

Updates in Pharmacotherapy for CHF and Reducing Hospital Readmission

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Heart Failure Hospitalizations

- Hospital discharges (2012): > 1 million
 - Unchanged in 10 years
 - Average incidence age ≥ 55 years = 11.6/1000 people/year
- 80% admits = **worsening chronic HF**
- HF admission
 - 15% ↑ risk mortality / 30% ↑ risk re-admit
 - PARADIGM data: recent decompensation = ↑ risk of death/readmit vs never been hospitalized (HR 1.45)
 - Medicare 30 day re-hospitalization = 27%
 - 37% are for HF
 - OPTIMIZE HF 60-90 day re-hospitalization = 30%

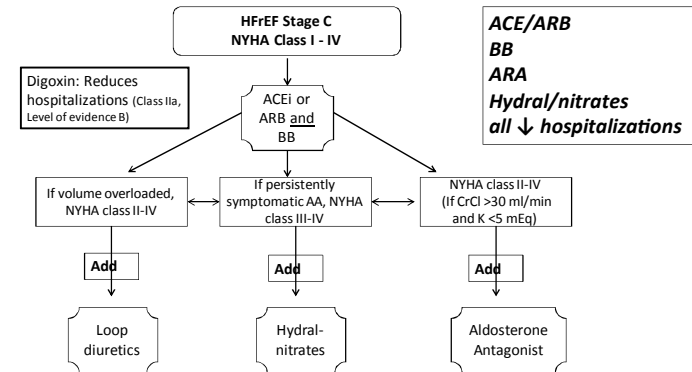
Mozaffarian D, Benjamin EJ, Go AS, et al. Circulation 2016;133:e38-360, Gheorghiu M et al. JACC 2013;61:391-403, Solomon SD et al. JACC: Heart Failure 2016;4:816-822

Objective: Tackling Readmissions

- Review the Guideline Update
- Review pharmacology, outcomes and dosing of ivabradine and sacubatril/valsartan
- Identify Opportunities to Improve Care



Heart Failure Guidelines

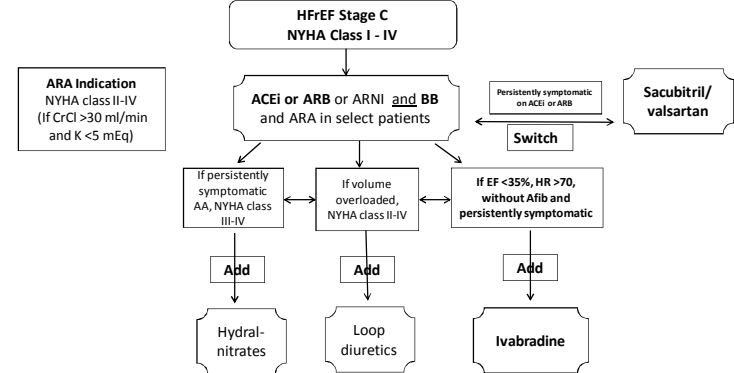


Yancy, Clyde W., et al. JACC 2013; 62: e147-e239.

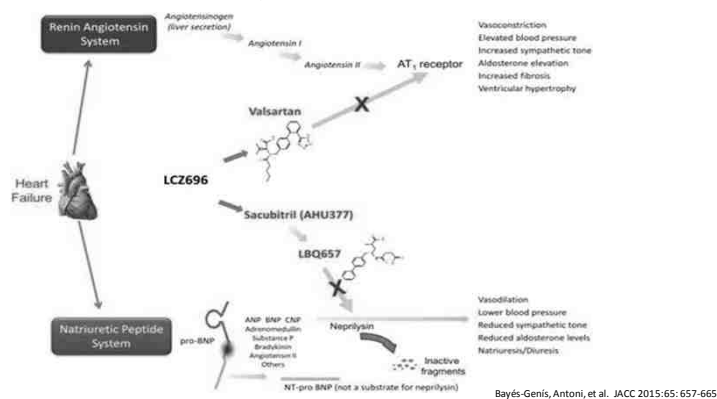
2016 Stage C HF Guideline Update:

- **Level 1:** Use ACE inhibitors, **or** ARBs **or** ARNI in conjunction with evidence-based beta blockers **and** aldosterone antagonists in **selected** patients, is recommended for patients with chronic HFref to reduce morbidity and mortality.
- **Level 1:** In patients with chronic symptomatic HFref NYHA class II or III who tolerate an ACE inhibitor or ARB, **replacement by an ARNI** is recommended to further reduce morbidity and mortality.
- **Level IIIa:** Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic NYHA class II-III stable chronic HFref (LVEF < 35%) who are receiving GDEM, including a beta blocker at maximum tolerated dose and who are in sinus rhythm with a HR of 70 bpm or > at rest.

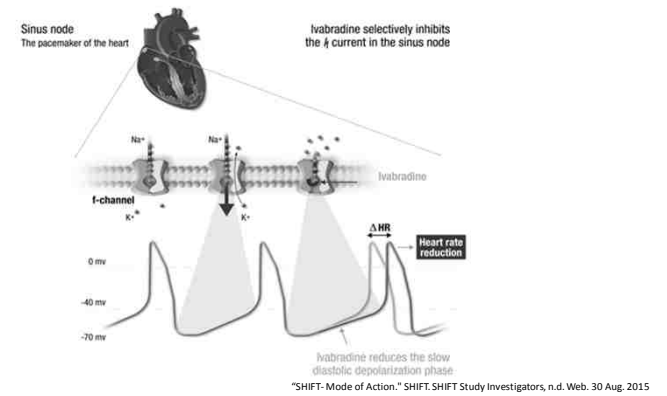
2016 Stage C HF Guideline Update:



ARNI: sacubitril/valsartan: MOA



Ivabradine: MOA



Study Designs

SHIFT Trial

- Ivabradine vs Placebo
- Inclusion
 - EF ≤ 35%
 - HR > 70 bpm in SR
 - Current symptoms
 - Prior HF hospitalization
- Exclusion
 - Afib
 - Pacer dependent
 - Low BP
- CV death or hospitalization for HF

Paradigm Trial

- Sacubitril/Valsartan vs Enalapril
 - Currently on ACEi or ARB
 - EF ≤ 35%
 - Current symptoms
 - Prior HF hospitalization or ↑BNP
- Exclusion
 - GFR < 30 ml/min
 - K > 5.2 mmol/L
 - Hx angioedema
 - Low BP
- CV death or hospitalization for HF

Swedberg, Karl, et al. Lancet 2010; 376:875-885, McMurray, John JV, et al. NEJM 2014; 371: 993-1004

Study Results

Swedberg, Karl, et al. Lancet 2010; 376:875-885, McMurray, John JV, et al. NEJM 2014; 371: 993-1004
Zannad, F et al. NEJM 2011; 364: 11-21

Study Observations

SHIFT

- Beta-blocker: 89%
 - Only 25% target dose
 - 56% on > 50% target
 - Low BP, fatigue, dizzy, SOB brady
- Aldosterone Antag: 60%
- Side Effects
 - 4-5% ↑ bradycardia
 - 1% ↑ New Afib
 - 2% ↑ Phosphenes
 - Visual changes/Bright lights
- Primary endpoint driven by ↓ hospitalizations

PARADIGM

- FC II >> FC III (72%)
- Aldosterone Antag: 54%
- Side Effects
 - 5% ↑ Symptomatic hypotension
 - 1.2% ↓ Cr ≥ 2.5 mg/dl
 - 1.3% ↓ K > 6.0 mmol/L
 - 3% ↓ Cough
 - No diff angioedema
 - PI states increased incidence in blacks
- Primary endpoint: both components in favor of ARNI
- No available data for new-onset heart failure or < target dose ACEi/ARB

Swedberg, Karl, et al. Lancet 2010; 376: 875-885, McMurray, John JV, et al. NEJM 2014; 371: 993-1004

Dosing

Ivabradine

Starting Dose	5 mg BID x 2 weeks
Heart rate	Dose adjustment
>60 bpm	Increased by 2.5 mg BID
50-60 bpm	Maintain dose
<50 bpm or symptomatic bradycardia	Decrease by 2.5 mg BID; if current dose is 2.5 mg BID, discontinue

Cost considerations:

- > \$400/month
- Medicare D: will hit donut hole faster
- Prior Authorization required

Corlanor Package Insert 4/2015, Entresto Package Insert 8/2015

Sacubitril/Valsartan

ACEi or ARB dose	Sacubitril/Valsartan Initial Dose
none or low dose	24/26 mg BID
target or max dose	49/51 mg BID
Clinical characteristic	
Severe renal impairment	24/26 mg BID
Mod hepatic impairment	
Angioedema	contraindicated
Double every 2-4 weeks to target of 97/103 mg BID	

If switching from ACEi:

- 36 hour washout required**
- Clear instructions to patient
- d/c ACEi Rx at the pharmacy

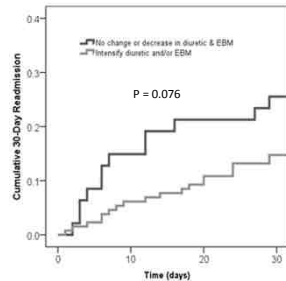
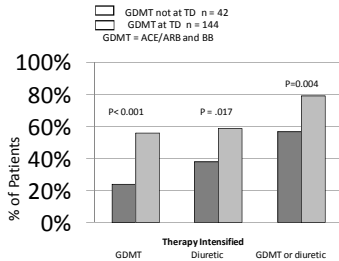
Opportunities to Improve Care/Prevent Hospitalizations

Readmissions: *What is Happening at Your Institution?*

- What is your readmission rate? (30-day, 60-90 day)
- Why are your patients getting re-admitted?/ Where they ready for discharge?
 - Complications from initial hospital stay
 - **HF adequately treated?**
 - Signs/symptoms of congestion reassessed at rest and activity
 - **Optimization of Chronic Oral Therapy?**
 - Co-morbidities managed?
 - Hospitalized pts have higher rates of comorbidities-
 - Progression of disease/ recurrence of HF
 - Poorly managed transitions
 - Adherence: diet/meds
 - Social Factors: income/literacy/support/substance abuse
 - End-stage

Gheorghide M et al. JACC 2013;61:391-403, Yancy CW et al. Circulation 2013 ;128:1810-1852

Hospitalization: *HF Therapy at Discharge*



ESC HF Registry 2011-2013	N	ACEi or ARB	B-blocker	MRA
Hospitalized HF-admit	5,039	64	55	34
Hospitalized HF-discharge		77	72	55

Goncharenko A et al. J Cardiac Fail 2016;22:598
Maggioli AP et al. European J of Heart Failure 2013;15:1173-1184

Hospitalization: *Transitioning to Home ACC H2H*

- See You in 7
- Home Risk Prediction tools
 - <http://cvquality.acc.org/Initiatives/H2H/Projects/See-You-in-7/Toolkit.aspx>
 - LACE Index Scoring Tool
 - Project BOOST, 8P Screening Tool
- Follow-up appointment in 7 days
 - GWTG QI program:
 - Hospitals with higher rates of early follow-up = ↓ readmissions 20.9% vs 23.3% (p < 0.001)
 - Medicare claims data show highest % of readmission within 10 days

Hernandez AF et al. JAMA 2010;303:1716-1722, Jencks SF et al. N Engl J Med. 2009;360:1418-1428

Hospitalization: *Transitioning to Home ACC H2H*

- **Mind Your Meds**
 - Med reconciliation admit, discharge, follow-up
 - Patient brings meds or current list to appointments
 - Don't assume they made the changes you last prescribed
 - Barriers
 - Obtaining Rx (insurance, cash, transportation)
 - Adherence (education/polypharmacy/cost)
 - Side Effects
- Once at home, can HF therapy continue to be optimized?

Hospitalization: *Transitioning to Home*

- Care Transitions Intervention:
 - APN transitions coach visits patient: hospital, home (72 hrs), phone x 3 (28d)
 - Medication self-management (med reconciliation)
 - Patient centered record (how to use)
 - Timely follow up visit
 - Red Flags (signs of condition worsening and who to contact)
 - Readmission = 8.3% Intervention vs 11.9% control (p 0.048)
- Allied Health Transition clinic: (APN and PharmD)
 - Visits at 1 week & 4-6 weeks (volume assessments and med reconciliation)
 - 44.3% ↓ readmissions compared to hospital average

Coleman EA et al. Arch Intern Med 2006;166:1822-1828, Donaho EK et al. J Am Heart Assoc 2015;4:e002296

Preventing Hospitalizations: *Underuse of GDMT*

Study	Dates	N	Use of Guideline Directed Medical Therapy				
			ACEi or ARB	B blocker	MRA	Dual	Triple
Utah Health	2007-2013	989	69	79	28	58	19
Target dose			31	24	13		
ESC HF Registry	2011-2013						
Ambulatory HF		4,792	92	93	67		
Ambulatory HF Target Dose*			29	17	30		
Use of GDMT prior to ICD#	2007-2011	78,665				61^	

* 1/3 reported to still be in up-titration
 ^ only 28% had enough meds to cover 80% of days
 # GDMT associated with ↓ mortality (11.1 vs 16.2%)

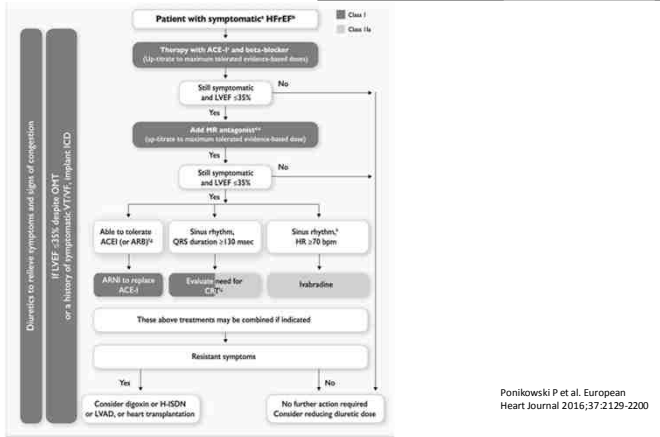
Bress AP et al. Pharmacotherapy 2016;36:174-186, Maggioni AP et al. European J of Heart Failure 2013;15:1173-1184, Roth GA et al. JACC 2016;67:1062-1069

GDMT to reduce hospitalizations

- Sacubatil/valsartan
 - Delayed 1st hospitalization for HF—consider in FC II-III with elevated BNP
 - Decreased total hospitalizations for HF (12.8 vs 15.6%)
 - Decreased 30 day readmission (9.7 vs 13.4%)
- Ivabradine
 - All-cause (38 vs 42%), worsening HF (16 vs 21%), any CV (30 vs 34%)
 - SHIFT placebo arm: outcomes based on HR
 - ≥ 87 bpm vs 70-72 bpm = 2 fold ↑ in primary outcome
 - For every 5 bpm ↑, 16% higher risk of primary outcome

McMurray, John JV, et al. NEJM 2014; 371: 993-1004, Desai AS et al. JACC 2016;68:241-248, Packer M et al. Circulation 2015;131:54-61, Swedberg, Karl, et al. Lancet 2010; 376:875-885, Bohm M et al. Lancet 2010;376:886-894

ESC HF Guidelines 2016



Hospitalization: *Transitioning to Home ACC H2H*

- Signs and Symptoms
 - Can the patient recognize signs/symptoms of deterioration?
 - **Does the patient have a place to call?**
 - *Do you have a provider to return their calls?*
 - Does the patient have support at home?
 - Self Care
 - Daily weights
 - Sodium / fluid restriction
 - Diuretic self management

Final Thoughts: *Tackling Readmissions*

- Use of GDMT can reduce hospitalizations
- New therapies are an option but don't forget about optimizing the old standards
- It takes more than meds to reduce hospitalizations

