 30 % of patients were recorded with a history of CAD, complicated by acute myocardial infarction in 20–30 % of cases, frequently resulting in systolic left ventricular dysfunction. Similarly, non-cardiac comorbidities including diabetes mellitus, chronic kidney disease, and chronic obstructive pulmonary disease are reported in over 30 % of patients [1]. Our database is in keeping with community registries; both cardiac and non-cardiac comorbidities were extremely prevalent, but non-cardiac comorbidities were of particular importance and highly prevalent: COPD (36.1 %), diabetes (32.9 %), CKD (26.3 %), cerebrovascular diseases (29.4 %), diagnosis of impaired cognitive status (31.2 %). Approximately 20 % of the subjects had 2 or more comorbidities (Table 1) and most comorbidities were more represented in subjects with a history of AHF than in subjects with new-onset AHF (Table 2).

Diabetes was confirmed as an important, independent predictor of mortality. In patients hospitalized for AHF, diabetes is associated with poorer prognosis and increased risk for combined cardiovascular mortality in several reports [35, 36]. Also the presences of multiple comorbidities and low compliance with treatment have been indicated as important outcome predictors in older subjects with AHF, and both the number and the severity of comorbidities increase progressively with advancing age [21] [28]. In a recent French survey on subjects over 80 with AHF, only 16 % of cases were being treated with ACE-Is or ARBs plus BB before hospital admission. [27] In our survey, the percentage of treated subjects was 39.6 % (with diuretics being taken in over 90 %). The higher prevalence of specific treatment highlights the severity of the condition, which per se does not systematically predict a favorable outcome, as reported in different settings [27].

In most clinical registries, admission to hospital is explained by a worsening condition of chronic HF, where one or more acute precipitating factors may be identified, and about 50 % of our patients are reported as uncontrolled hypertension at presentation. In contrast, only 2 % of patients are recorded with an initial systolic blood pressure <90 mm Hg, suggestive of cardiogenic shock and systemic hypo-perfusion and 15 % with acute pneumonia [24]. In our series, uncontrolled hypertension is rarely reported (only 12.7 %), acute pneumonia is very frequent (over 30 % of cases), and only cardiogenic shock (2.1 %) was in keeping with the literature.

ED disposition largely depended on the specific characteristics of the Italian Health System. The possibility of maintaining patients inside ED for a maximum of 24 h before admission, a possibility used to reduce formal

admission to hospital and costs, was used in less than 15 % of cases, due to severe conditions at presentation.

Most large studies and clinical registries focus on recurrence and outcome after hospital discharge from an episode of AHF, with poor outcome in cases with history of AHF [37–39]. An Italian registry in a cardiologic setting reports a 30-day mortality of 2.8 % and unplanned readmissions in 6.2 %. In a logistic model, worsening chronic heart failure as clinical presentation, inotropes use, length of stay and renin–angiotensin system inhibitors at discharge were selected as predictors of all-cause mortality or readmission but with low accuracy (c-statistic = 0.695) [40]. In a recent large cohort study in over 110,000 ED visits for AHF [7], one-third (31 %) of the patients have frequent ED visits at 1-year follow-up, associated with race/ethnicity and lower socio-economic status. In our series, recurrence rate is similar (31.0 %), but the mortality is higher. Thus, in our setting, higher mortality, driven by age and comorbidities, is likely to maintain a steady recurrence rate as expression of disease severity.

Some limitations must be acknowledged. Firstly, selection criteria are based on diagnosis after ED arrival, and medical evaluations were discussed during the investigator meetings, and centers were invited to follow current guidelines [13]. However, the diagnoses were made by the investigators according to their clinical judgment, and were not validated centrally. Secondly, representativeness is often recognized as a limitation in retrospective studies. To limit this issue, the participating centers were selected in proportion to the size of the population of reference, taking into account the different technological levels of the selected centers. Thirdly, the aforementioned independent predictors of mortality and the risk models may have limited external validity, since data have been obtained by post hoc analysis of a chart review analysis. Fourthly, the patients were selected in a large spectrum of disease severity, also including cases visited in EDs for mild symptoms and then referred to their GPs after few hours. Accordingly, the present population differs from the population of the large international registries, based only on hospitalized cases.

Conclusions: our analysis shows that subjects admitted to the participating Italian EDs and diagnosed as AHF (any disease severity) have a poorer prognosis in comparison to subjects considered in most international registries. The subjects are older, frail from cardiac and non-cardiac comorbidities (in particular diabetes), with 50 % death rate at 1-year, much higher than observed in large community-derived registries [1]. Whatever the severity of the event, the clinical variables have a limited discriminant capacity on outcome, which remains remarkably driven by age. Only preventive measures might change a clinical scenario in the presence of population aging.

Acknowledgments The authors thank all medical and nursing personnel of the participating centers for their valuable contributions.

Compliance with ethical standards

Conflict of interest All authors have no conflicts of interest to declare.

Statement of human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study formal consent is not required.

Source of support The study was endorsed by SIMEU (Società Italiana di Medicina d'Emergenza-Urgenza). The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

References

1. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M et al (2014) The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. J Am Coll Cardiol 63:1123–1133
2. Oliva F, Mortara A, Cacciatore G, Chinaglia A, Di Lenarda A, Gorini M et al (2012) Acute heart failure patient profiles, management and in-hospital outcome: results of the Italian Registry on Heart Failure Outcome. Eur J Heart Fail 14:1208–1217
3. Maggioni AP, Dahlstrom U, Filippatos G, Chioncel O, Crespo Leiro M, Drozdz J et al (2013) EURObservational Research Programme: regional differences and 1-year follow-up results of the Heart Failure Pilot Survey (ESC-HF Pilot). Eur J Heart Fail 15:808–817
4. Logeart D, Isnard R, Resche-Rigon M, Seronde MF, de Groote P, Jondeau G et al (2013) Current aspects of the spectrum of acute heart failure syndromes in a real-life setting: the OFICA study. Eur J Heart Fail 15:465–476
5. Butler J, Kalogeropoulos A (2008) Worsening heart failure hospitalization epidemic we do not know how to prevent and we do not know how to treat! J Am Coll Cardiol 52:435–437
6. Gheorghiade M, Zannad F, Sopko G, Klein L, Pina IL, Konstam MA et al (2005) Acute heart failure syndromes: current state and framework for future research. Circulation 112:3958–3968
7. Hasegawa K, Tsugawa Y, Camargo CA Jr, Brown DF (2014) Frequent utilization of the emergency department for acute heart failure syndrome: a population-based study. Circ Cardiovasc Qual Outcomes 5:735–742
8. Joffe SW, Webster K, McManus DD, Kiernan MS, Lessard D, Yarzebski J et al (2013) Improved survival after heart failure: a community-based perspective. J Am Heart Assoc 2:e000053
9. Stiell IG, Clement CM, Brison RJ, Rowe BH, Borgundvaag B, Aaron SD et al (2013) A risk scoring system to identify emergency department patients with heart failure at high risk for serious adverse events. Acad Emerg Med 20:17–26
10. Lee DS, Stitt A, Austin PC, Stukel TA, Schull MJ, Chong A et al (2012) Prediction of heart failure mortality in emergent care: a cohort study. Ann Intern Med 156:767–775

11. Gloth FM, 3rd (2007) The 2005 White House Conference on Aging: a new day for White House conferences on aging and food for the future. J Am Geriatr Soc 55:305–307
12. Felker GM, Pang PS, Adams KF, Cleland JG, Cotter G, Dickstein K et al (2010) Clinical trials of pharmacological therapies in acute heart failure syndromes: lessons learned and directions forward. Circ Heart Fail 3:314–325
13. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K et al (2012) ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 14:803–869
14. Diercks DB, Fonarow GC, Kirk JD, Emerman CL, Hollander JE, Weber JE et al (2008) Risk stratification in women enrolled in the Acute Decompensated Heart Failure National Registry Emergency Module (ADHERE-EM). Acad Emerg Med 15:151–158
15. Giannitsis E, Kurz K, Hallermayer K, Jarausch J, Jaffe AS, Katus HA (2010) Analytical validation of a high-sensitivity cardiac troponin T assay. Clin Chem 56:254–261
16. Apple FS (2009) A new season for cardiac troponin assays: it's time to keep a scorecard. Clin Chem 55:1303–1306
17. Chioncel O, Ambrosy AP, Filipescu D, Bubenek S, Vinereanu D, Petris A et al (2014) Patterns of intensive care unit admissions in patients hospitalized for heart failure: insights from the RO-AHFS registry. J Cardiovasc Med (Hagerstown)
18. Earley A, Miskulin D, Lamb EJ, Levey AS, Uhlig K (2012) Estimating equations for glomerular filtration rate in the era of creatinine standardization: a systematic review. Ann Intern Med 156:785–795
19. Harrell FE Jr, Lee KL, Mark DB (1996) Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 15:361–387
20. Malek MH, Berger DE, Coburn JW (2007) On the inappropriateness of stepwise regression analysis for model building and testing. Eur J Appl Physiol 101:263–264 **(author reply 265–266)**
21. Ahluwalia SC, Gross CP, Chaudhry SI, Leo-Summers L, Van Ness PH, Fried TR (2011) Change in comorbidity prevalence with advancing age among persons with heart failure. J Gen Intern Med 26:1145–1151
22. Martin-Sanchez FJ, Marino-Genicio R, Rodriguez-Adrada E, Jacob J, Herrero P, Miro O et al (2013) Management of acute heart failure in spanish emergency departments based on age. Rev Esp Cardiol (Engl Ed) 66:715–720
23. Lee DS, Ezekowitz JA (2014) Risk stratification in acute heart failure. Can J Cardiol 30:312–319
24. Atherton JJ, Hayward CS, Wan Ahmad WA, Kwok B, Jorge J, Hernandez AF et al (2012) Patient characteristics from a regional multicenter database of acute decompensated heart failure in Asia Pacific (ADHERE International-Asia Pacific). J Card Fail 18:82–88
25. Mahjoub H, Rusinaru D, Souliere V, Durier C, Peltier M, Tribouilloy C (2008) Long-term survival in patients older than 80 years hospitalised for heart failure. A 5-year prospective study. Eur J Heart Fail 10:78–84
26. Komajda M, Hanon O, Hochadel M, Lopez-Sendon JL, Follath F, Ponikowski P et al (2009) Contemporary management of octogenarians hospitalized for heart failure in Europe: euro Heart Failure Survey II. Eur Heart J 30:478–486
27. Vorilhon C, Chenaf C, Mulliez A, Pereira B, Clerfond G, Authier N et al (2015) Heart failure prognosis and management in over-80-year-old patients: data from a French national observational retrospective cohort. Eur J Clin Pharmacol 71:251–260
28. Gustafsson F, Torp-Pedersen C, Seibaek M, Burchardt H, Kober L, Group Ds (2004) Effect of age on short and long-term mortality in patients admitted to hospital with congestive heart failure. Eur Heart J 25:1711–1717
29. Teerlink JR, Cotter G, Davison BA, Felker GM, Filippatos G, Greenberg BH et al (2013) Serelaxin, recombinant human relaxin-2, for treatment of acute heart failure (RELAX-AHF): a randomised, placebo-controlled trial. Lancet 381:29–39
30. O'Connor CM, Starling RC, Hernandez AF, Armstrong PW, Dickstein K, Hasselblad V et al (2011) Effect of nesiritide in patients with acute decompensated heart failure. N Engl J Med 365:32–43
31. Gheorghiade M, Abraham WT, Albert NM, Gattis Stough W, Greenberg BH, O'Connor CM et al (2007) Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure: an analysis from the OPTIMIZE-HF registry. Eur Heart J 28:980–988
32. Butler J, Subacius H, Vaduganathan M, Fonarow GC, Ambrosy AP, Konstam MA et al (2013) Relationship between clinical trial site enrollment with participant characteristics, protocol completion, and outcomes: insights from the EVEREST (efficacy of vasopressin antagonism in heart failure: outcome study with tolvaptan) trial. J Am Coll Cardiol 61:571–579
33. Hsich EM, Pina IL (2009) Heart failure in women: a need for prospective data. J Am Coll Cardiol 54:491–498
34. Galvao M, Kalman J, DeMarco T, Fonarow GC, Galvin C, Ghali JK et al (2006) Gender differences in in-hospital management and outcomes in patients with decompensated heart failure: analysis from the Acute Decompensated Heart Failure National Registry (ADHERE). J Card Fail 12:100–107
35. Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Follath F, Harjola VP et al (2006) EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. Eur Heart J 27:2725–2736
36. Sarma S, Mentz RJ, Kwasny MJ, Fought AJ, Huffman M, Subacius H et al (2013) Association between diabetes mellitus and post-discharge outcomes in patients hospitalized with heart failure: findings from the EVEREST trial. Eur J Heart Fail 15:194–202
37. Jencks SF, Williams MV, Coleman EA (2009) Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med 360:1418–1428
38. Ross JS, Mulvey GK, Stauffer B, Patlolla V, Bernheim SM, Keenan PS et al (2008) Statistical models and patient predictors of readmission for heart failure: a systematic review. Arch Intern Med 168:1371–1386
39. Vashi AA, Fox JP, Carr BG, D'Onofrio G, Pines JM, Ross JS et al (2013) Use of hospital-based acute care among patients recently discharged from the hospital. JAMA 309:364–371
40. Di Tano G, De Maria R, Gonzini L, Aspromonte N, Di Lenarda A, Feola M et al (2015) The 30-day metric in acute heart failure revisited: data from IN-HF Outcome, an Italian nationwide cardiology registry. Eur J Heart Fail. doi:10.1002/ejhf.290
41. Teerlink JR, Metra M, Felker GM, Ponikowski P, Voors AA, Weatherley BD et al (2009) Relaxin for the treatment of patients with acute heart failure (Pre-RELAX-AHF): a multicentre, randomised, placebo-controlled, parallel-group, dose-finding phase IIb study. Lancet 373:1429–1439
42. Fonarow GC, Peacock WF, Horwich TB, Phillips CO, Givertz MM, Lopatin M et al (2008) Usefulness of B-type natriuretic peptide and cardiac troponin levels to predict in-hospital mortality from ADHERE. Am J Cardiol 101:231–237