Classification of acute heart failure: Presentation, treatment and outcome.

Data from Euro HF Survey II and ALARM-HF

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Switzerland
ESC Clinical classification of AHF

AHF classified according to clinical presentation
- decompensated (congestive) heart failure (AdHF)
- pulmonary oedema (POE)
- cardiogenic shock (CS)
- acute HF heart failure related to hypertension (HTHF) (SBP >180 mmHg)
- right ventricular heart failure (RVHF)
- high output HF (HOHF)

¹The Task Force on Acute Heart Failure of the ESC. Eur Heart J. 2005; 26(4):384-416
Patients included for analysis: 3580

Active centres: 133

Active countries: 30

3 month follow-up CRFs complete: 3107

12 month follow-up CRFs complete: 2597
Objectives:

1. Assess presentation of AHF under ‘real life conditions’ in different countries and regions
2. Validation of the ESC classification, comparison of presentation, treatment and outcomes in EHS HF II and ALARM-HF

Methods:

- Retrospective in-hospital observational study
- Geographic coverage of 10 countries including France, Germany, Italy, Spain, UK, Greece, Turkey, Australia, Brasil and Mexico
- Representative hospital sample designed according to geographic region, hospital size (by number of beds), funding and academic status
- CRF-based data collection, Oct 2006 – March 2007
- 5-8 consecutive patients per hospital (anonymised data)
- Classification according to ESC guidelines
ALARM-HF Study: 10 Country total

Patients:
- France: 588
- Germany: 617
- Italy: 679
- Spain: 700
- UK: 632
- Greece: 225
- Turkey: 628
- Australia: 262
- Brasil: 600
- Mexico: 601

Total respondents: 5,553

- No. patients: 5,553
- No. hospitals: 744
- Total respondents: 1,087
- No. ICU consultants: 338
- No. cardiologists: 749
EURO HF II and ALARM HF:

<table>
<thead>
<tr>
<th></th>
<th>EHFS II</th>
<th>ALARM-HF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients:</strong></td>
<td>3580</td>
<td>5553</td>
</tr>
<tr>
<td>- Age:</td>
<td>69.9 (12.5)</td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>61.3 %</td>
<td>62.1 %</td>
</tr>
<tr>
<td><strong>Type of HF:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>De novo HF:</td>
<td>37.0 %</td>
<td>34.0 %</td>
</tr>
<tr>
<td>ADCHF</td>
<td>63.0 %</td>
<td>66.0 %</td>
</tr>
</tbody>
</table>
Patient classification (main types of AHF):

EHFS II: 3,580 patients,

ALARM-HF: 5,553 patients (3,659 ADCHF, 1,894 De Novo AHF)
Pulmonary oedema (16% vs 37%) and cardiogenic shock (4% vs 12%) are significantly different between the two studies.
Acute /decompensated heart failure: Clinical presentation (ADCHF & POE)

High jugular venous pressure

Peripheral vasoconstriction

Pulmonary congestion/edema (high or low BP)

Haemodynamic findings:
- Low cardiac output (CI < 2.5 L/m²)
- High PCWP (>16 mmHg)
- High systemic vascular resistance
ALARM-HF vs. EHS HF II: Clinical Classification By Country

Combined AdHF + Pulmonary Oedema: 76% of ALARM-HF vs 81% in EHS HF II
# EHFS II: Characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>ADCHF</th>
<th>De novo AHF</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>3580</td>
<td>2251 (62.9%)</td>
<td>1329 (37.1%)</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>69.9 (12.5)</td>
<td>69.5 (12.1)</td>
<td>70.5 (13.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male (%)</td>
<td>61.3</td>
<td>63.7</td>
<td>57.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Underlying diseases (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>53.6</td>
<td>62.0</td>
<td>39.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>62.5</td>
<td>64.3</td>
<td>59.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32.8</td>
<td>34.4</td>
<td>30.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>38.7</td>
<td>46.5</td>
<td>25.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous stroke or TIA</td>
<td>13.3</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Valvular disease</td>
<td>34.4</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal failure</td>
<td>16.8</td>
<td>20.2</td>
<td>11.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anaemia</td>
<td>14.7</td>
<td>16.8</td>
<td>11.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>19.3</td>
<td>21.5</td>
<td>15.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pacemaker implanted</td>
<td>9.1</td>
<td>12.0</td>
<td>4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>19.3</td>
<td>25.1</td>
<td>9.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*ALL MORE COMMON IN ADCHF*

*Niemiinen MS et al. Eur Heart J 2006; 27: 2725–2736*
### EHFS II: Precipitating factors for AHF

**Table: Precipitating factors for AHF**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>ADCHF</th>
<th>De novo AHF</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Precipitating factors (on admission)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS (%)</td>
<td>30.2</td>
<td>23.1</td>
<td>42.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STEMI</td>
<td>11.1</td>
<td>6.0</td>
<td>19.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-STEMI</td>
<td>10.0</td>
<td>7.1</td>
<td>14.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>9.1</td>
<td>9.9</td>
<td>7.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Arrhythmia (%)</td>
<td>32.4</td>
<td>32.5</td>
<td>32.2</td>
<td>NS</td>
</tr>
<tr>
<td>Valvular cause (%)</td>
<td>26.8</td>
<td>30.3</td>
<td>20.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Infection (%)</td>
<td>17.6</td>
<td>19.2</td>
<td>15.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Non-compliance with therapy (%)</td>
<td>22.2</td>
<td>31.8</td>
<td>6.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*P*-value for difference between ADCHF and *de novo* AHF. TIA, transient ischaemic attack. Renal failure defined as any of the following: patient’s serum creatinine recurrently >177 µmol/L (>2.0 mg/dL) at present or in the past or patient on dialysis or with renal transplant; anaemia as reported.

**Niemiinen MS et al. Eur Heart J 2006; 27: 2725–2736**
### ALARM-HF: Precipitating factors of AHF

<table>
<thead>
<tr>
<th></th>
<th>total</th>
<th>ADCHF</th>
<th>De novo HF</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS %</td>
<td>36.8</td>
<td>30.5</td>
<td>49.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>26.2</td>
<td>30.0</td>
<td>18.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>valve dysf.</td>
<td>12.6</td>
<td>14.4</td>
<td>9.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Infection</td>
<td>19.9</td>
<td>18.0</td>
<td>11.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Poor compliance</td>
<td>13.2</td>
<td>18.9</td>
<td>2.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
LVEF by AHF Classification

ALARM-HF / EHFS II in %

Sample = 3,795 AHF patients with specified LVEF values
Goals of treatment in AHF

- Improvement of symptoms (dyspnea, low cardiac output & hypoperfusion of organs)

- Correction of precipitating factors (acute coronary syndrome, arrhythmia, infection)

- Improvement of short-term mortality, optimisation of treatment before discharge
EHFS II vs. ALARM-HF: Comparison of i.v. vasodilator and inotrope use

<table>
<thead>
<tr>
<th></th>
<th>All AHF</th>
<th>ADCHF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EHFS II</td>
<td>ALARM-HF</td>
</tr>
<tr>
<td>i.v. vasodilator</td>
<td>39%</td>
<td>43%</td>
</tr>
<tr>
<td>i.v. Inotrope</td>
<td>29%</td>
<td>39%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- dobutamine</td>
<td>10%</td>
<td>22%</td>
</tr>
<tr>
<td>- dopamine</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>- levosimendan</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>- adrenaline</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>- noradrenaline</td>
<td>2%</td>
<td>3%</td>
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</tbody>
</table>
Drug Therapy in AHF in ALARM-HF

- All AHF
  - IV diuretics: 90%
  - IV vasodilators: 43%
  - IV inotropes: 39%
  - *Levosimendan: 7%
  - Pulmonary Oedema
    - IV diuretics: 87%
    - IV vasodilators: 39%
    - IV inotropes: 32%
    - *Levosimendan: 8%
  - Cardiogenic shock
    - IV diuretics: 95%
    - IV vasodilators: 53%
    - IV inotropes: 37%
    - *Levosimendan: 7%

Driven by Cardiogenic Shock sub-group
I.V. Drug Treatment by Country

i.v. diuretics, vasodilators and inotropes

Levosimendan launched in 7/10 countries (It, Sp, Gr, Tk, Aus, Br, Mx)
ALARM-HF: i.v. combination therapy in 62% of patients

Total 5,553 ALARM-HF patients (AdHF 2254, P-OE 1955, Cardiogenic Shock 635)
Inotropes: Dobutamine remains the most frequently used drug across all AHF indications.
Levosimendan – a calcium sensitiser with a dual mechanism of action

- **Increase of cardiac contractility** without increasing calcium levels and myocardial oxygen demand

- **Vasodilation** via ATP dependent potassium channel opening antiischemic and antistunning effects (preconditioning)
Change (%) in Haemodynamic Variables at 24 Hours

- CO: 23\% increase with Dobutamine, 29\% increase with Levosimendan, P=0.048
- PCWP: -12\% decrease with Dobutamine, -26\% decrease with Levosimendan, P=0.26
- SV: 16\% increase with Dobutamine, 22\% increase with Levosimendan, P=0.22
- HR: 5\% increase with Dobutamine, 7\% increase with Levosimendan, P=0.002
- sBP: 5\% increase with Dobutamine, 2\% increase with Levosimendan, P=0.002

Dobutamine
Levosimendan
Effect of Levosimendan not attenuated by β-blockers

Median Change in Cardiac Output (L/min)

Levosimendan
n=69

Dobutamine
n=33

p-value = 0.01

Median Change in Pulmonary Capillary Wedge Pressure (mm Hg)

Levosimendan
n=67

Dobutamine
n=28

p-value = 0.03

In-hospital mortality: 11% in ALARM-HF vs. 7% in EHFS II

Sample = EHS HF II (3,580), All ALARM-HF patients (5,553)
Hospital mortality according to SBP and LVEF in ALARM-HF

![Graph showing hospital mortality according to SBP and LVEF in ALARM-HF.](image)

*Figure 1. Hospital mortality according to SBP and LVEF*
Mortality in EHFS II

- Decompensated HF
- Pulmonary oedema
- Cardiogenic shock
- Hypertensive HF
- Right ventricular HF

Mortality [%]
- 1-year mortality
- 3-months mortality
- In-hospital mortality
EHFS II: Independent predictors of
1-year mortality after discharge

Decompensated Chronic Heart Failure
Age (per decade)
Previous MI
Stroke or TIA
SBP < 100 mmHg
Diabetes mellitus
Crea > 1.3 mg/dl
Hyponatremia (Na < 135 mmol/l)
ACE inhibitors or ARB
Beta-blockers

Adjusted Hazard Ratio

0.25 0.5 1 2 5

1.32 (1.10-1.60)
1.28 (1.18-1.39)
1.35 (1.13-1.61)
1.39 (1.11-1.73)
1.70 (1.30-2.23)
1.26 (1.06-1.50)
1.76 (1.48-2.10)
1.48 (1.22-1.79)
0.62 (0.51-0.75)
0.78 (0.66-0.93)
Practical recommendations for prehospital and early in-hospital management of patients presenting with acute heart failure syndromes

Alexandre Mebazaa, MD, PhD; Mihai Gheorghiade, MD, FACC; Ileana L. Piña, MD, FACC; Veli-Pekka Harjola, MD; Steven M. Hollenberg, MD; Ferenc Follath, MD; Andrew Rhodes, MD; Patrick Plaisance, MD; Edmond Roland, MD; Markku Nieminen, MD; Michel Komajda, MD; Alexander Parkhomenko, MD; Josep Masip, MD; Faiez Zannad, MD, PhD; Gerasimos Filippatos, MD
## Management at admission

### Tailored therapy

- **CS1 (SBP > 140 mmHg):** NIV and Nitrates; diuretics are rarely indicated unless volume overload
- **CS2 (SBP 100-140 mmHg):** NIV and Nitrates; diuretics if systemic chronic fluid retention
- **CS3 (SBP < 100 mmHg):** Volume loading with initial fluid challenge if no overt fluid retention; inotrope; PAC if no improvement; if BP fails to improve above 100 mmHg and hypoperfusion persists, then consider vasoconstrictors
- **CS4 (ACS):** NIV; Nitrates; Cardiac catheterization lab, follow guideline recommended management for ACS (aspirin, heparin, reperfusion therapy); IABP
- **CS5 (RVF):** Avoid volume loading; diuretics if SBP >90 mmHg and systemic chronic fluid retention; inotropes if SBP <90 mmHg; If SBP fails to improve above 100 mmHg, then begin vasoconstrictors

### Additional diagnostic studies
- Lab tests
  - BNP or NT-pro BNP when diagnosis is uncertain
  - ECG
  - Chest X-Ray
- **ECG**, **Chest X-Ray**

### Transfer to tertiary care center

- **ECHO** if not recently done
- Central or arterial line
- Additional diagnostic studies
- **CCU/ICU admission**
  - ECHO if not recently done
  - Central or arterial line
  - Additional diagnostic studies
- **Transfer to tertiary care center**

**Initial 90-120 minutes**

- Non-invasive monitoring (SaO₂, BP, temperature)
- NIV as indicated
- Physical exam
- Management at admission
- Lab tests
- **BNP or NT-pro BNP** when diagnosis is uncertain
- ECG
- Chest X-Ray

**Tailored therapy**

- CS1 (SBP > 140 mmHg): NIV and Nitrates; diuretics are rarely indicated unless volume overload
- CS2 (SBP 100-140 mmHg): NIV and Nitrates; diuretics if systemic chronic fluid retention
- CS3 (SBP < 100 mmHg): Volume loading with initial fluid challenge if no overt fluid retention; inotrope; PAC if no improvement; if BP fails to improve above 100 mmHg and hypoperfusion persists, then consider vasoconstrictors
- CS4 (ACS): NIV; Nitrates; Cardiac catheterization lab, follow guideline recommended management for ACS (aspirin, heparin, reperfusion therapy); IABP
- CS5 (RVF): Avoid volume loading; diuretics if SBP >90 mmHg and systemic chronic fluid retention; inotropes if SBP <90 mmHg; If SBP fails to improve above 100 mmHg, then begin vasoconstrictors

**At discharge:**

- Please keep or introduce oral β-blockers etc…
Drug treatment in acute heart failure: Recommendations

- Drug selection according to the type of AHF, clinical presentation & precipitating factors.
- Avoid delays in treatment initiation!
- Patients with low SBP < 100 mmHg are a high risk sub-group even without signs of cardiogenic shock
  1st step: exclusion/correction of hypovolemia
- Vasodilators ARE drugs of 1st choice, diuretics only in low-moderate dose if signs of congestion present
- Inotropic agents in cases with low SBP may be needed, but are associated with increased risks
  levosimendan as an exception in beta-blocker treated patients (see LIDO an SURVIVE !)
The utility of the ESC guidelines for classifying AHF is confirmed in a large patient population from different countries and geographic areas.

Causes, distribution and frequency of the main classes of AHF in ALARM-HF and EHFS II is comparable.

Initial i.v. drug therapy: diuretics > 90% in both, vasodilators 43/39%, inotropes 39/29% (mostly dobutamine).

62% combination of 2-3 drugs in ALARM-HF.

Hospital mortality: total 11% ALARM-HF vs. 7% in EHFS II. ALARM HF: 10% in ADCHF vs. 13% in de novo HF.

Increased risks: Systolic blood pressure < 100 mmHg (even if cardiogenic shock excluded) and serum creatinine >1.5 mg/dl.
Drug use and systolic blood pressure:
Diuretics and vasodilators are often used in hypotensive patients! i.v. inotropes in 31% of AHF patients with initial SBP>=100mmHg compared to 72% in patients <100mmHg.
Mortality in patients with initial SBP > 100 vs <100mmHg: ADCHF vs De Novo AHF (cardiogenic shock excluded)

**ALARM-HF:** 951(19%) patients with initial SBP < 100mmHg (648 ADCHF, 303 De Novo AHF)
Driving Waves of Coronary Blood Flow: Is coronary perfusion the critical factor in AHF and low SBP?

As the cardiac cycle progresses, contraction of the ventricle lumen generates the dominant forward-travelling pushing wave.

With continued ventricular relaxation, relief of myocardial compression generates the dominant backward-travelling suction wave.
Timing of i.v. AHF drug therapies (Primary AHF only)

### Diuretics
- 0-1 hours: 60%
- 1-3 hours: 24%
- 3-6 hours: 8%
- 6-12 hours: 3%
- >12 hours: 5%

### Vasodilators
- 0-1 hours: 53%
- 1-3 hours: 10%
- 3-6 hours: 8%
- 6-12 hours: 6%
- >12 hours: 3%

### Inotropes
- 0-1 hours: 37%
- 1-3 hours: 33%
- 3-6 hours: 6%
- 6-12 hours: 28%
- >12 hours: 6%

### Average time to initiation
- Furosemide: 5.6 hrs
- Nitroglycerin: 6.7 hrs
- Dopaminergics: 24.9 hrs
- Levosimendan: 38.4 hrs
Site of initial i.v. drug treatment in ALARM-HF

Sample = All i.v. patients with specified data: diuretics 4378, vasodilators 2098, inotropes 1909
ALARM-HF in-hospital mortality and clinical parameters

Sample = All AHF patients (5,333)
# Underlying diseases in ALARM-HF

<table>
<thead>
<tr>
<th></th>
<th>total</th>
<th>ADCHF</th>
<th>De novo HF</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD %</td>
<td>30.8</td>
<td>33.3</td>
<td>26.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>71.5</td>
<td>73.8</td>
<td>67.2</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>46.0</td>
<td>49.5</td>
<td>39.3</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Renal dysf.</td>
<td>30.3</td>
<td>34.5</td>
<td>22.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>COPD</td>
<td>24.0</td>
<td>28.3</td>
<td>15.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>6.2</td>
<td>7.4</td>
<td>3.8</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
ALARM-HF: Systolic BP and LVEF

- highest proportion of low LV ejection fractions (<30%) seen in patients with initial SBP <100mmHg (44%)

Sample = All patients with specified initial SBP and LVEF values (3,272)
ADHERE registry (187,565 patients): Timing of i.v. diuretic and vasoactive medications

Mean time to i.v. diuretic 8.1 hrs
Mean time to iv vasoactive medication (vasodilator or inotrope) 21.9 hrs

- Importance of early intervention (site of drug administration):
  - emergency dept: inpatient unit
  Time to vasoactive drugs 1 – 2 h 20 - 22 h
  Hospital stay 4.5 days 7.0 days***
  Hospital mortality 4.3 % 10.9 %***

Heart Failure Reviews 2004; 9: 187