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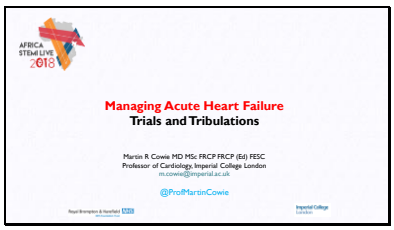

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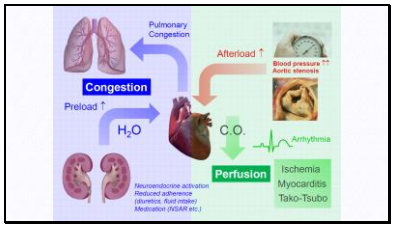

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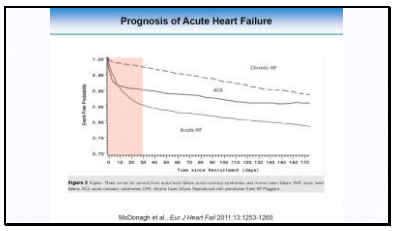

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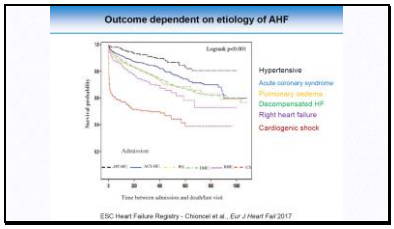

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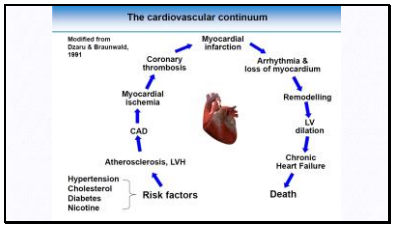

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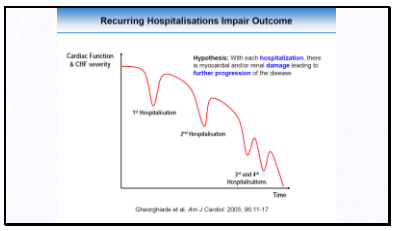

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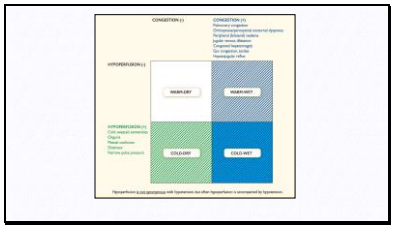

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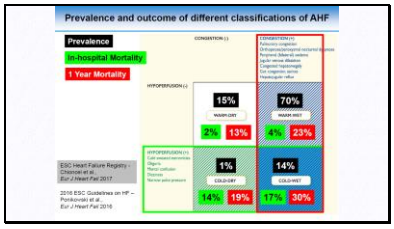

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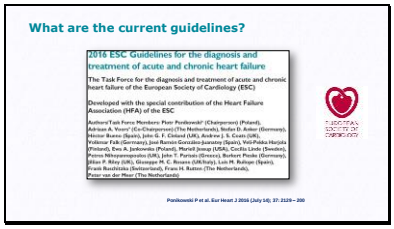

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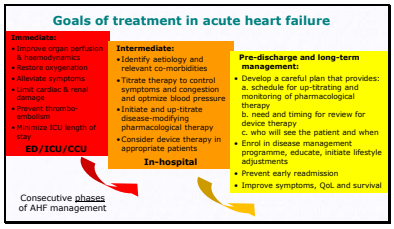

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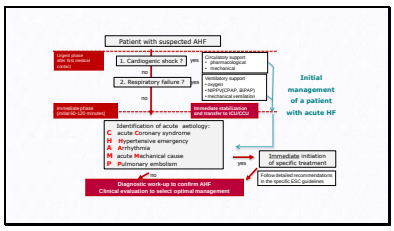

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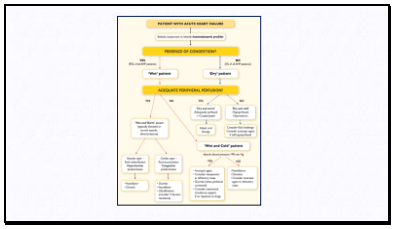

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Slide 16

Intermediate management and criteria for discharge

Identify aetiology and relevant co-morbidities

Slide 17

Intermediate management

Identify aetiology and relevant co-morbidities

Coexistence of two clinical conditions – **ACS and AHF** – always identifies a **very-high-risk group** where an **immediate invasive strategy** with intent to perform revascularization is recommended, irrespective of ECG or biomarker findings

Recommendations for coronary angiography in chronic HF

Invasive coronary angiography is recommended in patients with HF and angina pectoris recalcitrant to pharmacological therapy or symptomatic ventricular arrhythmias or aborted cardiac arrest (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity.	I	C
Invasive coronary angiography should be considered in patients with HF and intermediate to high pre-test probability of CAD and the presence of ischaemia in non-invasive stress tests (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity.	IIa	C

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Intermediate management

Titrate therapy to control symptoms & congestion and optimize blood pressure

Recommendations	Class [a]	Level [b]
Standard non-invasive monitoring of heart rate, rhythm, respiratory rate, oxygen saturation and blood pressure is recommended.	I	C
It is recommended that patients should be weighed daily and have an accurate fluid balance chart completed.	I	C
It is recommended to evaluate signs and symptoms relevant to HF (e.g. dyspnoea, pulmonary rales, peripheral oedema, weight) daily to assess correction of fluid overload.	I	C
Frequent, often daily,measurement of renal function (blood urea, creatinine) and electrolytes (potassium, sodium) during i.v. therapy and when renin-angiotensin-aldosterone system antagonists are initiated is recommended.	I	C

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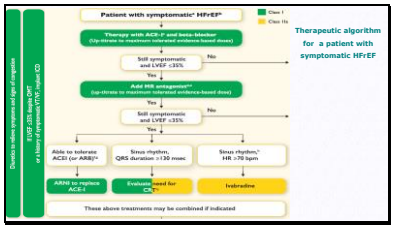
Pre-discharge management and criteria for discharge

Initiate and up-titrate disease-modifying pharmacological therapy

Recommendations	Class[a]	Level[b]
In case of worsening of chronic HFrEF, every attempt should be made to continue evidence-based, disease-modifying therapies, in the absence of haemodynamic instability or contra-indications.	I	C
In the case of de novo HFrEF, every attempt should be made to initiate these therapies after haemodynamic stabilization.	I	C

"In the case of haemodynamic instability/contraindications the daily dosage of oral therapy may be reduced or stopped temporarily until the patient is stabilized. In particular, β-blockers can be safely continued during AHF presentations except in cardiogenic shock."

Slide 20



Therapeutic algorithm for a patient with symptomatic HFrEF

Slide 21

Criteria for discharge from hospital and follow-up in the "high-risk" period

Patients admitted with AHF are medically fit for discharge:

- when **haemodynamically stable, euvolemic**, established on **evidence-based oral medication** and with **stable renal function** for at least 24 h before discharge
- once provided with **tailored education** and advice about self-care

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Develop a careful plan that provides:

a. schedule for up-titrating and monitoring of pharmacological therapy

b. need and timing for review for device therapy

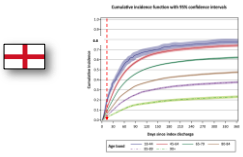
c. who will see the patient and when

Patients should be:

- enrolled in a disease management program
- seen by their general practitioner within 1 week of discharge
- seen by the **hospital cardiology team within 2 weeks of discharge** (if feasible)

Slide 23

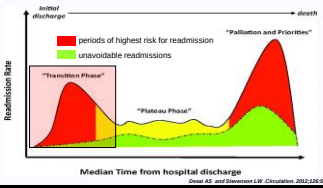
Cardiology follow-up after discharge
in NHS hospitals in England (2009-11)



Bottle A et al. BMJ Open 2016; 6: e010669

Slide 24

3 phase terrain of readmission risk after HF Hospitalization



Desai AS and Stevenson LW. Circulation. 2012;126:501-506

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Serelaxin

NOVARTIS

Novartis provides update on Phase III study of RLX030 (serelaxin) in patients with acute heart failure

- Phase III RELAX-AHF-2 study did not meet primary endpoint of reduced cardiovascular death or worsening heart failure in patients with acute heart failure
- Novartis remains committed to improving and extending the lives of patients with cardiovascular disease and will continue to invest in ways to improve their outcomes

Basel, March 31, 2017 – Novartis today announced results from the global Phase III RELAX-AHF-2 study investigating the efficacy, safety and tolerability of RLX030 (serelaxin) in patients with acute heart failure (AHF).

RELAX-AHF-2 did not meet its primary endpoints of reduction in cardiovascular death through day 180 and worsening heart failure through day five when added to standard therapy in patients with AHF

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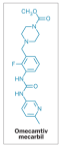
ATOMIC-HF



Omecamtiv mecarbil

- "in patients with AHF, intravenous omecamtiv did NOT meet the primary endpoint of dyspnoea improvement, but it was generally well tolerated, increased systolic ejection time, and may have improved dyspnoea in the high dose group"

Teerlink JR et al. JACC 2016; 67: 1444-55

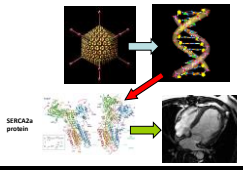
Slide 28

Ularatide

NEJM 2017; 376: 1956-64

Slide 29

SERCA2a Gene Therapy



Slide 30

- "A lot of us were very optimistic and hopeful that CUPID2 would meet its endpoint," says Barry Greenberg of the University of California, San Diego (UCSD), who chaired the CUPID2 executive clinical steering committee. "There was a very logical and appropriate scientific rationale and the study was done very well," he says. "But it just didn't work out."

Greenberg B et al. Lancet 2016; 387: 1178 – 86

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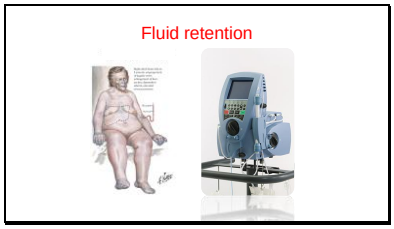

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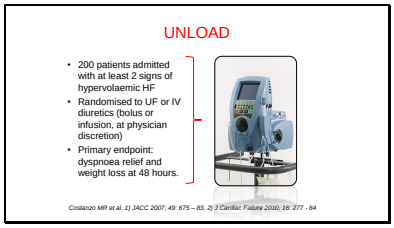

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The results of this analysis from the UNLOAD trial show that despite the lack of a statistical difference in weight and fluid loss by UF and IV diuretics administered by continuous infusion, UF was associated with fewer rehospitalizations. Additional prospective, randomized studies are needed to confirm or refute the hypothesis that removal of *isotonic* rather than *hypotonic* fluid is a key factor in producing sustained clinical benefit in congested HF patients

Costanzo MR et al. J Cardiac Failure 2010; 16: 277 - 84

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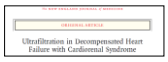
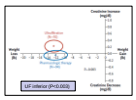


Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome

- CARESS
- 188 patients
- Acute decompensated HF admission + persistent congestion + worsening renal function (>26 µmol/l in the 12 weeks before or 10 days after admission)
- Strategy: stepped drug therapy versus ultrafiltration
- Primary endpoint:
  - Bivariate change from baseline in serum creatinine and body weight at 96 hours from randomisation
- 60 day follow-up



Bart BA et al. N Engl J Med 2012; 367: 2296 - 304

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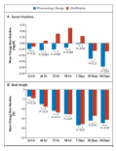
CARESS-HF



- Serious adverse events higher in UF group (72% vs 57% P=0.03)
- No difference in deaths or hospitalisations out to 60 days

Bart BA et al. N Engl J Med 2012; 367: 2296 - 304

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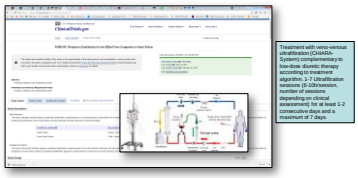
PURE-HF



Treatment with veno-venous ultrafiltration (CHIARA-System) complementary to low-dose diuretic therapy according to treatment algorithm. 1-7 Ultrafiltration sessions (6-12h/session, number of sessions depending on clinical assessment) for at least 1-2 consecutive days and a maximum of 7 days.

Slide 38

Conclusions

- New guidance from ESC on AHF (2016) is pragmatic and focused on reducing delay and identifying aetiologies that require specific management
- Much disappointment in trying to identify new treatments
- Mechanical approaches to circulatory and renal support being examined closely
- Put effort into doing what we do know more consistently and efficiently & ensuring efficient transition into CHRONIC care, with early follow-up

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