Heart Failure Hospitalization: Key Moment to OPTIMIZE Care

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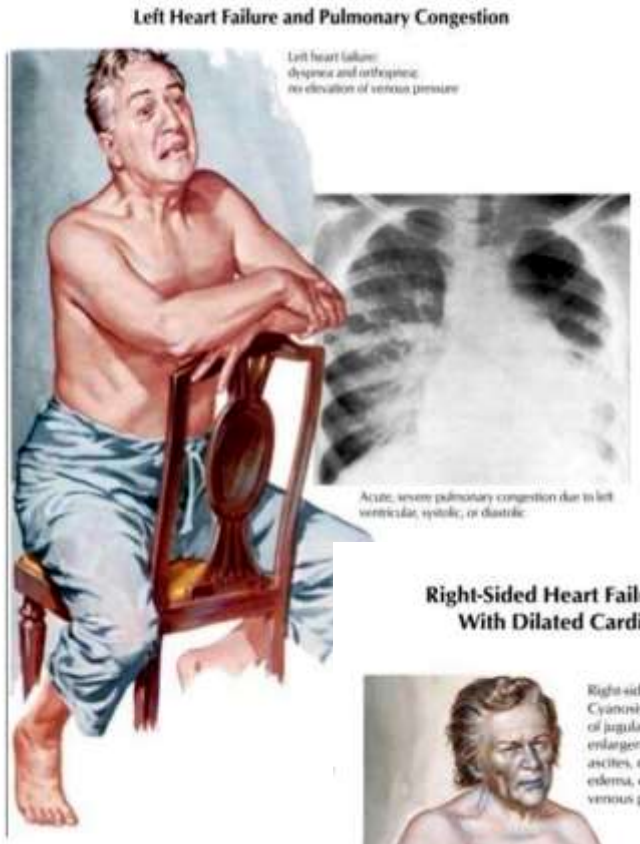
Definitions

- Heart Failure: A complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood[1]
- A clinical syndrome characterized by typical symptoms that may be accompanied by signs caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress[2]

1. **2013 ACCF/AHA Guideline for the Management of Heart Failure**
2. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure



Heart Failure

Unmet needs

- **Poor survival**
- **Poor quality of life if symptoms not controlled**
- **High risk of (re)hospitalisation**
- **Delivering comprehensive services to all**

The Burden of Heart Failure Hospitalization

Overview in figures…

- Heart failure is a life-threatening disease estimated to be present in 1% to 2% of the general population.
- The prevalence of the disease is tending to increase due to aging of the population and improved survival in many diseases. This global pandemic is known to have a survival rate that is worse than that of some cancers.

26 million

Worldwide number of patients affected by heart failure

74%

Heart failure patient suffering from at least 1 comorbidity: more likely to worsen the patient's overall health status

1. McMurray J et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2012;14(8):803-869. 2. Ambrosy PA et al. The Global Health and Economic Burden of Hospitalizations for Heart Failure. Lessons Learned From Hospitalized Heart Failure Registries. J Am Coll Cardiol. 2014;63:1123–1133. 3. Butler J, Braunwald E, Gheorghiade M. Recognizing worsening chronic heart failure as an entity and an end point in clinical trials. JAMA. 2014;312(8):789-790. 4. van Deursen VM et al. Co-morbidities in patients with heart failure: an analysis of the European Heart Failure Pilot Survey. Eur J Heart Fail. 2014;16:103-111.

The Burden of Heart Failure Hospitalization

from the society's perspective …

Increase in health care expenses

3 X

higher

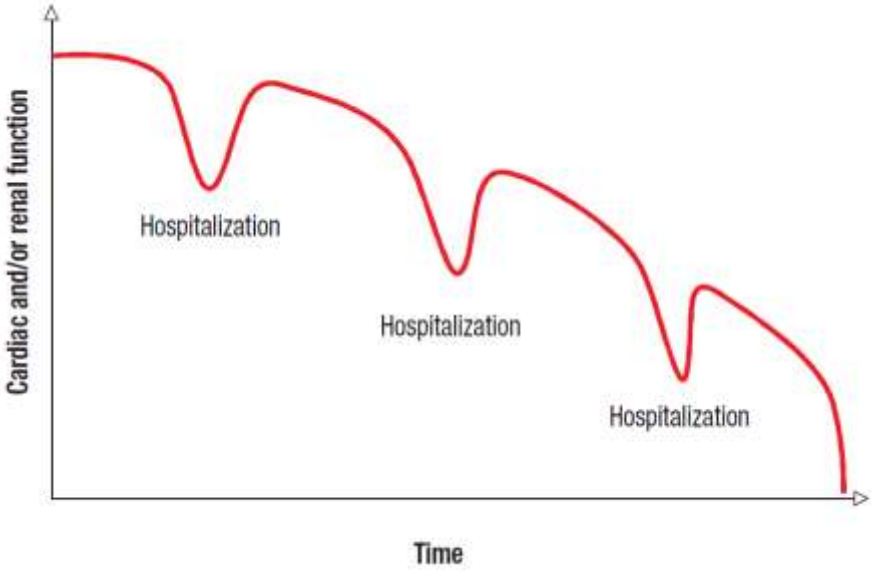
by *2030*

The 2030 projected cost estimates of treating patients with heart failure will be 3 fold higher than in 2010, mainly due to the aging of the population

PATIENT'S JOURNEY

Why is Hospitalization So Important?

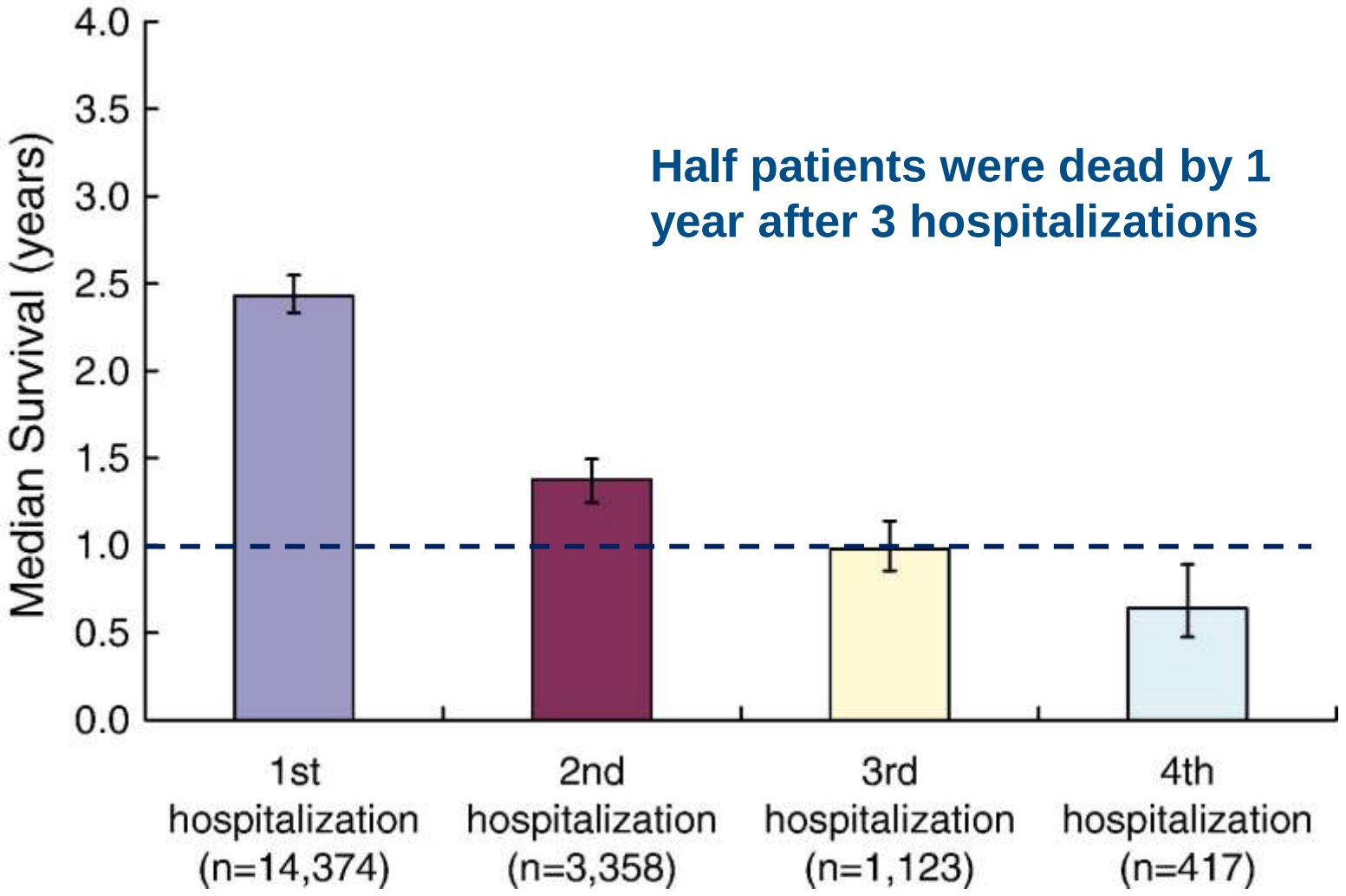
Cumulative adverse consequence of hospitalizations



With each hospitalization, there is likely **myocardial and renal damage** which contributes to progressive left ventricular or renal dysfunction, leading to an inevitable downward spiral.[1]

1. Gheorghiade M et al. *Am J Cardiol*. 2005;96:11-17.

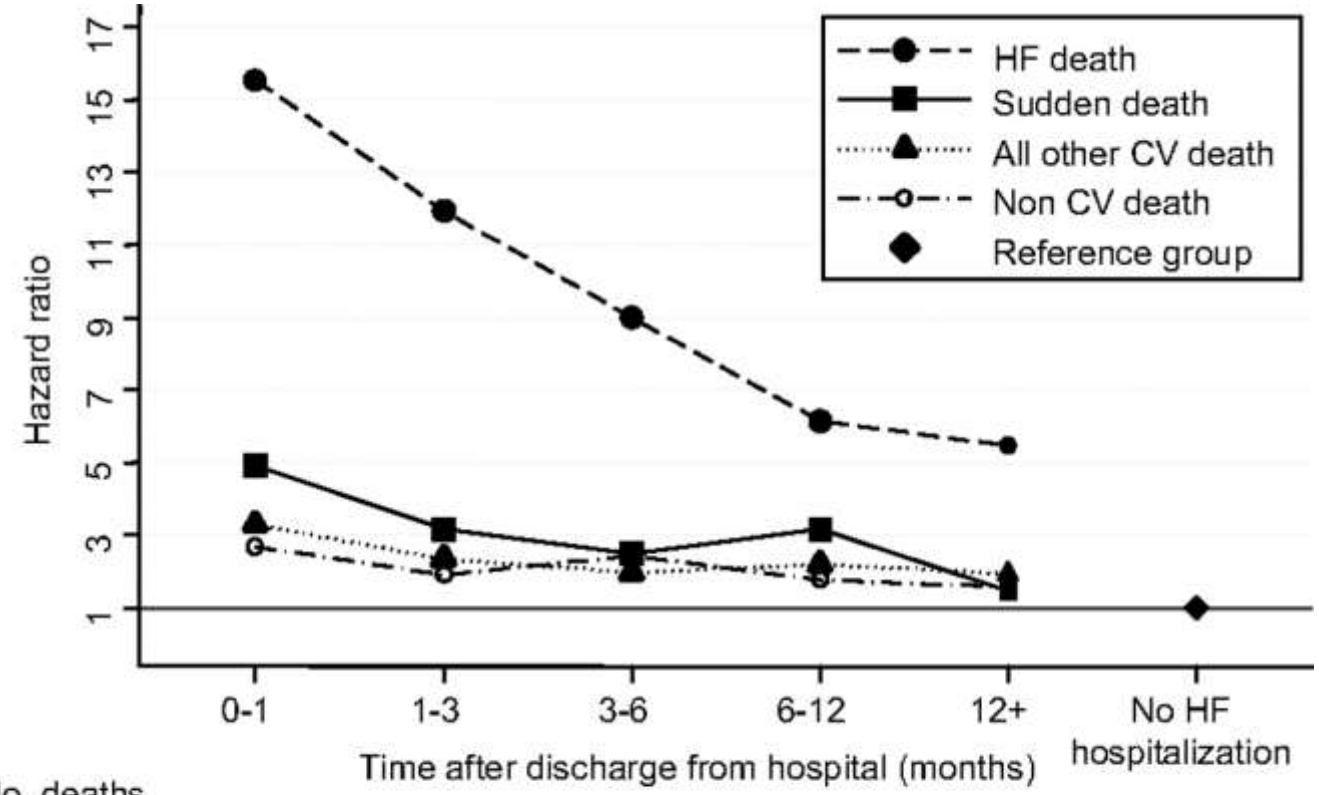
Strong Predictor for Increased Mortality



Setoguchi S, et al. *Am Heart J*. 2007;154:260-266.

Timing: Mortality After a First HF Hospitalization*

CHARM trial



No. deaths						
HF	33	44	44	45	88	209
Sudden	20	22	24	47	47	481
Other CV	7	9	11	20	38	262
Non CV	6	8	15	18	40	281

* Adjusted for other baseline predictors of all-cause mortality

Solomon SD, et al. *Circulation*.2007;116:1482-1487.

PATIENT'S JOURNEY

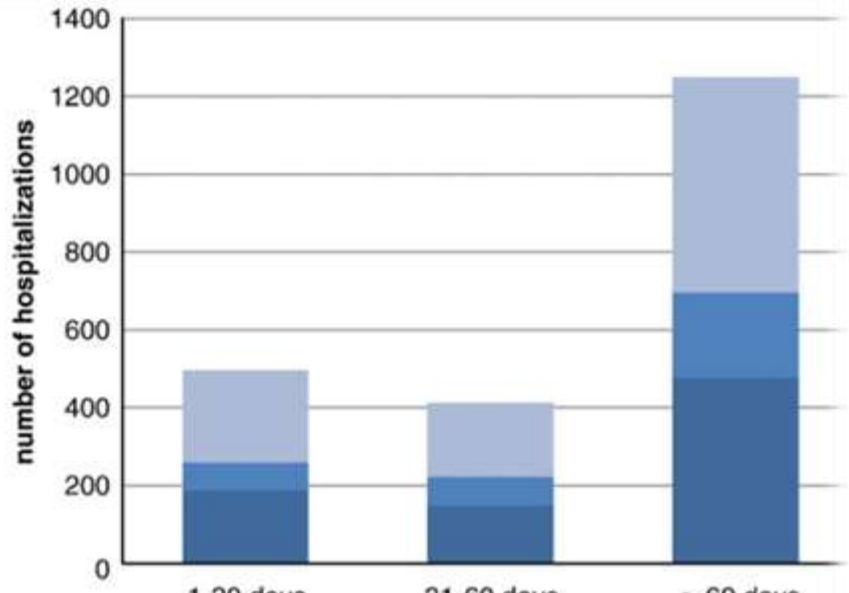
Rehospitalization is Particularly High in The Early Phase After Hospitalization:

1 out of 2 patients rehospitalized within 2 months

EVEREST

Timing of major causes of first hospitalization[1]

[2159 patients]



	1-30 days	31-60 days	> 60 days
HF hospitalization	237 (24.1%)	191 (19.5%)	554 (56.4%)
Non-HF CV hospitalization	71 (19.5%)	74 (20.3%)	219 (60.2%)
Non-CV hospitalization	188 (23.1%)	148 (18.2%)	477 (58.7%)
Total	496 (23.0%)	413 (19.1%)	1250 (57.9%)

1. O'Connor CM et al. Causes of death and rehospitalization in patients hospitalized with worsening heart failure and reduce left ventricular ejection fraction: results from efficacy of vasopressin antagonism in heart failure outcome stuy with tolvaptan (EVEREST) program. *Am Heart J.* 2010;159:841-849.e1.

Hospitalization is The Key Moment to Optimize Treatment

Recognizing Hospitalized Heart Failure as an Entity and Developing New Therapies to Improve Outcomes

Academics', Clinicians', Industry's, Regulators', and Payers' Perspectives

Mihai Gheorghiade, MD[a,*], Ami N. Shah, MD[a], Muthiah Vaduganathan, MD, MPH[b], Javed Butler, MD, MPH[c], Robert O. Bonow, MD, MS[b], Giuseppe M.C. Rosano, MD, PhD[d], Scott Taylor, RPh, MBA[e], Stuart Kupfer, MD[f], Frank Misselwitz, MD, PhD[g], Arjun Sharma, MD[h], Gregg C. Fonarow, MD[i]

KEYWORDS

• Hospitalized heart failure • Heart failure • Postdischarge mortality

KEY POINTS

- Hospitalized heart failure (HHF) is associated with unacceptably high postdischarge mortality and rehospitalization rates.
- This heterogeneous group of patients, however, is still treated with standard, homogenous therapies that are not preventing their rapid deterioration.
- The costs associated with HHF have added demands from society, government, and payers to improve outcomes.
- It is important to consider that once HHF patients are stabilized by discharge, the majority of them should be considered to be in a chronic heart failure state at a significantly high risk for adverse outcomes. Delaying initiation of potentially effective therapies for weeks to months post discharge risks unabated high risk for adverse events in the meantime. Initiating therapies in patients who are stabilized in the hospital and continued long term provides a potent option to improve long-term clinical outcomes.
- With coordinated and committed efforts in the development of new therapies, improvements may be seen in outcomes for patients with HHF.
- This article summarizes concepts in developing therapies for HHF discussed during a multidisciplinary panel at the Heart Failure Society of America's Annual Scientific Meeting, September 2012.

Initiating therapies in patients who are **stabilized in the hospital** and continued long term provides a potent option **to improve long-term clinical outcomes.**[1]

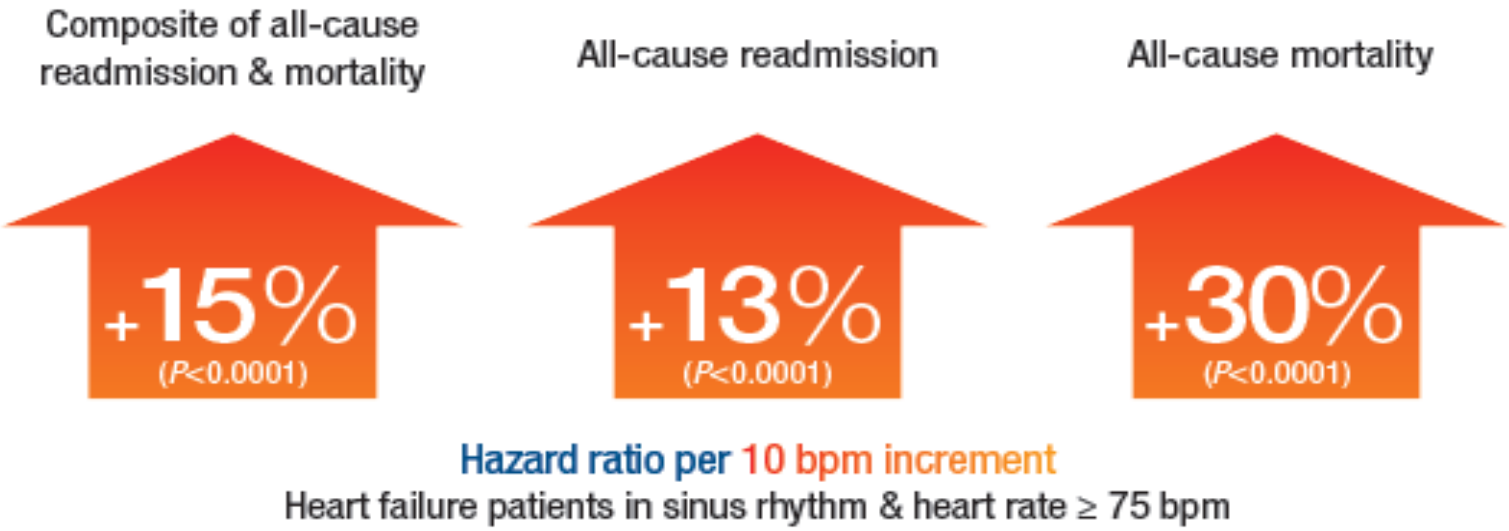
Delaying initiation of potentially effective therapies for weeks to months post discharge risks unabated **high risk for adverse events in the meantime.**[1]

1. Gheorghiade M et al. Recognizing hospitalized heart failure as an entity and developing new therapies to improve outcomes. Academics', clinicians', industry's, regulators', and payers' perspectives. *Heart Failure Clin.* 2013:9;285-290.

Heart Failure Hospitalization: a key opportunity

in view of discharge phase …

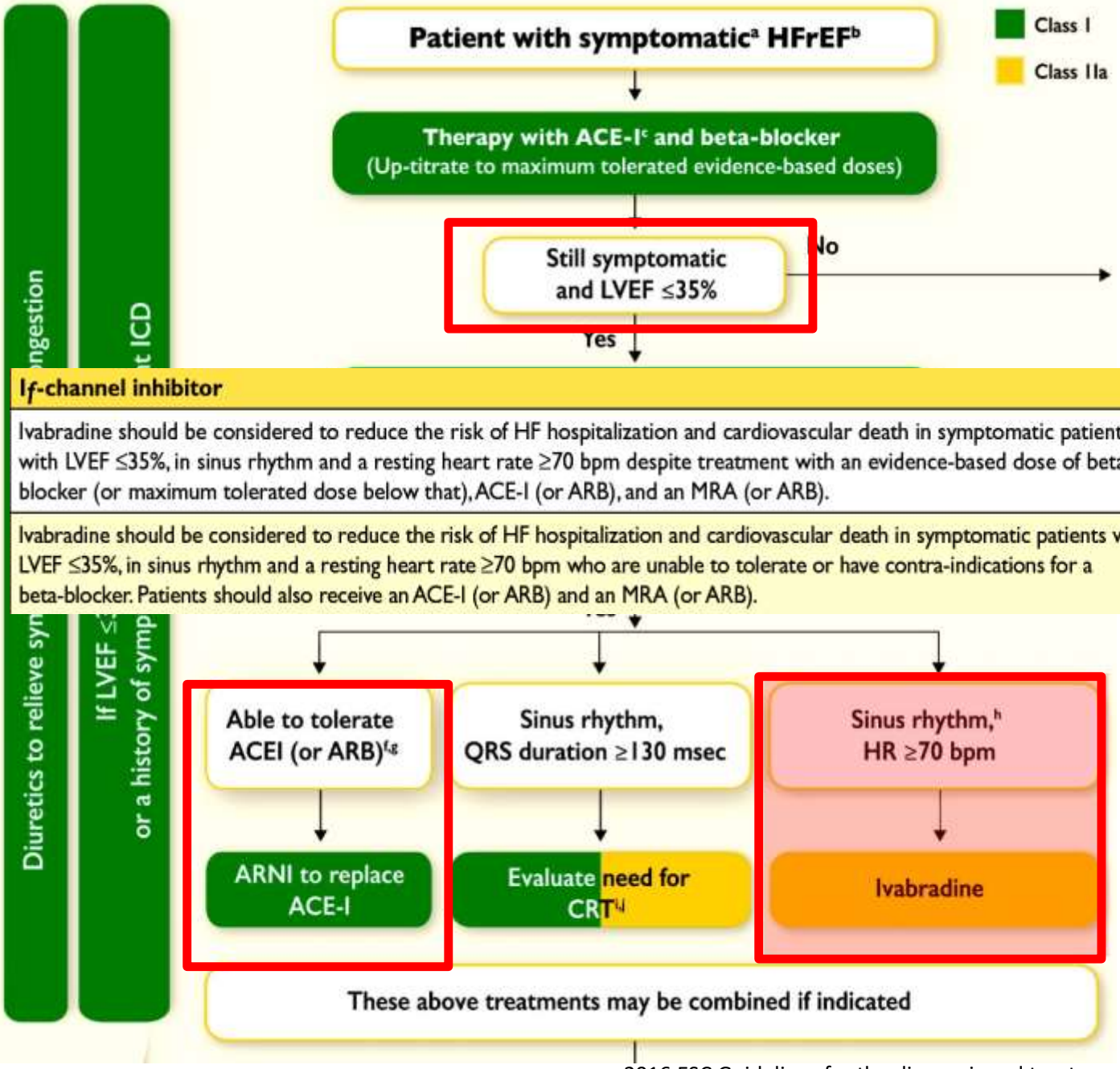
Elevated discharge heart rate increases the risk of adverse 30-day outcomes.



"By targeting heart rate as a potentially modifiable risk factor in the progression of HF, the SHIFT trial has implicated heart rate in the causal pathway of HF progression

1. Laskey WK et al. Heart rate at hospital discharge in patients with heart failure is associated with mortality and rehospitalization. J Am Heart Assoc. 2015;4:e001626. 2. Habal MV et al. Association of heart rate at hospital discharge with mortality and hospitalizations in patients with heart failure. Circ Heart Fail. 2014;7(1):12-20

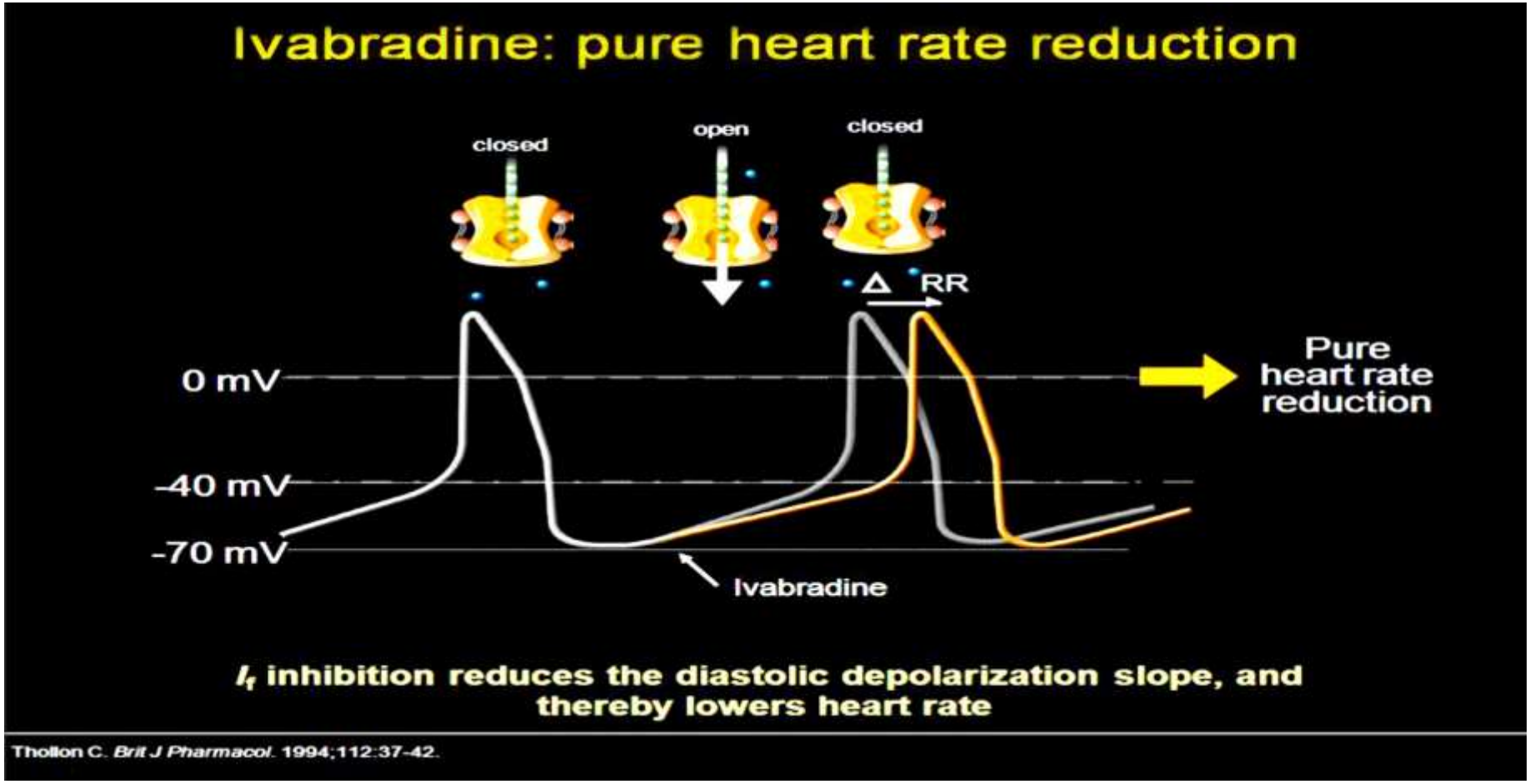
Therapeutic algorithm for a patient with symptomatic HFrEF



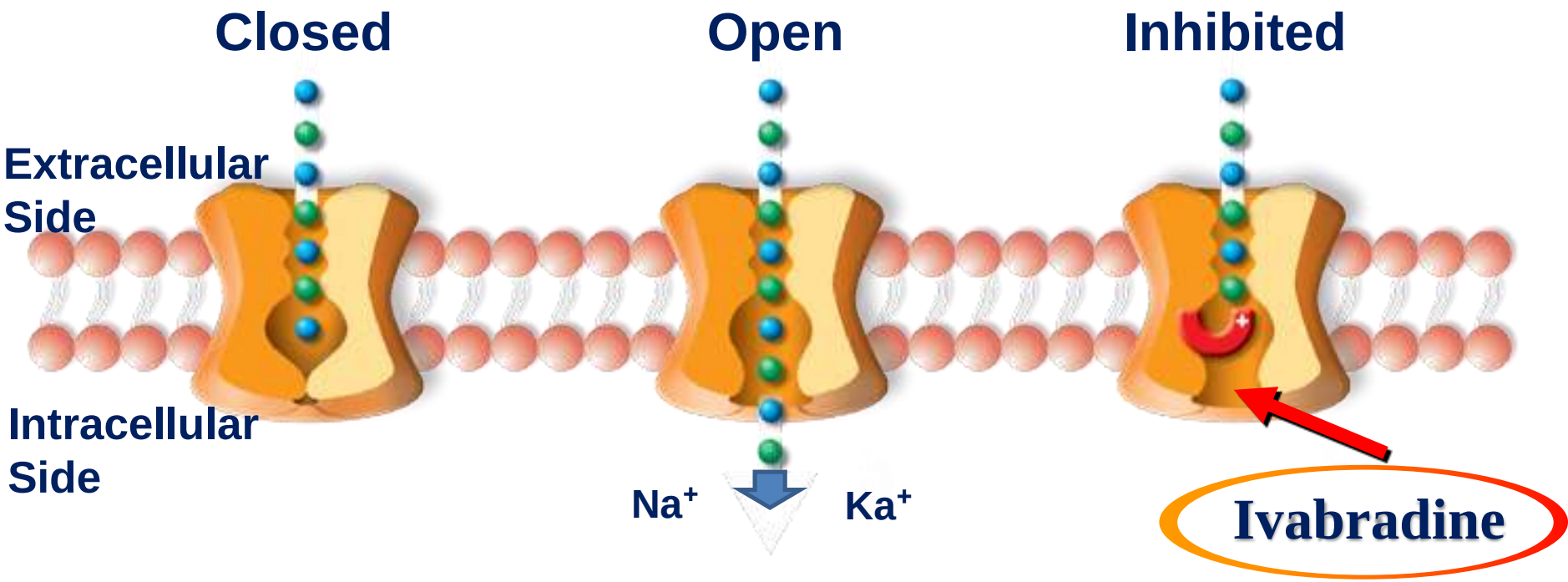
If-channel inhibitor			
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I (or ARB), and an MRA (or ARB).	IIa	B	180
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm who are unable to tolerate or have contra-indications for a beta-blocker. Patients should also receive an ACE-I (or ARB) and an MRA (or ARB).	IIa	C	181

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

- Ivabradine
  - Specific Inhibitor of the I_f current in the SA Node
  - Decreases resting heart rate



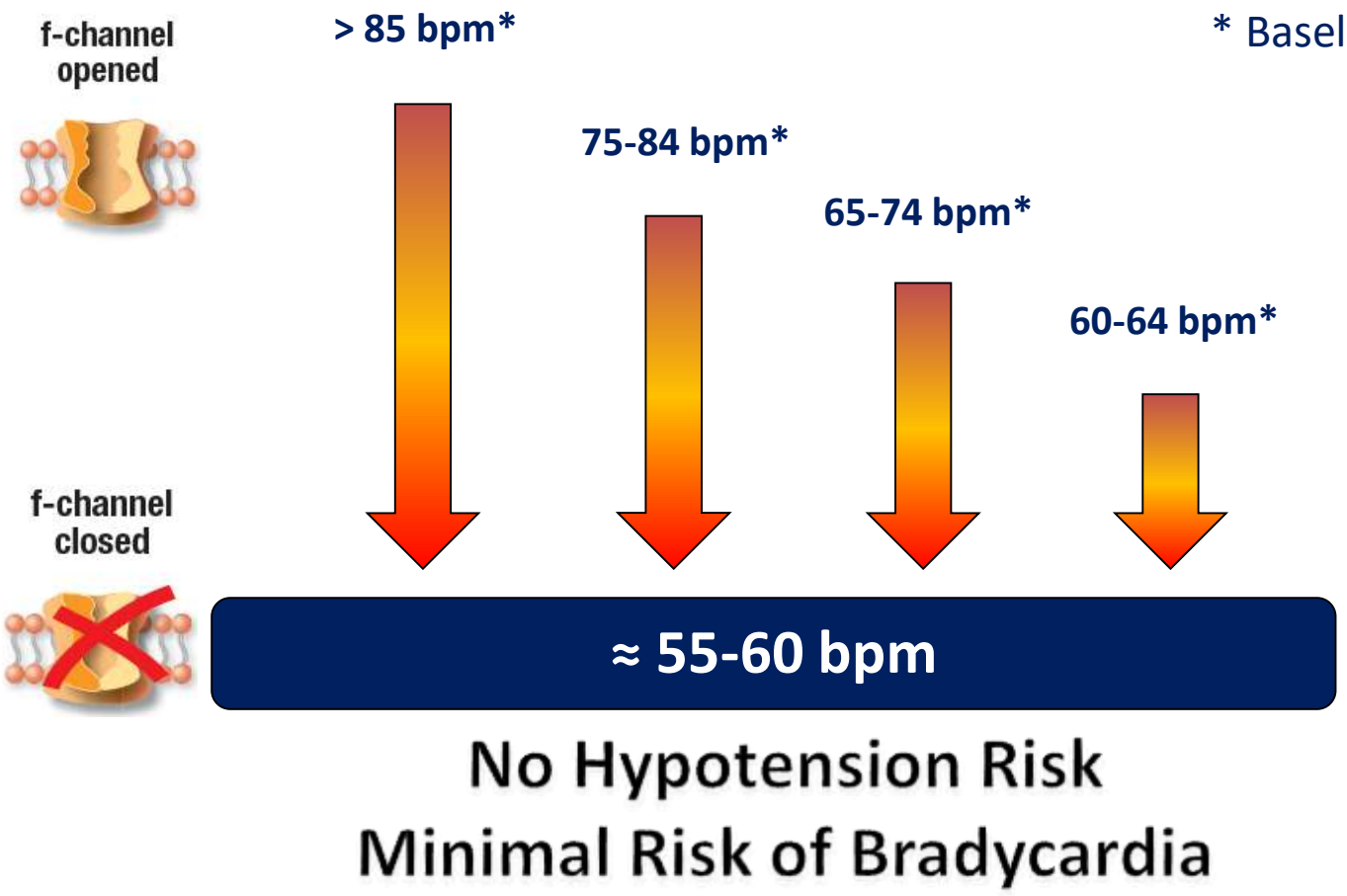
Ivabradine Interacts Internaly With The I_f Channel: a Safety Valve



When the channel is in closed state (*bradycardia*) Ivabradine is inactive

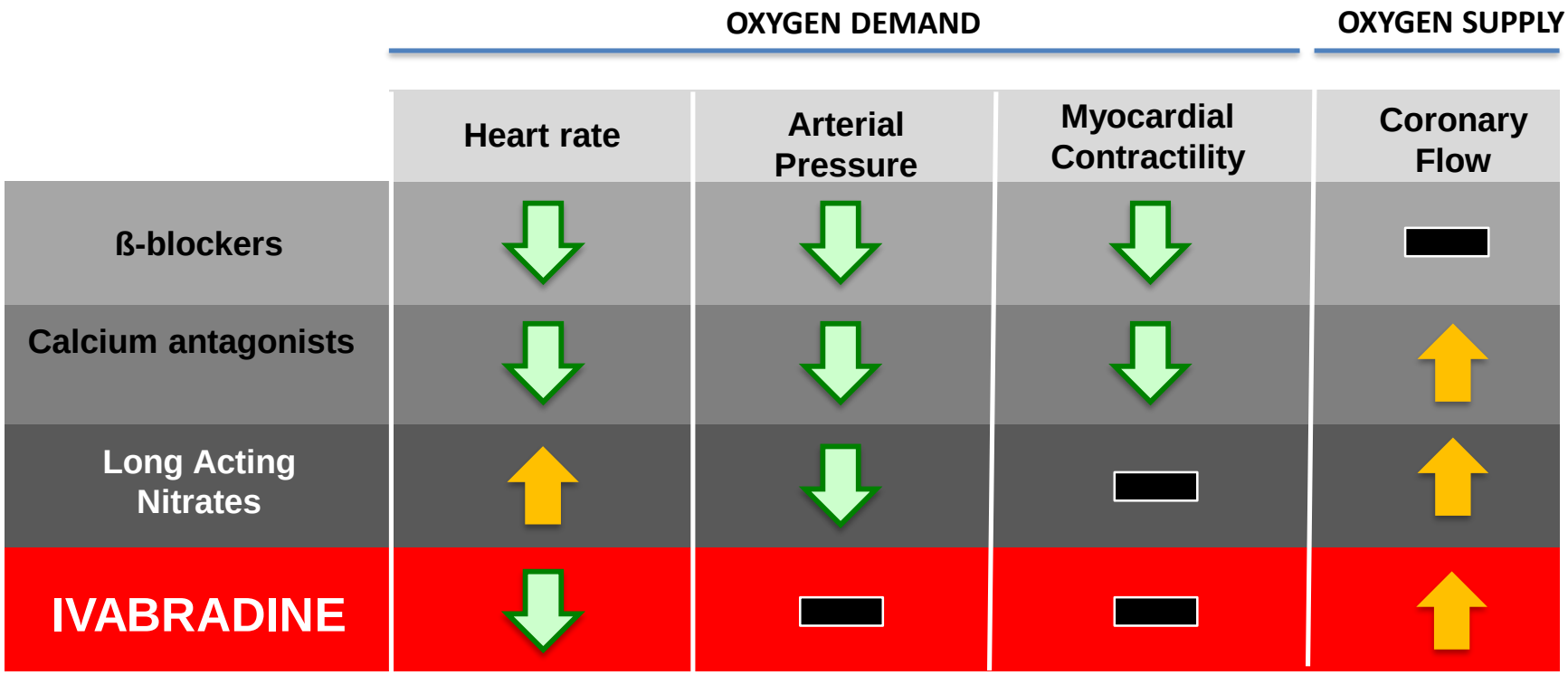
Bucchi A, Baruscotti M, DiFrancesco D. J Gen Physiol. 2002;120:1-13

Achieves Target Heart Rate of 60 bpm With Excellent Tolerability [1,2]



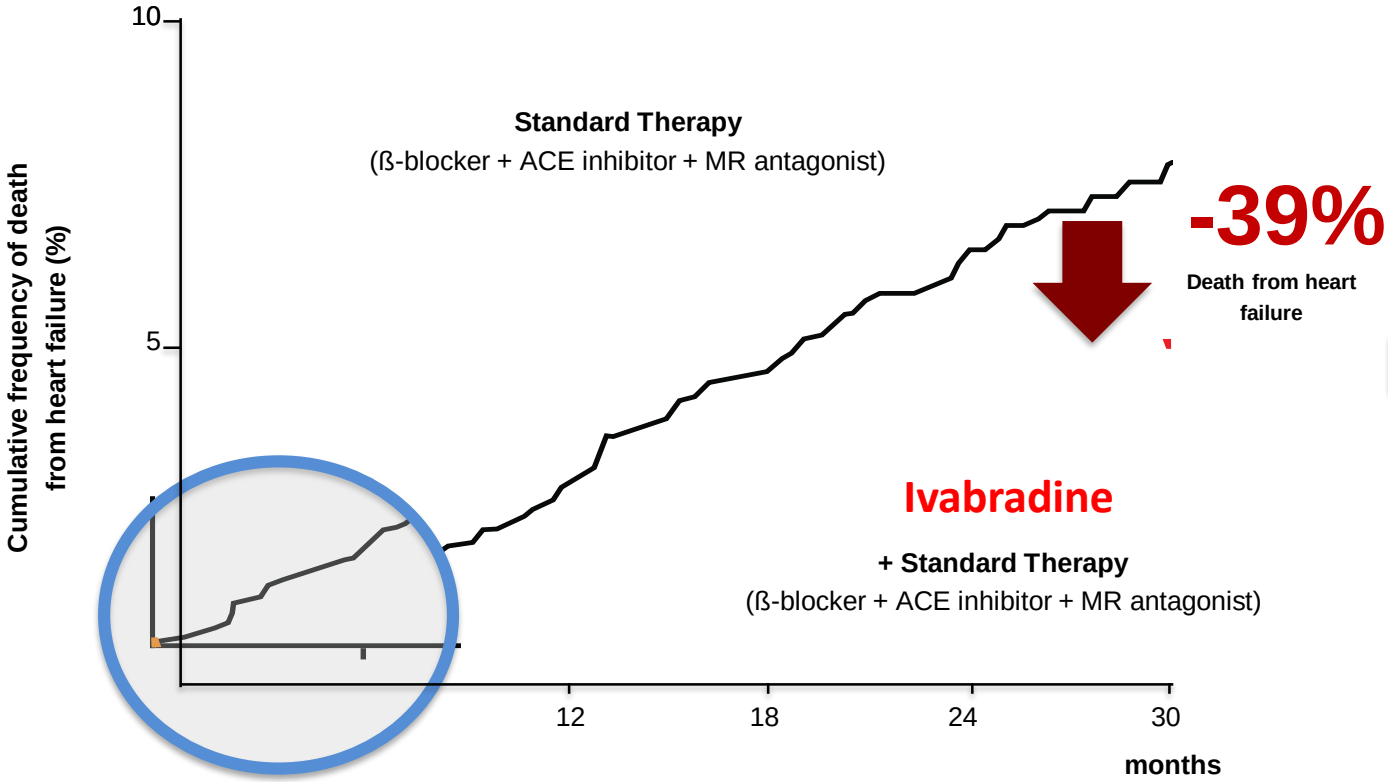
1. Borer JS, Heuzey JY. Characterization of the heart rate-lowering action of ivabradine, a selective I(f) current inhibitor. Am J Ther. 2008;15:461-473.
2. Swedberg K, Komajda M, Böhm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. Lancet. 2010;376:875-885.

Unlike Any Hemodynamic Agent



Fox et al. Eur Heart J.2009:30:2337-2345
Borer et al. Am J Ther 2008:15:461-473

Ivabradine : Ensure Survival Patients



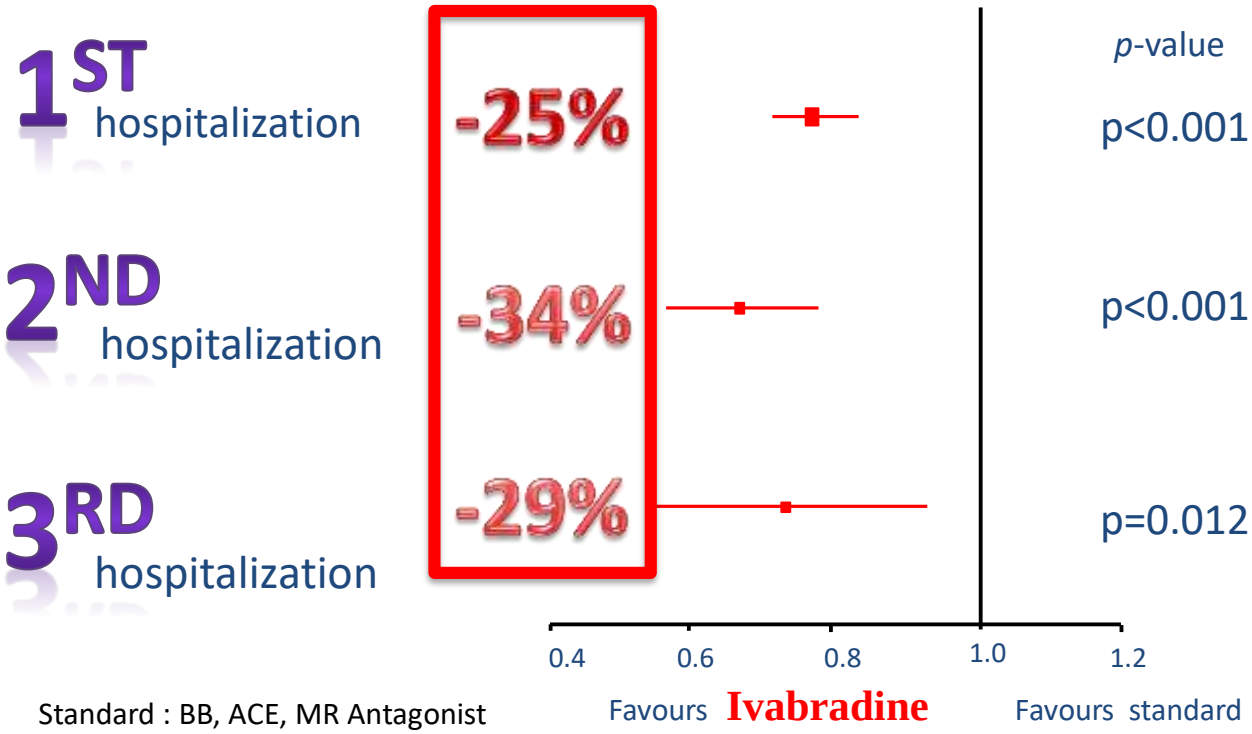
Heart rate ≥ 75 bpm n=4150 Hazard rate=0.61 p=0.0006

Benefit for Patients

More Living Time

. Zugok C et al. Adv Ther. 2014;31:961-974

Ivabradine : Reduces Recurrent Hospitalization for Heart Failure



Standard : BB, ACE, MR Antagonist

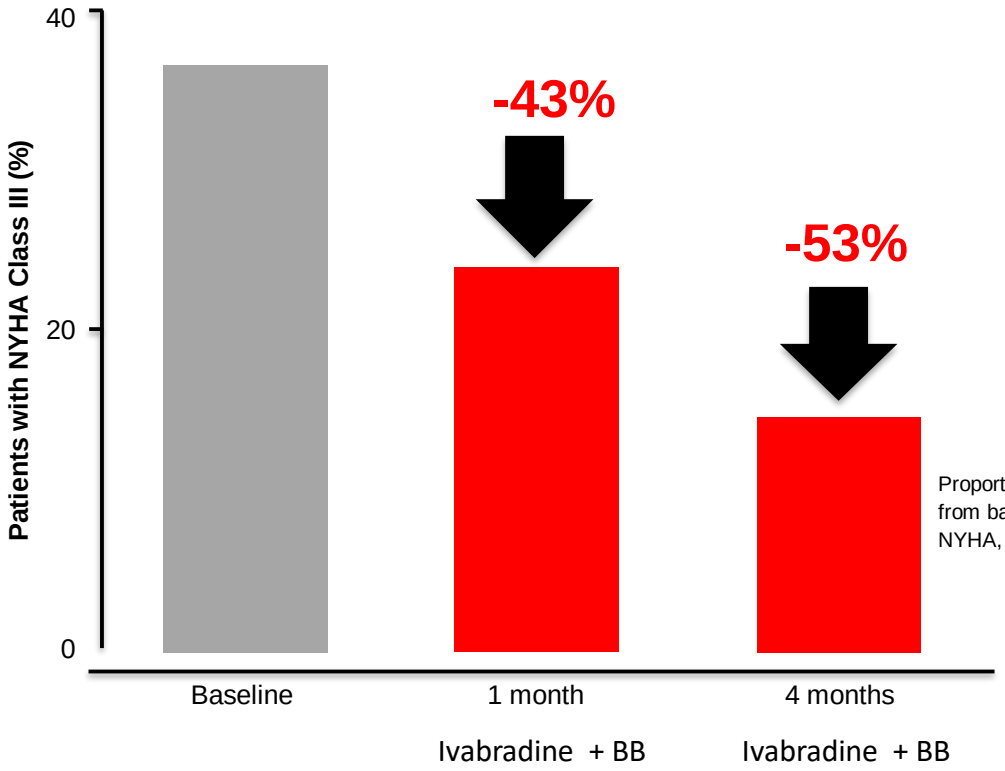
SHIFT

Benefit for Patients

Free from Fear and Social Isolation

Borer JS et al. Eur Heart J. 2012;33:2813-2820.

Ivabradine : Reduces NYHA Class RAPIDly



Proportion of patients with NYHA class III from baseline to study end (month 4).
NYHA, New York Heart Association

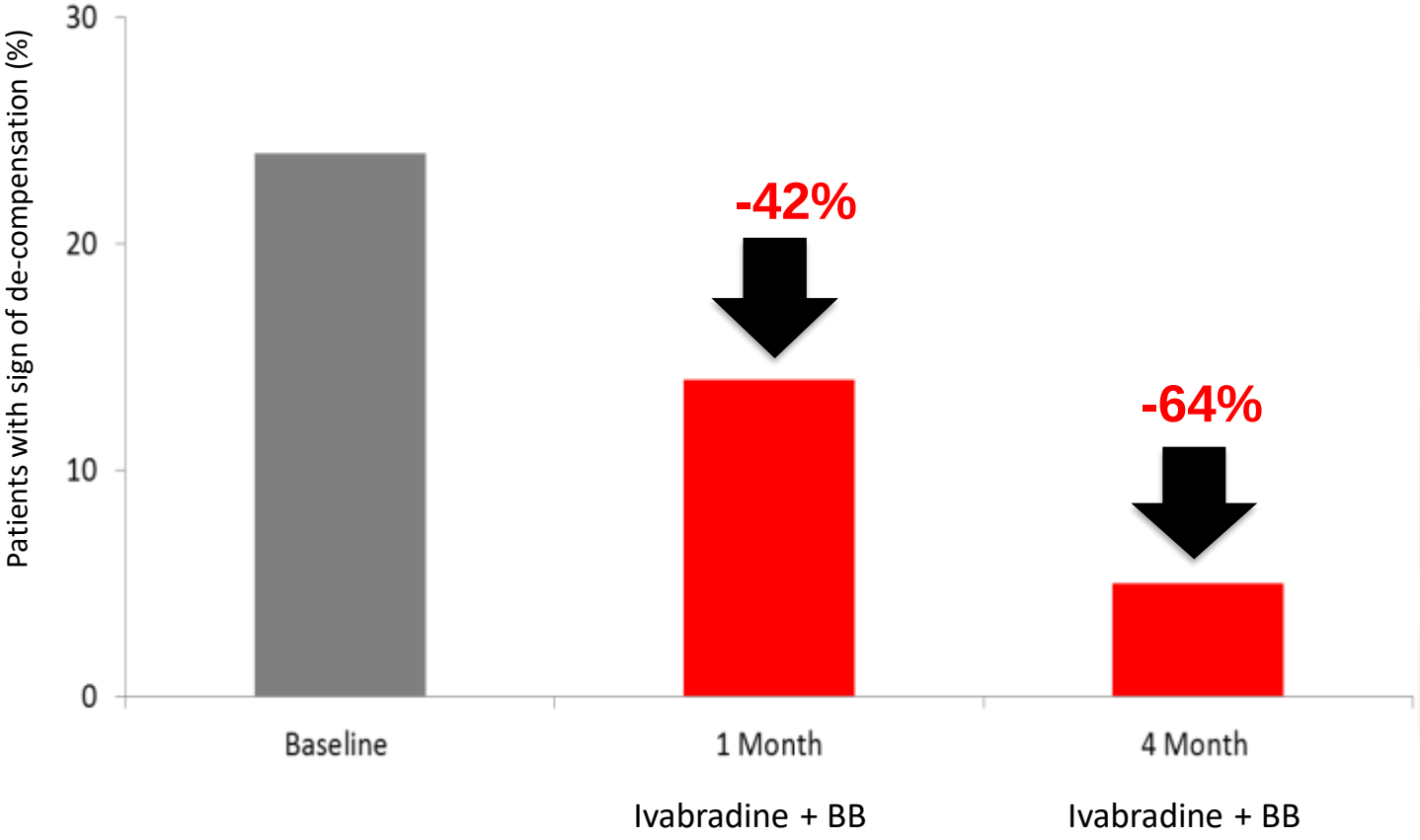
INTENSIfY

Benefit for Patients

Less shortness of breath, no swelling and dizziness

Zugck C et al.. *Adv Ther*. 2014;31(9):961-974.

Ivabradine :Ensure Less De-compensation

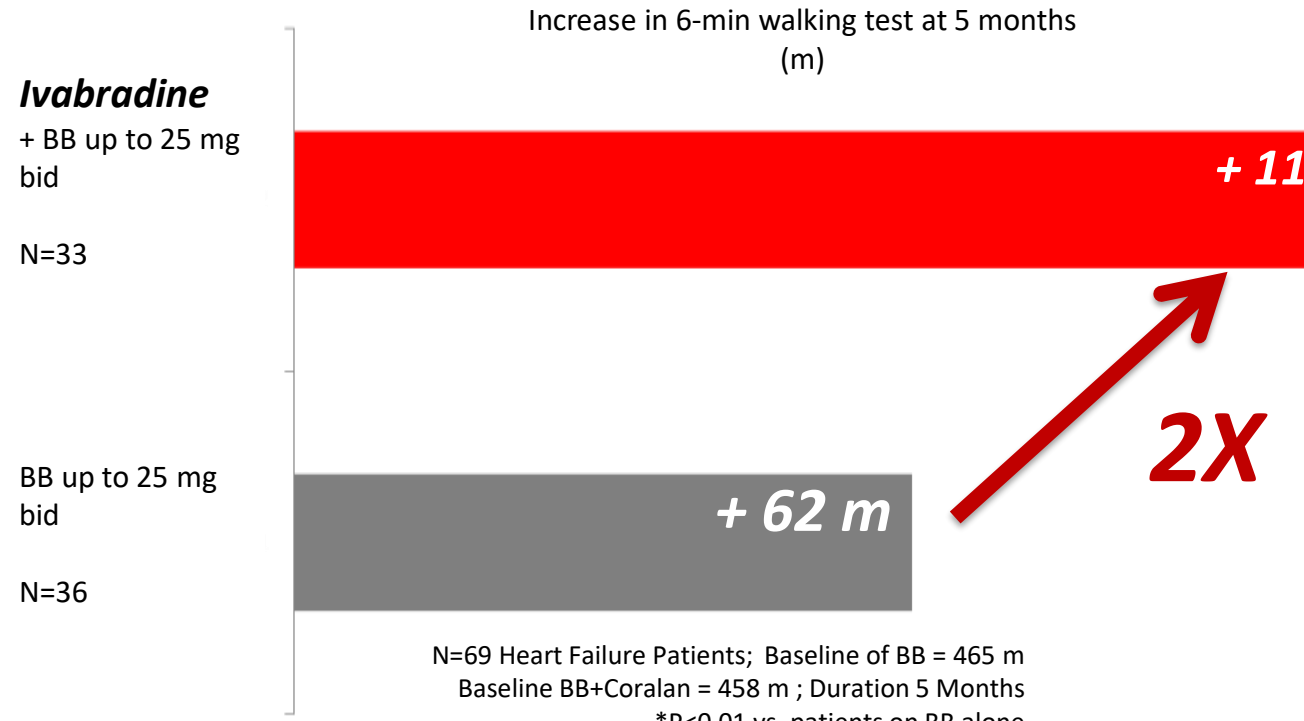


Benefit for Patients

Reduces Worsening HF

. Zugck C et al. Adv Ther. 2014;31:961-974

The Early Addition of Ivabradine to β-Blockers Increases Exercise Capacity RAPIDly



N=69 Heart Failure Patients; Baseline of BB = 465 m
Baseline BB+Coralan = 458 m ; Duration 5 Months
*P<0.01 vs. patients on BB alone

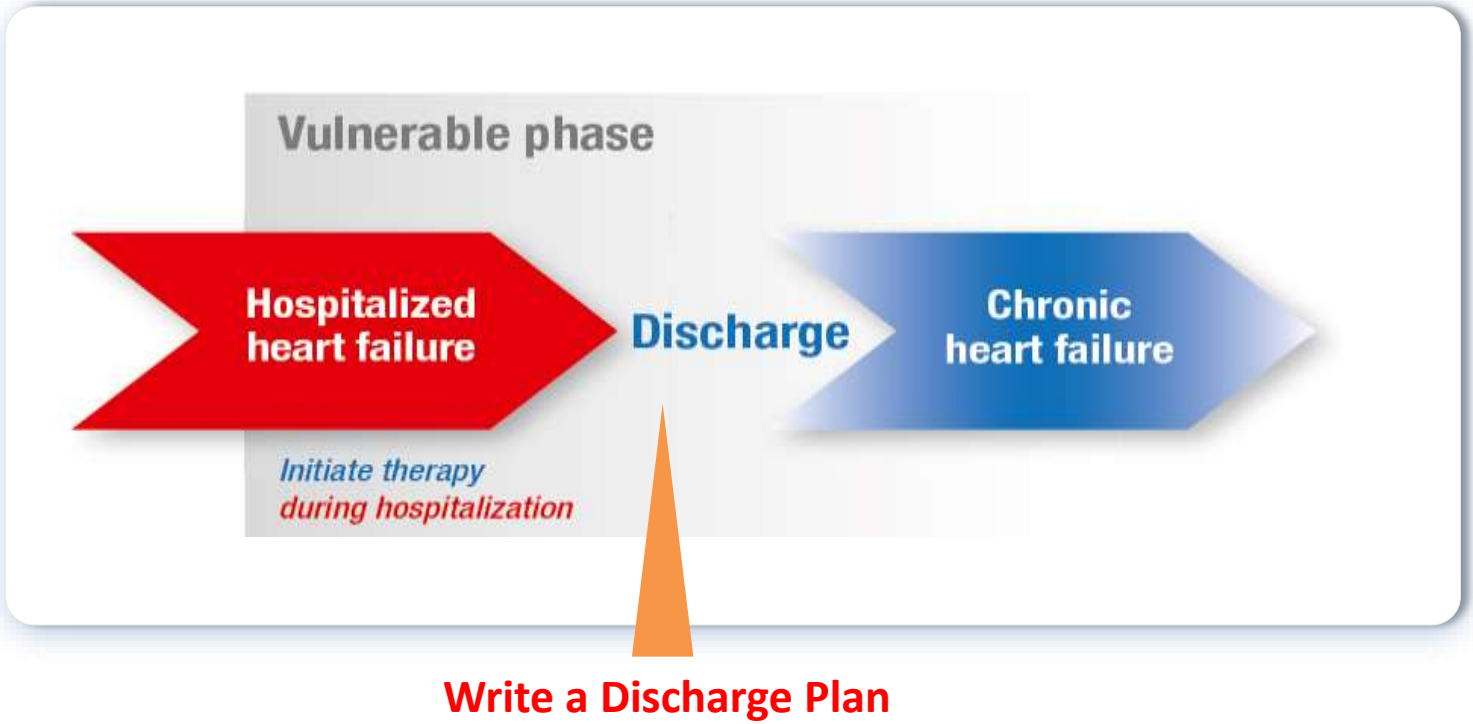
Benefit for Patients

Able doing sport activities

Bagriy AE et al. Adv Ther. 2015;32:108-119.

RIGHT ACTION

Discharge Planning



Don't Forget Vital Link With Chronic HF Programme: ESC 2012 guidance

Pre-discharge and long-term management

Plan follow-up strategy

Enrol in disease management programme, educate, and initiate appropriate lifestyle adjustments

Plan to up-titrate/optimize dose of disease-modifying drugs

Ensure assessed for appropriate device therapy

Prevent early readmission

Improve symptoms, quality of life and survival

McMurray et al. Eur Heart J 2012;33:1787–847

2013 ACCF/ AHA Recommendations For Hospital Discharge[1]

Table 29. Recommendations for Hospital Discharge

Recommendations or Indications	COR	LOE	References
Performance improvement systems in the hospital and early postdischarge outpatient setting to identify HF for GDMT	I	B	82, 365, 706, 792–796
Before hospital discharge, at the first postdischarge visit, and in subsequent follow-up visits, the following should be addressed: a. initiation of GDMT if not done or contraindicated; b. causes of HF, barriers to care, and limitations in support; c. assessment of volume status and blood pressure with adjustment of HF therapy; d. optimization of chronic oral HF therapy; e. renal function and electrolytes; f. management of comorbid conditions; g. HF education, self-care, emergency plans, and adherence; and h. palliative or hospice care	I	B	204, 795, 797–799
Multidisciplinary HF disease-management programs for patients at high risk for hospital readmission are recommended	I	B	82, 800–802
A follow-up visit within 7 to 14 d and/or a telephone follow-up within 3 d of hospital discharge are reasonable	IIa	B	101, 803
Use of clinical risk-prediction tools and/or biomarkers to identify higher-risk patients are reasonable	IIa	B	215

COR indicates Class of Recommendation; GDMT, guideline-directed medical therapy; HF, heart failure; and LOE, Level of Evidence.

1. Yancy C et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;128:e240-e327.

Discharge Planning

According to NICE Guidelines in HF

"Patients with heart failure should generally be discharged from hospital only **when their clinical condition is stable and the management plan is optimized.**

Timing of discharge should take into account patient and carer wishes, and the level of care and support that can be provided in the community.

The primary care team, patient and carer must be **aware of the management plan."**[1]

1. NICE clinical guideline 108. Chronic heart failure. Management of chronic heart failure in adults in primary and secondary care . August 2010. Available at guidance.nice.org.uk/cg108

Conclusions

Chronic heart failure patient: a life time burden of hospitalisation

Despite stabilisation at discharge, patients hospitalized for heart failure are at high risk of rehospitalisation and death.

The risk is particularly high within 30 days after hospitalisation.

Before hospital discharge, the patient has to receive evidence-based therapies: initiation or uptitration of therapies should not be delayed

Early post-discharge assessment is key: further adjustments to therapy will be required.

Ivabradine is recommended as an integral part of therapy in the recent 2016 HF guidelines
Ivabradine reduces early readmissions during the vulnerable phase

The early co-administration of ivabradine and beta-blockers during hospital admission for ADHF is safe and clinically beneficial

Don’t wait until it’s too late …

Thank You For Listening

Borer JS et al. *Eur Heart J* Online,2012