Characteristics, outcomes, and predictors of 1-year mortality in patients hospitalized for acute heart failure

Krista Siirilä-Waris¹, Johan Lassus¹, John Melin², Keijo Peuhkurinen³, Markku S. Nieminen¹, and Veli-Pekka Harjola⁴* for the FINN-AKVA study group

¹ Division of Cardiology, Department of Medicine, Helsinki University Central Hospital, Helsinki, Finland; ² Department of Medicine, Central Finland Central Hospital, Jyväskylä, Finland; ³ Department of Cardiology, Kuopio University Hospital, Kuopio, Finland; and ⁴ Division of Emergency Care, Department of Medicine, Helsinki University Central Hospital, PO Box 340, 00029 HUS, Helsinki, Finland

Received 31 March 2006; revised 11 October 2006; accepted 6 November 2006; online publish-ahead-of-print 24 November 2006

Aims Acute heart failure (AHF) is associated with poor prognosis and requires recurrent hospitalizations. However, studies on AHF characteristics, treatment, and prognostic factors are few. Our aim was to investigate the characteristics, treatment, and 1-year prognosis of AHF and identify prognostic factors in different clinical groups.

Methods and results We conducted a prospective multicentre study with 620 patients hospitalized due to AHF; mean age 75.1 (10.4) years, 50% male. Half of the patients had new-onset heart failure. Acute congestion (63.5%) and pulmonary oedema (26.3%) were the most common clinical presentations. Left ventricular ejection fraction (LVEF) was reported in two-thirds of patients. Half of these had preserved systolic function (LVEF ≥45%). At discharge, 86% of patients had beta-blockers and 76% either ACE-inhibitors or angiotensin receptor blockers in use. The 12-month all-cause mortality was 27.4%. We identified several clinical and biochemical prognostic risk factors in univariate analysis. Independent predictors of 1-year mortality were older age, male gender, lower systolic blood pressure (SBP) on admission, C-reactive protein, and serum creatinine (≥120 μmol/L).

Conclusion We present the characteristics and prognosis of an unselected population of AHF patients. One-year mortality is high, and independent clinical risk factors include age, male gender, lower SBP on admission, C-reactive protein, and renal dysfunction.

KEYWORDS
Acute heart failure; Multicentre study; Decompensated chronic heart failure; New-onset heart failure; De novo heart failure; Risk markers

Introduction

Acute heart failure (AHF) is one of the most common diseases in emergency medicine and associated with a poor prognosis. Its clinical classification has been described in the recently published guidelines of European Society of Cardiology (ESC).¹ The clinical presentation ranges from acute pulmonary congestion to pulmonary oedema and cardiogenic shock. It can also be seen as heart failure caused by hypertension, high output, or right ventricular failure.¹

Even though common and fatal at its worse, there is limited data on the epidemiology, treatment, and prognosis of AHF.²⁻⁵ The largest European survey, the Euro Heart Failure Survey (EHFS)² with 11 327 patients, includes both patients with AHF and patients with chronic heart failure (CHF) hospitalized primarily due to other reasons, as well as 17% of patients with only suspected heart failure with a follow-up of only 3 months. Only 40% of patients in EHFS had heart failure as primary cause for hospitalization, i.e. AHF.

Identification of prognostic risk factors in the setting of AHF is of high priority, and follow-up might be tailored in the high-risk patients. Several markers of poor prognosis have been described in CHF. Widely recognized risk factors are age, coronary artery disease (CAD), reduced left ventricular ejection fraction (LVEF), and renal dysfunction.⁶⁻⁸ Also anaemia, hyponatraemia, male gender, and diabetes have been associated with poor prognosis.⁸⁻¹⁰ The values of these prognostic factors in AHF patients are less well documented.

Finnish Acute Heart Failure Study (FINN-AKVA) is a national observational prospective multicentre study on AHF. It is the first population of all consecutive AHF patients characterized according to the ESC criteria—distinct to the EHFS survey. Our aim was to investigate the aetiology, concomitant diseases, treatment modalities, morbidity, mortality, and prognostic markers of AHF.

Methods

All consecutive patients hospitalized with AHF during 3 months were enrolled at 14 university, central, and regional hospitals in Finland between 2 February 2004 and 30 May 2004. Patients with new-onset...
AHF as well as with exacerbation of CHF were included and enrolled only once during the study period. They were characterized according to the recently published ESC AHF guideline criteria to five groups on the basis of their clinical presentation on admission: cardiogenic shock, pulmonary oedema, congestive heart failure, hypertensive crisis with heart failure, and right ventricular failure. Patients with high-output heart failure were not included. Anthropometric measures, underlying diseases, precipitating factors, the most recent echocardiography findings, clinical presentation, in-hospital treatments, and medication at discharge were recorded by local research fellows. Mortality as well as in-hospital mortality and length of stay (LOS) in the hospital were also documented. At discharge, the diagnosis of heart failure had to be confirmed. Mortality was assessed for all patients from the Finnish National Population Register. The patients gave a written consent and blood samples were drawn twice during the hospital stay and stored in −20°C. The study was approved by local ethical committees.

We sought to identify demographic characteristics, clinical variables, and biochemical markers with prognostic impact. χ² test, independent t-test, and Cox proportional hazards regression analysis were used as appropriate. We compared 1-year mortality in relation to age, gender, body mass index (BMI), and previous medical history. The use of beta-blockers, ACE-inhibitors, and/or angiotensin receptor blockers (ARB) on admission was tested for impact on prognosis, as was the use of these medications at discharge in the population discharged alive. We further evaluated the effect of left ventricular systolic function on survival (LVEF ≤ 40%), clinical presentation, acute coronary syndrome (ACS), as well as systolic and diastolic blood pressures on admission. Biochemical variables included in the analysis were anaemia (blood haemoglobin < 120 g/L in females and < 130 g/L in males), hyponatraemia (sodium < 135 mmol/L), C-reactive protein (over median of 10 mg/L), serum creatinine >120 µmol/L, and BNP on admission (over median of 174 pg/mL). All variables were then included in the Cox multivariable analysis to identify independent predictors of mortality. There was a large number of missing values for BMI, BNP, and LVEF. Therefore, these variables were tested both separately and all together in multivariable analyses, but since found non-significant, they were not retained in the final multivariable model. The proportional hazards assumption was confirmed using weighted residuals score test. We used SPSS 12.0.1 statistical software (SPSS Inc.). The results are given as mean (SD), median (interquartile range [IQR]), percentages [95% confidence interval (CI)], or hazard ratios (95% CI) as appropriate.

Results

Patient characteristics

Altogether 620 patients entered the study, 58% from university hospitals, 21% from central hospitals, and 21% from regional hospitals. The patient demographics are shown in Table 1 with a comparison between new-onset and acutely decompensated CHF patients. Of the latter, 40% had been hospitalized for AHF at least once during the previous 6 months.

Clinical manifestation and hospital course

Acute congestion (63.5%) was the most common manifestation of AHF, whereas 26.3% had pulmonary oedema. The rest had either cardiogenic shock (2.3%) or hypertensive crisis (3.1%) or right ventricular failure (4.8%). Half of the patients had a history of heart failure. Compared with patients with congestive heart failure, those with pulmonary oedema had more often a history of CAD (66 vs. 53%, P < 0.01) as well as ACS (51 vs. 25%, P < 0.001) and angiography (22 vs. 14%, P < 0.01), percutaneous coronary intervention (PCI), or coronary artery bypass surgery (CABG) performed during hospital stay (15 vs. 6%, P < 0.001), along with treatment in the cardiac care unit (CCU) and/or intensive care unit (ICU) (71 vs. 35%, P < 0.001). Hospital stay was similar with a median of 8 (IQR 5–10) vs. 7 (IQR 6–14) days, whereas in-hospital mortality was slightly higher (10 vs. 6%, n.s.) in the pulmonary oedema group. On the contrary, compared with patients with congestive heart failure, those with pulmonary oedema had less often atrial fibrillation as a precipitating factor (20 vs. 34%, P < 0.01).

The 14 cardiogenic shock patients were mostly men (71%), with ACS as the most common precipitating factor (64%). Eight out of nine cardiogenic shock patients with ACS underwent angiography during the hospital stay. PCI was performed in five of these patients and one patient underwent CABG during hospital stay. All shock patients needed inotropic or vasopressor support, and levosimendan was used in 71% of these patients. Invasive ventilatory support was needed in 50% of the shock patients, and 22% received intra-aortic balloon pump (IABP) support. The median in-hospital LOS was 12 days (IQR 8–25) in shock patients. All these patients were treated in the CCU and/or ICU for a total median time of 13 (IQR 5–19) days. Still, in-hospital mortality was 28.6% in the shock patients.

Therapeutic and diagnostic management of the total study population

Continuous positive airway pressure support was used in 26% of the patients, but invasive ventilatory support only in 4%. Intravenous furosemide infusions/boluses were given during the first 12 h to 76% of all patients, and 42% received intravenous nitrates. Inotropic treatment or vasopressors were used in 13% of the patients, and 49% of these received two or more inotropes. Levosimendan (7%), dopamine (7%), nor-adrenaline (5%), and dobutamine (4%) were the most commonly used. Few patients received adrenaline or milrinone. Before hospitalization, 23% of the study patients had undergone either coronary angiography or PCI or CABG, and during hospitalization, these were performed to 17% of the patients. Of the ACS patients, 37% underwent angiography, PCI, or CABG during hospitalization (PCI 5%), whereas 11% had undergone angiography, PCI, or CABG only before hospitalization. Pacemakers were present in 9% of all patients on admission, 12% in the CHF patients, and 6% in de novo patients. Of all patients, 6% had paced rhythm on admission, and of these, 49% had right ventricular pacing and the rest had physiological pacing.

Data from echocardiography were available in 71% of the patients, of which 72% had been performed during hospital stay. Two-thirds of all patients had LVEF reported and half of these had preserved systolic function (LVEF ≥ 45%) (Table 1). Regarding distinct types of hospitals, echocardiography was available in only 32% of patients in regional hospitals, in contrast to 68% in central hospitals and 78% in university hospitals. The echocardiograms were least often performed to the oldest patients (data not shown).

Overall, the median LOS was 7 days (IQR 5–11). CCU care was needed in 39.5% of the patients for a median of 2 (IQR 2–4) days. ICU care was given to 11.9% of the patients for a median of 3 (IQR 2–5) days. In-hospital mortality was
7.1%. Although 78% of the patients were hospitalized from home, only 58% were discharged directly to home and the others either to regional hospitals or nursing homes for further rehabilitation.

The medication on admission and at discharge is shown in Table 2. Before hospitalization, nine out of 10 patients received cardiovascular medication. ARBs were mostly used as an alternative to ACE-inhibitors because only eight patients received both. ACE-inhibitors/ARBs were prescribed more often to patients with systolic dysfunction than with preserved systolic function [85% if LVEF < 45% and 73% if LVEF ≥ 45% (P = 0.004), 70% if LVEF missing]. The patients without prescribed ACE-inhibitors/ARBs at discharge had higher creatinine levels (111 vs. 95 μmol/L, P = 0.001) compared with those discharged with these medications. Of the patients with systolic dysfunction, 92% received beta-blockers at discharge, whereas in patients with preserved systolic function and with unknown systolic function, the use was 86 and 78%, respectively (P = 0.001). Use of beta-blockers and/or ACE-inhibitors/ARBs at discharge and differences in age and echocardiographic data are shown in Table 3. At discharge, ~90% of all patients had either aspirin or oral anticoagulant in use. Two-thirds of our patients with a known history of hypercholesterolaemia had lipid-lowering agents in use.

### Follow-up

The cumulative 3-month and 6-month mortality rates were 15.0 and 20.0%. At year 1, 171 patients (27.4%) had died. One-year mortality was higher in the decompensated CHF group (21.1%, P < 0.001). Demographic and biochemical variables associated with all-cause mortality at 12 months are shown in Table 4. In patients with C-reactive protein above or below median, the proportion with diagnosed infection was similar. Using Cox multivariable analysis, we identified older age, male gender, lower systolic blood pressure (SBP) on admission, C-reactive protein > 10 mg/L, and creatinine > 120 μmol/L as independent prognostic factors (Table 5). The 12-month mortality in the congestive group was 25.1%, and in the pulmonary oedema group, it was 31.9%. Mortality in the cardiogenic shock group was high, reaching 35.7% at 12 months. In the right ventricular heart failure group, all patients were
Table 2: Medication on admission and at discharge in patients with decompensated CHF or de novo AHF

<table>
<thead>
<tr>
<th>Medication</th>
<th>On admission</th>
<th>De novo HF</th>
<th>At discharge</th>
<th>De novo HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blocker</td>
<td>75.9</td>
<td>50.2*</td>
<td>86.0**</td>
<td>85.1**</td>
</tr>
<tr>
<td>ACE-inhibitor</td>
<td>50.8</td>
<td>26.4*</td>
<td>59.7***</td>
<td>62.3**</td>
</tr>
<tr>
<td>ARB</td>
<td>17.5</td>
<td>9.9***</td>
<td>19.8</td>
<td>13.5***</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>16.9</td>
<td>1.0*</td>
<td>26.7**</td>
<td>12.5***</td>
</tr>
<tr>
<td>Furosemide</td>
<td>79.0</td>
<td>16.5*</td>
<td>93.8***</td>
<td>83.6***</td>
</tr>
<tr>
<td>Other diuretic</td>
<td>8.9</td>
<td>10.9</td>
<td>7.5</td>
<td>8.2</td>
</tr>
<tr>
<td>Digoxin</td>
<td>34.7</td>
<td>5.6*</td>
<td>40.1**</td>
<td>25.0***</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>2.9</td>
<td>0.3</td>
<td>4.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Other anti-arrhythmic medication</td>
<td>1.0</td>
<td>1.0</td>
<td>0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>ASA</td>
<td>37.5</td>
<td>36.6</td>
<td>41.1</td>
<td>47.9**</td>
</tr>
<tr>
<td>Warfarin</td>
<td>44.1</td>
<td>17.5*</td>
<td>51.0***</td>
<td>40.7**</td>
</tr>
<tr>
<td>Lipid-lowering medication</td>
<td>34.6</td>
<td>22.8</td>
<td>39.6</td>
<td>42.7</td>
</tr>
<tr>
<td>Oral diabetes medication</td>
<td>23.8</td>
<td>17.2</td>
<td>24.2</td>
<td>14.2</td>
</tr>
<tr>
<td>Insulin</td>
<td>20.0</td>
<td>6.9</td>
<td>18.7</td>
<td>8.9</td>
</tr>
</tbody>
</table>

*P < 0.001 for difference between de novo HF and decompensated CHF groups.
***P < 0.001 for difference between admission and discharge medication.
****P < 0.05 for difference between admission and discharge medication.
*****P < 0.01 for difference between de novo HF and decompensated CHF groups.

Table 3: Use of beta-blockers and/or ACE-inhibitor/ARB at discharge, and differences in age and echocardiographic data

<table>
<thead>
<tr>
<th></th>
<th>With beta-blocker</th>
<th>Without beta-blocker</th>
<th>P-value</th>
<th>With ACE-inhibitor/ARB</th>
<th>Without ACE-inhibitor/ARB</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean, years</td>
<td>74.5</td>
<td>77.0</td>
<td>0.048</td>
<td>74.1</td>
<td>77.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Echocardiography available (%)</td>
<td>71</td>
<td>52</td>
<td>0.0007</td>
<td>70</td>
<td>60</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean LVEF%</td>
<td>44</td>
<td>51</td>
<td>0.01</td>
<td>44</td>
<td>51</td>
<td>0.0002</td>
</tr>
<tr>
<td>LVEF ≥ 45% (%)</td>
<td>49</td>
<td>63</td>
<td>0.1</td>
<td>47</td>
<td>65</td>
<td>0.004</td>
</tr>
</tbody>
</table>

ACE-inhibitor, angiotensin converting enzyme inhibitor.

Discussion

FINN-AKVA, a national observational prospective multicentre study yields new important information on real-life AHF patients. It is the first population of all consecutive AHF patients characterized according to the ESC criteria—distinct to the EHFS survey.

Decompensated CHF and new-onset heart failure

For the first time, we describe significant differences between patients with new-onset heart failure and acutely decompensated CHF. In this study, half of the patients had new-onset (de novo) heart failure, a greater number than in the previous literature.1,4,5 This may have been due to meticulous screening of the patients to the present study. The majority of de novo patients were men, and they were younger than patients with CHF. Importantly, de novo patients had more often ACS as the precipitating factor. Moreover, there was a significant difference in the distribution of underlying diseases in these two groups: e.g. diabetes, valvular diseases, and chronic kidney disease were more common in patients with CHF. Only history of hypertension was equally common in both groups. The finding that de novo patients more often had ACS and atrial fibrillation as precipitating factors could imply that cardiac dysfunction in some forms of de novo heart failure is transient in nature and might thus be curable along with the precipitating factor. This might explain, at least partly, the better survival of de novo patients at 1 year, which is a novel finding.

Patients and clinical groups

As previously reported,2,11 the average age of the patients in our study was high and women were older than men. CAD and hypertension were the most common cardiovascular underlying factors of heart failure in our study. Patients in our study were classified for the first time with similar criteria as those in the ESC guidelines on AHF,1 except that no high-output heart failure patients were included. Those patients, actually, are difficult to recognize, and their treatment is principally aimed at the factors causing high-output circulation. Indeed, the identification of curable, causative, and predisposing factors is essential in the management of all patients with AHF. Acute congestion, the most common form of AHF, was most often precipitated by atrial fibrillation, whereas pulmonary oedema and cardiogenic shock were more often caused by ACS. In fact, half of the discharged alive, but 12 month mortality was as high as 43.3%. Best prognosis was seen in the hypertensive heart failure group, with no in-hospital mortality and 84.2% survival at 1 year.
pulmonary oedema patients and most of those with cardiogenic shock had no history of CAD or CHF. Interestingly, the majority of AHF patients with a history of CAD did not have ACS on admission.

Echocardiography

Preserved LVEF is a common finding in patients with AHF and in elderly CHF patients. Half of our patients with information on LVEF had preserved systolic function (LVEF ≥ 45%) and one-third had LVEF over 50%. However, transient systolic heart failure cannot be excluded. LVEF was more frequently reported in university and central hospitals than in regional hospitals, to a same degree as in a previous study from two European academic hospitals. In regional hospitals, echocardiography is mostly performed by internists in contrast to university hospitals with more cardiologists. Anyhow, like in EHFS, echocardiography was not performed to a third of all patients. The probability of not having echocardiogram increased with age and was higher in women than men. The patients lacking an estimate of the LVEF also carried the worst prognosis. However, we did not record reasons for not performing an echocardiogram.

Medication

Owing to other cardiovascular diseases, a large proportion of even the new-onset heart failure patients had beta-blocker and ACE-inhibitor/ARB in use on admission. During hospital stay, especially these medications, as well as furosemide, digoxin, spironolactone, aspirin, and oral anticoagulants

| Table 4 | Patient characteristics by vital status at 12 months and results of univariate Cox regression analysis |
|----------------|-------------------------------------------------|---------------------|-----------------|------------------|
| Characteristics | Deceased (95% CI) n = 171 | Alive (95% CI) n = 449 | P-value | HR (95% CI) |
| Age, years (SD) | 78.0 (9.4) | 74.0 (10.6) | 0.0001 | 1.04* | 1.02–1.05 |
| Gender (%male) | 57.0 (49.2–64.5) | 48.0 (43.3–52.7) | 0.05 | 1.3 | 0.98–1.79 |
| Male gender (HR adjusted for age) | | | | 1.8** | 1.31–2.47 |
| BMI (kg/m²) mean (SD) | 25.9 (5.3) | 28.2 (6.3) | 0.004 | 0.5** | 0.31–0.83 |
| History of (%) | | | | | |
| Previous heart failure | 62.2 (54.5–69.5) | 46.7 (42.0–51.4) | 0.001 | 1.7** | 1.22–2.27 |
| CAD | 65.1 (57.5–72.2) | 51.3 (46.6–56.1) | 0.002 | 1.6** | 1.17–2.20 |
| Previous MI | 34.9 (27.8–42.5) | 25.0 (21.1–29.3) | 0.01 | 1.5*** | 1.08–2.02 |
| Hypertension | 47.7 (40.0–55.4) | 57.4 (52.6–62.0) | 0.03 | 0.7*** | 0.55–0.99 |
| Diabetes | 36.0 (28.9–43.7) | 30.6 (26.6–35.3) | 0.2 | 1.2 | 0.88–1.65 |
| Cerebrovascular disease | 21.5 (15.6–28.4) | 15.8 (12.6–19.6) | 0.1 | 1.4 | 0.94–1.95 |
| Chronic kidney disease | 17.4 (12.1–24.0) | 6.3 (4.2–8.9) | <0.0001 | 2.4* | 1.64–3.60 |
| COPD | 14.5 (9.6–20.7) | 11.8 (9.0–15.2) | 0.4 | 1.2 | 0.80–1.87 |
| Smoker/ex-smoker | 27.3 (20.8–34.6) | 29.7 (25.5–34.2) | 0.6 | 0.9 | 0.66–1.28 |
| ACS on admission | 34.3 (27.2–41.9) | 31.0 (26.8–35.5) | 0.4 | 1.2 | 0.87–1.62 |
| Medication on admission (%) | | | | | |
| Beta–blocker | 67.4 (59.9–74.4) | 61.8 (57.2–66.3) | 0.2 | 1.2 | 0.88–1.67 |
| ACE-inhibitor/ARB | 50.6 (42.9–58.3) | 51.6 (46.8–56.3) | 0.8 | 1.0 | 0.71–1.30 |
| LVEF ≤ 40% | 57.4 (46.8–67.6) | 43.6 (38.1–49.2) | 0.02 | 1.6*** | 1.08–2.45 |
| LVEF missing | 45.3 (33.6–56.6) | 28.8 (21.1–37.3) | 0.0001 | 1.9* | 1.37–5.20 |
| SBP (mmHg) mean (SD) | 137 (32) | 151 (33) | <0.0001 | 0.9* | 0.83–0.92 |
| DBP (mmHg) mean (SD) | 76 (18) | 85 (20) | <0.0001 | 0.9* | 0.87–0.95 |
| Sodium <135 mmol/L | 23.4 (17.2–30.5) | 16.1 (12.8–19.9) | 0.04 | 1.5*** | 1.05–2.14 |
| Anaemia | 54.9 (46.9–62.6) | 35.9 (31.4–40.7) | <0.0001 | 1.9* | 1.41–2.61 |
| Creatinine >120 μmol/L | 45.8 (38.0–53.7) | 22.4 (18.5–26.6) | <0.0001 | 2.4* | 1.78–3.27 |
| C-reactive protein >10 mg/L | 63.6 (55.3–71.2) | 41.8 (37.1–46.7) | <0.0001 | 2.2* | 1.53–3.00 |
| BNP >174 pg/mL (n = 325) | 62.5 (52.0–72.2) | 44.5 (38.0–51.2) | 0.003 | 1.9** | 1.23–2.81 |
| Medication at discharge (%) | | | | | |
| Beta-blocker | 79.7 (71.7–86.3) | 87.3 (83.8–90.2) | 0.03 | 0.6*** | 0.38–0.91 |
| ACE-inhibitor/ARB | 70.3 (61.6–78.1) | 77.9 (73.8–81.7) | 0.08 | 0.7 | 0.47–1.01 |
| Both | 57.8 (48.8–66.5) | 69.4 (64.9–73.7) | 0.01 | 0.6** | 0.44–0.88 |

*P < 0.0001. **P < 0.01. ***P < 0.05.

Table 5 | Adjusted hazard ratios for predictors of mortality at 12 months from multivariable Cox regression analysis |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>HR</td>
<td>95% CI</td>
<td>P-value</td>
</tr>
<tr>
<td>Age (per 10 year increase)</td>
<td>1.6</td>
<td>1.30–1.97</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>1.5</td>
<td>1.02–2.17</td>
<td>0.04</td>
</tr>
<tr>
<td>SBP (per 10 mmHg increase)</td>
<td>0.9</td>
<td>0.80–0.94</td>
<td>0.0003</td>
</tr>
<tr>
<td>C-reactive protein &gt;10 mg/L</td>
<td>1.9</td>
<td>1.32–2.65</td>
<td>0.0005</td>
</tr>
<tr>
<td>Creatinine &gt;120 μmol/L</td>
<td>1.9</td>
<td>1.29–2.69</td>
<td>0.0009</td>
</tr>
</tbody>
</table>

Adjusted for variables in Table 4. Non-significant adjusted HR not shown.

DBP, diastolic blood pressure on admission. Anaemia defined as haemoglobin <120 g/L for women and <130 g/L for men. Numbers are means (SD) and percentage (95% CI). P-values shown are for differences between groups by vital status. HR from Cox univariate analysis. HR for SBP/10 mmHg and for DBP/5 mmHg increase.
were frequently initiated to the de novo patients and also to a number of decompensated CHF patients. Surprisingly, the use of beta-blockers, ACE-inhibitors/ARBs, or both on admission did not affect long-term prognosis. In fact, the deterioration and need for hospitalization in patients with CHF could partly be regarded as a treatment failure. This seems to emphasize that AHF and CHF are in themselves two different conditions.

Beta-blocker and ACE-inhibitor/ARB therapy were better implemented in our patients than before, and lipid-lowering agents and especially beta-blockers were used more often than in a recent Italian survey. The use of ARBs in heart failure has increased noticeably. Patients without prescribed beta-blockers or ACE-inhibitors/ARBs at discharge were older and had higher LVEF, a possible explanation for not prescribing these medications. Also, patients without ACE-inhibitors/ARBs at discharge had higher average creatinine levels than those with medication prescribed, although these features cannot be considered as contraindications.

Intravenous diuretics were used in three-fourths of the patients in our study. Many patients had the precipitating factor treated and obviously did not have significant fluid overload. Spironolactone was rather infrequently used, since only one-third of the patients with a history of systolic heart failure were discharged with this medication. However, the use was similar to EHFS. Inotropes are needed in AHF to support and to stabilize haemodynamics if basic treatment modalities are not sufficient. The more common use of inotropes in our study than in EHFS is most likely explained by a minority of patients in EHFS having AHF; however, in a recent Italian study with more severe AHF patients, inotropes were required more often. We show for the first time prevalence of the use of levosimendan, a calcium sensitizer, in an ordinary AHF population. Interestingly, it was used in our study as often as dopamine and twice as often as dobutamine. Over one-third of our patients were treated in the CCU and one-eighth required intensive care, on average five days. All in all, the total LOS was comparable with the average in the literature.

Treatment and prognostic factors

We identified several demographic variables as significant predictors of poor survival in unadjusted analysis. Since women were significantly older than men, male gender emerged as a prognostic risk factor only after correction for age. The association of a previous history of heart failure with worse prognosis seems meaningful, although it is in contrast to a previous study. Patients with new-onset heart failure more frequently presented with ACS. Two-thirds of the ACS patients in our study were older than 75 years, and in line with the recent Euro Heart Survey on ACS, invasive procedures were less often performed in the aged. On the other hand, not all of the participants hospitals had angiography laboratories and still the rate of PCI is similar to a recent Italian study of more severe AHF patients. Ischaemia being successfully treated, decompenation might be of transient nature in patients without myocardial infarction.

In multivariable analysis, we found older age, male gender, lower SBP on admission, admission C-reactive protein level, and renal dysfunction to be independently associated with prognosis in AHF patients. Although mortality increases progressively with declining LVEF in CHF, in our study, LVEF ≤ 40% was not independently associated with outcome. Among biochemical variables, a strong relationship between renal dysfunction and mortality has been reported both in CHF and in AHF. Our results confirm these findings and the importance of the cardiorenal syndrome. C-reactive protein is a novel prognostic risk marker in heart failure, and in our analysis, elevated C-reactive protein levels were indeed associated with worse prognosis. Certainly, in acute cardiac decompenation, elevated C-reactive protein levels may reflect concomitant infection, with impact on survival. However, in our study, C-reactive protein above median was an independent predictor of mortality irrespective of whether infection was diagnosed or not.

We also found a relationship between higher SBP on admission and better 1-year survival. The association between blood pressure and in-hospital outcome was recently reported. In contrast to previous reports in CHF, anaemia, hyponatraemia, and diabetes did not emerge as predictors of mortality in our population. BNP values obtained on admission were not predictive of long-term outcome on multivariable analysis. Indeed, in a previous study evaluating serial BNP measurements in AHF, predischarge BNP values had better prognostic significance compared with admission values. Our findings are representative of an unselected population hospitalized for AHF. In contrast, patients in randomized clinical trials are younger, the proportion of women is smaller than in real-life, and moderate-to-severe renal dysfunction and significant anaemia are common exclusion criteria.

This paper describes the first population of all consecutive AHF patients characterized according to the ESC criteria from a wide range of hospitals. The all-cause mortality at 12 months in our study is similar to a recently published data. Owing to the short 3 month follow-up in EHFS I, no comparison can be done on long-term prognosis; however, the 3 month mortality data are rather similar. Survival was expectedly better in patients with less severe presentation of heart failure. A third of the pulmonary oedema patients died during the 1-year follow-up, however, although a 40% 1-year mortality has been reported. The mortality in patients with cardiogenic shock was high, although less than previously reported. Interestingly, all deaths in cardiogenic shock patients occurred in the first 3 months. Surprisingly, mortality in right ventricular heart failure increased steadily after discharge and the outcome was in fact worst among clinical classes. Almost half of these patients had either dilated cardiomyopathy or end-stage heart failure, which most probably accounts for the negative prognosis. Hypertensive crisis on the other hand was interestingly associated with a fairly good survival. Owing to the limited number of patients in these latter three groups, the results should, however, be interpreted with caution.

Conclusion

FINN-AKVA is a large multicentre study comprising a broad spectrum of patients with AHF. AHF patients are on average old and the amount is still to increase due to growing old age groups. New-onset AHF patients are as
common as those with exacerbation of CHF. These two
groups differ in regard to co-morbidities, precipitating
factors, and mortality. As a whole, 1-year mortality is high
and independent clinical risk factors include age, male
gender, lower SBP on admission, C-reactive protein, and
renal dysfunction. LOS in hospital is fairly long. Better
understanding of AHF may help develop protocols for trials
to improve prognosis of patients with AHF. Indeed, in con-
test to studying AHF as a single entity, more refined
trials, which take into account diverse aetiologies and man-
ifestations of AHF, are needed. To this point, there is still
room for improvement in adherence to diagnostic and thera-
peutic strategies as described in the recently published
guidelines.14–18

Acknowledgements
This study was supported by grants from the Finnish foundation for
vascular research, Paulo Foundation, and an unrestricted
grant from Orion Pharma. BNP analysis was supported by an unrestr-
icted grant from Abbott Laboratories.

Conflict of interest: none declared.

Appendix
FINN-AKVA study group

Study physicians. Mikko Hakolaari, Central Hospital of Central
Ostrobotnia; Kai-Petri Hanninen, Central Hospital of Kymenlaakso;
Tuomo Ilva and Taisto Talvensaari, Kanta-Hame Central Hospital;
Hautakoski, Central Hospital of Central Ostrobotnia; Johanna
Lammisen, Hyvinkaa Hospital; Kai Kiilavuori, HUCH, Jorvi
Hospital; Kirsi Marjamaa-Voltti, Oulu University Hospital; Heikki
Makinen and Vesa Virtanen, Tampere University Hospital; Taina
Salmena-Mattila, Rauma Hospital; Kari Soiminen, Kuusankoski
Hospital; Marjatta Strandberg and Heikki Ukkonen, Turku
University Central Hospital; Irja Vehmanen, Turku City Hospital;
and Esa-Pekka Sandell, OrionPharma. Research nurses. Kirsi
Hautakoski, Central Hospital of Central Ostrobotnia; Johanna
Lammisen, Hyvinkaa Hospital; Minna-Liisa Niskanen, Kuopio
Central Hospital; Outi Surakka, Central Finland Central Hospital;
and Mervi Pietilä, Helsinki University Central Hospital.

References
1. Nieminen MS, Bohm M, Cowie MR, Drexler H, Filippatos GS, Jondeau G,
Haas Y, Lopez-Sendon J, Mebazaa A, Metra M, Rhodes A, Swedberg K,
Priori SG, Garcia MA, Blanc JJ, Budaj A, Deckers J, Burgos EF, Lekakis J,
Lindahl B, Mazzotta G, Morais J, Otto A, Smiseth OA, Dickstein K,
Janssens U, Komajda M, Morais J, Moreno R, Singer M, Singh S, Tendlera M,
Thygesen K. Guidelines on the diagnosis and
treatment of acute heart failure. Task Force on acute heart failure
Dietz R, Gavazzi A, Hobs R, Korewicki J, Madeira HC, Moiseyev VS,
Presca I, Widimska J, Freemantle N, Eastaugh J, Mason J. The
EuroHeart Failure Survey programme—a survey on the quality of
Dietz R, Gavazzi A, van Gilst WH, Hobs R, Korewicki J, Madeira HC,
Moiseyev VS, Preda I, Widimska J, Freemantle N, Eastaugh J, Mason J.
The EuroHeart Failure Survey programme—a survey on the quality of
care among patients with heart failure in Europe. Part 1: Executive
Dietz R, Gavazzi A, van Gilst WH, Hobs R, Korewicki J, Madeira HC,
Moiseyev VS, Preda I, Widimska J, Freemantle N, Eastaugh J, Mason J.
The EuroHeart Failure Survey programme—a survey on the quality of
5. Varela-Roman A, Grigorian L, Barge E, Bassante P, de la Pena M,
Gonzalez-Juanatey JR. Heart failure in patients with preserved and dete-
and heart failure. Prognostic and therapeutic implications from a pros-
7. Pocock SJ, Wang D, Pfeffer MA, Yusuf S, McMurray JJ, Swedberg K,
Ostergren J, Michelson EL, Pieper KS, Granger CB. Predictors of mortality
and morbidity in patients with chronic heart failure. Eur Heart J 2006;
27:65–75.
8. Swedberg K, Cleland JG, Dargie H, Drexler H, Follath F, Komajda M,
Tavazzi L, Smiseth OA, Gavazzi A, Haverich A, Hoes A, Jaarsma T,
Korewicki J, Levy S, Linde C, Lopez-Sendon JL, Nieminen MS, Pierard L,
Remme WJ. Guidelines for the diagnosis and treatment of chronic
heart failure: executive summary (update 2005): The Task Force for
the diagnosis and treatment of chronic heart failure of the European
9. Gustafsson F, Torp-Pedersen C, Burchardt H, Buch P, Selbaek M, Kjoller E,
Gustafsson I, Kober L. Female sex is associated with a better long-term
survival in patients hospitalized with congestive heart failure. Eur
10. Ezeokwuzi J, McAlister F, Armstrong P. Anemia is common in heart failure
and is associated with poor outcomes: insights from a cohort of 12 065
12. Varela-Roman A, Grigorian L, Barge E, Bassante P, de la Pena M,
Gonzalez-Juanatey JR. Heart failure in patients with preserved and dete-
Dietz R, Gavazzi A, van Gilst WH, Hobs R, Korewicki J, Madeira HC,
Moiseyev VS, Preda I, Widimska J, Freemantle N, Eastaugh J, Mason J.
The EuroHeart Failure Survey programme—a survey on the quality of
Age, clinical presentation, and outcome of acute coronary syndromes
in the Euroheart acute coronary syndrome survey. Eur Heart J 2006;
and renal insufficiency are independent risk factors for death among
patients with congestive heart failure admitted to community hospitals:
Inflammation and long-term mortality in acute congestive heart
17. Kearney MT, Fox KA, Lee AJ, Prescott RJ, Shah AM, Batin PD, Baig W,
Lindsay S, Callahan TS, Shell WE, Eckberg DL, Zaman AG, Williams S,
Neilson JM, Nolan J. Predicting death due to progressive heart failure
18. Dries DL, Swietzer NK, Drazner MH, Stevenson LW, Gersh BJ. Prognostic
impact of diabetes mellitus in patients with heart failure according
to the etiology and left ventricular systolic dysfunction. J Am Coll
Cardiol 2001; 38:421–428.
Solal A. Predischarge B-type natriuretic peptide assay for identifying
patients at high risk of re-admission after uncomplicated heart failure.
20. Lenzen B, Boersma E, Scholte op Reimer W, Balk A, Komajda M, Swedberg K,
Follath F, Jimenez-Narvarro M, Simoons M, Cleland J. Under-utilization
of evidence-based drug treatment in patients with heart failure is only partially
explained by dissimilarity to patients enrolled in landmark trials: a report
from the Euro Heart Survey on Heart Failure. Eur Heart J 2005;
26:2706–2713.
Long-term prognosis of acute pulmonary oedema—an ominous outcome.
Blin P, Barlet M, Paolozzi L, Vincent C, Desnos M, Samii K. Clinical profile,
contemporary management and one-year mortality in patients with
severe acute heart failure syndromes: the EFICA study. Eur Heart J 2006;
27:697–705.