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SHM Clinical Rapid Updates: Heart Failure

Moderated by Joseph Sweigart, MD Ebrahim Barkoudah, MD | Nurcan Ilksoy, MD July 29, 2021, 4 PM Eastern



Learning Objectives

- Recognize the importance of rapid decongestion
- Recognize the importance of initiation of GDMT
- Describe inpatient initiation/titration of ARNI including PIONEER-HF trial

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- Dr. Barkoudah is the Associate Director of Brigham Heath Hospital Medicine and a Medical Director in the Department of Medicine at Brigham and Women's Hospital in Boston. Dr. Barkoudah is an Assistant Professor of Medicine, Harvard Medical School.
- He is the President of SHM Boston Chapter and a member of the SHM education and the research committees
- Dr. Barkoudah serves as the Editor-in-Chief for the Journal of Clinical Outcomes Management
- Dr. Barkoudah's research interest lies in clinical research outcomes through his role in the Clinical Endpoint Center at the Brigham and Women's Hospital and implementation science with the focus on the care during hospitalization







Disclosures

Ebrahim Barkoudah discloses the following relevant financial or advisory relationships:

- Advisory fees from Portola, Janssen, Novartis, and Pfizer/Bristol-Myers-Squibb to Hospital Medicine and Cardiovascular Medicine research
- Research support payments from National Institutes of Health/National Heart, Lung, and Blood Institute; Bristol Myers Squibb; Janssen. Payments made to Brigham and Women's Hospital for performing clinical endpoints sponsored by various entities

Dr. Nurcan Ilksoy, MD, FACP, FHM

Associate Professor of Medicine Emory University School of Medicine Atlanta, GA

- Established a HF task force as the Chair Heart failure Best Practice Team in 2006 and expanded that program resulting significant reduction in HF readmissions at Emory in Grady. She has continued to serve in the HF transition of clinic.
- Involved in SHM HF curriculum development, HF quality resource room development and creating HF implementation guide for SHM.
- Served on multiple regional, national committees and led resident education and faculty development in Quality Improvement and Patient Safety in her institution.







Disclosures

Nurcan Ilksoy has no relevant financial or advisory relationships with corporate organizations related to this activity.

Congestive Heart Failure

- Heart Failure is a clinical syndrome with symptoms and or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion.
- Approximately 6.2 million people 20 years of age or older in the United States have HF, with approximately 1 million new HF cases diagnosed annually, and the prevalence continues to rise.
- Heart failure is the primary diagnosis in over 1 million hospitalizations annually, and the total cost of HF care in the United States exceeds \$30 billion annually.



N Engl J Med 2020;383:2603-15.

American Heart Association

J Card Fail. 2021 Mar 1:S1071-9164(21)00050-6

At Risk for Heart Failure

Heart Failure







Integrated Care for Heart Failure (2014)



N Engl J Med 2020;383:2603-15.

Heart Failure guideline update: a guide for general practice



The cycle of quality as a model for improving health outcomes





Robert M. Califf: European Heart Journal Supplements (2007) 9 (Supplement B), B8–B12

Gaps in Clinical Care of Heart Failure

- Diagnosing and treating HF throughout its progression stages
- Acute Care during hospitalization
- Transition of care and adherence
- Follow up and access to HF specialist
- Disease progression and comorbidities



Universal Definition and Classification of Heart Failure

Parameter	Explanation
NYHA functional class ³	I, II, III, IV based on symptoms severity
EF^4	HFrEF, HFmrEF, or HFpEF based on LVEF
Etiology ²⁵	Specific etiology of HF, for example, ischemic/nonischemic, valvular, hypertensive, infiltrative cardiomyopa thy such as cardiac amyloidosis, peri- partum cardiomyopathy, viral myocarditis chemotherapy-induced cardiomyopathy
Disease progression (ACCF/AHA) ^{3,54}	Stages A, B, C, or D according to pres- ence of HF symptoms and signs and cardiac structural changes
MOGES ²⁸	Morphofunctional phenotype (M), organ (s) involvement (O), genetic inheri- tance pattern (G), etiological annota- tion (E) including genetic defect or underlying disease/substrate, and the functional status (S)
INTERMACS Profiles for Advanced HF ¹⁰⁸	Profiles 1–7 according to symptoms, functional capacity, hemodynamic sta- bility for patients who are considered for advanced HF therapies

Classification Frameworks Currently Used for HF

Current HF Classifications According to LVEF in Contemporary Clinical Practice Guidelines

Society Name	HF Classification According to LVEF	LVEF
ACCF/AHA (2013) ³	Heart failure with reduced ejection fraction (HFrEF) Heart failure with preserved ejection fraction (HFpEF) HFpEF, borderline HFpEF, improved	$\leq 40\%$ $\geq 50\%$ 41% - 49% > 40%
ESC (2016) ⁴	Heart failure with reduced ejection fraction (HF <i>r</i> EF) Heart failure with mid-range ejection fraction (HFmrEF)	<40 % 40-49%
	Heart failure with preserved ejection fraction (HFpEF)	≥50%
JCS/JHFS (2017) ⁵	Heart failure with reduced ejection fraction (HF <i>r</i> EF) Heart failure with mid-range ejection fraction (HFmrEF) Heart failure with preserved ejection fraction (HF <i>p</i> EF) Heart failure with preserved ejection fraction, improved (HF <i>p</i> EF improved) or heart failure with recovered EF (HFrecEF)	<40% 40% to $<50\%$ $\ge50\%$ $\ge40\%$



https://doi.org/10.1016/j.cardfail.2021.01.022

Classification of HF according to LVEF

HF with reduced EF (HFrEF):	
 HF with LVEF ≤ 40% 	
HF with mildly reduced EF (HFmrEF):]
• HF with LVEF 41-49%	
HF with preserved EF (HFpEF):]
 HF with LVEF	
HF with improved EF (HFimpEF):]
 HF with a baseline LVEF ≤ 40%, a ≥ 10 point incre baseline LVEF, and a second measurement of LV 	ase from EF > 40%



https://doi.org/10.1016/j.cardfail.2021.01.022

Stages in the development and progression of HF





https://doi.org/10.1016/j.cardfail.2021.01.022

CENTRAL ILLUSTRATION: Heart Failure Hospitalization Associations With Guideline-Directed Medical Therapy Changes and Subsequent Hazards of All-Cause Mortality

Α

Asso	ciation	of Heart	Failure Hospitalizat	ion wi	th GDM1	T Dose Cha	inge	
Dose	Change F	Rate at 12	Months Cha	Characteristics of Patients with Dose Cha				
	HFH	No HFH	Adjusted Probability Ratio (95% CI)	Age, Years	Female	Systolic Blood Pressure, mm Hg	Heart Rate, Beats per Minute	
Initiation								
ACEI/ARB ARNI Beta Blocker MRA	13.9% 13.9% 56.8% 14.7%	11.9% 9.2% 25.1% 6.6%	2.62 (1.83-3.73) 1.63 (1.25-2.13) 13.23 (6.42-27.27) 3.35 (2.50-4.50)	62.6 61.9 67.6 66.6	36.4% 25.9% 33.3% 23.3%	120.2 120.3 124 120.5	74.0 76.9 77.9 76.0	
Dose Escalati	on							
ACEI/ARB ARNI Beta Blocker MRA	20.5% 18.9% 11.8% 15.6%	16.9% 22.5% 13.9% 8.5%	1.71 (1.36-2.16) 1.02 (0.57-1.80) 1.29 (0.95-1.75) 8.71 (4.19-18.10)	61.2 59.0 61.7 55.6	26.3% 55.0% 40.0% 25.0%	118.8 122.3 116.8 115.2	77.0 75.0 78.3 79.3	
Dose De-Esca	lation							
ACEI/ARB ARNI Beta Blocker MRA	29.0% 35.8% 23.6% 27.2%	10.9% 14.0% 8.0% 15.2%	2.96 (2.34-3.76) 4.34 (3.09-6.09) 3.30 (2.62-4.16) 2.26 (1.75-2.93)	65.4 60.8 64.2 65.6	26.8% 27.9% 25.3% 28.8%	114.9 109.9 112.8 112.6	78.0 75.3 75.6 77.1	
Discontinuati	on							
ACEI/ARB ARNI Beta Blocker	18.0% 28.4% 8.1%	5.7% 9.3% 2.0%	3.16 (2.47-4.06) 6.05 (3.91-9.36) 4.41 (3.28-5.93)	66.6 61.2 65.1	28.9% 25.0% 28.3%	114.3 110.3 112.4	77.6 74.5 74.0	
MRA	21.1%	10.4%	2.58 (1.98-3.36)	66.3	26.8%	112.9	76.9	



Compares Dose Initiation/Escalation After Heart Failure Hospitalization vs. Not

Srivastava, P.K. et al. J Am Coll Cardiol HF. 2021;9(1):28-38.

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Heart Failure Hospitalization and **Guideline-Directed Prescribing Patterns Among Heart Failure** With Reduced **Ejection Fraction Patients**

Intercountry **Differences in Guideline-Directed Medical Therapy** and Outcomes **Among Patients** With Heart Failure

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J Am Coll Cardiol HF. 2021 Jul, 9 (7) 497–505

Multidisciplinary Management of Chronic Heart Failure: Principles and Future Trends



https://doi.org/10.1016/j.clinthera.2015.08.021



Hospital Readmissions: Not Just a Problem for Medicare

Many hospitals are working hard at lowering readmissions among Medicare patients. But another patient group – adults covered by Medicaid – have readmission rates that are just as high, or even higher, than Medicare patients, 2012 data from AHRQ show. This graphic compares 30-day readmission rates for Medicare and Medicaid patients for acute myocardial infarction, congestive heart failure, pneumonia, and hip and knee replacement.



Source: AHRQ Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID), 2012. http://hcupnet.ahrq.gov.

Time-to-Furosemide Treatment and Mortality in Patients Hospitalized With Acute Heart Failure





INI-CRCT, Great Network, and the EF-HF Group. Integrative Assessment of **Congestion in Heart Failure** Throughout the Patient Journey.

JACC Heart Fail. 2018 Apr;6(4):273-285.



the hospitalist

CENTRAL ILLUSTRATION: Early Clinical Management of Acute HF

<u>Early Hospital Management</u>

- Emergency Department Management
 - First 6 hours
 - Priority is stabilization and treating life-threatening complications of AHF
 - Goals are to improve congestion and hemodynamics
 - Initiation of vasodilators, diuretics, etc.
 - 24-48 hrs: Observation Unit management for select patients

- approx. 6-16 hours after presentation
- Priority is early initiation of IV diuretics and
- vasoactive agents if needed
- Goals are to prevent long hospital stay and improve long-term outcomes
- Also initiate/titrate ACE-I, ARB, BB, etc
- Certain patients can be referred to Same Day Access Clinic for early follow-up

- Patients referred from PCP or ED for acute symptoms
- Priority is for lower-acuity patients that require short IV diuresis
- Goals are to manage acute episode without using ED or hospital resources
- Use of same-day
 Furosemide bolus or IV
 infusion

Clinic

Same Day Access

 Close outpatient follow-up after resolution of acute episode

Zsilinszka, R. et al. J Am Coll Cardiol HF. 2017;5(5):329-36.



Inpatient Diuretic Management of Acute Heart Failure



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DOI:10.1007/s40256-020-00463-5

Figure 1: Shifting the Paradigm of Guideline-directed Medical Therapy Initiation



A suggested timeline of initiating guideline-directed medical therapy (GDMT) for patients admitted with heart failure with reduced ejection fraction during their hospitalization. ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor—neprilysin inhibitor; MRA = mineralocorticoid receptor antagonist; RAAS-I = renin-angiotensin-aldosterone system inhibitor; SGLT2i = sodium—glucose cotransporter-2 inhibitor.

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https://doi.org/10.15420/usc.2020.29

Thank you!

Heart-Healthy (CDC Tips)







GDMT in HF patients

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HOSPITALISTS have a KEY role in HF management

- HF remains most common, morbid, complex syndrome, and costly disease in the US, and its prevalence is expected only to increase.
- Hospitalists provide care for the majority of HF patients, and their comorbidities, usually they are the first to see the patients with HF.

• Thorough understanding of the guidelines and how to apply them to the management of ADHF has critical importance.



GDMT is proven to reduce morbidity and mortality

Many eligible Pts (HFrEF) are NOT receiving recommended txs

Hospitalization serves as a key point to initiate and titrate GDMT

Four therapies have clinical benefit within 30 days of initiation:

- 1. Renin-angiotensin-aldosterone system inhibitors with or without a neprilysin inhibitor (ACE/ARB/ARNI)
- 2. β-blockers
- 3. Mineralocorticoid-receptor-antagonists
- 4. Sodium-glucose cotransporter-2 inhibitors



Poll: How comfortable are you to initiate/switch/titrate up GDMT in HF patients in the hospital?

- 1. Comfortable
- 2. Somewhat
- 3. Not comfortable
- 4. Not sure. Need more information



2021 update to the 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 Solution Set Oversight Committee. J Am Coll Cardiol 2021;77:772–810



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10 Principles for Successful Treatment of Heart Failure

How to implement GDMT...

I. Initiate & Switch

Treatment algorithm for guideline-directed medical therapy including novel therapies (*Figure 2* and 3)

II. Titration

Target doses of select guideline-directed heart failure therapy (*Tables 1, 2, 3, 4, 5*)

Considerations for monitoring

How to address challenges with...

III. Referral Triggers for referral to HF specialist (Table 6)

IV. Care Coordination Essential skills for a HF team (Table 7)

Infrastructure for team-based HF care (*Table 8*)

V. Adherence Causes of non-adherence (Table 9)

Interventions for adherence (Table 10, 11)

VI. Specific Patient Cohorts

Evidence based recommendations and assessment of risk for special cohorts: African Americans; older adults; frail (*Table 12*)

VII. Cost of Care

Strategies to reduce cost (Table 13)

Helpful information for completion of prior authorization forms (*Table 14*)

How to manage...

VIII. Increasing Complexity Ten pathophysiologic targets in HFrEF and treatments (Table 15)

Ten principles and actions to guide optimal therapy

IX. Comorbidities

Common cardiac and non-cardiac comorbidities with suggested actions (*Table 16*)

X. Palliative/Hospice Care Seven principles and actions to consider regarding palliative care

PIONEER-HF

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Open label extension:

- Further reduction in NTproBNP (both groups)
- In-hospital sac-val group experienced lower incidence of death or re-hospitalization over 12 weeks follow-up

Velazquez et al, N Engl J Med 2019 Devore et al, JAMA Cardiol 2020

DAPA-HF and EMPEROR-Reduced

Outcome	Dapagliflozin	Placebo	
	Events/100 patient-yr	Events/100 patient-yr	HR (95%CI)
Primary outcome	11.6	15.6	0.74 (0.65- 0.85)
HHF	6.9	9.8	0.70 (0.59- 0.83)
CV death	6.5	7.9	0.82 (0.69- 0.98)

Outcome	Empagliflozin	Placebo	
	Events/100 patient-yr	Events/100 patient-yr	HR (95%CI)
Primary outcome	15.8	21.0	0.75 (0.65- 0.86)
HHF	10.7	15.5	0.69 (0.59- 0.81)
CV death	7.6	8.1	0.92 (0.75- 1.12)

McMurray JJV, et al. N Engl J Med. 2019

Packer M, et al. N Engl J Med. 2020

- Significantly reduced combined endpoint of CV death or HF hospitalization compared to placebo, with very few adverse events
- EMPEROR Reduced patients with both higher risk and more aggressively treated with HF therapies
- Benefit similar in patient WITH and WITHOUT diabetes





*ACEI/ARB should only be considered in patients with contraindications, intolerance or inaccessibility to ARNI. In those instances, please consult Figure 3 and text for guidance on initiation.

[†]Carvedilol, metoprolol succinate, or bisoprolol.

ACEI = angiotensin-converting enzyme inhibitors; ARNI = angiotensin receptor-neprilysin inhibitors; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate; HFrEF = heart failure with reduced ejection fraction; HR = heart rate; $K^* =$ potassium; NYHA = New York Heart Association; SGLT2 = sodium-glucose cotransporter-2.







ACEI = angiotensin-converting enzyme inhibitors; ARNI = angiotensin receptor-neprilysin inhibitors; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate.

*Carvedilol, metoprolol succinate, or bisoprolol.





ACEI = angiotensin-converting enzyme inhibitors; ARNI = angiotensin receptor-neprilysin inhibitors; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate; SGLT2 = sodium-glucose cotransporter-2.





Treatment of HFrEF Stage C and D



⁺Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored. [‡]See 2013 HF guideline.

§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.

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ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD, isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSR, normal sinus rhythm; and NYHA, New York Heart Association.

Recommendation	Strength of Rec	Quality of Evidence
ARNI can be used in place of ACE/ARB in Pts with HFrEF with sxs despite tx with GDMT to decrease CV death, HF admissions, and sxs	Strong	High
Pts admitted for ADHF with HFrEF should be switched to ARNI (from ACE/ARB) when stabilized and before discharge	Strong	Moderate
Pts admitted to hospital with new dx of HFrEF should be tx'd with ARNI as 1 st line tx (as an alternative to ACE/ARB)	Weak	Moderate



Recommendation	Strength of Rec	Quality of Evidence
SGLT2 inhibitors (such as dapagliflozin or empaglifozin) can be used in Pts w/ HFrEF with or without DM-II to improve sxs and QoL and to reduce risk of HF and/or CV mortality	Strong	High



- For Pts with newly dx'd Stage C HFrEF:
 - BB and ACEI/ARB/ARNI should be started in any order
 - Each agent should be up-titrated to maximally tolerated or target dose
 - Initiation of BB is better tolerated when Pts are dry
 - Initiation of ACEI/ARB/ARNI is better tolerated when Pts are wet
- Guideline-recommended BB for HFrEF: carvedilol, metop succinate, or bisoprolol
- ARNIs are preferred over ACE/ARB
 - Renal function and potassium should be checked 1-2 weeks after starting or titrating
- Diuretics should be used to achieve decongestion
 - If furosemide >80 mg BID, consider different loop or thiazide



- Consider <u>aldosterone antagonist</u> after BB and ACE/ARB/ARNI with close monitoring of electrolytes
- Consider <u>SGLT-2 inhibitors</u> for HFrEF with NYHA class ≥II
- Consider <u>isosorbide dinitrite + hydralazine</u> for persistently symptomatic black patients after max tolerated BB, ACE/ARB/ARNI, aldosterone antagonist
- Consider <u>ivabradine</u> if resting HR ≥70 bpm despite max tolerated BB
- Optimize therapy during hospitalizations
- Adjust meds q2 wks as outpatient
- Repeat TTE q3-6 months to guide device mgt (ICD and/or CRT)



- Hyperkalemia and/or abnormal renal function
 - Common barriers to achieving target medication doses
 - Require patient education about dietary changes
 - May be managed with potassium binders
- Socioeconomic barriers may pose major barriers to ARNI, SGLT-2 inhibitors, etc
 - Financially feasible options should be considered



- Resume GDMT in Pts with recovery of LVEF to >40%, in the absence of a defined, reversible cause.
- Consider repeat TTE only if change in clinical status or other high-risk features
- BNP or NT-proBNP
 - Useful for risk assessment and decision making regarding specialist referral or need for other imaging studies
 - BNP levels may rise with ARNI therapy
 - NT-proBNP levels are not affected



- Consider referral to a HF specialist if
 - Inotropes needed
 - NYHA class IIIB/IV sxs or persistently elevated natriuretic peptides
 - End-organ dysfunction, persistent hypotension, persistent tachycardia
 - EF ≤35%
 - ICD shocks
 - Recurrent hospitalizations
 - Congestion despite escalating diuretics
 - Intolerance to GDMT



- Build a team
- Use infrastructure
 - Scales, smartphones, EHRs, etc
- Assess medication adherence
 - Improve adherence with Pt education, medication management strategies, pharmacy involvement, and/or incentives
- Address goals of care



HF Case #1

A 68-year-old female presents with progressive worsening of DOE over a month and increased swelling of both lower extremities. Admitted to hospital with ADHF. She denies concurrent chest pain or cough.

PMH: HFrEF (30%), HTN, DM , dyslipidemia. She takes Insulin, simvastatin, Out of Lasix and lisinopril > 1 week She is not checking her weights at home, not following low salt diet.



HF Case #1 cont'd

She has gained 15 lbs in a month

BP 160/90 mm Hg, P 86/min, RR 18

CV exam --JVD elevated, RRR (+) S3, 3/6 HSM at the apex. Lungs- few crackles at the bases

Ext-- 2(+) peripheral edema bilaterally

Labs- renal function and electrolytes are stable.

What is your approach? How to optimize this patient's HF care?



HF Case #2

A 54 -year-old male with long standing uncontrolled HTN, obesity,

dyslipidemia, presents with gradually worsening of DOE and

increased weight over few months

Edema presents on up to knees.

Admitted to hospital with new onset ADHF.

Denies CP. Troponins normal. Cardiac cath revealed no significant CAD

Echo obtained- LVH, EF 35%

Medications- Carvedilol 12.5 mg BID .He took some other BP meds few years ago. Not recently.

BP 145/ 85 HR 72

What is your approach?

How to optimize this patient's HF care?



HF Case #3

A 42 year-old male with morbid obesity, OSA/OHS on CPAP and home O2, Nonischemic CM with EF 15% admitted with significant volume overload. Edema presents on up to thighs. Admitted to hospital with ADHF. Denies CP. Troponins normal. BP 100-110/70 HR 78 Medications- Lasix 80 mg BID , metoprolol XL 50 mg daily. Lisinopril 5mg daily (stopped recently because of cough) Adherent to meds , reports that Lasix not working

During hospitalization received significant diuresis with high dose Lasix and Thiazide +- Diamox combination. Renal function – almost at baseline. Metoprolol cont'd at reduced dose at 25mg daily. How to optimize this patient's HF care?



Figure 2: Pre-discharge Checklist

Medications	Follow-up	Patient Education
 GDMT initiation: ACEi/ARB/ARNI, β-blocker, MRA, SGLT2i Assessment of oral diuretic 	 Telehealth/in-person visit within 1 week Heart failure clinic referral Labs: creatinine, electrolyte 	 Medication education Nutrition counseling Physical exercise education Daily weight and blood
efficacy	panel, glucose, BNP	pressure monitoring
Assess for potential drug–drug interactions	referral	cessation counseling

A suggested pre-discharge checklist to help clinicians ensure that patients who are hospitalized with heart failure with reduced ejection fraction receive optimal guideline-directed medical therapy (GDMT). ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor—neprilysin inhibitor; BNP = brain natriuretic peptide; MRA = mineralocorticoid receptor antagonist; SGLT2i = sodium glucose cotransporter-2 inhibitor.

US Cardiology Review 2021;15:e07



Summary

- HF is a major public health problem
- High hospital admissions and high mortality rate
- Key elements of management
 - early dx
 - hemodynamic stabilization and
 - initiation of GDMT
 - Comprehensive Pt education and life style modification should be started at early stages of admission and continued as an outpatient



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SHM Clinical Rapid Updates: Heart Failure Thank you: Ebrahim Barkoudah, MD Nurcan Ilksoy, MD