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ΒΑΣΙΛΗΣ ΣΤΑΣΙΝΟΣ, ΚΑΡΔΙΟΛΟΓΟΣ.

ΕΠΙΣΤΗΜΟΝΙΚΟΣ ΣΥΝΕΡΓΑΤΗΣ
Β΄ΠΑΝΕΠΙΣΤΗΜΙΑΚΗΣ ΚΑΡΔΙΟΛΟΓΙΚΗΣ ΚΛΙΝΙΚΗΣ, ΤΜΗΜΑ ΗΛΕΚΤΡΟΦΥΣΙΟΛΟΓΙΑΣ, ΑΤΤΙΚΟΝ ΝΟΣΟΚΟΜΕΙΟ

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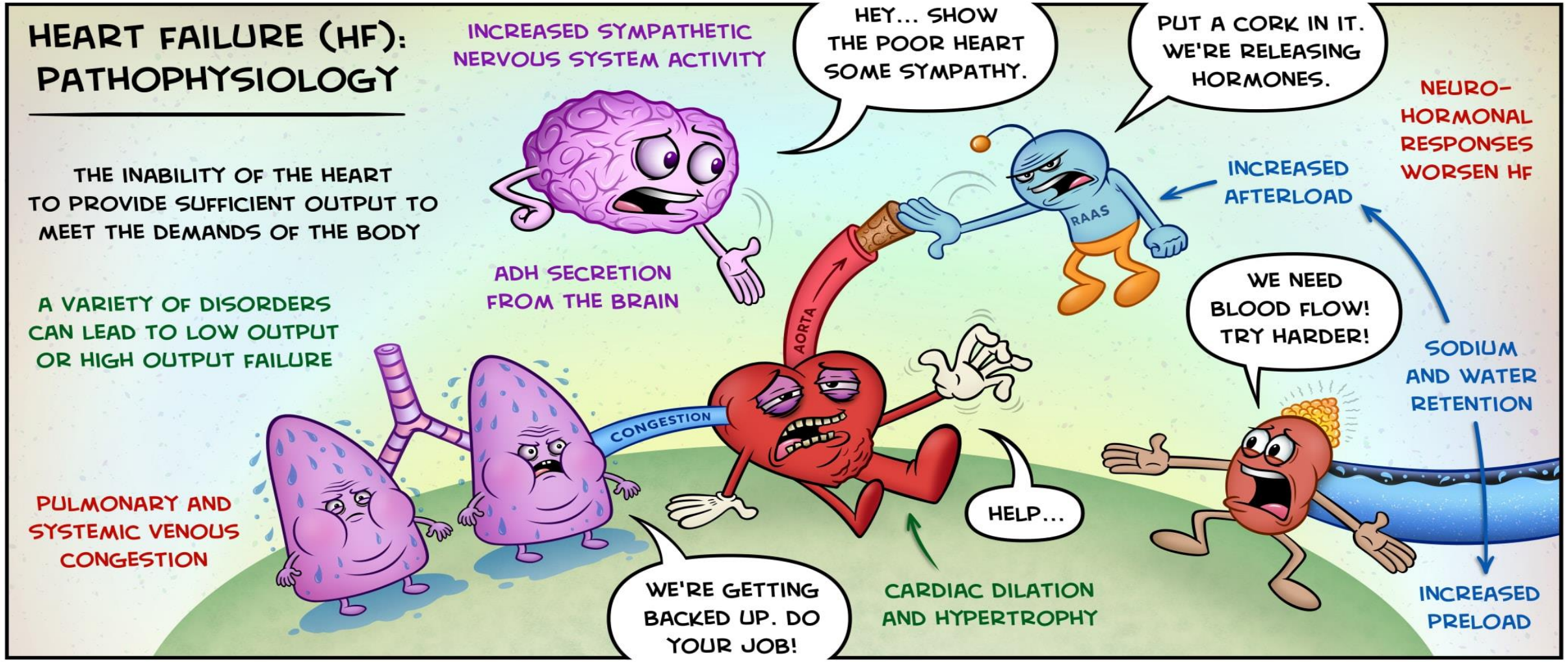
- NO DISCLOSURES

ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ

Watch the disease in time: For when, within
the dropsy rages, and extends the skin,
in vain for hellebore the patient cries,
and sees the doctor, but too late is wise:
Too late for cure, he proffers half his wealth;
ten thousand doctors cannot give him health.

Benjamin Franklin,
Poor Richard's Almanack, 1749

ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ



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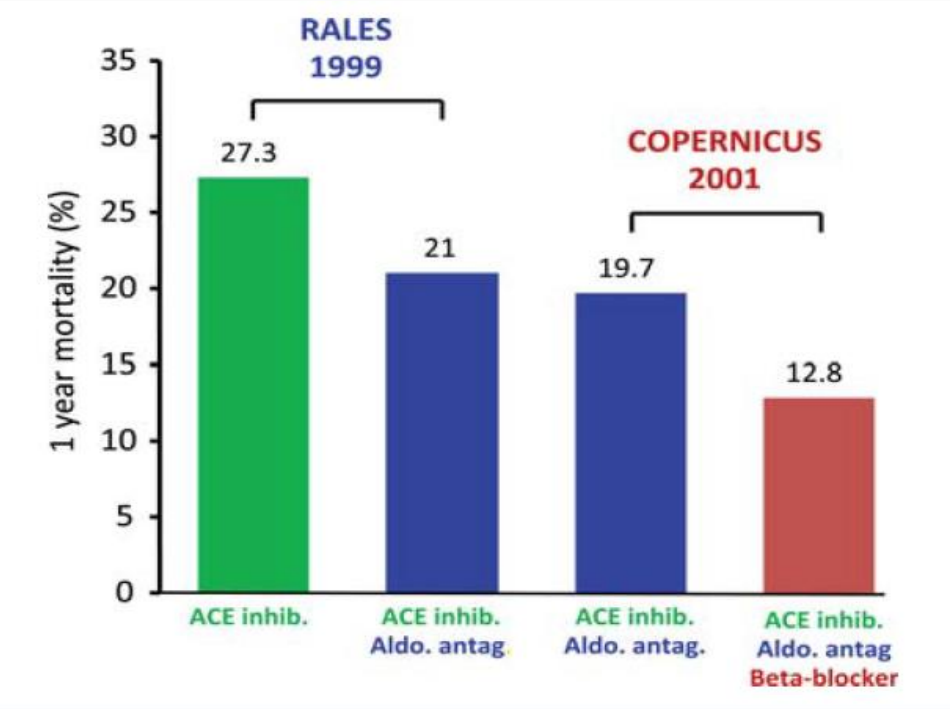

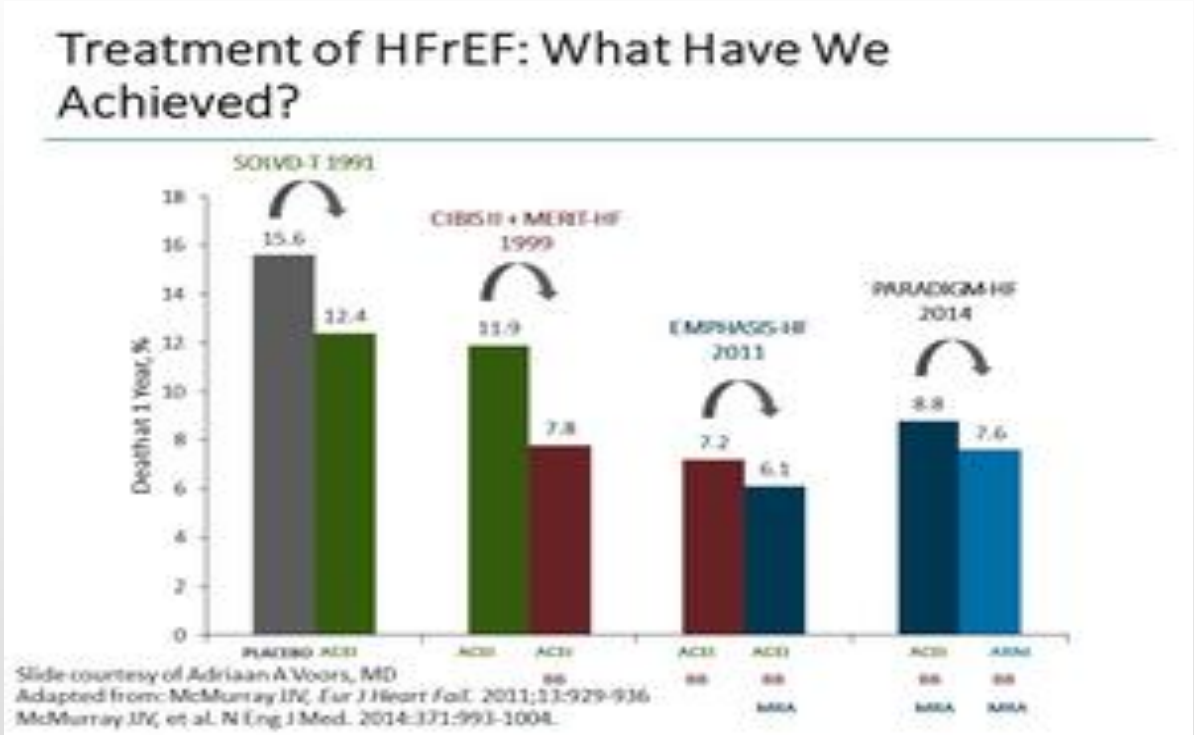

CONSENSUS to EMPHASIS: the overwhelming evidence which makes blockade of the renin–angiotensin–aldosterone system the cornerstone of therapy for systolic heart failure

John J.V. McMurray*

EUROPEAN SOCIETY OF CARDIOLOGY®
European Journal of Heart Failure (2011) **13**, 929–936
doi:10.1093/eurjhf/hfr093

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Ten Pivotal Issues in HFrEF

1. How to initiate, add, or switch therapy to new evidence-based guideline-directed treatments for HFrEF.
2. How to achieve optimal therapy given multiple drugs for HF including augmented clinical assessment that may trigger additional changes in guideline-directed therapy (e.g., imaging data, biomarkers, and filling pressures).
3. When to refer to an HF specialist.
4. How to address challenges of care coordination.
5. How to improve adherence.
6. What is needed in specific patient cohorts: African Americans, the frail, and older adults.
7. How to manage your patients' cost of care for HF.
8. How to manage the increasing complexity of HF.
9. How to manage common comorbidities.
10. How to integrate palliative care and transition to hospice care.

Definitions

HFrEF: Clinical diagnosis of HF and LVEF ≤40%.

New York Heart Association (NYHA) functional classification:

- *Class I:* No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF.
- *Class II:* Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
- *Class III:* Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF.
- *Class IV:* Unable to perform any physical activity without symptoms of HF, or symptoms of HF at rest.

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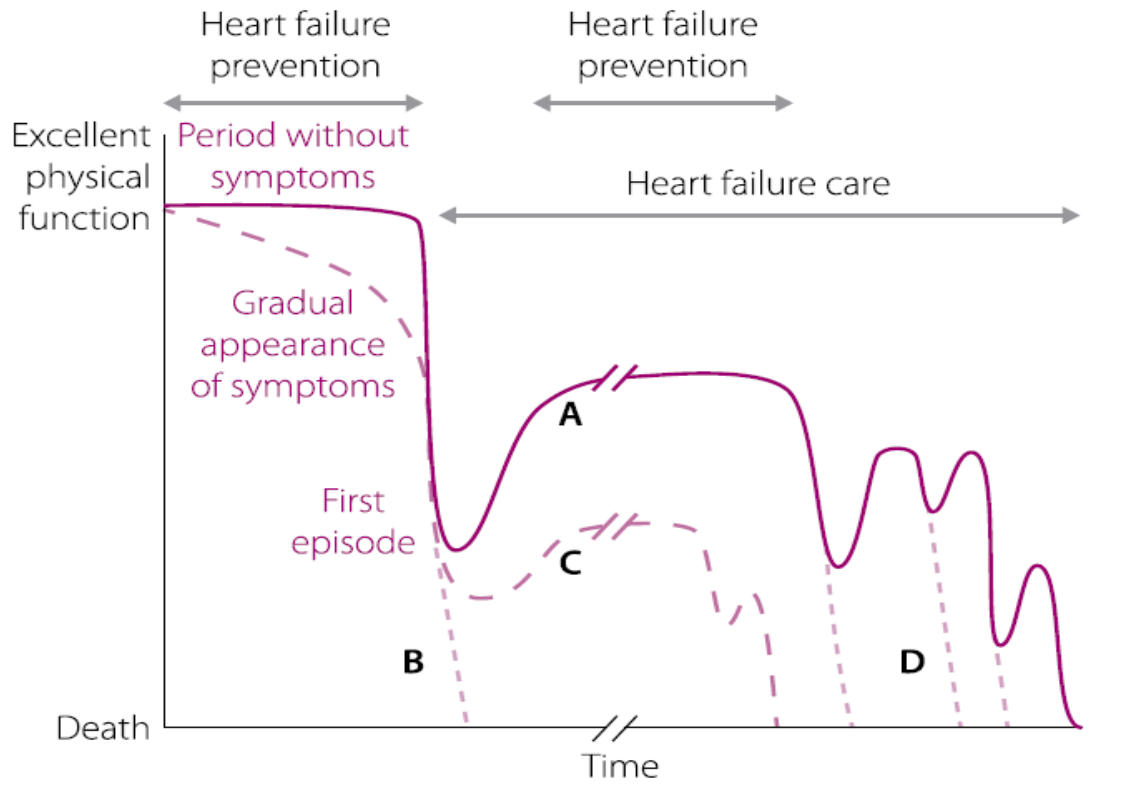
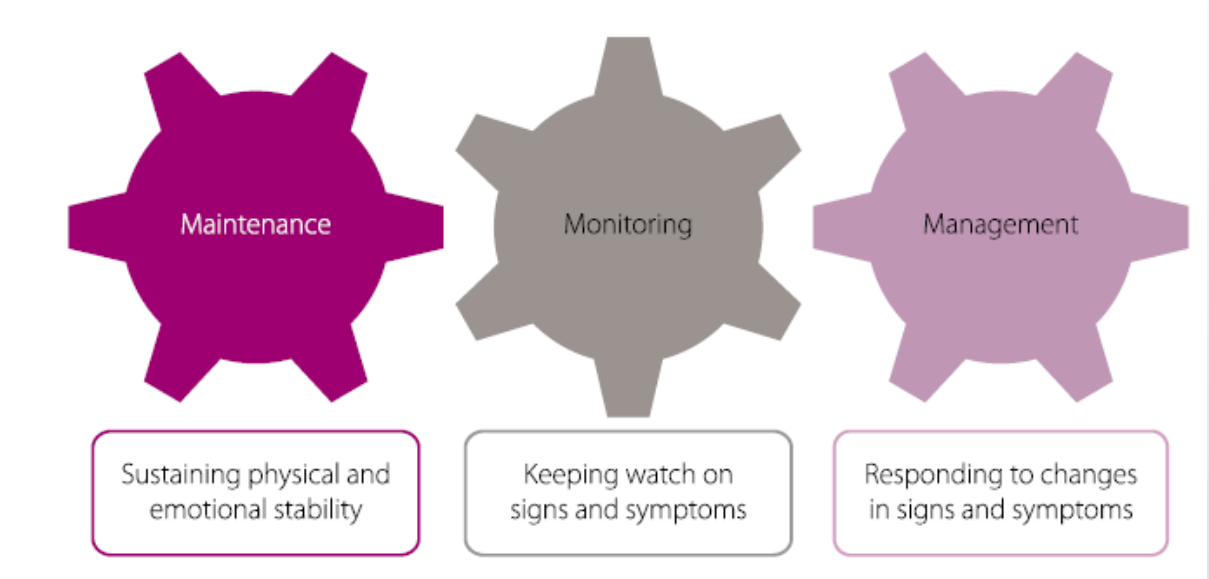
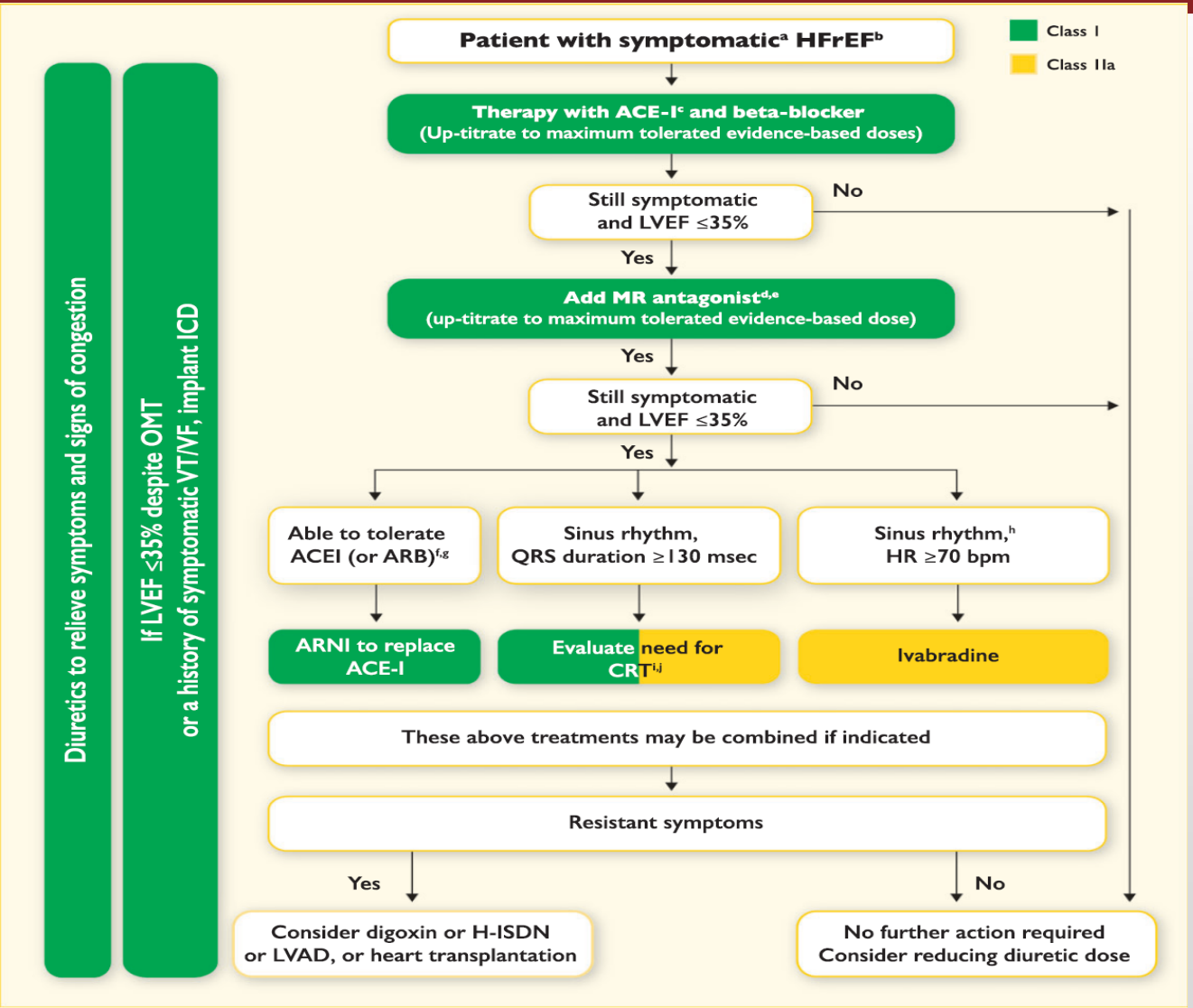
Improving care for patients with acute heart failure: before, during and after hospitalization





Martin R. Cowie Stefan D. Anker John G. F. Cleland G. Michael Felker Gerasimos Filippatos Tiny Jaarsma Patrick Jourdain Eve Knight Barry Massie Piotr Ponikowski José López-Sendón
ESC HEART FAILURE 2014

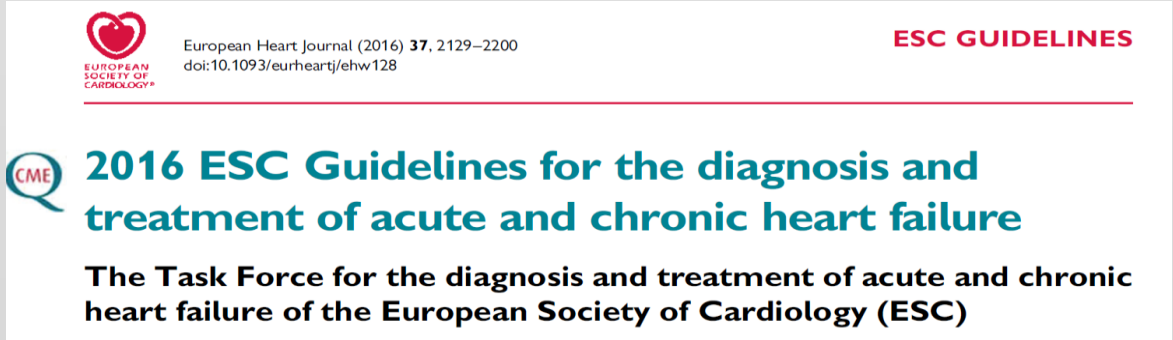
ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ



HF is a complex syndrome typically associated with multiple comorbidities; most patients are on multiple medications.

No clinical trials have specifically evaluated the potential for greater benefit or excessive risk of indicated therapies among patients with multimorbidity.

To assess tolerability of medications and best assess the trajectory of HF, it is often necessary for patients to have more frequent follow-up, especially after initiation or titration of therapy.


European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

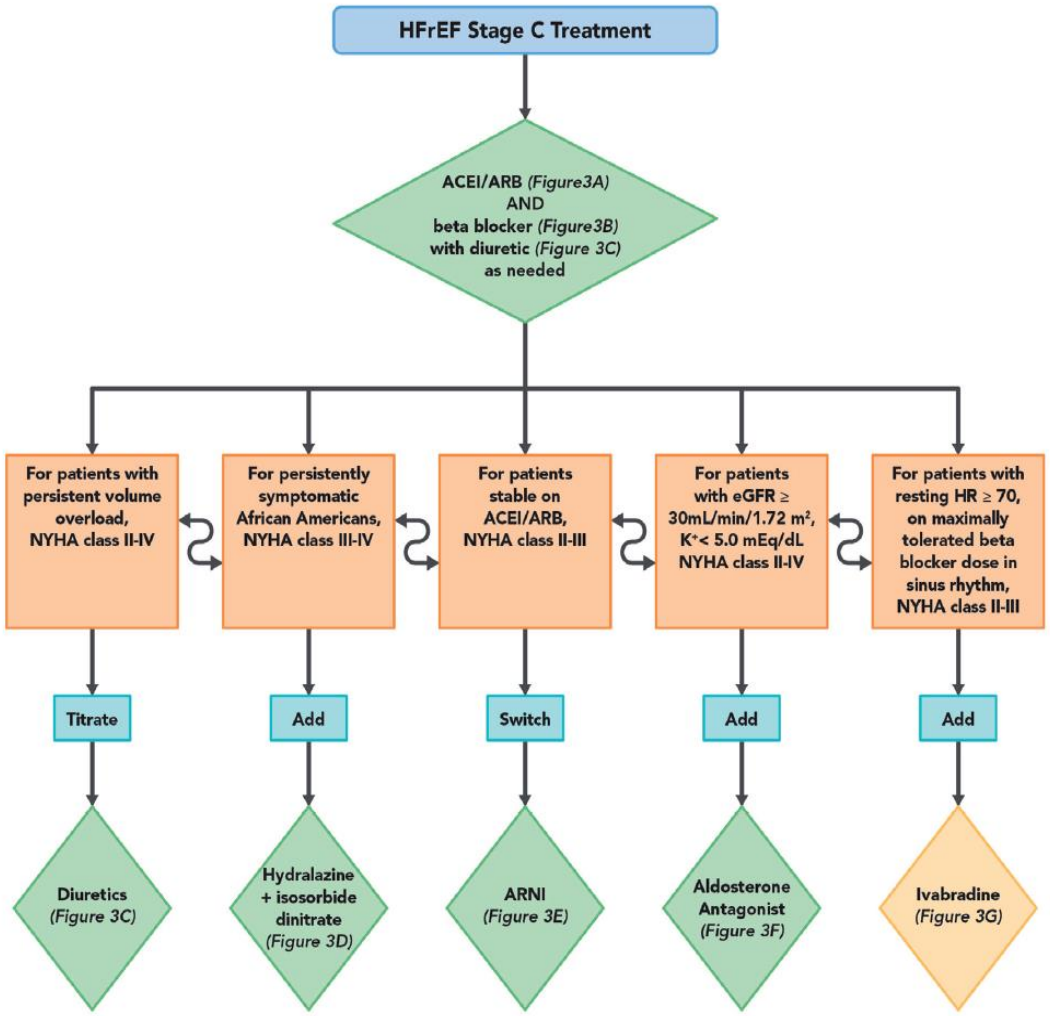
ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ

FIGURE 2 Treatment Algorithm for Guideline-Directed Medical Therapy Including Novel Therapies (2,9)



Whether to initiate b-blocker or ACE-inhibitor first?

Data from the randomized CIBIS (Cardiac Insufficiency Bisoprolol) III trial suggest that either is safe.

Initiation of ACEI or ARB is often better tolerated when the patient is still **congested** ("wet"; when renin-angiotensin-aldosterone system activation is less), whereas beta blockers are better tolerated when the patient is **less congested** ("dry") with adequate resting heart rate. **Only evidence-based beta blockers should be used in patients with HFrEF.**

In selected patients with HFrEF, a clinician may choose to start a low dose of a beta blocker and an ACEI/ARB; in persistently symptomatic patients who tolerate an ACEI or ARB, switching to an ARNI would be recommended.

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Beta Blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg
Metoprolol succinate	12.5–25 mg/d	200 mg daily
ARNI		
Sacubitril/valsartan	24/26 mg–49/51 mg twice daily	97/103 mg twice daily
ACEI		
Captopril	6.25 mg 3× daily	50 mg 3x daily
Enalapril	2.5 mg twice daily	10–20 mg twice daily
Lisinopril	2.5–5 mg daily	20–40 mg daily
Ramipril	1.25 mg daily	10 mg daily
ARB		
Candesartan	4–8 mg daily	32 mg daily
Losartan	25–50 mg daily	150 mg daily
Valsartan	40 mg twice daily	160 mg twice daily
Aldosterone antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5–25 mg daily	25–50 mg daily
Vasodilators		
Hydralazine	25 mg 3× daily	75 mg 3× daily
Isosorbide dinitrate*	20 mg 3× daily	40 mg 3× daily
Fixed-dose combination isosorbide dinitrate/hydralazine†	20 mg/37.5 mg (one tab) 3× daily	2 tabs 3× daily
Ivabradine		
Ivabradine	2.5–5 mg twice daily	Titrate to heart rate 50–60 bpm. Maximum dose 7.5 mg twice daily

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 11, 2014 VOL. 371 NO. 11

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Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

Karl Swedberg, Michel Komajda, Michael Böhm, Jeffrey S Borer, Ian Ford, Ariane Dubost-Brama, Guy Lerebours, Luigi Tavazzi, on behalf of the SHIFT Investigators*

Indications for Use of an ARNI

- HFrEF (EF ≤40%)
- NYHA class II or III HF

Indications for Use of Ivabradine

- HFrEF (EF ≤35%)
- On maximum tolerated doses of beta blocker
- Sinus rhythm with a resting heart rate ≥70 bpm
- NYHA class II or III HF

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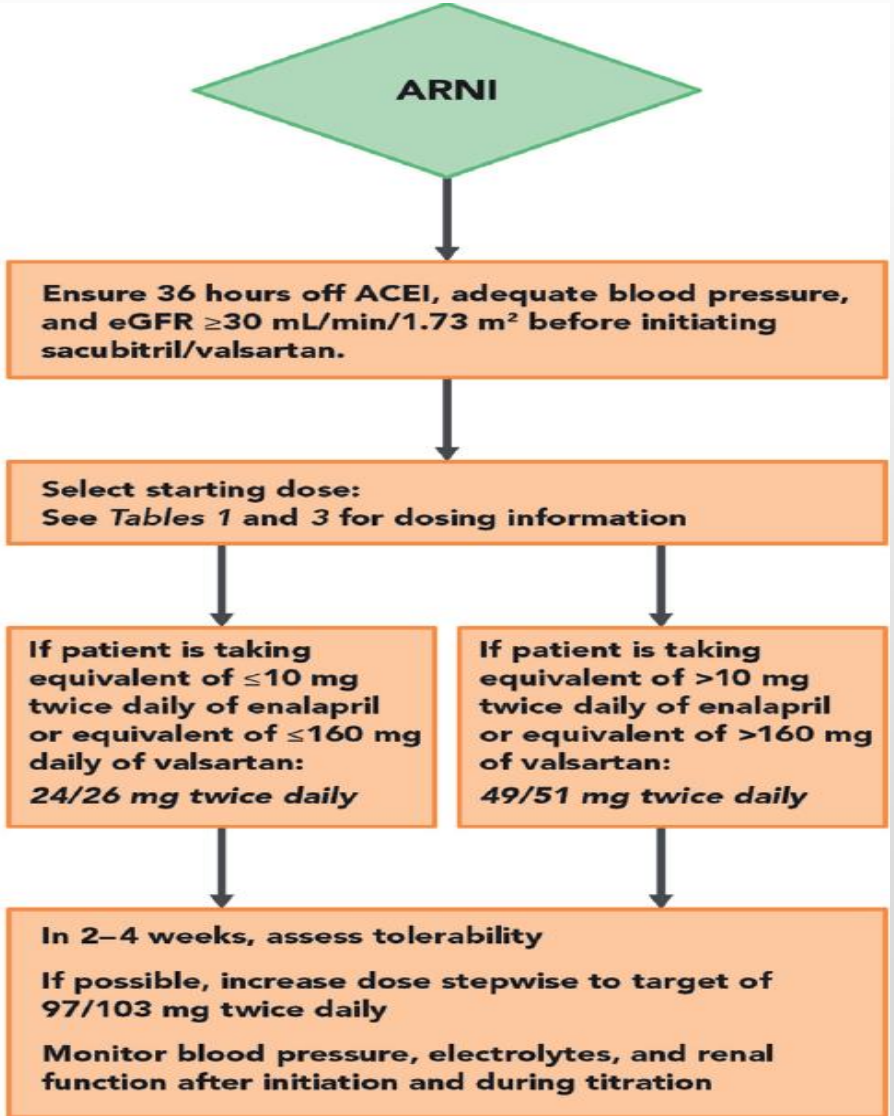


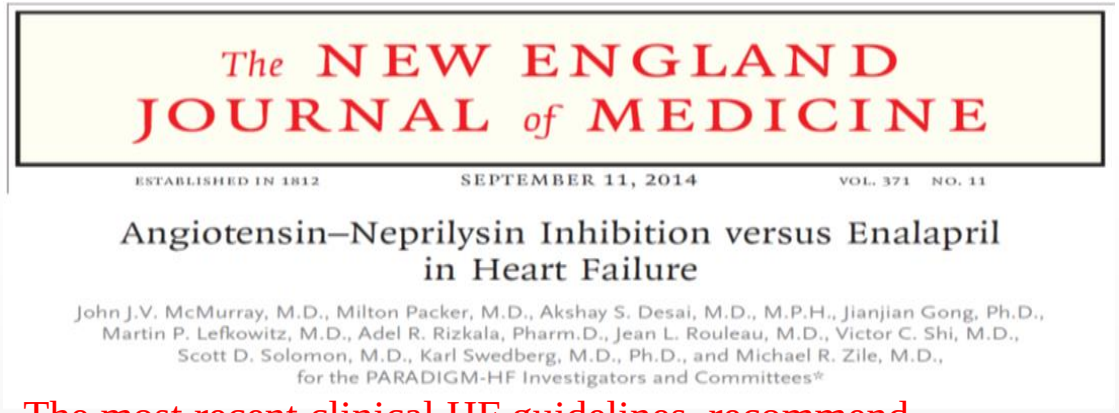
Neprilysin, also known as neutral endopeptidase, is a zinc-dependent metalloprotease that inactivates several vasoactive peptides, including the natriuretic peptides, adrenomedullin, bradykinin, and substance P, each of which has an important role in the pathogenesis and progression of HF.

Because angiotensin II is also a substrate for neprilysin, neprilysin inhibitors raise angiotensin levels, which explains the rationale for coadministration of ARB.

Neprilysin inhibitors are not combined with ACEI due to a higher risk of angioedema.

Sacubitril/valsartan was tested among patients with chronic HFrEF in a randomized controlled trial, PARADIGM HF (Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure). The trial enrolled patients with NYHA class II to IV symptoms with an EF<40% (modified to < 35% 1 year into the trial), stable on doses of ACEI/ARB, and on other background GDMT. Patients with a history of angioedema, estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m2, symptomatic hypotension, or current decompensated HF were excluded. The trial began with a sequential run-in period to ensure that every patient randomized could tolerate both sacubitril/valsartan and the comparator enalapril target doses. Of the 10,513 candidates screened, 2,079 were not randomized due to the inability to achieve target dose therapy on enalapril or sacubitril/valsartan. Most patients enrolled in PARADIGM-HF had NYHA class II to III symptoms (<100 patients with NYHA class IV symptoms).

PARADIGM-HF demonstrated a 20% reduction in the primary outcome of cardiovascular death or HF hospitalization (hazard ratio: 0.80; 95% confidence interval: 0.73 to 0.87; p < 0.001) in patients treated with sacubitril/valsartan. The number needed to treat to prevent 1 primary endpoint over 27 months was 21. These differences in outcomes included a 20% reduction in sudden cardiac death.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The most recent clinical HF guidelines recommend ARNI, ACEI, or ARB to reduce morbidity and mortality in patients with chronic HFrEF and that patients with NYHA class II to III symptoms who can tolerate an ACEI or ARB should transition to an ARNI to further reduce morbidity and mortality (Class I, Level of Evidence: B-R) . Use of an aldosterone antagonist, although also recommended to improve outcomes, is not considered mandatory prior to changing a patient to ARNI.

When making the transition from an ACEI to ARNI, a 36-hour washout period should be strictly observed to avoid angioedema, a delay that is not required when switching from an ARB to ARNI. In a recent study , a condensed and conservative approach to initiation of sacubitril/valsartan was explored; the investigators compared titration to a target dose between 3 and 6 weeks. Both approaches were tolerated similarly.

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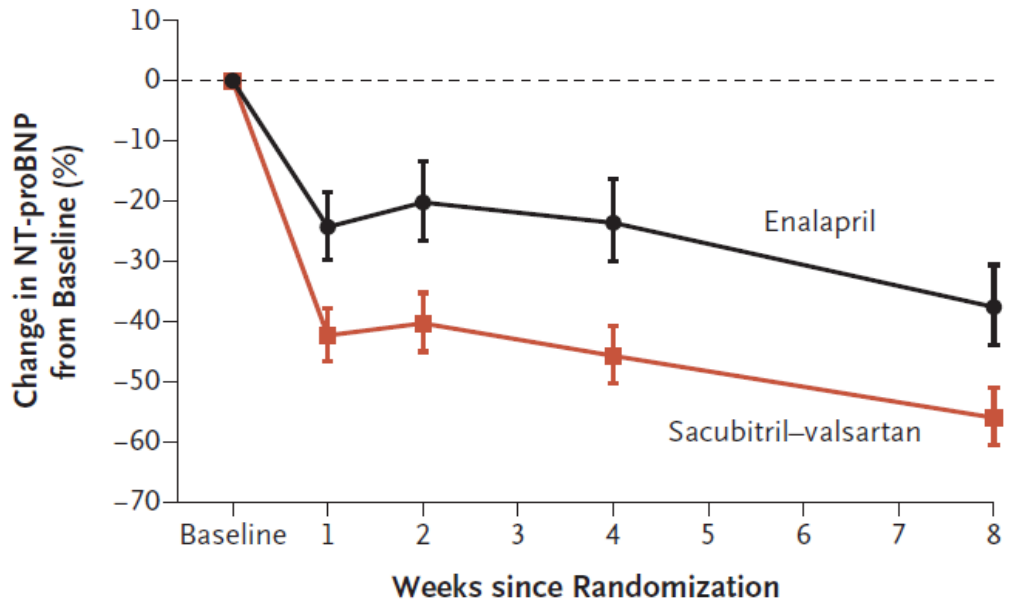
ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

Eric J. Velazquez, M.D., David A. Morrow, M.D., M.P.H., Adam D. DeVore, M.D., M.H.S., Carol I. Duffy, D.O., Andrew P. Ambrosy, M.D., Kevin McCague, M.A., Ricardo Rocha, M.D., and Eugene Braunwald, M.D., for the PIONEER-HF Investigators*

Initiation of an ARNI de novo without prior exposure to ACEI or ARB

It is possible that a patient may be identified who meets all criteria for initiation of ARNI, but the patient has not yet been treated with an ACEI or ARB. **The committee is aware that clinicians may occasionally consider initiating ARNI in patients who have not previously been treated with ACEI or ARB. To be explicitly clear, no predicate data supports this approach**. For well-informed patients who, within a framework of shared-decision making, accept the uncertainty about effectiveness and safety as well as potentially greater out-of-pocket costs, de novo initiation of ARNI with close follow-up and serial assessments (blood pressure, electrolytes, and renal function) might be considered. Any such usage should consider concerns regarding risk of angioedema or hypotension



No. at Risk					
Enalapril	394	359	351	350	348
Sacubitril–valsartan	397	355	363	365	349

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Outcome	Sacubitril–Valsartan (N=440)	Enalapril (N=441)	Sacubitril–Valsartan vs. Enalapril
Key safety outcomes — no. (%)			**Relative risk (95% CI)**
Worsening renal function†	60 (13.6)	65 (14.7)	0.93 (0.67 to 1.28)
Hyperkalemia	51 (11.6)	41 (9.3)	1.25 (0.84 to 1.84)
Symptomatic hypotension	66 (15.0)	56 (12.7)	1.18 (0.85 to 1.64)
Angioedema	1 (0.2)	6 (1.4)	0.17 (0.02 to 1.38)
Secondary biomarker outcomes — % (95% CI)‡			**Ratio of change (95% CI)**
Change in high-sensitivity troponin T concentration	−36.6 (−40.8 to −32.0)	−25.2 (−30.2 to −19.9)	0.85 (0.77 to 0.94)
Change in B-type natriuretic peptide concentration	−28.7 (−35.5 to −21.3)	−33.1 (−39.5 to −25.9)	1.07 (0.92 to 1.23)
Change in ratio of B-type natriuretic peptide to NT-proBNP	35.2 (28.8 to 42.0)	−8.3 (−3.6 to −12.7)	1.48 (1.38 to 1.58)
Exploratory clinical outcomes — no. (%)			**Hazard ratio (95% CI)§**
Composite of clinical events	249 (56.6)	264 (59.9)	0.93 (0.78 to 1.10)
Death	10 (2.3)	15 (3.4)	0.66 (0.30 to 1.48)
Rehospitalization for heart failure	35 (8.0)	61 (13.8)	0.56 (0.37 to 0.84)
Implantation of left ventricular assist device	1 (0.2)	1 (0.2)	0.99 (0.06 to 15.97)
Inclusion on list for heart transplantation	0	0	NA
Unplanned outpatient visit leading to use of intravenous diuretics	2 (0.5)	2 (0.5)	1.00 (0.14 to 7.07)
Use of additional drug for heart failure	78 (17.7)	84 (19.0)	0.92 (0.67 to 1.25)
Increase in dose of diuretics of >50%	218 (49.5)	222 (50.3)	0.98 (0.81 to 1.18)
Composite of serious clinical events¶	41 (9.3)	74 (16.8)	0.54 (0.37 to 0.79)

Among patients with heart failure with reduced ejection fraction who were hospitalized for acute decompensated heart failure, the initiation of sacubitril–valsartan therapy led to a greater reduction in the NT-proBNP concentration than enalapril therapy. Rates of worsening renal function, hyperkalemia, symptomatic hypotension, and angioedema did not differ significantly between the two groups.

TO PIONEERING OR NOT TO PIONEERING?

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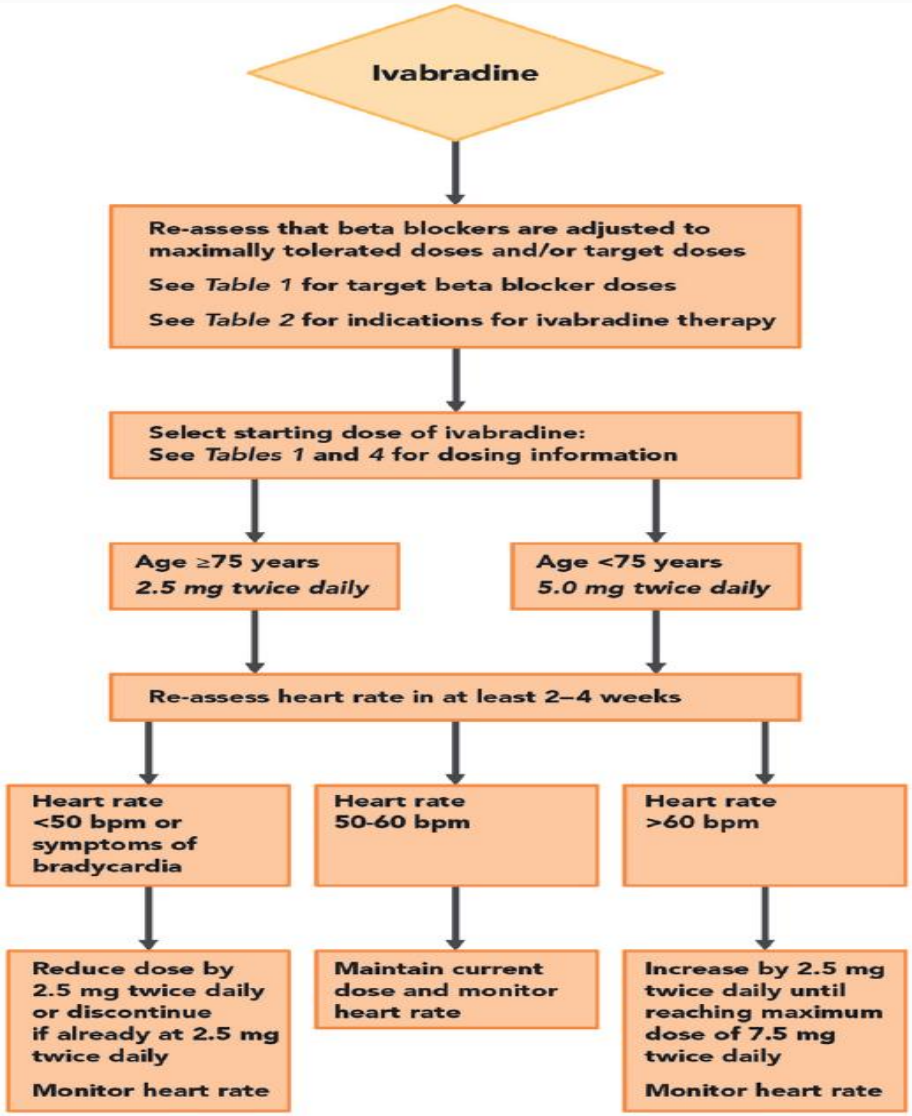

In the SHIFT (Systolic HF Treatment with the If Inhibitor Ivabradine Trial) trial of 6,505 subjects with stable, chronic, predominantly NYHA class II and III HFrEF, ivabradine therapy, when added to GDMT, resulted in a significant reduction in HF hospitalizations.

Benefits were noted especially for those patients with: 1.contraindications to beta blockers, 2.beta blocker doses <50% of GDMT targets , and 3.resting heart rate >77 bpm at study entry .

It is important to emphasize that ivabradine is indicated only for patients in sinus rhythm, not in those with atrial fibrillation, patients who are 100% atrially paced, or unstable patients. From a safety standpoint, patients treated with ivabradine had more bradycardia and developed more atrial fibrillation as well as transient blurring of vision

European Heart Journal (2017) 38, 1883–1890
doi:10.1093/eurheartj/ehx026

CLINICAL RESEARCH
Heart failure/cardiomyopathy

Determinants and clinical outcome of uptitration of ACE-inhibitors and beta-blockers in patients with heart failure: a prospective European study

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	ACE-inhibitor/ARB				Beta-blocker			
	0%	1–49%	50–99%	≥100%	0%	1–49%	50–99%	≥100%
n	305	686	639	470	200	1062	581	257
Mortality rate, % (n)	29% (89)	25% (172)	14% (92)	15% (70)	27% (53)	22% (233)	16% (93)	17% (44)
Mortality and/or HF-hospitalization rate, % (n)	50% (152)	39% (267)	29% (185)	29% (137)	41% (82)	36% (286)	31% (182)	35% (91)
HR Mortality	1.76 (1.54–1.98)	1.50 (1.33–1.67)	0.82 (0.61–1.02)	–	2.41 (2.13–2.68)	1.91 (1.74–2.08)	1.29 (1.07–1.51)	–
HR Mortality and/or HF-hospitalization	1.77 (1.61–1.94)	1.23 (1.09–1.36)	0.86 (0.71–1.00)	–	1.51 (1.29–1.72)	1.27 (1.15–1.39)	1.04 (0.89–1.20)	–

There is little known about the comparison of 0%, 1–49%, 50–99%, and >100% of recommended ACE-inhibitors/ARBs doses. The results of CONSENSUS, SOLVD, and V-HeFT II trials have clearly shown benefit of ACE-inhibitors at high doses. The NETWORK trial compared 25, 50, and 100% of recommended enalapril dose, although there was a trend in mortality reduction they did not find any significant
difference in mortality and heart failure related hospitalizations.
The ATLAS trial suggests that higher doses does reduce heart failure related hospitalizations (12% lower risk of death or hospitalization, 24% lower risk of hospitalizations).

Independent predictors of reaching lower ACEinhibitor/ARB doses were country of inclusion, female gender, lower BMI and eGFR, and higher alkaline phosphatase.
Predictors for lower doses of beta-blockers were higher age, country of inclusion and lower DBP, heart rate and more signs of congestion
Reaching less than 50% of the recommended dose of ACE-inhibitor/ARB and beta-blocker doses was associated with worse survival.

European Journal of Heart Failure (2013) **15**, 1173–1184
doi:10.1093/eurjhf/hft134

Are hospitalized or ambulatory patients with heart failure treated in accordance with European Society of Cardiology guidelines? Evidence from 12 440 patients of the ESC Heart Failure Long-Term Registry

	At target, *n* (%)	Not at target, *n* (%)	Reason for not at target, *n* (%)	
ACE-I (4710 pts)	1380 (29.3)	3330 (70.7)	1123 (33.7)	Still in up-titration
			866 (26.0)	Symptomatic hypotension
			264 (7.9)	Worsening renal function
			85 (2.6)	Hyperkalaemia
			29 (0.9)	Cough
			5 (0.2)	Angioedema
			958 (28.8)	Other/unknown
ARBs (1500 pts)	362 (24.1)	1138 (75.9)	369 (32.4)	Still in up-titration
			295 (25.9)	Symptomatic hypotension
			115 (10.1)	Worsening renal function
			25 (2.2)	Hyperkalaemia
			1 (0.1)	Angioedema
			333 (29.3)	Other/unknown
Beta-blockers (6468 pts)	1130 (17.5)	5338 (82.5)	1871 (35.1)	Still in up-titration
			904 (16.9)	Symptomatic hypotension
			586 (11.0)	Bradyarrhythmia
			185 (3.5)	Worsening HF
			146 (2.7)	Bronchospasm
			56 (1.1)	Worsening PAD
			33 (0.6)	Sexual dysfunction
			1557 (29.2)	Other/unknown
MRAs (4226 pts)	1290 (30.5)	2936 (69.5)		
			864 (29.4)	Still in up-titration
			350 (11.9)	Hyperkalaemia
			284 (9.7)	Worsening renal function
			60 (2.0)	Gynaecomastia
			1378 (46.9)	Other/unknown

Considering just the patients with reduced EF, for whom these drugs are recommended by guidelines, the rate of use of ACE inhibitors/ARBs, betablockers, and MRAs was 92.2, 92.7, and 67.0%, respectively.

With respect to the target dosages of these drugs, far fewer than one-third of the patients were on the target dosages suggested by the current guidelines:
29.3% for ACE inhibitors,
24.1% for ARBs,
17.5% for beta-blockers, and
30.5% for MRAs
WHY B-BLOCKERS SO LOW?

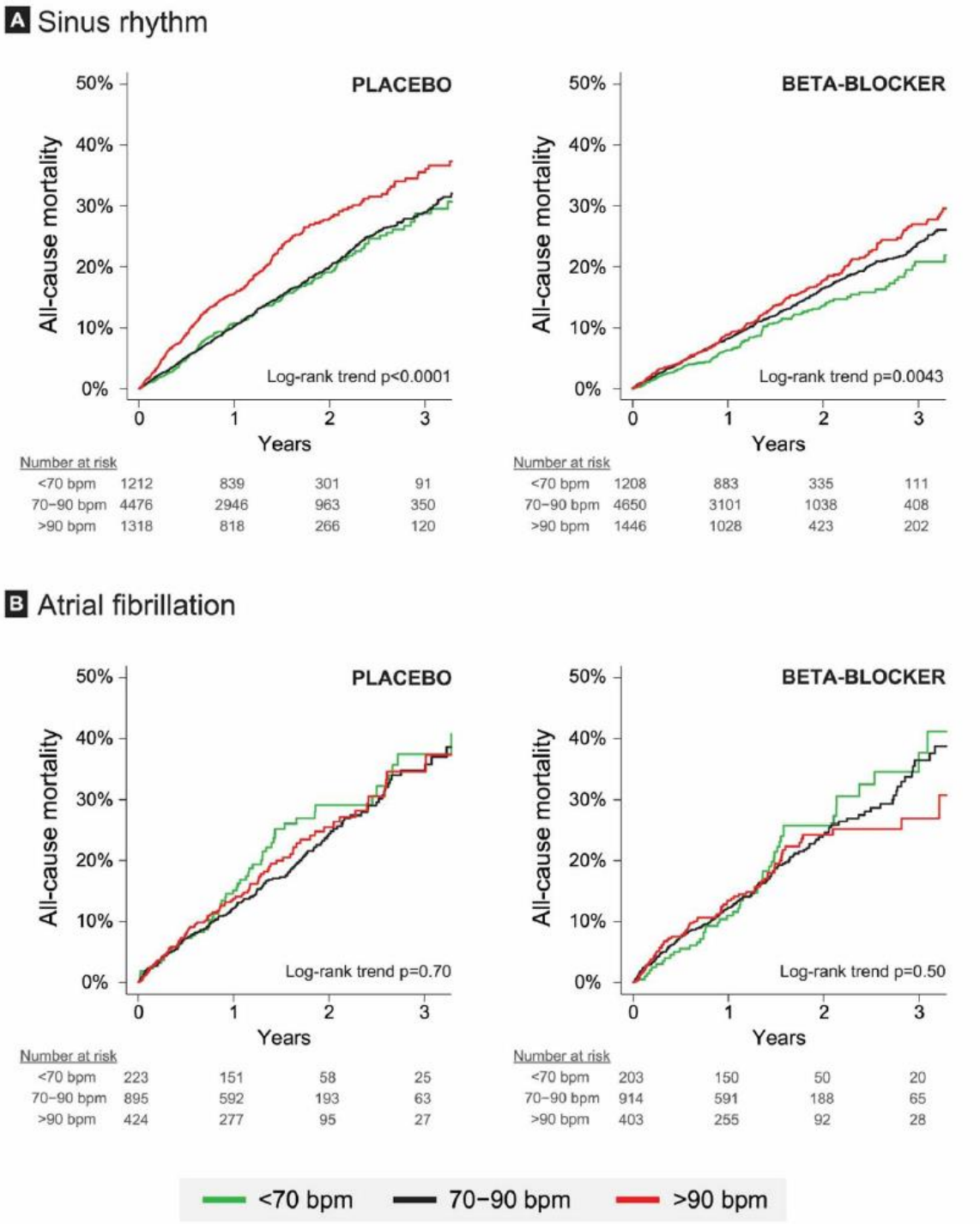
Accepted Manuscript

JACC

Heart Rate, Heart Rhythm, and Prognostic Benefits of Beta-Blockers in Heart Failure: Individual Patient-Data Meta-Analysis

Dipak Kotecha, PhD, Marcus D. Flather, MBBS, Douglas G. Altman, DSc, Jane Holmes, PhD, Giuseppe Rosano, PhD, John Wikstrand, PhD, Milton Packer, MD, Andrew J.S. Coats, DSc, Luis Manzano, MD, Michael Böhm, Dirk J. van Veldhuisen, Bert Andersson, PhD, Hans Wedel, PhD, Thomas G. von Lueder, PhD, Alan S. Rigby, MSc, Åke Hjalmarson, PhD, John Kjekshus, PhD, John G.F. Cleland, MD

Beta-blockers versus placebo	Heart rate <70 bpm		Heart rate 70-90 bpm		Heart rate >90 bpm		Interaction p-value for heart rate as a continuous variable
	N (events /patients	HR, 95% CI, p-value	N (events /patients	HR, 95% CI, p-value	N (events /patients	HR, 95% CI, p-value	
Sinus rhythm	328 / 2,386	0.64, 0.51-0.80, p<0.0001	1,293 / 9,042	0.79, 0.71-0.89, p<0.0001	520 / 2,738	0.62, 0.52-0.74, p<0.0001	0.35
Atrial fibrillation	104 / 423	0.76, 0.51-1.13, p=0.18	345 / 1,791	1.07, 0.87-1.33, p=0.51	160 / 820	0.87, 0.63-1.19, p=0.38	0.48



European Journal of Heart Failure (2011) **13**, 670–680
doi:10.1093/eurjhf/hfr020

Titration to target dose of bisoprolol vs. carvedilol in elderly patients with heart failure: the CIBIS-ELD trial

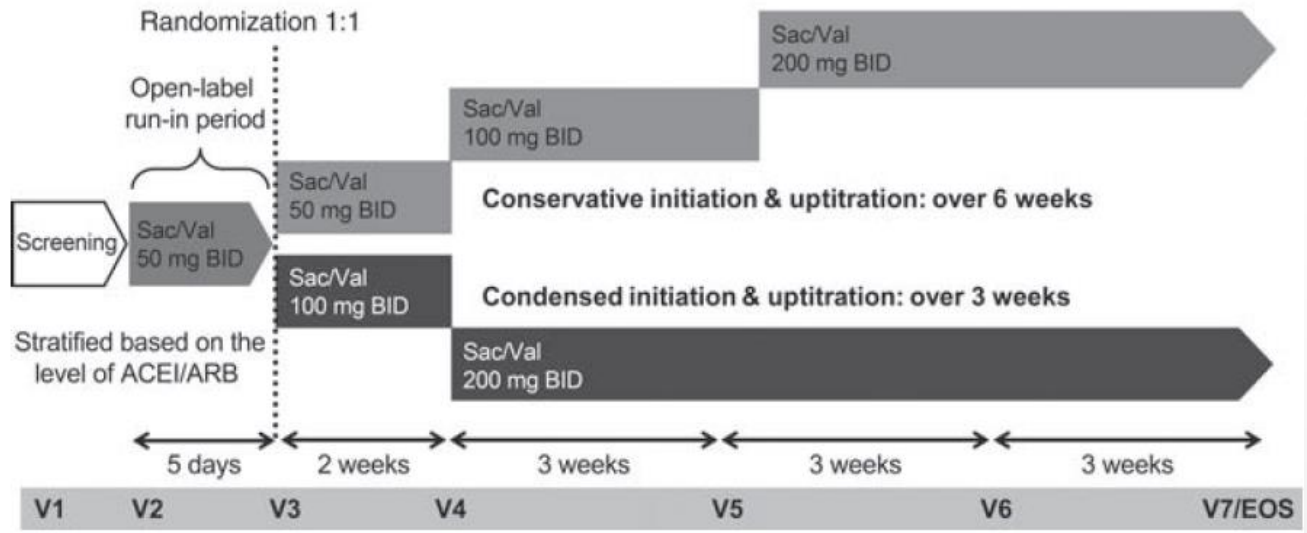
	Patients in treatment groups		*P*-value
	Bisoprolol (*n* = 431)	Carvedilol (*n* = 445)	
Primary endpoint achieved[a], no. (%)	102 (24)	112 (25)	0.64
95% CI for rate	20–28	21–29	
Dose level at follow-up, no. (%)			0.58
0 (study medication stopped before follow-up)	46 (11)	51 (11)	
12.5% (1.25 mg bisoprolol or 3.125 mg carvedilol)	47 (11)	45 (10)	
25% (2.5 mg bisoprolol or 6.25 mg carvedilol)	108 (25)	97 (22)	
50% (5 mg bisoprolol or 12.5 mg carvedilol)	98 (23)	110 (25)	
100% (10 mg bisoprolol or 1–2 × 25 mg carvedilol)	132 (31)	142 (32)	

Overall, 31% of patients reached the full, and 55% tolerated at least half of the target doses. The mean daily dose reached at follow-up was 5.0 mg for bisoprolol and 23.9 mg for carvedilol in patients ≤ 85 kg (47.7 mg in patients > 85 kg).

Age > 65y. , BB-naïve at baseline or on < 25% of recommended target dose.

SHOULD WE TRY MORE??

Initiating sacubitril/valsartan (LCZ696) in heart failure: results of TITRATION, a double-blind, randomized comparison of two uptitration regimens



Tolerability criteria:

-hypotension,
-renal dysfunction
- hyperkalaemia
- adjudicated angioedema

REAL WORLD DATA???

Initiation/uptitration of sacubitril/valsartan from 50 to 200 mg twice daily over 3 or 6weeks had a tolerability profile in line with other HF treatments. More gradual initiation/uptitration maximized attainment of target dose in the low-dose ACEI/ARB group.

Pre-specified 'treatment success' and 'tolerability success'		Sacubitril/valsartan Condensed, $n/N^{\dagger}$ (%)	Sacubitril/valsartan Conservative, $n/N^{\dagger}$ (%)	Odds ratio (95% CI)	
Treatment success	High	90/109 (82.6)	98/117 (83.8)	0.91 (0.45, 1.83)	0.783
	Low	89/121 (73.6)	101/119 (84.9)	0.50 (0.26, 0.94)	0.030
	All	179/230 (77.8)	199/236 (84.3)	0.65 (0.41, 1.05)	0.078
Tolerability success	High	94/109 (86.2)	103/117 (88.0)	0.84 (0.38, 1.84)	0.657
	Low	97/121 (80.2)	103/119 (86.6)	0.63 (0.32, 1.26)	0.189
	All	191/230 (83.0)	206/236 (87.3)	0.72 (0.43, 1.20)	0.207

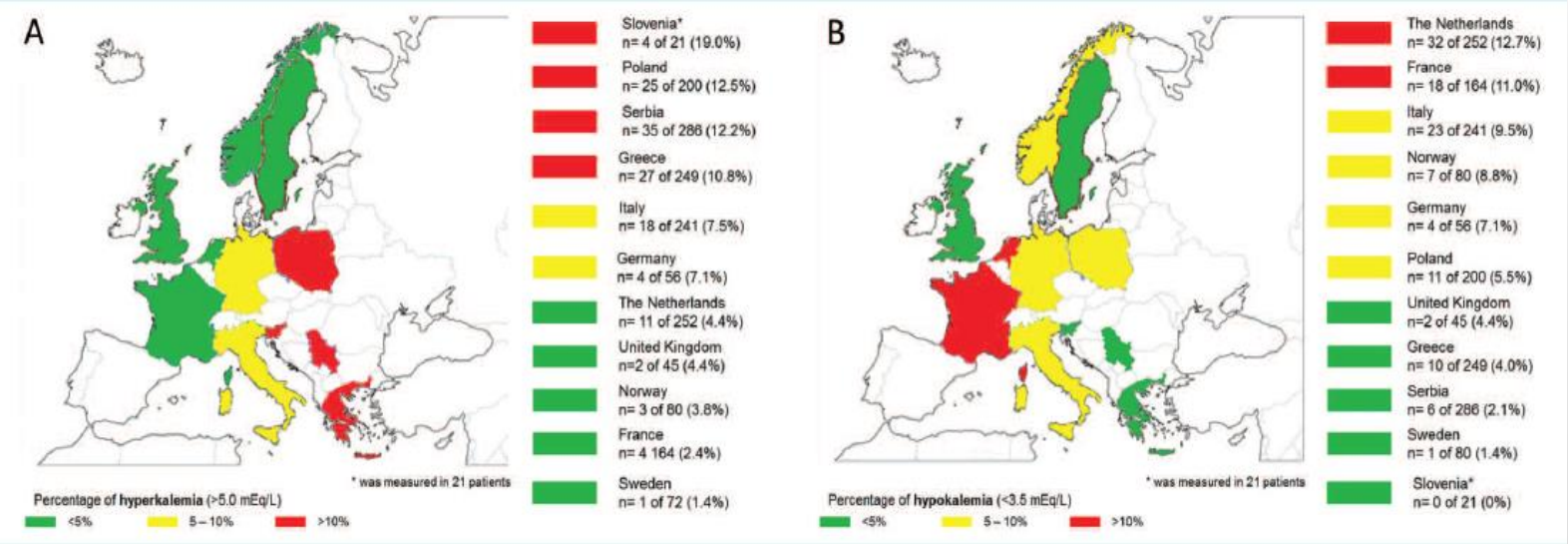
ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ

- Why are drugs NOT uptitrated in HFrEH?
- 1. Dizziness or low BP being experienced patient asks for dose reduction
- 2. Patients do not usually request dose to be increased
- 3. Symptoms relief, the patient may not expect uptitration
- 4. physician’s satisfaction
- 5. Borderline exams (eg Potassium, Creatinine levels etc.)

European Journal of Heart Failure (2018) **20**, 923–930
doi:10.1002/ejhf.1079

RESEARCH ARTICLE

Potassium and the use of renin–angiotensin–aldosterone system inhibitors in heart failure with reduced ejection fraction: data from BIOSTAT-CHF



In this study, higher potassium levels at baseline were associated with less uptitration of ACEi/ARB. This suggests that HF patients with hyperkalaemia at the start of therapy are at greater risk for lower doses or discontinuation of ACEi/ARB, which impede outcomes.

This is consistent with earlier reports from a general patient population where high potassium levels were found to be responsible for a significant proportion of discontinuation or lowering of ACEi/ARB dosage.

ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ

Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:		
• IHD (unless they have had an MI in the prior 40 days – see below).	I	A
• DCM.	I	B
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A
ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C

European Heart Journal (2016) **37**, 2129–2200
doi:10.1093/eurheartj/ehw128

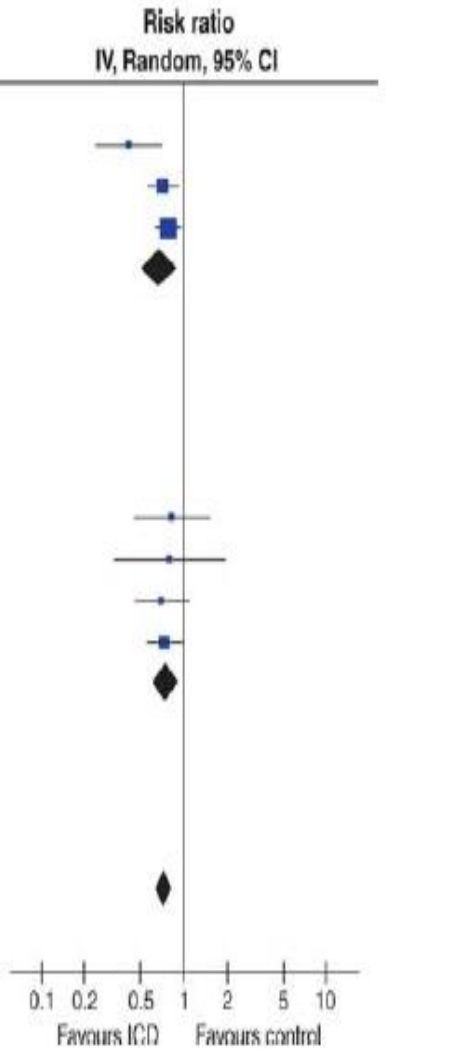
ESC GUIDELINES

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ

Study or subcategory	ICD Events	ICD Total	Control Events	Control Total	Weight	Risk ratio IV, Random, 95% CI
2.1.1 Ischaemic cardiomyopathy						
01 - MADIT	15	95	39	101	5.5%	0.41 [0.24, 0.69]
04 - MADIT II	105	742	97	490	24.1%	0.71 [0.56, 0.95]
08 - SCD-HeFT	120	431	161	453	39.6%	0.78 [0.64, 0.95]
Subtotal (95% CI)		**1268**		**1044**	**69.3%**	**0.67 [0.51, 0.88]**
Total events:	240		297			
Heterogeneity: $\tau^2=0.03$; $\chi^2=5.17$, df = 2 ($P=0.08$); $I^2=61\%$						
Test for overall effect: $Z=2.88$ ($P=0.004$)						
2.1.2 Non-ischaemic cardiomyopathy						
03 - CAT	13	50	17	54	4.1%	0.83 [0.45, 1.52]
05 - AMIOVIRT	7	51	9	52	1.8%	0.79 [0.32, 1.97]
06 - DEFINITE	28	229	40	229	7.6%	0.70 [0.45, 1.09]
08 - SCD-HeFT	62	398	83	394	17.2%	0.74 [0.55, 1.00]
Subtotal (95% CI)		**728**		**729**	**30.7%**	**0.74 [0.59, 0.93]**
Total events:	110		149			
Heterogeneity: $\tau^2=0.00$; $\chi^2=0.20$, df = 3 ($P=0.98$); $I^2=0\%$						
Test for overall effect: $Z=2.61$ ($P=0.009$)						
Total (95% CI)		**1996**		**1773**	**100.0%**	**0.73 [0.64, 0.82]**
Total events:	350		446			
Heterogeneity: $\tau^2=0.00$; $\chi^2=5.42$, df = 6 ($P=0.49$); $I^2=0\%$						
Test for overall effect: $Z=5.05$ ($P<0.00001$)						



Thus, this analysis confirms that ICD-only therapy reduces the RR for all-cause mortality by 27% for patients with a LVEF ≤35%, if they are 40 days from myocardial infarction and ≥3 months from a coronary revascularization procedure, without a previous cardiac arrest or symptomatic ventricular arrhythmias.

This beneficial effect of ICD-only therapy on survival exists regardless of whether a patient has left ventricular dysfunction due to CAD or DCM.

EUROPEAN SOCIETY OF CARDIOLOGY®
Europace (2010) **12**, 1564–1570
doi:10.1093/europace/euq329

CLINICAL RESEARCH
Implantable Cardioverter-Defibrillators

Effectiveness of prophylactic implantation of cardioverter-defibrillators without cardiac resynchronization therapy in patients with ischaemic or non-ischaemic heart disease: a systematic review and meta-analysis

The NEW ENGLAND JOURNAL of MEDICINE

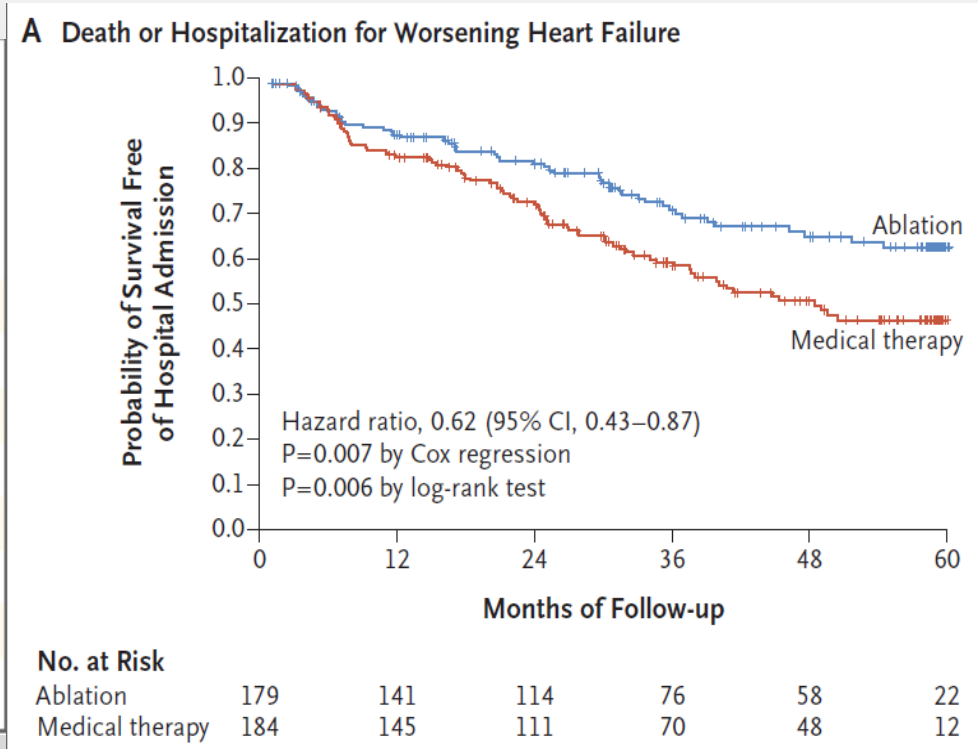
ESTABLISHED IN 1812 FEBRUARY 1, 2018 VOL. 378 NO. 5

Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

In the ablation group, 63% of patients were in sinus rhythm at 60 months versus 22% in the medical-therapy group, which suggests that maintenance of sinus rhythm is beneficial when achieved without the use of antiarrhythmic drugs.

End Point	Ablation (N=179)	Medical Therapy (N=184)	Hazard Ratio (95% CI)	P Value	
				Cox Regression	Log-Rank Test
	number (percent)				
Primary†	51 (28.5)	82 (44.6)	0.62 (0.43–0.87)	0.007	0.006
Secondary					
Death from any cause	24 (13.4)	46 (25.0)	0.53 (0.32–0.86)	0.01	0.009
Heart-failure hospitalization	37 (20.7)	66 (35.9)	0.56 (0.37–0.83)	0.004	0.004
Cardiovascular death	20 (11.2)	41 (22.3)	0.49 (0.29–0.84)	0.009	0.008
Cardiovascular hospitalization	64 (35.8)	89 (48.4)	0.72 (0.52–0.99)	0.04	0.04
Hospitalization for any cause	114 (63.7)	122 (66.3)	0.99 (0.77–1.28)	0.96	0.96
Cerebrovascular accident	5 (2.8)	11 (6.0)	0.46 (0.16–1.33)	0.15	0.14



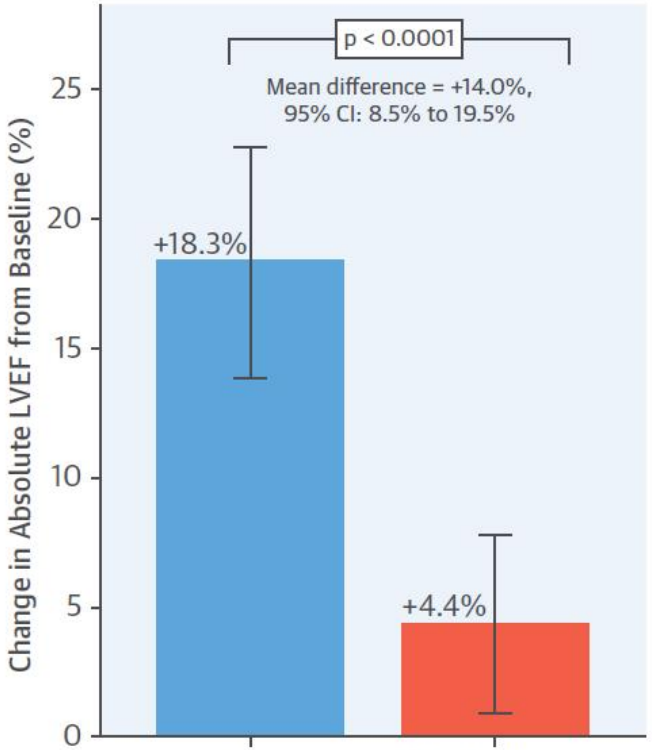
Catheter Ablation Versus Medical Rate Control in Atrial Fibrillation and Systolic Dysfunction

The CAMERA-MRI Study

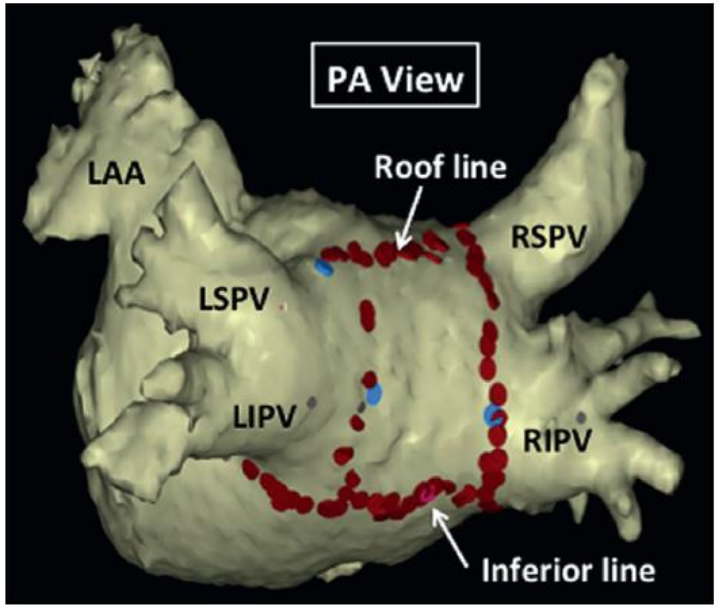
Sandeep Prabhu, MBBS,[a,b,c,d] Andrew J. Taylor, MBBS, PHD,[a,b,e] Ben T. Costello, MBBS,[a,b]
David M. Kaye, MBBS, PHD,[a,b,e] Alex J.A. McLellan, MBBS, PHD,[a,b,c,d] Aleksandr Voskoboinik, MBBS,[a,b,c,d]
Hariharan Sugumar, MBBS,[a,b,c,d] Siobhan M. Lockwood, MBBS,[f] Michael B. Stokes, MBBS,[f] Bhupesh Pathik, MBBS,[c,d]
Chrishan J. Nalliah, MBBS,[c,d] Geoff R. Wong, MBBS,[c,d] Sonia M. Azzopardi, RN,[a,b] Sarah J. Gutman, MBBS,[a,b]
Geoffrey Lee, MBBS, PHD,[c] Jamie Layland, MBCHB, PHD,[e] Justin A. Mariani, MBBS, PHD,[a,b,d]
Liang-han Ling, MBBS, PHD,[a,b,d] Jonathan M. Kalman, MBBS, PHD,[c,d] Peter M. Kistler, MBBS, PHD[a,b,d]

CONCLUSIONS: AF is an underappreciated reversible cause of LVSD in this population despite adequate rate control.
The restoration of sinus rhythm with CA results in significant improvements in ventricular function, particularly in the absence of ventricular fibrosis on CMR. This outcome challenges the current treatment paradigm that rate control is the appropriate strategy in patients with AF and LVSD.

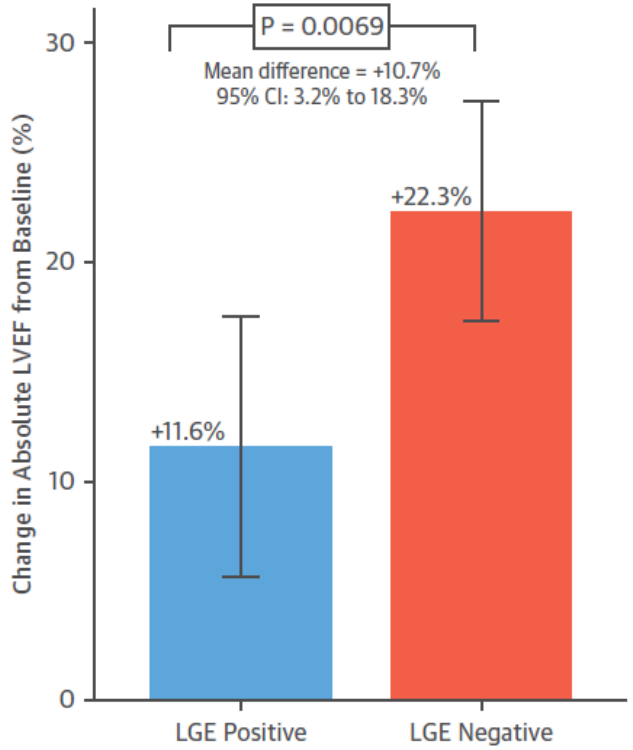
A Primary Endpoint: Change in LVEF at Baseline and 6 Months by Treatment Arm



B Catheter Ablation Lesion Set in Left Atrium: Pulmonary Vein and Posterior Wall Isolation



A ΔLVEF Stratified by LGE Status in Patients Following Catheter Ablation



ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ

Comorbidity	Association With Heart Failure Outcomes	Clinical Trial Evidence for Modulating Comorbidity	Suggested Action
		Cardiovascular	
Coronary Artery Disease	Strong	Strong	Evaluate and revascularize in appropriate patients
Atrial Fibrillation/Flutter	Strong	Intermediate	Treat according to current ACC/AHA/HRS Guideline for the Management of Patients with Atrial Fibrillation (94)
Mitral Regurgitation	Strong	Intermediate	Refer to structural heart disease expert & treat according to current AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (95)
Aortic Stenosis	Strong	Strong	Refer to structural heart disease expert & treat according to current AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease (95)
Hypertension	Uncertain	Strong for prevention	Treat according to current ACC/AHA hypertension guidelines
Dyslipidemia	Uncertain	Strong for prevention	Treat according to ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults (96). Also see the nonstatin treatment of dyslipidemia clinical pathways (97)
Peripheral Vascular Disease	Moderate	None	Treat according to current AHA/ACC vascular guidelines (98)
Cerebrovascular Disease	Moderate	Weak	Treat according to current AHA stroke guidelines (99)
		Noncardiovascular	
Obesity	Moderate (inverse association)	Weak	Further data needed
Chronic Lung Disease	Strong	Weak	Optimize therapy, consider pulmonary consultation
Diabetes Mellitus	Strong	Intermediate	Optimize therapy, consider SGLT2 inhibitors, consider endocrine consult and follow current American Diabetes Association Standards of Medical Care in Diabetes (100)
Chronic Renal Disease	Strong	Weak	Optimize RAASi therapy, consider nephrology consult
Anemia	Moderate	Weak	Evaluate secondary causes, consider transfusing in severe cases
Iron Deficiency	Strong	Intermediate	Consider intravenous iron replacement for symptom improvement
Thyroid Disorder—hypo or hyper	Strong	Weak	Consider referral to endocrinologist and/or treatment
Sleep Disordered Breathing	Strong	Intermediate	Consider sleep study and treat severe obstructive sleep apnea to improve sleep quality, consider referring to sleep specialist

Reasons for Nonadherence (World Health Organization)

Patients need support. “Blame” is counterproductive.

Patient → Perceived lack of effect
Poor health literacy
Physical impairment (vision, cognition)
Depression and social isolation
Cognitive impairment

Medical condition → High HF regimen complexity
Polypharmacy due to multiple comorbidities

Therapy → Frequency of dosing
Polypharmacy
Side effects

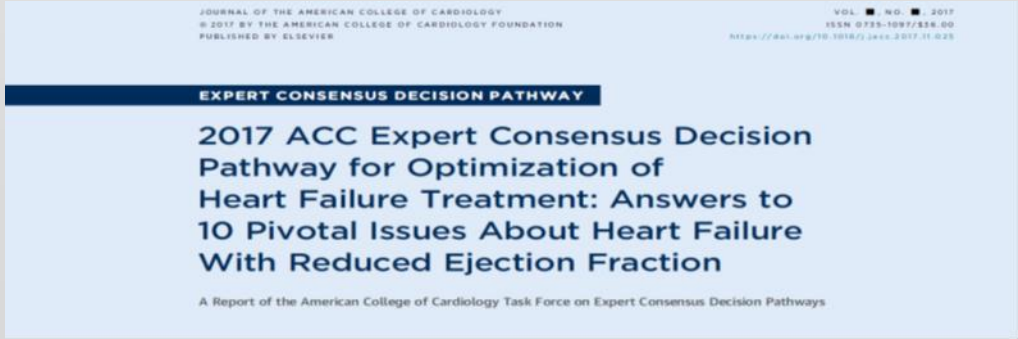
Socioeconomic → Out-of-pocket cost
Difficult access to pharmacy
Lack of support

Health system → Poor communication
Silos of care
No automatic refills

ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ

How to Improve Adherence

Example	Scenario	Intervention
Medication education	Patient confusion about polypharmacy	Pharmacist and other clinician-based education
Disease education	Misunderstanding about HF and its management	Support groups, one-on-one disease teaching
Improved integration of care	Fragmented care due to multiple comorbidities	Team-based care (see answers to Issues 4 and 8), involvement of a case manager. Effective use of electronic health record and patient portal access
Self-management teaching	Challenges in salt avoidance or fluid restriction	Clinic and home-based nursing program.
Self-monitoring	Difficulties in achieving optimal fluid and weight monitoring.	Home-based monitoring programs for select patients, biomarker and/or (for those with implantable devices) impedance monitoring in the office, in select patients implantable pulmonary artery pressure monitoring.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EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Improving medication titration in heart failure by embedding a structured medication titration plan

International Journal of Cardiology

Annabel Hickey [a,1], Jessica Suna [b,1], Louise Marquart [c,1], Charles Denaro [d,1], George Javorsky [a,1], Andrew Munns [e,1], Alison Mudge [b,1], John J. Atherton [f,*,1]

Queensland Government

Heart Failure Medication Titration

(Affix identification label here)

URN:
Family Name:
Given Name(s):
Address:
Date of Birth:

To:

- Titration to maximum tolerated doses of ACE Inhibitor and Beta-blocker redu
ventricular systolic heart failure.
- Clinical review of the patient should precede each dose adjustment.
- Patients over 75 years old with co-morbidities are more likely to experience

Heart Failure Medications To Be Titrated By (nominate person

Echo date: EF: %

Titrate first (tick one box only):
☐ ACE Inhibitor ☐ Beta-blocker

Avoid titrating both the ACE inhibitor and beta-blocke

ACE Inhibitor or Angiotensin II Receptor Antagonist			**Beta-Blocker**
Medication:			Medication:
Current dose:			Current dose:
Target dose:			Target dose:
Increase dose by:	every	wks	Increase dose by

Instructions eg. special requirements, relevant allergies:
Check urea and electrolytes 1 week after titrating ACE inhibitor.

Tip for GPs: Use your recall system. See over for problem solving guidelines

Variable Dose Diuretic Action Plan

Current Diuretic: Dose:

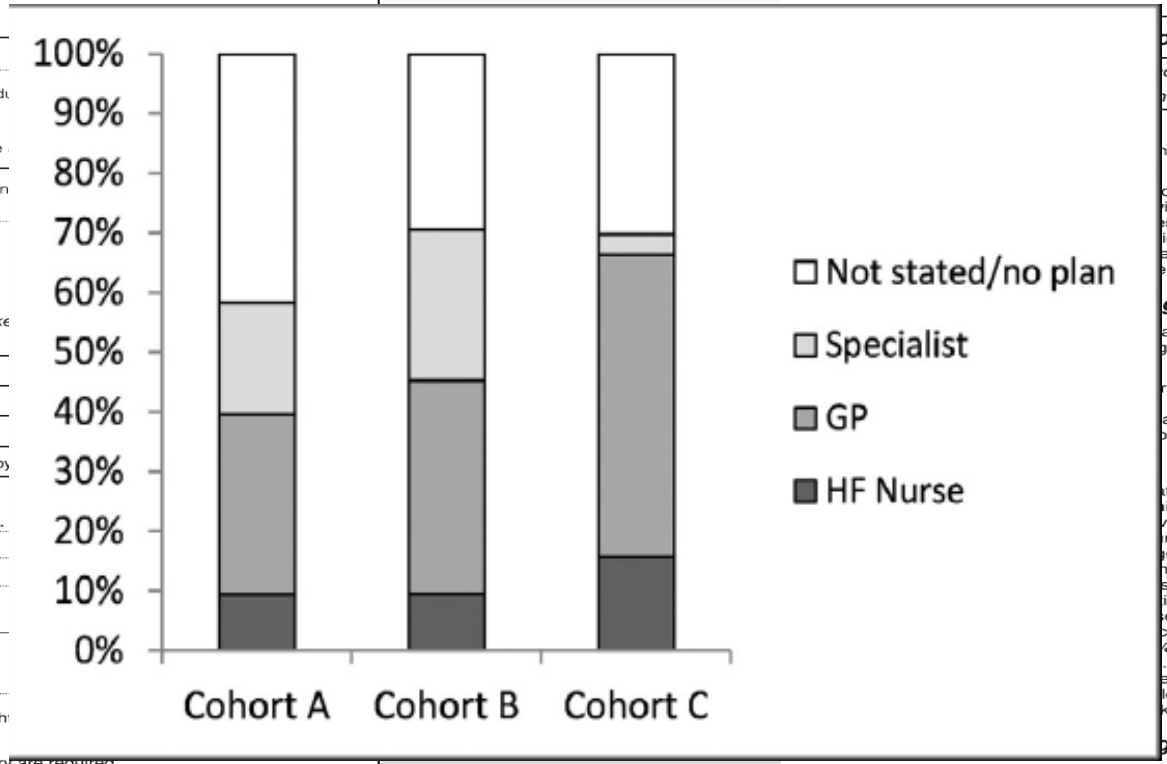
Fluid overload: If daily weight increases by more than 1kg above stable weigh
increase dose to until
diuretic dose is required beyond 3 days, then medical review and blood chemistry are required.

Dehydration: If daily weight decreases by more than 1kg below stable weight for 2 days and there are signs of dehydration (dizziness, postural hypotension, dry mucosa) then:- decrease dose to .
Further assessment of fluid status and blood chemistry are required 3-7 days post reduction.

Dr's signature: Print name: Date:
Consultant's name: Contact:
Hospital discharge date:

- This form is intended to support dose titration of heart failure medications.
- This form is not intended to replace clinical judgement.

Phone: **Fax:**



Queensland Government

Heart Failure Medication Titration

(Affix identification label here)

URN:
Family Name:
Given Name(s):
Address:
Date of Birth: Sex: ☐ M ☐ F ☐ I

oblem Solving Guidelines

ontraindicated in patients with heart failure
-channel blockers (verapamil, diltiazem) in systolic heart failure

therapy (systolic BP 90 -100 mmHg).

c hypotension or in shock to an emergency department immediately.
ith dizziness, light-headedness and/or confusion, stop or reduce calcium-channel
ss absolutely essential e.g. for angina.
igns or symptoms of congestion.
er reducing ACE inhibitor or Beta-blocker dose *temporarily.*
(daily – weekly). If these measures do not work, seek specialist advice.

g ACE inhibitors in heart failure

at any time when using ACE inhibitors. Stop immediately and seek specialist
gonist should only occur on specialist advice (possible cross-sensitivity).

rt failure. This may be due to pulmonary oedema, which should be excluded if

at is likely to be caused by the ACE inhibitor, it is not always necessary to
ough is troublesome and/or interferes with sleep, consider substituting an

ted even in patients with significant renal impairment (creatinine over 200
in). However, these patients are more vulnerable. A destabilising event such as a
omiting), dehydration from overdiuresis or addition of nephrotoxic medications
re leading to hospital admission.
ent medical attention in these situations, and to withhold the ACE inhibitor
hemistry checked.
ssium is expected after commencing an ACE inhibitor due to a decrease in eGFR.
ic, no action is necessary, but blood chemistry must be checked several days after
ely thereafter to ensure kidney function is not worsening.
ceptable provided it stabilises within 2 weeks.
%, the patient should be reviewed urgently for clinical assessment of volume status
. Seek specialist advice regarding the safety of continuing therapy.
ed. With an increase to 5.0 – 5.5, review and reduce potassium
loride, spironolactone, eplerenone). If 5.6 – 5.9, cease all potassium supplements/
k immediate specialist advice.

g Beta-blockers in heart failure

Worsening symptoms/signs (eg. increasing dyspnoea, fatigue, oedema, weight gain)

- If congestion develops, increase the diuretic dose.
- If increasing the diuretic dose does not work, halve dose of beta-blocker and liaise with the heart failure service.
- If marked fatigue and/or bradycardia (see below), halve dose of beta-blocker (rarely necessary).
- Review patient as clinically appropriate (daily – weekly). Seek specialist advice if not improved.
- If serious deterioration, refer patient to an emergency department immediately.

Low heart rate

- If < 50 beats/min and worsening symptoms, halve dose of beta-blocker (rarely necessary).
- Review the need for other drugs that slow heart rate (e.g. digoxin, amiodarone) in consultation with specialist.
- Arrange ECG to exclude heart block.
- Review patient as clinically appropriate (daily – weekly). Seek specialist advice.
- If severe deterioration, stop beta-blocker and refer patient to an emergency department immediately.

Endorsed by Queensland Heart Failure Steering Committee October 2009

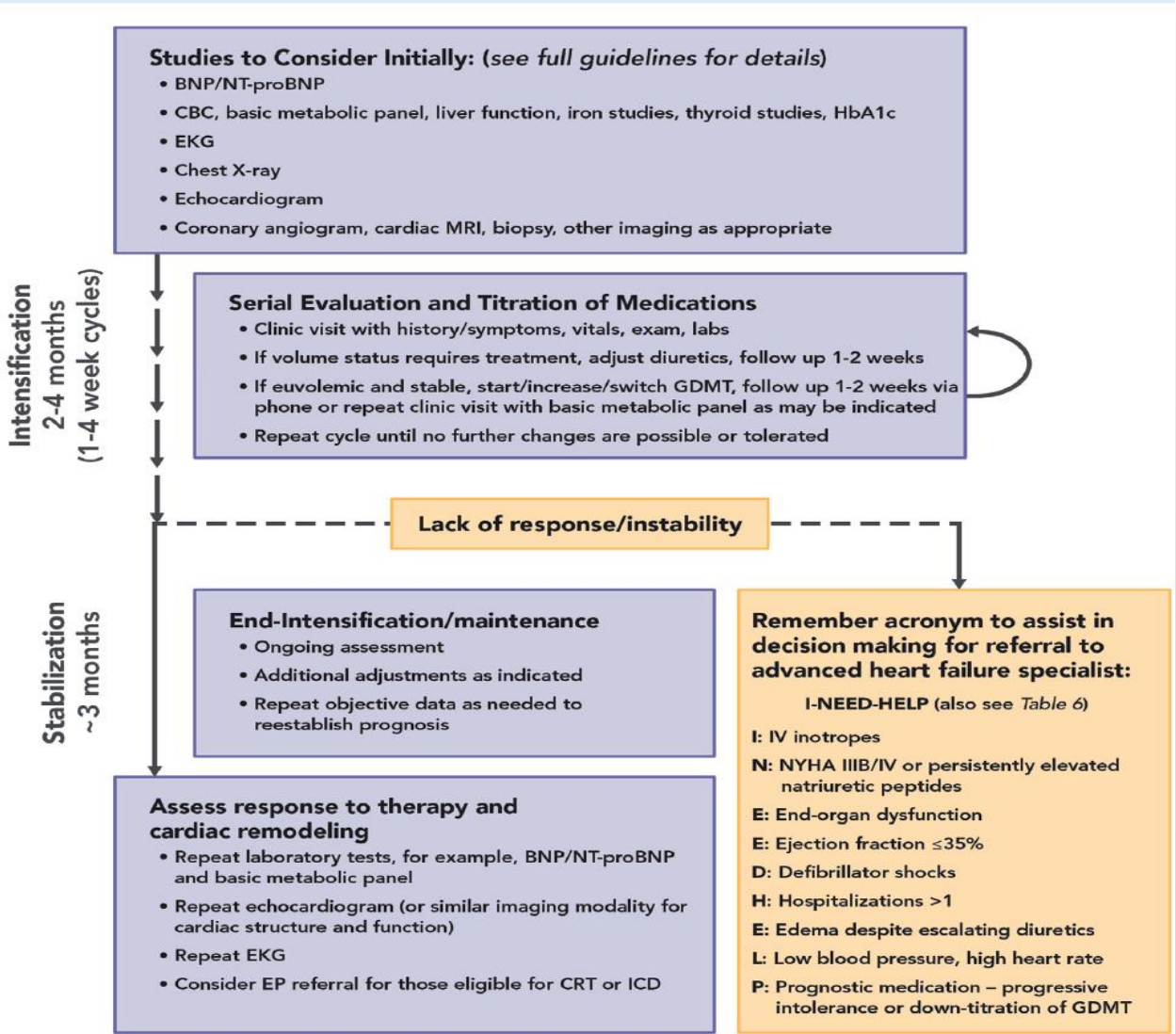
Phone: **Fax:**

I-NEED-HELP: TRIGGERS FOR HF PATIENT REFFERAL TO A SPECIALIST

1. New onset HF (regardless of EF) for evaluation of etiology, guideline-directed evaluation and management of recommended therapies, and assistance in disease management.
2. Chronic HF with high-risk features, such as development of 1 or more of the following risk factors:
A- Need for chronic IV inotropes
B- Persistent NYHA functional class III–IV symptoms of congestion or profound fatigue
C- Systolic blood pressure < 90 mm Hg or symptomatic hypotension
D- Creatinine >1.8 mg/dL or BUN > 43 mg/dL
E- Onset of atrial fibrillation or ventricular arrhythmias or repetitive ICD shocks
F- Two or more emergency department visits or hospitalizations for worsening HF in prior 12 months
G- Inability to tolerate optimally-dosed beta blockers and/or ACEI/ARB/ARNI and/or aldosterone antagonists
H- Clinical deterioration as indicated by worsening edema, rising biomarkers (BNP, NT-proBNP, others), worsened exercise testing, decompensated hemodynamics, or evidence of progressive remodeling on imaging
I- High mortality risk using validated risk model for further assessment and consideration of advanced therapies

3. To assist with management of GDMT, including replacement of ACEI or ARB therapy with ARNI for eligible patients, or to address comorbid conditions such as chronic renal disease or hyperkalemia, which may complicate treatment.
4. Persistently reduced LVEF < 35% despite GDMT for > 3 months for consideration of device therapy in those patients without prior placement of ICD or CRT, unless device therapy contraindicated.
5. Second opinion regarding etiology of HF; for example:
- Evaluation for potential ischemic etiology
- Suspected myocarditis
- Established or suspected specific cardiomyopathies, e.g., hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, Chagas disease, restrictive cardiomyopathy, cardiac sarcoidosis, amyloid, aortic stenosis.
- Valvular heart disease with or without HF symptoms
6. Annual review for patients with established advanced HF in which patients/caregivers and clinicians discuss current and potential therapies for both anticipated and unanticipated events, possible HF disease trajectory and prognosis, patient preferences, and advanced care planning.
7. Assess the possibility of participation in a clinical trial.

ΚΑΡΔΙΑΚΗ ΑΝΕΠΑΡΚΕΙΑ ΜΕ ΜΕΙΩΜΕΝΟ ΚΛΑΣΜΑ ΕΞΩΘΗΣΗΣ: Ο ΚΑΘΟΡΙΣΤΙΚΟΣ ΡΟΛΟΣ ΤΗΣ ΕΓΚΑΙΡΗΣ ΠΑΡΕΜΒΑΣΗΣ



Remember acronym to assist in decision making for referral to advanced heart failure specialist:

I-NEED-HELP (also see *Table 6*)

I: IV inotropes

N: NYHA IIIB/IV or persistently elevated natriuretic peptides

E: End-organ dysfunction

E: Ejection fraction ≤35%

D: Defibrillator shocks

H: Hospitalizations >1

E: Edema despite escalating diuretics

L: Low blood pressure, high heart rate

P: Prognostic medication – progressive intolerance or down-titration of GDMT

Final model	HR (95% CI)	Coefficient	P-value	Integer score
Age ≤ 65 years	Reference	–	–	–
Age 65–75 years	1.09 (0.91–1.30)	0.09	0.35	–
Age > 75 years	1.34 (1.12–1.60)	0.29	0.002	+1
HFH in the last year	1.44 (1.25–1.65)	0.36	< 0.001	+1
Peripheral oedema	1.31 (1.11–1.53)	0.26	0.001	+1
SBP ≤ 110 mmHg	1.28 (1.11–1.47)	0.25	0.001	+1
eGFR > 60 mL/min/1.73 m^2	Reference	–	–	–
eGFR 45–60 mL/min/1.73 m^2	1.19 (0.99–1.42)	0.17	0.058	–
eGFR < 45 mL/min/1.73 m^2	1.37 (1.14–1.65)	0.32	0.001	+1
Urea < 8 mmol/L	Reference	–	–	–
Urea 8–16 mmol/L	1.26 (1.04–1.54)	0.23	0.019	+1
Urea > 16 mmol/L	1.50 (1.20–1.86)	0.40	< 0.001	+1
NT-proBNP 2000–3000 pg/mL	Reference	–	–	–
NT-proBNP 3000–7000 pg/mL	2.04 (1.65–2.54)	0.71	< 0.001	+2
NT-proBNP > 7000 pg/mL	2.86 (2.26–3.62)	1.05	< 0.001	+3
Anaemia	1.32 (1.15–1.52)	0.28	< 0.001	+1
HDL-cholesterol < 1 mmol/L	1.20 (1.03–1.40)	0.19	0.017	+1
Sodium < 135 mmol/L	1.16 (0.97–1.38)	0.15	0.10	–
No beta-blocker at baseline	1.37 (1.16–1.61)	0.31	< 0.001	+1

ESC European Society of Cardiology
European Journal of Heart Failure (2019) 21, 112–120
doi:10.1002/ejhf.1323
RESEARCH ARTICLE

Heart failure in the outpatient versus inpatient setting: findings from the BIOSTAT-CHF study

Risk category	Total		Outpatients		Inpatients	
	n. pts/events (%)	Incidence rate (95% CI)	*n*. pts/events (%)	Incidence rate (95% CI)	*n*. pts/events (%)	Incidence rate (95% CI)
HFH or death						
Low (0–4)	1058/230 (22)	11.8 (10.4–13.4)	437/68 (16)	8.4 (6.6–10.6)	621/162 (26)	14.3 (12.3–16.7)
Intermediate (5–6)	746/338 (45)	34.3 (30.8–38.1)	233/100 (43)	29.8 (24.5–36.2)	513/238 (46)	36.6 (32.2–41.5)
High (7–15)	712/446 (63)	64.0 (58.3–70.2)	152/79 (52)	43.3 (34.7–54.0)	560/367 (66)	71.3 (64.4–79.0)
Death						
Low (0–4)	1058/131 (12)	6.3 (5.3–7.4)	437/44 (10)	5.2 (3.8–7.0)	621/87 (14)	7.0 (5.7–8.6)
Intermediate (5–6)	746/200 (27)	16.3 (14.2–18.7)	233/59 (25)	14.6 (11.3–18.9)	513/141 (27)	17.2 (14.5–20.2)
High (7–15)	712/326 (46)	35.1 (31.5–39.1)	152/52 (34)	23.2 (17.7–30.4)	560/274 (49)	38.9 (34.5–43.7)
HFH						
Low (0–4)	1058/142 (13)	7.3 (6.2–8.6)	437/39 (9)	4.8 (3.5–6.6)	621/103 (17)	9.1 (7.5–11.1)
Intermediate (5–6)	746/213 (29)	21.5 (18.8–24.6)	233/63 (27)	18.7 (14.6–23.9)	513/150 (29)	23.0 (19.6–27.0)
High (7–15)	712/253 (36)	36.1 (31.9–40.8)	152/50 (33)	27.2 (20.6–35.9)	560/203 (36)	39.2 (34.1–45.0)

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Heart failure in the outpatient versus inpatient setting: findings from the BIOSTAT-CHF study

-The five strongest predictors of mortality were more advanced age, higher blood urea nitrogen and N-terminal pro-B-type natriuretic peptide, lower haemoglobin, and failure to prescribe a beta-blocker.

-The five strongest predictors of hospitalization owing to HF were more advanced age, previous hospitalization owing to HF, presence of oedema, lower systolic blood pressure and lower estimated glomerular filtration rate.

-BUT the final decision cannot replace the clinical expertise and the information obtained from the complexicity of the whole history of any single patient. (scores support and NOT replace clinical judgement)

TAKE HOME MESSAGES

1. More **education** is needed for both clinicians and patients

2. Maximum recommended or tolerated **doses** should be described to avoid HF deterioration

START LOW, AIM HIGH AND STAY HIGH

3. Follow up is important, can be provided by **nursing**

   - Does not require office visit

   -Frequent lab monitoring for creatinine and potassium is needed

   -Phone follow-up may be possible

   -Blood pressure and weight monitoring

4. Heart failure teams and **clinics** must be established.

5. We need a lot of **different specialists** for each one “heart failure patient”

Ευχαριστώ θερμά