

De ESC Hartfalen Richtlijnen: Actualiteit en praktijk

Hartfalen, Guidelines en impact nieuwe trials

Symposium tijdens NVVC Voorjaarscongres, Rotterdam, 12 april 2019

Dr. Gerard Linssen, cardioloog
ZGT, Almelo en Hengelo
g.linssen@zgt.nl

Disclosure belangen Dr. G.C.M. Linssen, cardioloog Ziekenhuisgroep Twente (ZGT) Almelo en Hengelo

(potentiële) belangenverstrengeling	
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
<ul style="list-style-type: none">• Sponsoring of onderzoeksgeld• Adviesraden en sprekersvergoedingen• Aandeelhouder• Andere relatie	<ul style="list-style-type: none">• WCN – contracten Nationaal Coördinator PARAGON-HF en PARALLAX-HF onderzoeken• Novartis Pharma, Roche Diagnostics, Servier, Vifor Pharma Ned.• Geen• Geen

De ESC Hartfalen Richtlijnen: Actualiteit en praktijk

- **Introductie en rationale**
- **ESC medicatie richtlijnen in Nederland 2001 – 2015: Pharmo Data**
- **ESC 2012 richtlijn in Nederlandse praktijk: CHECK-HF register**
- **2016: introductie nieuwe medicatie (ARNi)**
- **Barrières en oplossingen...**

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How guidelines evolve from bench to bedside...

Burden of disease: heart failure symptoms, disability, worse outcome

Pathophysiology and associated therapeutic interventions

From phase 1 to phase 3, Randomized clinical trials

Established, evidence-based medication / intervention

Guideline-directed medical therapies (GDMT): clinical roadmaps

Adoption and Implementation in family / clinical practice

Real-world, observational studies and registries

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ESC Guidelines: medication profiles after HF-hospitalization in 22,476 Dutch patients: 2001 - 2015

Dutch PHARMO Database Network:

- Diagnosis of HF at hospital discharge (after a first HF admission)
- Focus on ACEI/ARB, BB, MRA and diuretics
- Drug dispenses from outpatient pharmacies (representing 3.8 million Dutch residents)
- WHO – ATC classification system
- Linked Hospitalization Database

Kruik-Kollöffel WJ, Linssen GCM, Kruik HJ, Movig KLL, Heintjes EM, van der Palen J.
Heart Fail Rev. 2019 (online 8 March).



UNIVERSITEIT TWENTE.

ESC Guidelines: medication profiles after HF-hospitalization in 22,476 Dutch patients: 2001 - 2015

Dutch PHARMO Database Network:

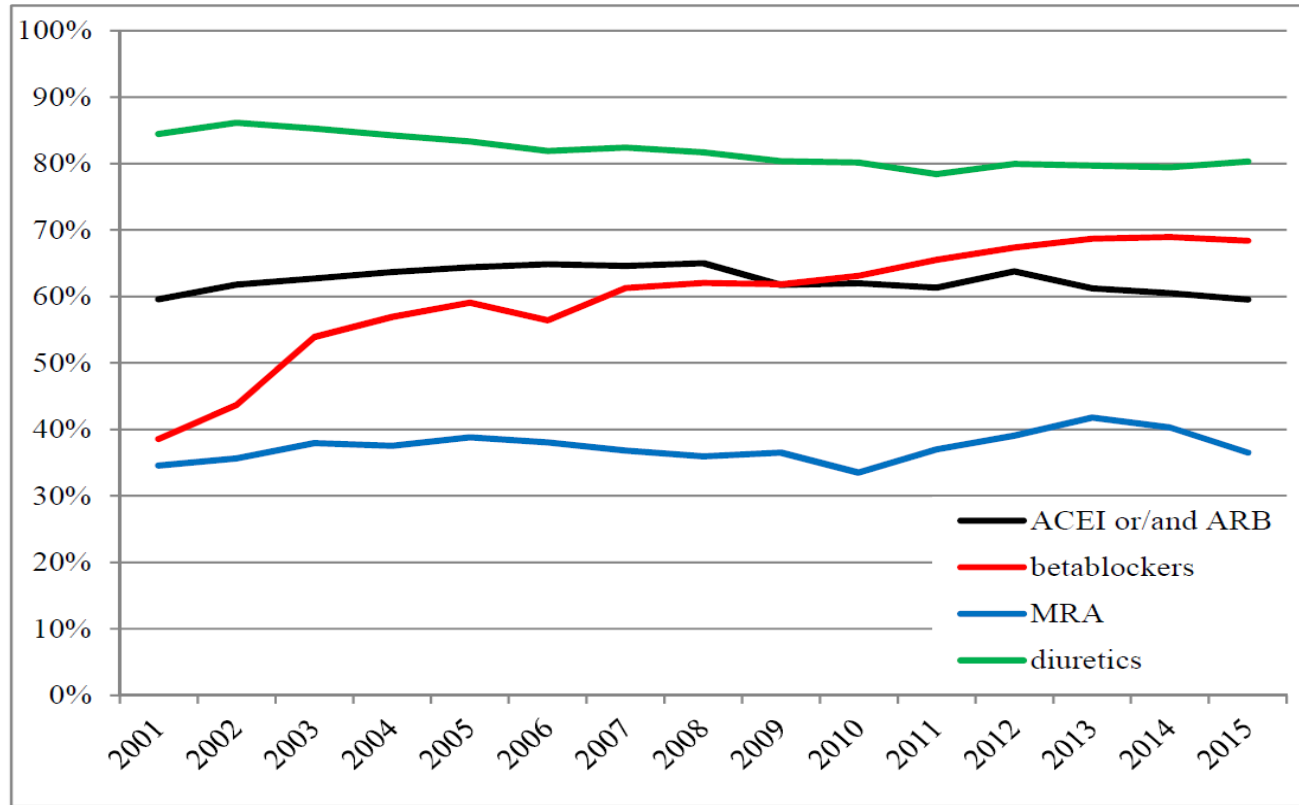
- Patients-study year (SD): 1498 (455)
- Mean age (SD) 76.8 years (10.9)
- Females: 50.9 %
- Median length of hospital stay: (IQR): 6 days (3.0; 11.0)
- Prescribed HF, CV and non-CV medication, mean (SD): 7,6 drugs (3.6)
- No data available on HF etiology, NYHA class, LV function
- Comorbidities by proxy methods (medication profiles)

Kruik-Kollöffel WJ, Linssen GCM, Kruik HJ, Movig KLL, Heintjes EM, van der Palen J.
Heart Fail Rev 2019 (online 8 March).

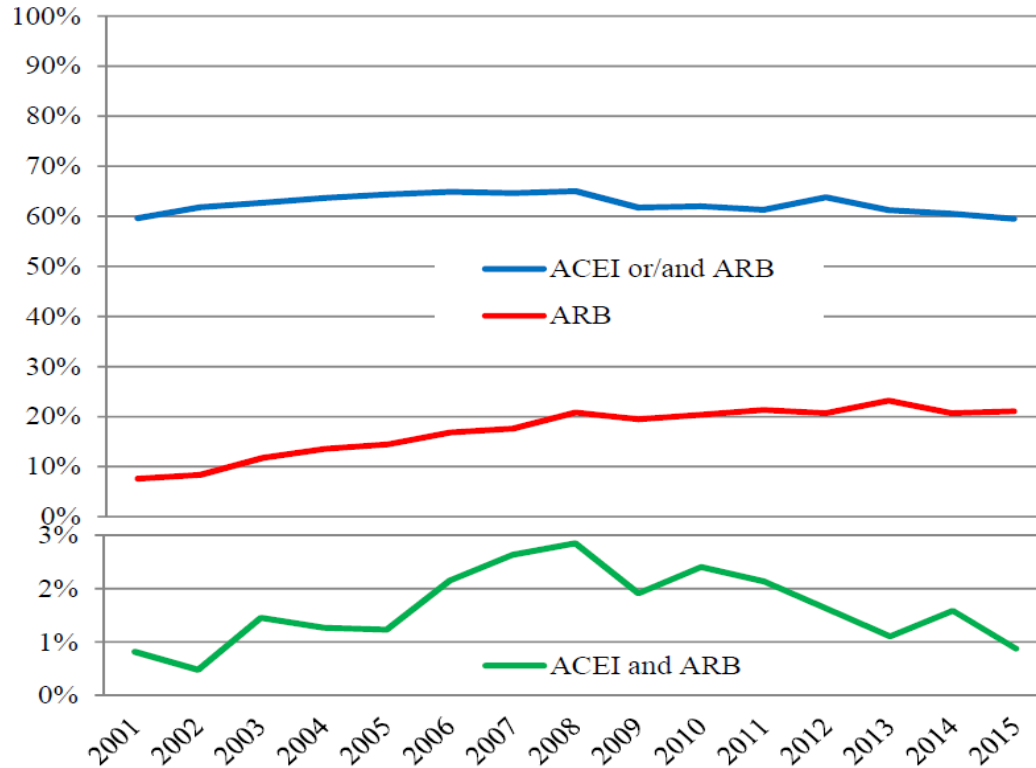


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Prescription of heart failure medication in 22,476 Dutch patients: 2001 - 2015



Prescription of ACEI and/or ARB in 22,476 Dutch HF patients



CHECK-HF: Dutch registry of chronic HF patients

- Chronisch Hartfalen ESC-richtlijn Cardiologische praktijk Kwaliteitsproject HartFalen
- 2013 - 2016, diagnosed HF
- Based on 2012 ESC Guidelines
- 34 participating Dutch centers
- 10,910 patients
- 96% at HF outpatient clinic
- Unselected patients



Brugts JJ, Linssen GCM, Hoes AW, et al. Neth Heart J. 2018;26:272-279.

Brunner-La Rocca HP, Linssen GC, Smeele FJ, et al. J Am Coll Cardiol HF. 2019;7:13–21.

CHECK-HF: Dutch registry of chronic HF patients

N = 10,910 patients

- Mean age 73 years (SD 12)
- 40% Females
- 47% Ischemic HF
- 21% HFpEF
- 81% NYHA 2 en 3

Comorbidities:

- 30% Diabetes
- 43% Hypertension
- 19% COPD
- 58% Renal insufficiency (or eGFR < 60)

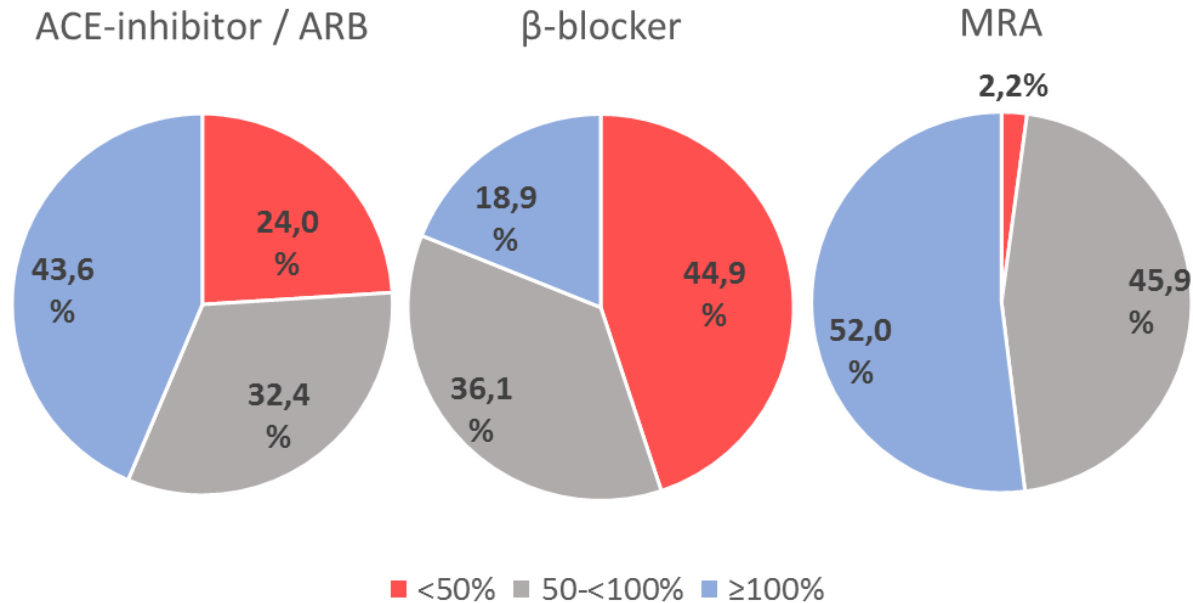


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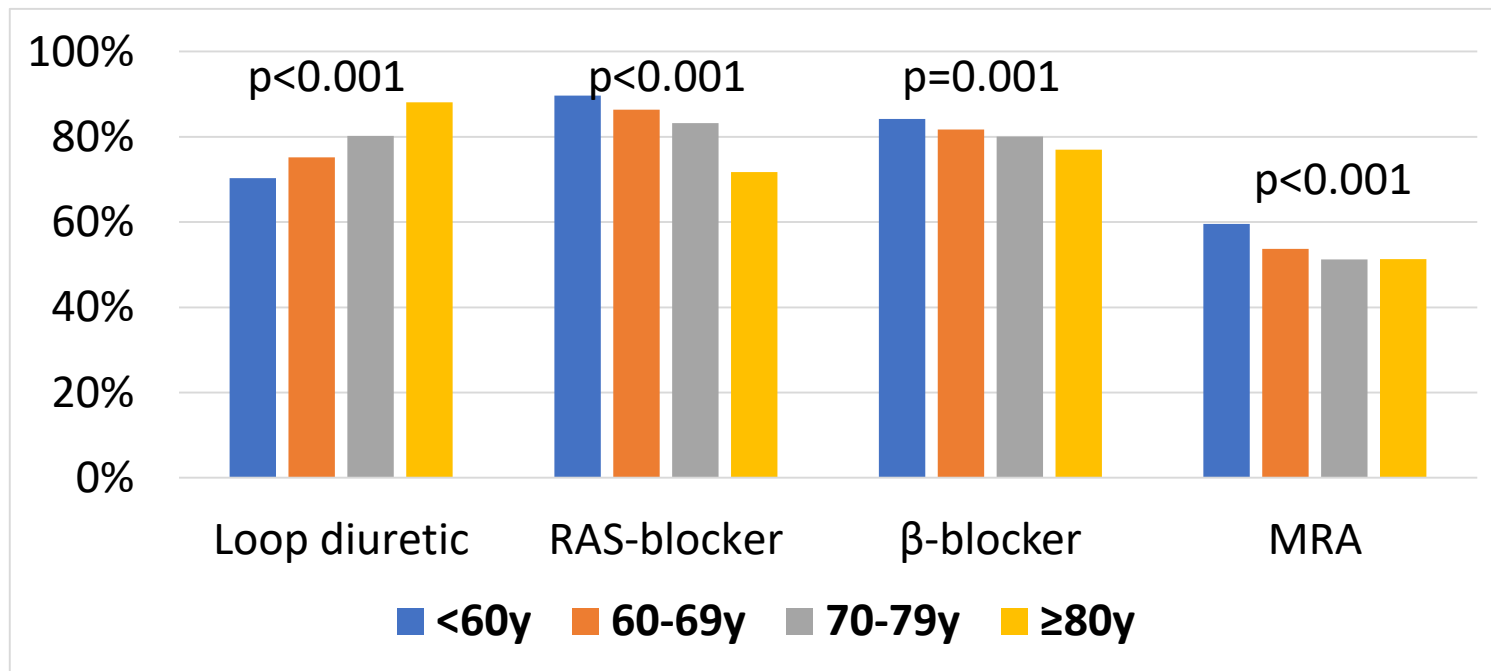
CHECK-HF: Dutch registry of chronic HF patients

Target doses of medication in HFrEF (<40%), n = 5,701 patients



CHECK-HF: Dutch registry of chronic HF patients

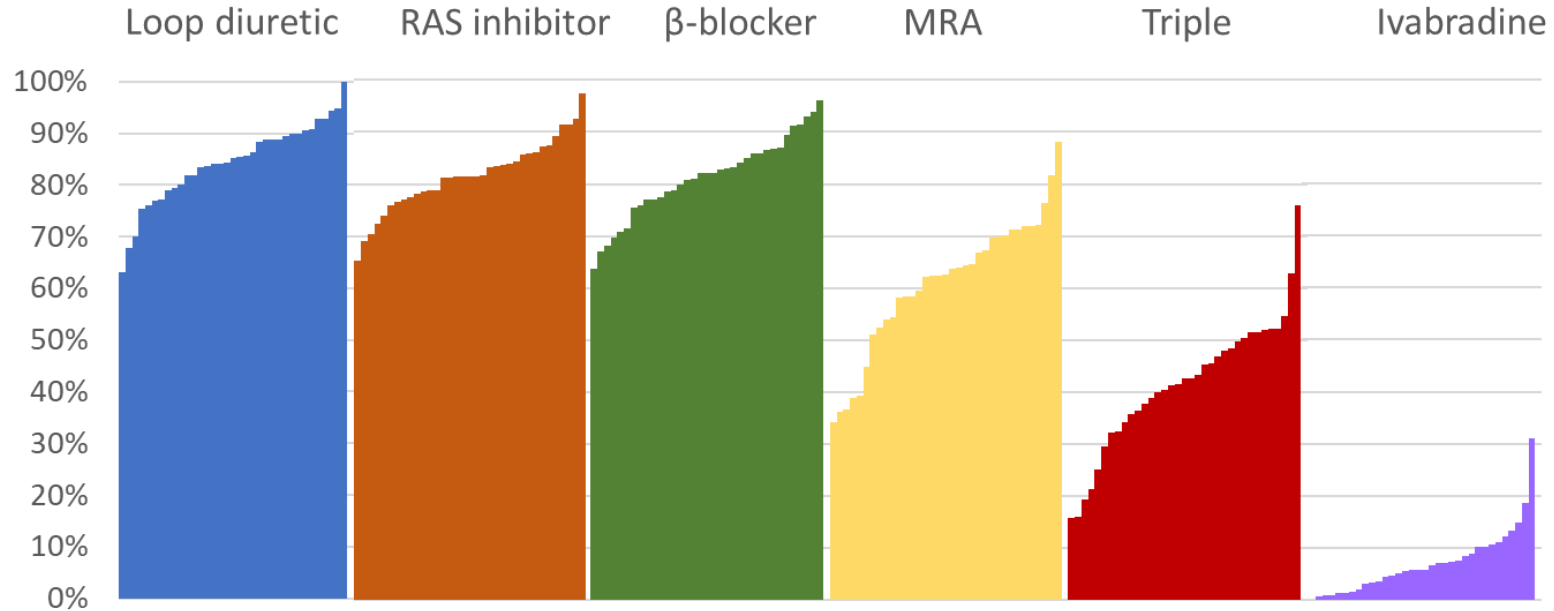
Prescription Rate of Medication in Different Age Groups in HFrEF Patients, n = 5,701



Brunner-La Rocca HP, Linssen GC, Smeele FJ, et al. J Am Coll Cardiol HF.2019;7:13–21.

CHECK-HF: Dutch registry of chronic HF patients

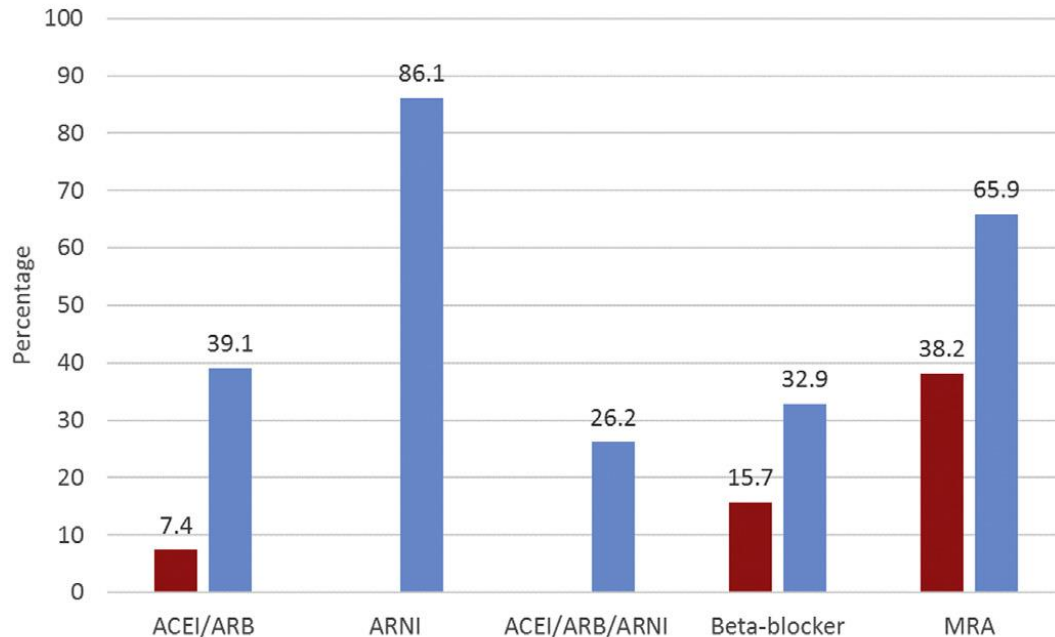
Differences in treatment between 34 Dutch centres in HFrEF Patients, n = 5,701



Brunner-La Rocca HP, Linssen GC, Smeele FJ, et al. J Am Coll Cardiol HF.2019;7:13–21.

CHECK-HF (n=5,701) vs CHAMP-HF (U.S.; n=3,518) HFrEF

Percentage of Patients Not Treated and Without Contraindications



Brunner-La Rocca HP, Linssen GC, Smeele FJ, et al. J Am Coll Cardiol HF.2019;7:13–21 and Editorial by Greene & Felker.
Greene SJ, Butler J, Albert NM, et al. J Am Coll Cardiol. 2018;72:351-366.

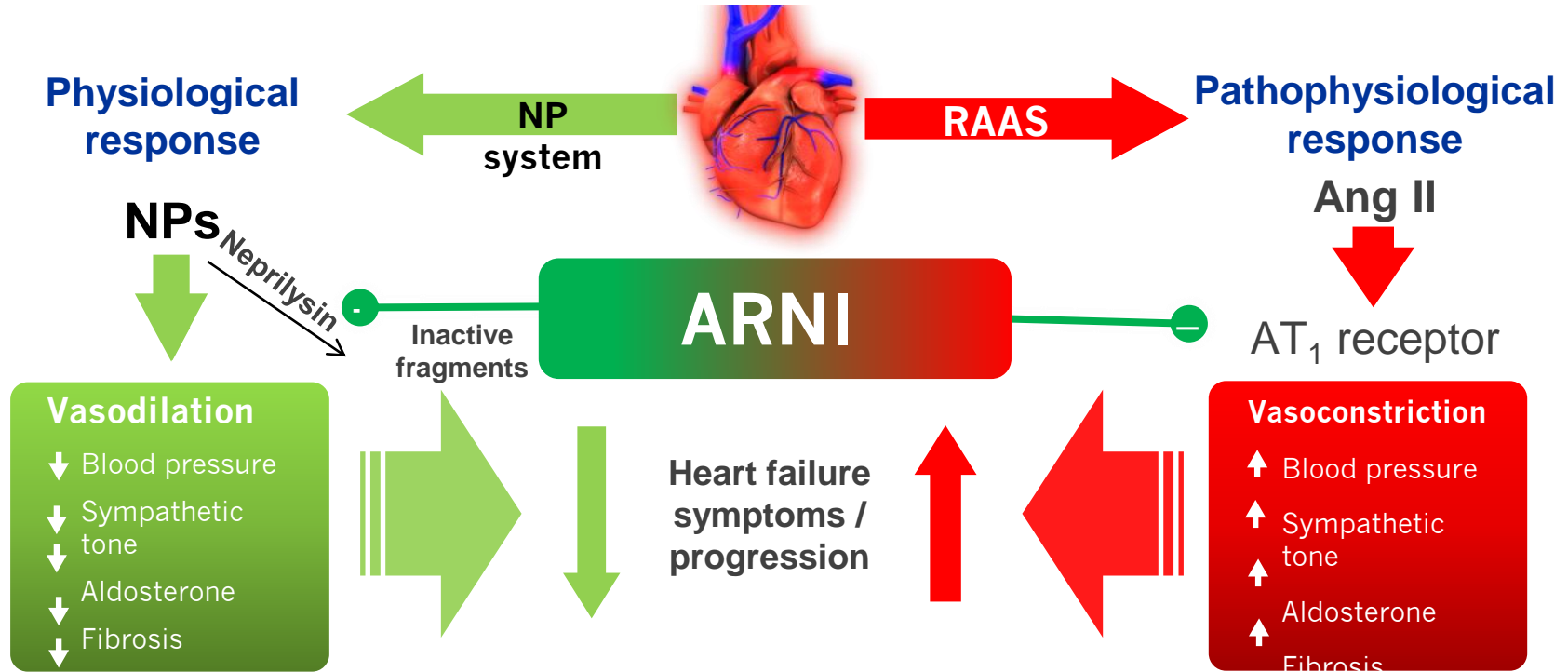
2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

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

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

Authors/Task Force Members: Piotr Ponikowski* (Chairperson) (Poland), Adriaan A. Voors* (Co-Chairperson) (The Netherlands), Stefan D. Anker (Germany), Héctor Bueno (Spain), John G. F. Cleland (UK), Andrew J. S. Coats (UK), Volkmar Falk (Germany), José Ramón González-Juanatey (Spain), Veli-Pekka Harjola (Finland), Ewa A. Jankowska (Poland), Mariell Jessup (USA), Cecilia Linde (Sweden), Petros Nihoyannopoulos (UK), John T. Parissis (Greece), Burkert Pieske (Germany), Jillian P. Riley (UK), Giuseppe M. C. Rosano (UK/Italy), Luis M. Ruilope (Spain), Frank Ruschitzka (Switzerland), Frans H. Rutten (The Netherlands), Peter van der Meer (The Netherlands)

Angiotensin Receptor + Neprilysin Inhibition (ARNI) has the potential to restore the natural balance of the RAS and NPs



#In-vitro evidence

1) Ferro et al. *Circulation* 1998;97:2323–30; 2) Levin et al. *N Engl J Med* 1998;339:321–8; 3) Nathisuwan & Talbert. *Pharmacotherapy* 2002;22:27–42; 4) Schrier et al. *Kidney Int* 2000;57:1418–25; 5) Schrier & Abraham. *N Engl J Med* 1999;341:577–85; 6) Stephenson et al. *Biochem J*. 1987;241:237–47

Pharmacological treatments indicated in patients with symptomatic (NYHA Class II-IV) HFrEF

Recommendations	Class	Level
An ACEi is recommended, in addition to a beta blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death	I	A
A beta blocker is recommended, in addition an ACEi, for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death	I	A
An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACEi and a beta-blocker, to reduce the risk of HF hospitalization and death	I	A
Sacubitril/valsartan is recommended as a replacement for an ACEi to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACEi, a beta-blocker and an MRA*	I	B

Sacubitril/valsartan in management of ventricular arrhythmias

Recommendations	Class	Level
Treatment with beta-blocker, MRA and sacubitril/valsartan reduces the risk of sudden death and is recommended for patients with HFrEF and ventricular arrhythmias (as for other patients) (Section 10.2).	I	A

ARNI (angiotensine-receptor-neprilysine-inhibitor) LCZ696 bij HFrEF patiënten die voldoen aan de criteria van het klinische onderzoek: **ambulant stabiel NYHA 2-4, LVEF \leq 35%, eGFR \geq 30 ml/min/1,73 m², Kalium \leq 5,4 mmol/l, EN:**

1. Verhoogde BNP \geq 150 pg/mL (**45 pmol/L**) of NT-proBNP \geq 600 pg/mL (**70 pmol/L**)

Of: ingeval van ziekenhuisopname voor HF in voorgaande 12 maanden, dan: BNP \geq 100 pg/mL (30 pmol/L) of **NT-proBNP \geq 400 pg/mL (50 pmol/L)**

2. **En:** verdraagt enalapril tweemaal daags 10 mg (of equivalente ACE-I/ARB).

“LCZ696 is cost effective compared with enalapril under the former and current Dutch guidelines....

The incremental cost-effectiveness ratio obtained was €17,600 per quality-adjusted life-year (QALY) gained.....”

Corro Ramos I, Versteegh MM, de Boer RA, Koenders JMA, Linssen GCM, Meeder JG, Rutten-van Mölken MPMH



2017; 20 (Dec.): 1260-9

What proportion of patients with chronic heart failure are eligible for sacubitril–valsartan?

Pierpaolo Pellicori^{1*}, Alessia Urbinati¹, Parin Shah¹, Alexandra MacNamara¹, Syed Kazmi¹, Riet Dierckx¹, Jufen Zhang¹, John G.F. Cleland^{1,2}, and Andrew L. Clark¹

ARNi in the EU



- 4 million HFrEF patients

Milton Packer. Eur J Heart Fail. 2017;19:779-781

ARNi in the EU



- 4 million HFrEF patients
- < 200.000 pts fulfill ESC 2016 Guidelines – ARNi

Milton Packer. Eur J Heart Fail. 2017;19:779-781

ARNi in the EU



- 4 million HFrEF patients
- < 200.000 pts fulfill ESC 2016 Guidelines – ARNi
- 3 million pts comply with FDA, EMA and US guidelines

Milton Packer. Eur J Heart Fail. 2017;19:779-781

ARNi in the EU



- 4 million HFrEF patients
- < 200.000 pts fulfill ESC 2016 Guidelines – ARNi
- 3 million pts comply with FDA, EMA and US guidelines
- *Authors of the Guidelines, if they have HF, they would personally take ARNi, outside the confines of the Guidelines, but consistent with the recommendations of government agencies.*

Milton Packer. Eur J Heart Fail. 2017;19:779-781

EDITORIAL COMMENT

The Urgency of Doing

Addressing Gaps in Use of Evidence-Based Medical Therapy for Heart Failure*

Stephen J. Greene, MD,^{a,b} G. Michael Felker, MD, MHS^{a,b}



Barriers for guideline-adherence

- “Risk-treatment paradox”: HF patients with greatest need are less likely to receive appropriate therapy
- Therapeutic inertia
 - Clinician
 - Patient
 - Systems



Jefferies JL and Ibrahim NE. **Are guidelines merely suggestions?** J Am Coll Cardiol. 2018;72:367-9.

How to improve use and dosing of GDMT in heart failure

- Awareness of suboptimal therapy, side-effects, comorbidities
- Heart failure specialists, allied professionals, implementation tools
- Sense of urgency in bringing new modalities to practice
- Education by professional societies and in regional networks
- Patient empowerment, coaching, self management
- Technological innovation (monitoring, motivational tools)

GDMT: guideline-directed medical therapies

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Professional education in NL



nvvconnect
Toolkit HF Educatie



Nationale Hartfalendag
Zeist, vrijdag 27 sept. 2019



Dank voor uw aandacht

Vragen en discussie

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