Factors associated with in-hospital mortality in acute decompensated heart failure

PHILIPPE LE CORVOISIER1, SYLVIE BASTUJI-GARIN2, BERTRAND RENAUD3, ISABELLE MAHÉ4, JEAN-FRANÇOIS BERGMANN5, HERVE PERCHET6, ELENA PAILLAUD7, DOMINIQUE MOTTIER8, OLIVIER MONTAGNE1

1Inserm, Clinical Investigation Centre 1430, APHP, Henri Mondor Hospital, F-94010 Creteil, France
2Paris Est University (UPE), IJC EA4393 and APHP, Henri Monod hospital, Clinical Research Unit (URC Mondor), F-94010 Créteil, France
3APHP, Cochin Hospital, Emergency Department, F-75014 Paris, France
4APHP, Louis Mourier Hospital, Department of Internal Medicine and Paris 7 University, EA REMES Paris Diderot University, Sorbonne Paris Cité, F-92700 Colombes, France
5APHP, Lariboisière-Fernand Vidal Hospital, Department of Internal Medicine, F-75010 Paris, France
6Meaux Hospital, Department of Cardiology, F-77100 Meaux, France
7APHP, Henri Mondor Hospital, Department of Geriatry, F-94010 Creteil, France
8Cavale Blanche Hospital, Department of Internal Medicine and Pneumology, EA 3878 (GETBO), F-29609 Brest, France

Address correspondence to: P. Le Corvoisier. Tel: (+33) 149813796; Fax: (+33) 149813797. Email: philippe.lecorvoisier@hmn.aphp.fr

Abstract

Background: among patients admitted for acute decompensated heart failure (ADHF), half are aged 75 years or over. The high prevalence of co-morbidities and functional impairments in this age group may affect patient outcomes.

Objective: to assess the association between co-morbidities, functional status and in-hospital mortality in patients with ADHF aged ≥75 years.

Design: a prospective, multicentre cohort study.

Setting: five French hospitals.

Subjects: five hundred and fifty-five patients aged ≥75 years admitted to the emergency department with ADHF.

Methods: baseline clinical data and co-morbidities were recorded at admission. Functional status and cognition were assessed using the Katz index and Mini-Mental Status Examination score, respectively. The primary outcome was in-hospital mortality.

Results: we found high prevalences of co-morbidities and functional impairments including hypertension (74.0%), atrial fibrillation (40.2%), prior acute coronary syndrome (32.3%) and diabetes (18.2%). The average creatinine clearance was 56.3 ml/min/1.73 m² (interquartile range, 39.2–77.0). In-hospital mortality was 67/555 (12.1%; 95% confidence interval, 9.4–14.8).
multivariate analysis, in-hospital mortality showed a statistically positive association with prior loss of self-sufficiency (Odds ratio [OR]: 5.85 [2.25–12.19]), hyperglycaemia (OR: 1.80 [1.26–2.54] per 1 SD increase), prior cerebral ischaemic event (OR: 3.56 [1.51–8.44]) and troponin I elevation above upper limit of normal (OR: 2.81 [1.37–5.77]). In addition, systolic blood pressure (OR: 0.98 [0.97–0.99] per 1 mmHg increase) and creatinine clearance (OR: 0.72 [0.51–1.00] per 1 SD increase) were negatively associated with in-hospital mortality.

**Conclusion:** co-morbidities and functional impairments are associated with a worse short-term prognosis in patients aged ≥75 years admitted for ADHF. Assessing these parameters at admission may improve patient management.

**Keywords:** older patients, acute decompensated heart failure, mortality, co-morbidities, functional status

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**Introduction**

Heart failure affects over 15 million people in Europe and generates a significant economic burden for healthcare systems [1]. Despite recent advances in the long-term treatment of chronic heart failure, most patients experience repeated episodes of acute decompensated heart failure (ADHF). In addition, an increased proportion of the population lives into older age worldwide. This, coupled with an increasing prevalence of heart failure in the elderly, leads to expect increasing numbers of emergency department admissions with ADHF [2].

Among patients admitted for ADHF in Western countries, half are aged 75 years or over [2]. Few studies have specifically addressed heart failure in this age group, and current clinical guidelines for older patients with heart failure are extrapolations of data from younger patients or from subgroup analyses of clinical trial results [1]. However, older patients often have atypical clinical presentations and exhibit specific characteristics including a high prevalence of multiple co-morbidities [3]. Furthermore, the loss of self-sufficiency due to physical and cognitive impairments is common in older individuals [4–6].

Assessing the prognosis of ADHF in older patients is challenging [6]. Clinical assessment may be too subjective to reliably separate into useful risk categories. Identifying factors associated with short-term outcome would therefore be of considerable clinical benefit. In this article, our main objective was to assess the potential influence of functional status and co-morbidities on in-hospital mortality. This is a large, prospective cohort study of patients aged 75 and over admitted to the emergency departments of five French hospitals with a diagnosis of ADHF.

**Methods**

The study protocol was approved by the institutional review board of our institution. The study was conducted in compliance with the Declaration of Helsinki. Patients or relatives gave their written informed consent before study inclusion.

**Study design and patient population**

This multicentre, prospective cohort study was conducted in the emergency departments of five French hospitals. Inclusion criteria were (i) patients aged ≥75 years, (ii) dyspnoea at rest or with minimal exertion, (iii) admission to an emergency department with a diagnosis of ADHF according to Framingham criteria (at least two major criteria or one major criterion plus two minor criteria) (Supplementary data, Supplement 1 are available in *Age and Ageing* online) [7] and (iv) expected hospital stay duration ≥ 24 h. Exclusion criteria were (i) patients transferred to another hospital after their initial evaluation and (ii) ventricular arrhythmia at admission.

**Data collection**

A standardised clinical evaluation was performed in the emergency department. For patients whose physical or cognitive status precluded a medical interview, data were obtained from the relatives or medical records.

The baseline clinical data, biological parameters, socio-demographic characteristics, medical history and co-morbidities listed in Table 1 were recorded routinely. Diagnostic investigations and treatments were at the discretion of the emergency room physicians. The glomerular filtration rate was calculated using the abbreviated Modification of Diet in Renal Disease formula. Functional status was assessed using the Katz Index of Independence in activities of daily living (ADL) based on six items (Katz index) [8]: eating, dressing, bathing, transferring from bed to chair, using the toilet, and bladder and bowel continence. Each item is scored on a 0–2 scale where 0 indicates dependency, 1 need for help and 2 independence. We defined loss of self-sufficiency as a score of 0 or 1 for at least one of the six items and full self-sufficiency as a total score of 12. Cognitive status was assessed in the emergency department using the Mini-Mental State Examination (MMSE) as early as allowed by the patient’s condition then again on Day 3 or 4; the highest of the two scores was used for the analysis [9].

**Clinical follow-up**

Patients were monitored until discharge from the hospital or death. The primary outcome was in-hospital mortality.
Factors associated with in-hospital mortality in acute decompensated heart failure

Table 1. Baseline characteristics of the 555 patients ≥75 years of age admitted with ADHF

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>85.2 (81.1–90.8)</th>
<th>367 (66.1)</th>
<th>145 (126–163)</th>
<th>74 (63–86)</th>
<th>87 (73–102)</th>
<th>367 (66.1)</th>
<th>145 (126–163)</th>
<th>74 (63–86)</th>
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<tr>
<td>Age, year, median (IQR)</td>
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<td>Heart rate, bpm, median (IQR)</td>
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<td>Medical status, n (%)</td>
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<td>Arterial hypertension (n = 551)*</td>
<td>408 (74.0)</td>
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<td>Diabetes mellitus (n = 543)*</td>
<td>99 (18.2)</td>
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<td>Hypercholesterolaemia (n = 537)*</td>
<td>106 (19.7)</td>
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<td>History of heart failure (n = 555)*</td>
<td>344 (62.0)</td>
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<td>History of atrial arrhythmia (n = 534)*</td>
<td>368 (68.9)</td>
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<td>Coronary artery disease (n = 517)*</td>
<td>167 (32.3)</td>
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<td>History of myocardial infarction (n = 542)*</td>
<td>110 (20.3)</td>
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<tr>
<td>History of cerebral ischaemic event (n = 535)*</td>
<td>67 (12.5)</td>
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<td>Current and former smokers (n = 513)*</td>
<td>128 (25.0)</td>
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<td>MMSE score &lt; 17 (n = 488)*</td>
<td>118 (21.6)</td>
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<td>ADL score, median (IQR)</td>
<td>10 (5–12)</td>
<td>321 (65.8)</td>
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<td>Number of drugs/day, median (IQR)</td>
<td>7 (5–9)</td>
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<td>Laboratory parameters at admission, median (IQR)</td>
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<td>Potassium, mmol/l (n = 533)*</td>
<td>4.2 (3.8–4.6)</td>
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<td>Sodium, mmol/l (n = 547)*</td>
<td>138 (135–141)</td>
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<td>Urea, mmol/l (n = 545)*</td>
<td>9.3 (6.8–13.8)</td>
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<tr>
<td>Creatinine clearance, ml/min/1.73 m2 (n = 545)*</td>
<td>56.3 (39.2–77.3)</td>
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<td>Glucose, mmol/l (n = 521)*</td>
<td>7.3 (6.1–9.3)</td>
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<td>ASAT, IU/l (n = 244)*</td>
<td>26 (20–41)</td>
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<td>Creatine kinase, IU/l (n = 408)*</td>
<td>69 (40–120)</td>
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<tr>
<td>Troponin at admission, ng/ml (n = 397)*</td>
<td>0.11 (0.06–0.4)</td>
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<tr>
<td>Arterial pH (n = 364)*</td>
<td>7.42 (7.36–7.46)</td>
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<td>White blood cells, 109/l (n = 532)*</td>
<td>9.2 (7.3–11.8)</td>
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<tr>
<td>Haemoglobin, g/dl (n = 533)*</td>
<td>12.3 (11.0–13.6)</td>
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</table>

An extended version of this table (with living conditions and electrocardiogram findings) is presented in Supplementary data, Supplement 2 available in Age and Aging online.

BP, blood pressure; ASAT, serum aspartate aminotransferase level.

*Number of values.

†Patients unable to perform the MMSE were assigned an MMSE score <17.

Statistical analysis

For risk factors present in 15–70% of the patients, to detect an odds ratio (OR) of 2.5 or 3 with 80% power and a type I error of 5%, assuming a 10% mortality rate, 500 patients were required.

After double data entry, STATA software version 11 (Stata Corporation, College Station, TX, USA) was used for the analysis. Quantitative variables are described as median (inter-quartile range, IQR) and qualitative variables as number (%). No adjustment for multiple comparisons was performed. All tests were two tailed, and P values no greater than 0.05 were considered significant.

In-hospital mortality was computed using the total number of included patients as the denominator. The 95% confidence interval (95% CI) of the estimate was estimated. Pre-defined variables likely to influence in-hospital mortality (Table 2) were compared between survivors and non-survivors by a univariate analysis (χ2 test, or Fisher’s exact test where appropriate, and non-parametric Mann–Whitney test). Age- and sex-adjusted ORs (aORs) with their 95% CIs were computed separately for each variable when a trend for an association (P values < 0.15) was observed. The two quantitative variables with non-normal distributions were dichotomised using the following cut-offs: Katz index, <12 or ≥12; MMSE score, ≤17 or >17 [9, 10]. Patients with cognitive impairment precluding the MMSE assessment were assigned an MMSE score <17. Cut-offs for laboratory variables were the normal range limits provided by the hospital laboratories. Due to their skewed distributions, creatinine clearance, blood urea, blood glucose and leucocyte counts were log-transformed for logistic regression; the ORs and 95% CIs are reported for a change of 1 SD in the log-transformed levels.

Variables showing a trend for an association (P < 0.15) in the univariate analyses were considered for the multivariate analyses. First-order interactions and confounding factors were looked for using multiple pairwise analyses. Finally, a backward stepwise logistic regression analysis was performed. Goodness of fit of the model was evaluated using the Hosmer–Lemeshow statistic and discrimination using the Harrell c-index.

Results

Patient characteristics

We included 555 patients with ADHF over a 12 month period. Table 1 lists their main characteristics. Chronic congestive heart failure had been diagnosed previously in 344 (62.0%) patients. Co-morbidities, dependency and severe cognitive impairment were common. The Katz index was <12 in 65.8% of the population (median score: 10 [5–12]). A severe cognitive impairment (MMSE score <17) was observed in 21.6% of the population.

Median hospital stay length was 10 [4–16] days. Of the 555 patients, 67 died, yielding an in-hospital mortality rate of 12.1% [95% CI, 9.4–14.8]. Median time from admission to death was 9 [4–25] days.

Factors associated with in-hospital mortality by univariate analysis

Table 2 reports the findings from the univariate analysis. The non-survivors were older and more often had a history of cerebral ischaemic events. At admission, haemodynamic alterations were more common, and systolic blood pressure was lower in the group of non-survivors. Male gender and past or current smoking were associated with non-significant trends towards higher mortality.

Several laboratory parameters were associated with mortality after adjustment for age and sex, including markers for renal dysfunction (low creatinine clearance or high blood urea) and for myocardial ischaemia (high creatine kinase (CK) and high troponin I). Blood glucose and leucocyte count at admission were higher in the non-survivors. No differences were found between survivors and non-survivors for sodium, potassium, aspartate aminotransferase or haemoglobin levels.
We also assessed the association between functional or cognitive status and the prognosis of patients. A Katz index ≤12 at admission was more common among non-survivors (Table 2), and alterations in each individual ADL item were also associated with higher in-hospital mortality (data not shown). Severe cognitive impairment showed a non-significant trend towards an association with higher in-hospital mortality.

### Multivariate analysis

No significant interactions were observed in the bivariate analysis. Due to co-linearity between diastolic and systolic blood pressure, and between blood urea and creatinine clearance, diastolic blood pressure and urea nitrogen were not considered for the multivariate analyses. Because of strong correlations between CK in one hand and glycaemia, creatinine clearance, Katz index and troponin I elevation in the other hand, CK could not be introduced in the multivariate analysis. The following factors were considered in the multivariate models: age, systolic blood pressure, history of cerebral ischaemic event, glycaemia, troponin I elevation, leucocytosis, low MMSE score and low Katz index. Troponin I was assayed at admission only when clinically indicated (71.5% of patients), and we therefore performed two multivariate analyses, with and without troponin I, to avoid potential selection bias. By multivariate analysis (Table 3), five factors assessed at admission were significantly associated with in-hospital mortality: lower systolic blood pressure, hyperglycaemia, history of cerebral ischaemic event, lower creatinine clearance and loss of self-sufficiency. Similar results were observed with the model including troponin I. In this second model, troponin I elevation was also associated with in-hospital mortality. Both models showed good calibration (Hosmer–Lemeshow statistic, \( P = 0.56 \) and \( P = 0.42 \), respectively) and good discrimination (Harrell c-index, 0.75 and 0.82, respectively).

### Discussion

The in-hospital mortality rate was 12.1% in our prospective study of unselected older patients admitted with ADHF. Co-morbidities, functional limitations and cognitive impairments were common. Factors independently associated with in-hospital mortality were prior loss of self-sufficiency, low systolic blood pressure, hyperglycaemia, prior cerebral ischaemic event, renal dysfunction and troponin I elevation.

The number of admissions for ADHF is increasing steadily as the population ages. Surveys have identified age-related differences in the epidemiology, clinical presentation and management of ADHF [5, 11]. Improvements in the management of chronic heart failure have decreased the in-hospital mortality rate of ADHF that was recently high.
Factors associated with in-hospital mortality in acute decompensated heart failure

Table 3. Independent risk factors for in-hospital mortality identified by multivariate analysis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Model without troponin I (n = 486)</th>
<th>Model 2 with troponin I (n = 352)</th>
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<tbody>
<tr>
<td>Age</td>
<td>OR [95% CI]</td>
<td>P value</td>
</tr>
<tr>
<td>Age</td>
<td>1.04 [0.99–1.09]</td>
<td>0.15</td>
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<tr>
<td>Systolic BP</td>
<td>0.98 [0.97–0.99]</td>
<td>0.003</td>
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<tr>
<td>Glycaemia</td>
<td>1.47 [1.10–1.97]</td>
<td>0.008</td>
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<tr>
<td>History of cerebral ischaemic event</td>
<td>2.33 [1.13–4.79]</td>
<td>0.021</td>
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<tr>
<td>Creatinine clearance</td>
<td>0.67 [0.51–0.89]</td>
<td>0.006</td>
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<tr>
<td>ADL score &lt; 12</td>
<td>3.46 [1.56–7.68]</td>
<td>0.002</td>
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<tr>
<td>Troponin I at admission &gt; 0.15 ng/ml</td>
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</table>

BP, blood pressure.

*Multivariate ORs (95% CI) were adjusted simultaneously for all variables listed in the table.

b OR [95% CI] per additional year.

BP [95% CI] per 1 mmHg increase.

*a OR [95% CI] per 1 SD increase in the log-transformed value.

estimated to be between 4 and 6% in middle-aged patients [5, 11, 12]. Higher mortality rates of 10.7 and 11.8% were reported in elderly patients in the prospective Euro Heart Failure Survey II and in the Italian survey on heart failure [5, 11], in keeping with the 12.1% in-hospital mortality rate in our patients aged ≥75 years.

Our patients had a high prevalence of co-morbidities including hypertension, ischaemic events, atrial fibrillation, renal dysfunction and diabetes. These co-morbidities may influence the effectiveness of treatments, the in-hospital clinical course and patient outcomes. In previous studies, widely diverse factors were associated with an increased risk of death in patients with ADHF including demographic factors, medical history and co-morbidities [5, 11, 13–15]. However, most of these studies focused chiefly on middle-aged patients [13–15]. The prognostic models derived from these studies have not been validated in older patients, in whom they may underestimate the risk of death [16]. Few data are available on assessing the risk of in-hospital mortality among older patients admitted with ADHF [5].

One of the most interesting findings from our study is the association between functional impairments and in-hospital mortality. Functional impairments were common in our population, with two-thirds of patients having limitations for one or more ADL at admission. Similarly, in the Euro Heart Failure Survey II, many older patients required help for ADL [5]. Previous studies in other clinical settings showed that functional status predicted in-hospital mortality independently from the underlying medical condition [17, 18]. Thus, the loss of self-sufficiency in patients admitted with chronic obstructive pulmonary disease (COPD), dialysis or neoplasms predicted short-term mortality, longer hospital stays and subsequent institutionalisation [17, 18]. However, few studies have assessed the influence of functional status on outcomes in representative populations of heart failure patients [19]. At present, the ability of older patients to perform ADL is rarely assessed in emergency departments despite the availability of the simple semi-quantitative scale, whose completion does not require active patient participation. The Katz index is well suited to the assessment of clinically unstable patients. It was found reproducible and reliable in earlier studies [20, 21]. Our results support routine determination of the Katz index in older patients admitted for ADHF, and an earlier study established the 1 year prognostic significance of ADL assessment in a similar population [19]. Interestingly, we found that each of the six ADL items taken separately predicted in-hospital mortality.

Cognitive impairments affected a substantial proportion of our patients, in agreement with earlier data [6]. In earlier work, cognitive decline was associated with higher long-term mortality in older patients with chronic heart failure [22]. Few data are available on the prognostic impact of cognitive impairments in patients with ADHF [23]. In our population, cognitive impairment was not a significant independent risk factor for in-hospital mortality but was strongly associated with a history of cerebral ischaemic events.

Other risk factors for mortality in patients with ADHF have been reported [5, 13–15]. Some of them, such as hyponatraemia, were not significant in our study. These discrepancies may be related to differences in inclusion criteria across studies.

In contrast, low systolic blood pressure was associated with in-hospital mortality in our study, as well as in the Euro Heart Failure Survey II, and ALARM-HT survey [5, 24]. Furthermore, troponin I elevation at admission was associated with in-hospital mortality. These results strongly suggest that ADHF complicating an ischaemic event may carry a worse prognosis than ADHF precipitated by other factors. However, non-ischaemic mechanisms such as elevated left-ventricular-wall stress may increase troponin I levels in some patients [25]. Regardless of the mechanism responsible for troponin I elevation, these data indicate that troponin I is a prognostic indicator that may be useful to assay routinely in older patients with ADHF. Another factor associated with in-hospital mortality in our patients was hyperglycaemia. The glucose level has been identified as a prognostic factor in various clinical settings including acute myocardial infarction, stroke, COPD exacerbation and pneumonia [26]. In ADHF, hyperglycaemia was associated with
the prognosis in some studies [27, 28], but not in others [29]. This discrepancy is likely due to differences in population characteristics, particularly in the proportion of patients with ischaemic heart failure.

Most of the prognostic models developed for risk stratification of patients with ADHF include an assessment of renal function [13]. Our results show that creatinine clearance remains a relevant prognostic factor in a population of older patients with a high prevalence of renal dysfunction.

Strengths and limitations
The main strength of our study is the identification of short-term prognostic factors in a large population of unselected older patients admitted with ADHF. Thus, our work provides valuable data on patients who are generally excluded from clinical trials.

A limitation of our study is the absence of data on nutritional status. In several studies, the prognosis of patients with heart failure was associated with various nutritional markers [30]. However, the methods used to assess nutritional status including laboratory assays, bioelectrical impedance and anthropometric measurements are not suitable for risk stratification in the emergency department setting.

Conclusion
Impaired function and co-morbidities influenced in-hospital mortality in our population of patients aged 75 years or over and admitted with ADHF. These parameters must therefore be assessed at admission to help identify those patients at greatest risk, with the goal of improving the clinical management of the acute event, preventing further functional loss and scheduling appropriate rehabilitation therapy.

Key points
- High prevalences of co-morbidities and functional impairment among older patients admitted for ADHF.
- Co-morbidities and functional impairments are associated with a worse short-term prognosis in this population.
- Functional status should be assessed at admission in older patients admitted for ADHF.

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Conflicts of interest
None declared.

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Supplementary data
Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

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