Gerasimos Filippatos MD, FESC, FCCP, FACC

- Head of HF Unit at Athens University Hospital, Greece
- President (2014-2016) of the HF Association of the European Society of Cardiology (ESC)
  - Served as Chair of the ESC’s Working Group on Acute Cardiac Care, and in the Practice Guidelines Committee
  - Coordinator ESC Congress Programme Committee
- Associate Editor:
  - European Heart Journal, International J. of Cardiology, Archives of Medical Science
- Reviewer, guest editor and member of the editorial board for major cardiology and critical care journals
- Published over 300 articles in peer-reviewed journals and authored more than 30 book chapters
- Co-chairman REPORT-HF
REPORT-HF
The WORLD HEART FAILURE REGISTRY

Gerasimos Filippatos, MD, FESC, FHFA

Athens University Hospital, Greece
geros@otenet.gr
Outcome in AHF is still poor

AHF=acute heart failure; CI=confidence interval; ER=emergency room; HF=heart failure; HR=hazard ratio

Outcomes for patients with HF are poor in clinical practice

Chronic HF\(^3\)
IN-CHF Registry
1-year follow-up (n=1,315 patients)

<table>
<thead>
<tr>
<th></th>
<th>All-cause mortality</th>
<th>All-cause hospitalisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (%)</td>
<td>12.4</td>
<td>23.8</td>
</tr>
</tbody>
</table>

HF mortality remains high, with ~50% of patients with HF dying within 5 years of diagnosis\(^1,2\)

*From hospital discharge
IN-CHF=Italian Network on Congestive Heart Failure
HF has a detrimental effect on quality of life

- Patients with HF commonly report psychological distress, including\textsuperscript{1}
  - Depression and anxiety
  - Limitation in their activities of daily living
- Patient quality of life is reduced more by HF than many other chronic diseases, including diabetes, arthritis and chronic lung disease\textsuperscript{2,3}
- Patients with advanced HF had a greater number of physical symptoms, higher depression scores and lower spiritual well-being than patients with advanced cancer\textsuperscript{4}

Economic burden of chronic heart failure

Hospitalization accounts for most CHF-associated costs

In-hospital patients: clinical status at discharge (n. 1821 pts)

**Pulmonary congestion**
- At admission: 60.9%
- At discharge: 9.7%

**Peripheral congestion**
- At admission: 64.5%
- At discharge: 18.1%

**Pulmonary and/or Peripheral congestion**
- At admission: 81.6%
- At discharge: 24.1%
Acute HF: persisting congestion at discharge and all-cause mortality during the follow-up

**Pulmonary congestion**

- **No**
  - n. 1610, 90.3%
- **Yes**
  - n. 173, 9.7%
  - \( p=0.0007 \)

**Peripheral congestion**

- **No**
  - n. 1459, 81.9%
  - \( p<.0001 \)
- **Yes**
  - n. 323, 18.1%
  - \( p<.0001 \)

**Pulmonary and/or Peripheral congestion**

- **No**
  - n. 1355, 75.9%
  - \( p<.0001 \)
- **Yes**
  - n. 429, 24.1%
HF leads to adverse effects on the heart, lungs, kidneys and vasculature

- Inflammatory
  - Inflammation
  - Anaemia
  - Cell death
  - Fibrosis/remodelling

- Risk factors
  - Ageing
  - Diabetes
  - Hypertension
  - Atherosclerosis

- Sympathetic drive + outflow

- Heart failure
  - High central venous pressure (Backward failure)
  - Drug therapy
  - Low cardiac output (Forward failure)

- RAS inhibitors
- Diuretics

- High intra-abdominal pressure

- High pressure on Bowman’s capsule

- Low pressure in afferent arteriole

- Low urine output

- Sympathetic drive + outflow

- Renal dysfunction

Unmet therapeutic need in AHF:  
*The evidence base for many commonly used AHF treatments is limited with no proven long-term benefits*

<table>
<thead>
<tr>
<th>GROUP</th>
<th>MEDICATION</th>
<th>CLASS OF RECOMMENDATION (I–III)</th>
<th>LEVEL OF EVIDENCE† (A–C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>Loop diuretics</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Nitrates</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Sodium nitroprusside</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Opiates</td>
<td>Morphine</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Inotropes</td>
<td>Dobutamine</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

†A=data derived from multiple randomised controlled trials (RCTs) or meta-analyses; B=data derived from a single RCT or large non-randomised studies; C=consensus of opinion of experts and/or data from small studies, retrospective studies, or registries

McMurray et al. Eur Heart J 2012;33:1787–1847
Demographics and comorbidities of patients hospitalised with AHF from various registries

<table>
<thead>
<tr>
<th></th>
<th>ADHERE n=105,388</th>
<th>OPTIMIZE-HF n=48,612</th>
<th>EHFS II n=3,580</th>
<th>ARGENTINA n=2,974</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>72</td>
<td>73</td>
<td>70</td>
<td>68</td>
</tr>
<tr>
<td>Women, %</td>
<td>52</td>
<td>52</td>
<td>39</td>
<td>41</td>
</tr>
<tr>
<td>Prior HF, %</td>
<td>76</td>
<td>88</td>
<td>63</td>
<td>50</td>
</tr>
<tr>
<td>Preserved EF, %</td>
<td>40</td>
<td>49</td>
<td>52</td>
<td>26</td>
</tr>
<tr>
<td>Medical history, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td>57</td>
<td>50</td>
<td>54</td>
<td>–</td>
</tr>
<tr>
<td>Hypertension</td>
<td>73</td>
<td>71</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>31</td>
<td>–</td>
<td>–</td>
<td>22</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>31</td>
<td>31</td>
<td>39</td>
<td>27</td>
</tr>
<tr>
<td>Diabetes</td>
<td>44</td>
<td>42</td>
<td>33</td>
<td>23</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>30</td>
<td>20</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>COPD/asthma</td>
<td>31</td>
<td>34</td>
<td>19</td>
<td>15</td>
</tr>
</tbody>
</table>

COPD=chronic obstructive pulmonary disease; EF=ejection fraction

The ESC recommend a symptom-based treatment algorithm for HFrEF

ACEI=angiotensin-converting-enzyme inhibitor; ARB=angiotensin receptor blocker; CRT=cardiac resynchronization therapy; CRT-D=CRT-defibrillator; ESC=European Society of Cardiology; HFrEF=heart failure with reduced ejection fraction; H-ISDN=hydralazine-isosorbide dinitrate; HR=heart rate; ICD=implantable cardioverter defibrillator; LVAD=left ventricular assist device; LVEF=left ventricular ejection fraction; NHYA=New York Heart Association

McMurray et al. Eur Heart J 2012;33:1787–1847
Are ambulatory patients with heart failure treated in accordance with ESC guidelines?

**Rate of use**

- **ACE-I/ARB**
  - 1.9% (92 pts)
  - 7.8% (372 pts)
  - 92.7% (4439 pts)
  - 7.3% (353 pts)

- **ARBs**
  - 21.6% (1033 pts)
  - 68.8% (3295 pts)

- **B-blockers**
  - 67.0% (3209 pts)
  - 33.0% (1583 pts)

- **MRAs**
  - 67.0% (3209 pts)
  - 33.0% (1583 pts)

**Rate of patients at target dosage of recommended pharmacological treatments**

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Total Patients</th>
<th>Target Dosage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-I</td>
<td>4710 pts</td>
<td>1380 (29.3)</td>
</tr>
<tr>
<td>ARBs</td>
<td>1500 pts</td>
<td>362 (24.1)</td>
</tr>
<tr>
<td>B-blockers</td>
<td>6468 pts</td>
<td>1130 (17.5)</td>
</tr>
<tr>
<td>MRAs</td>
<td>4226 pts</td>
<td>1290 (30.5)</td>
</tr>
</tbody>
</table>

Maggioni et al, Eur J Heart Fail 2013;15:1173–84
Chronic HF survival rates have improved over time with the advent of new therapies

Population-based cohort study analysing data from the Rochester Epidemiology Project, Minnesota, USA. 4,537 patients with a diagnosis of HF between 1979 and 2000 were included. Framingham criteria and clinical criteria were used to validate the diagnosis.

Roger et al. JAMA 2004;292:344–50

... nevertheless, the 5-year mortality rate remains high
To date, no therapy has been proven to reduce morbidity and mortality in patients with HFpEF.

**I-PRESERVE**
- **HR** = 0.95 (95% CI, 0.86 to 1.05); p = 0.35
- Primary composite endpoint of death from any cause or hospitalisation for a CV cause (HF, MI, unstable angina, arrhythmia, or stroke) in HF patients with LVEF ≥45%

**CHARM-preserved**
- **HR** = 0.89 (95% CI, 0.77–1.03); p = 0.118
- Adjusted **HR** = 0.86, p = 0.051
- Primary composite outcome of CV death or admission to hospital for chronic HF in HF patients with LVEF >40%

CV = cardiovascular; HFpEF = heart failure with preserved ejection fraction; HR = hazard ratio; I-PRESERVE = Irbesartan In Patients With Heart Failure And Preserved Ejection Fraction; MI = myocardial infarction

HEART FAILURE

- There is an unmet need to identify safe and effective therapies for patients with AHF given the high post-discharge morbidity and mortality experienced by this group.
- The majority of AHF patients hospitalized with HF are patients with worsening chronic heart failure.
- Long term Follow up is necessary to understand the disease.