Heart failure and co-morbidities

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Although patients with 5 or more comorbidities comprised only 39% of the population, they accounted for 81% of total hospital days.
### Table 3. Association of Noncardiac Comorbidity With Ambulatory Care Sensitive CHF Hospitalization Among Medicare Beneficiaries With CHF

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk Ratio (95% CI) (n = 122,630)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic renal failure</td>
<td>1.91 (1.83–1.99)</td>
</tr>
<tr>
<td>Acute and unspecified renal failure</td>
<td>1.83 (1.74–1.93)</td>
</tr>
<tr>
<td>Hypertension—with complications or secondary</td>
<td>1.82 (1.76–1.88)</td>
</tr>
<tr>
<td>Lower respiratory disease, failure or insufficiency</td>
<td>1.57 (1.52–1.63)</td>
</tr>
<tr>
<td>COPD/bronchiectasis</td>
<td>1.49 (1.45–1.53)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.41 (1.37–1.44)</td>
</tr>
<tr>
<td>Essential hypertension</td>
<td>1.31 (1.28–1.35)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.31 (1.23–1.39)</td>
</tr>
<tr>
<td>Anxiety, somatoform disorders, and personality disorders</td>
<td>1.22 (1.14–1.31)</td>
</tr>
<tr>
<td>Peripheral or visceral atherosclerosis</td>
<td>1.19 (1.15–1.23)</td>
</tr>
<tr>
<td>Depression/affective disorders</td>
<td>1.16 (1.10–1.21)</td>
</tr>
<tr>
<td>Thyroid disorders</td>
<td>1.05 (1.01–1.09)</td>
</tr>
<tr>
<td>Chronic back disorders</td>
<td>1.01 (0.96–1.06)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>1.01 (0.97–1.05)</td>
</tr>
<tr>
<td>Cerebrovascular disease, late effects</td>
<td>0.98 (0.91–1.07)</td>
</tr>
<tr>
<td>Ocular disorders</td>
<td>0.98 (0.95–1.01)</td>
</tr>
<tr>
<td>Prostatic hyperplasia</td>
<td>0.93 (0.88–0.99)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>0.91 (0.86–0.97)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.90 (0.87–0.93)</td>
</tr>
<tr>
<td>Alzheimer’s disease/dementia</td>
<td>0.82 (0.78–0.86)</td>
</tr>
</tbody>
</table>

*Adjusted for patient race (white or nonwhite), age (65–69, 70–74, 75–79, 80–84, 85+) and gender, primary caring provider type (cardiologist, generalist, non-cardiac specialist), patient’s county of residence per capita hospital beds, total physicians and cardiovascular specialists; †Includes intravertebral injury, spondylosis, or other chronic back disorders.

CHF = chronic heart failure; CI = confidence interval; COPD = chronic obstructive pulmonary disease.
Main co-morbidities in patients with chronic HF

- Chronic renal failure
- Anaemia
- Chronic obstructive pulmonary disease
Main co-morbidities in patients with chronic HF

• Chronic renal failure
• Anaemia
• Chronic obstructive pulmonary disease
Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative

Claudio Ronco¹,²*, Peter McCullough³, Stefan D. Anker⁴,⁵, Inder Anand⁶, Nadia Aspromonte⁷, Sean M. Bagshaw⁸, Rinaldo Bellomo⁹, Tomas Berl¹⁰, Ilona Bobek¹, Dinna N. Cruz¹,², Luciano Daliento¹¹, Andrew Davenport¹², Mikko Haapio¹³, Hans Hillege¹⁴, Andrew A. House¹⁵, Nevin Katz¹⁶, Alan Maisel¹⁷, Sunil Mankad¹⁸, Pierluigi Zanco¹⁹, Alexandre Mebazaa²⁰, Alberto Palazzuoli²¹, Federico Ronco¹¹, Andrew Shaw²², Geoff Sheinfeld²³, Sachin Soni¹,²⁴, Giorgio Vescovo²⁵, Nereo Zamperetti²⁶, and Piotr Ponikowski²⁷ for the Acute Dialysis Quality Initiative (ADQI) consensus group
Relation between heart and renal diseases

Cardiac diseases can produce renal diseases

Renal diseases can produce cardiac diseases

 ↔ this mechanism shows a feed-back loop
Cardio-renal syndromes

• Definition: disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other

• Chronic abnormalities in heart function leading to kidney injury and/or dysfunction
• Nearly 60% of patients with chronic heart failure have a reduced renal function
• Chronic heart disease and CKD frequently co-exist, and often the clinical scenario does not permit to distinguish which disease came first.
Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization

- longitudinal glomerular filtration rate (GFR) among 1,120,295 adults within a large, integrated system of health care delivery in whom serum creatinine had been measured between 1996 and 2000

Drugs employed in both heart or renal failure

• ACE-Inhibitors/AT-1 antagonists
• Loop diuretics
• Aldosterone antagonists
Biomarkers of heart failure

Natriuretic peptides

- Useful biomarkers for diagnosis, clinical management, prognosis in heart failure patients
- Patients with CKD have higher levels of BNP and NT-proBNP than age- and gender-matched subjects without reduced renal function, even in the absence of clinical heart failure, due to reduced renal clearance.
Therapy of CHF with concomitant renal impairment is still not evidence-based, as these patients are generally excluded from CHF trials.

Diuretic treatment:
- Typically, these patients are hypervolemic, and more intensive diuretic treatment is needed.
- Thiazide diuretics may be less effective, and loop diuretics are preferred.
- In refractory cases, dialysis/ultrafiltration may be required.

Dose adjustment of drugs with renal clearance (i.e. digoxin)
Correction of anaemia
Lack of optimal treatment is especially observed in patients with renal failure
Quality of care and outcomes among patients with heart failure and chronic kidney disease: A Get With the Guidelines—Heart Failure Program study

Patel UD et al, Am Heart J 2008;156:674-81
Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients with congestive heart failure and chronic kidney disease

- Retrospective analysis of the Minnesota Heart Survey, identifying patients hospitalized in 2000 in the Minneapolis–St Paul metropolitan area with heart failure (2169 pts).

- The graphs shows the rate of prescription of standard medical therapies during hospitalization (a) and at hospital discharge (b), age- and sex-adjusted, and stratified by renal function.
In patients with heart failure, treatment with RAS blockers should be maintained despite high plasma creatinine or potassium levels.

Hyperkalemia is obviously dangerous, but before stopping the RAS blocker administration, it is important to try to manage it (diet, increase diuretic dose....).
Thirty-day adjusted mortality for CHF patients, stratified by in-hospital prescription of ACE-I or ARB

<table>
<thead>
<tr>
<th>Renal function (GFR)</th>
<th>Stage 1 (≥90 mL/min)</th>
<th>Stage 2 (60-89 mL/min)</th>
<th>Stage 3 (30-59 mL/min)</th>
<th>Stage 4 (15-29 mL/min)</th>
<th>Stage 5 (&lt;15 mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CHF hospitalizations*</td>
<td>469</td>
<td>546</td>
<td>773</td>
<td>238</td>
<td>143</td>
</tr>
<tr>
<td>ACE-I or ARB</td>
<td>6.1%</td>
<td>6.3%</td>
<td>5.4%</td>
<td>9.4%</td>
<td>11.9%</td>
</tr>
<tr>
<td>No ACE-I or ARB</td>
<td>11.3%</td>
<td>8.6%</td>
<td>14.0%</td>
<td>18.5%</td>
<td>22.8%</td>
</tr>
<tr>
<td>*P</td>
<td>.07</td>
<td>.37</td>
<td>.0001</td>
<td>.008</td>
<td>.03</td>
</tr>
</tbody>
</table>

Berger AK et al, Am Heart J 2007
If a sudden and consistent plasma creatinine increase is observed in a patient with heart failure, what is necessary to immediately exclude?

• Renal artery stenosis, caused by progression of atherosclerosis (especially if the patient is diabetic)

• Dehydration (especially in summer, in old patients treated with high dose diuretics)
Main co-morbidities in patients with chronic HF

- Chronic renal failure
- Anaemia
- Chronic obstructive pulmonary disease
Anaemia during chronic HF

• Anaemia is often present in patients with heart failure: hemoglobin <12 g/dL is present in 3–20% of ambulatory chronic HF patients, higher in hospitalized patients

von Heahing S et al, Heart Fail Rev 2011
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• The cause is typically CKD and/or chronic inflammation

• Heart failure, CKD and anaemia constitute the so-called “cardio-renal anaemia syndrome”, associated with poor outcome
Hemoglobin level, chronic kidney disease, and the risks of death and hospitalization in adults with chronic heart failure: the (ANCHOR) Study

- 59,772 adults with HF followed up for ~2 years
- At baseline, 42.6% of subjects were anemic by WHO criteria

Go AS et al, Circulation 2006
Correction of anaemia during chronic HF

Intravenous iron

- FAIR-HF study
  - 459 patients with chronic HF and iron deficiency (Hb between 9.5 and 13.5 g/ dL)
  - improved symptoms, exercise tolerance and quality of life without increasing survival, regardless of the presence of anaemia

Anker SD et al, NEJM 2009
Correction of anaemia during chronic HF

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Darbepoetin alfa

- Three randomized, double blind, placebo-controlled studies in patients with chronic HF and anaemia
  - improved symptoms, exercise tolerance and quality of life without increasing survival
  - Pooled analysis: trend in reduction death and HF hospitalizations

- RED-HF (ongoing)
  - aims to recruit 2600 patients with chronic HF patients with Hb between 9.0 and 12.0 g/dL

McMurray JJ et al, Eur J Heart Fail 2009

Anker SD et al, NEJM 2009

Ponikowski P et al. JACC 2007
van Veldhuisen DJ et al. EHJ 2007
Ghali JK et al, Circulation 2008
Main co-morbidities in patients with chronic HF

• Chronic renal failure
• Anaemia
• Chronic obstructive pulmonary disease
Cardiovascular comorbidities in COPD

• The prevalence of Chronic Obstructive Pulmonary Disease (COPD) is greater in patient with HF than in general population: 11 to 52% in US cohorts, 9 to 41% in European cohorts
COPD and chronic HF: epidemiology

- Severe COPD (GOLD stages III and IV) is associated with a worse prognosis in patients with HF; hospitalization is associated with a greater mortality and longer hospital stay in patients with COPD and CHF than in patients with CHF alone.

- Although coexisting of the two conditions is common, usually only one of the two is diagnosed resulting in under-treatment and unsatisfactory response.
Symptoms and signs

- Pulmonary disease may produce or obscure every symptom and sign defined by Framingham criteria for HF diagnosis
- Exertional breathlessness, nocturnal cough and paroxysmal nocturnal dyspnoea are common to both conditions.
- No qualitative features of dyspnoea are unique to HF
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### Radiology
- Asymmetric, regional and reticular pattern of pulmonary oedema are common in COPD and might mimic HF radiological alterations.
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Echocardiography

- Emphysema is associated with poor acoustic window (images are inadequate in 8-10% of cases).

- Doppler estimation of pulmonary artery pressure is less frequently possible.
# COPD and chronic HF: diagnostic pitfalls

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## Spirometry
- HF patients exhibit both obstructive and restrictive ventilatory defects that may mimic COPD.
• Natriuretic peptides are useful in the acute setting for excluding HF in subject with acute dispnoea

• However in the chronic setting the diagnostic accuracy of BNP in patients with concurrent COPD is less certain: plasma BNP is elevated in both primary pulmonary hypertension and right HF secondary to COPD
In the past β-blockers have been contraindicated in COPD patients with HF

- β-blockers are indicated in the management of chronic heart failure
- Clinicians are often hesitant to administer beta-blockers in the presence of COPD for fear of acute bronchospasm occurring during non cardioselective beta-blocker use
- Most of COPD patients were excluded from randomized placebo-controlled trials of β-blockers in CHF

### Beta-blockers: selectivity

<table>
<thead>
<tr>
<th>Name</th>
<th>B1 selective</th>
<th>B1-SI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol</td>
<td>☺</td>
<td></td>
</tr>
<tr>
<td>Atenolol</td>
<td>☺</td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>☺</td>
<td>☺</td>
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<tr>
<td>Carvedilol</td>
<td>☺</td>
<td>☺</td>
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<tr>
<td>Celiprolol</td>
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<td></td>
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<tr>
<td>Labetalol</td>
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<td></td>
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<tr>
<td>Nebivolol</td>
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<tr>
<td>Metoprolol</td>
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<tr>
<td>Pindolol</td>
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<td></td>
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<tr>
<td>Propranolol</td>
<td>☺</td>
<td></td>
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<tr>
<td>Sotalol</td>
<td>☺</td>
<td></td>
</tr>
</tbody>
</table>

**SI:** Selectivity Index. **Grey:** vasodilating properties. ***: evidence in CHF

Gorre F, Acta Cardiol 2010
Cardioselective beta-blockers, given as a single dose or for longer durations, produced no significant change in FEV1 or respiratory symptoms compared to placebo.

Cardioselective beta-blockers did not effect the FEV1 treatment response to beta2- agonists.
Agents with documented effects on morbidity and mortality such as ACEIs, beta-blockers, and ARBs are recommended in patients with co-existing pulmonary disease. The majority of patients with HF and COPD can safely tolerate beta-blocker therapy. Initiation at a low dose and gradual up-titration is recommended. Mild deterioration in pulmonary function and symptoms should not lead to prompt discontinuation. If symptoms worsen, a reduction of the dosage or withdrawal may be necessary. Selective b-blockade may be the preferable option. A history of asthma should be considered a contraindication to the use of any b-blocker.
Some studies have recognized deleterious cardiovascular effects (HF hospitalization, myocardial infarction, unstable angina, sudden cardiac death) of inhaled $\beta_2$ agonists, a cornerstone of COPD therapy.

Salpenter SR, Chest 2004

Such analyses were carried out in the absence of detailed clinical informations:

- Smoking status
- COPD status
- Measure of HF severity like Natriuretic Peptides
Inhaled $\beta_2$ agonists are not associated with increased mortality in community-managed HF patients when adjusted for BNP as well as other clinical, demographic, and medication variables.

Bermighan J et al, European Journal of Heart Failure, 2011
Conclusions

1. Management of patients with heart failure and co-morbidities is difficult due to clinical complexity and to lack of controlled trials.

2. Thus, the management of each single patient must be entrusted to the clinical ability of the physician which is determined by the wise cohesion of: culture, experience and common sense.
2015 Asia Pacific conference on cardiometabolic diseases management

4-5 July 2015
MUMBAI, INDIA

IMPROVING THE PATIENT’S LIFE THROUGH MEDICAL EDUCATION