Effective Management of Patients With Heart Failure During and After the COVID-19 Pandemic: Updates and Key Considerations for the Nurse Practitioner

NURSE PRACTITIONER



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Learning Objectives

- Discuss the safety of RAAS antagonist use in patients with CV and related comorbidities during the ongoing COVID-19 pandemic
- Outline how to apply evidence-based GDMT into the management of patients with HF
- Explain the burden of COVID-19 on patients with CV and related comorbidities
- Discuss how to integrate telemedicine initiatives into the effective management of patients with HF

COVID-19, coronavirus disease 2019; CV, cardiovascular; GDMT, guideline-directed medical therapy; HF, heart failure; RAAS, renin-angiotensin-aldosterone system.



Definition of HF

A clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood



Major clinical manifestations: dyspnea, fatigue, and fluid retention*

*Patient presentation varies.

Jessup M, Brozena SA. New Engl J Med. 2003;348:2007-2018; Yancy CW, et al. Circulation. 2013;128:e240-e327.

Classification of HF

Classification	EF (%)	Description
HFrEF	≤40	Also referred to as systolic HF . RCTs have mainly enrolled patients with HF <i>r</i> EF; to date, only in these patients have effective therapies been demonstrated.
HF <i>mr</i> EF	41-49	HF with mid-range ejection fraction . New category with overlapping characteristics of HF <i>r</i> EF and HF <i>p</i> EF. Clinical course and mortality are more like HF <i>r</i> EF than HF <i>p</i> EF.
HF <i>p</i> EF	≥50	Also referred to as diastolic HF . Several different criteria have been used to further define HF <i>p</i> EF. Diagnosis of HF <i>p</i> EF is challenging because it largely involves excluding other potential noncardiac causes of symptoms suggestive of HF. To date, no effective therapies have been identified.

RCTs, randomized control trials. Yancy CW, et al. *Circulation*. 2013;128:e240-e327; Bhambhani V, et al. *Eur J Heart Fail*. 2018;20(4): 651–659.





ESC Guidance on Management of CVD During the COVID-19 Pandemic

- The risk of COVID-19 infection may be higher in chronic HF patients due to the advanced age and presence of several comorbidities.
- Ambulatory stable HF patients (with no cardiac emergencies) should refrain from hospital visits.
- GDMT (including beta-blocker, ACE inhibitor, ARB, or sacubitril/valsartan and MRA), should be continued in chronic HF patients, irrespective of COVID-19.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CVD, cardiovascular disease; MRA, mineralocorticoid receptor antagonist. The European Society for Cardiology. ESC guidance for the diagnosis and management of CV disease during the COVID-19 pandemic. Updated June 10, 2020. https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance



ESC Guidance on Management of CVD During the COVID-19 Pandemic



Treatment of Stage C-D HF*r***EF**



Medications for HFrEF

Class	Mechanism of action	Drug	Initial daily dose(s)	Max dose(s)	Mean RCT dose
	Inhibits the conversion of angiotensin I to	Captopril	6.25 mg TID	50 mg TID	122.7 mg QD
	angiotensin II, and upregulates bradykinin,	Enalapril	2.5 mg BID	10-20 mg BID	16.6 mg QD
	RMS system and the effects of adverse cardiac	Fosinopril	5-10 mg QD	40 mg QD	NA
	remodeling	Lisinopril	2.5-5 mg QD	20-40 mg QD	32.5-35.0 mg QD
ACEIS		Perindopril	2 mg QD	8-16 mg QD	NA
		Quinapril	5 mg BID	20 mg BID	NA
		Ramipril	1.25-2.5 mg QD	10 mg QD	NA
		Trandolapril	1 mg QD	4 mg QD	NA
	Inhibits angiotensin II AT1 receptors, thereby	Candesartan	4-8 mg QD	32 mg QD	24 mg QD
ARBs	counteracting the overactivation of the RAAS	Losartan	25-50 mg QD	50-150 mg QD	129 mg QD
	cardiac remodeling	Valsartan	20-40 mg BID	160 mg BID	254 mg QD
ARNI	Inhibits neprilysin and blocks angiotensin II receptor; inhibition of neprilysin leads to increased circulating levels of natriuretic peptides, vasodilation and natriuresis	Sacubitril/ valsartan	49/51 mg BID Therapy may be initiated at 24/26 mg BID	97/103 mg BID	375 mg QD; target dose: 24/26 mg, 49/51 mg OR 97/103 mg BID

AT1, angiotensin II receptor type 1; BID, twice daily; QD, daily; TID, three times daily; RMS, records management system. Yancy CW, et al. *Circulation*. 2013;128(16):e240-e327.

Medications for HFrEF (cont'd)

Class	Mechanism of action	Drug	Initial daily dose(s)	Max dose(s)	Mean BCT dose
I _f Channel Inhibitor	Inhibits the I _f node, which slows the sinus nodal rate in patients who are in sinus rhythm	Ivabradine	5 mg BID	7.5 mg BID	6.4 mg BID (at 28 days) 6.5 mg BID (at 1 year)
Aldosterone antagonists (ie, MRAs)	Competitively bind to the aldosterone receptor, which increases the secretion of water and sodium in the distal tubule, and decreases the secretion of potassium	Spironolactone Eplerenone	4-8 mg QD 25-50 mg QD	32 mg QD 50-150 mg QD	24 mg QD 129 mg QD
β-blockers	Inhibits neprilysin and blocks angiotensin II receptor; inhibition of neprilysin leads to increased circulating levels of natriuretic peptides, vasodilation and natriuresis	Bisoprolol Carvedilol Carvedilol CR Metoprolol Succinate	1.25 mg QD 3.125 mg BID 10 mg QD 12.5-25 mg QD	10 mg QD 50 mg BID 80 mg QD 200 mg QD	8.6 mg QD 37 mg QD NA 159 mg QD
lsosorbide dinitrate (ID) and hydralazine (HYD)	Arterial and venous vasodilation and a nitric oxide donor (isosorbide)	Fixed-dose combination ID and HYD	20 mg ID/37.5 mg HYD TID 20-30 mg ID/25-50 mg HYD TID or QD	40 mg ID/75 mg HYD TID 40 mg ID TID with 100 mg HYD TID	90 mg ID/~175 mg HYD QD N/A

Yancy CW, et al. Circulation. 2013;128(16):e240-e327.

Diuretics Commonly Used in HF

Class	Mechanism of action	Drug	Initial dose	Usual daily dose		
Loop diuretics	Inhibits primarily the absorption of sodium	Furosemide	20-40 mg	40-240 mg		
	and chloride not only in the proximal and distal tubules but also in the loop of Henle	Bumetanide	0.5-1.0 mg	1-5 mg		
	distal tubules but also in the loop of riente.	Torsemide	5-10 mg	10-20 mg		
Thiazides	Inhibits sodium chloride transport in the	Bendroflumethiazide	2.5 mg	2.5-10 mg		
	distal convoluted tubule. More sodium is	Hydrochlorothiazide	25 mg	12.5-100 mg		
	accompanying fluid.	Metolazone	2.5 mg	2.5-10 mg		
		Indapamide	2.5 mg	2.5-5 mg		
	Potassium-sparing diuretics	Initial Dose	Usual Daily	Dose		
	Spironolactone/eplerenone	+ ACEi/ARB: 12.5-25 mg - ACEi/ARB: 50 mg	+ ACEi/ARB: - ACEi/ARB: 10	50 mg D-200 mg		
	Spironolactone/eplerenone	+ ACEi/ARB: 12.5-25 mg - ACEi/ARB: 50 mg + ACEi/ARB: 2.5 mg - ACEi/ARB: 5 mg	+ ACEi/ARB: - ACEi/ARB: 10 + ACEi/ARB: 1 - ACEi/ARB: 1	50 mg 0-200 mg 5-10 mg 0-20 mg		

https://www.ncbi.nlm.nih.gov/books/NBK430766/

2017 Focused Update of the 2013 Guideline for the Management of HF

Class (Strength) o	f Recommendation	Level	Level (Quality) of Evidence	
l (Strong)	Benefit >>> Risk	Α	High quality	
lla (Moderate)	Benefit >> Risk	B-R	Moderate quality, randomized	
llb (Weak)	Benefit ≥ Risk	B-NR	Moderate quality, non-randomized	
III: No Benefit (Moderate)	Benefit = Risk	C-LD	Limited data	
III: Harm (Strong)	Risk > Benefit	C-EO	Expert opinion	
N, et al. Circulation. 2013;128(16):e2	40-e327.			

Treatment of Stage C HF*r***EF**

	COR	LOE	Recommendation	
		ACE-I: A	The clinical strategy of inhibition of the RAAS with ACEI's, ARBs, or ARNIs in conjunction with	
NEW	I.	ARB: A	evidence-based β-blockers and aldosterone antagonists in selected patients is recommended for	
		ARNI: B-R	patients with chronic HFrEF to reduce morbidity and mortality.	
	I	ACE-I: A	The use of ACEi's is beneficial for patients with prior or current symptoms of chronic HFrEF to reduce morbidity and mortality.	
	I	ARB: A	The use of ARBs to reduce morbidity and mortality is recommended in patients with prior or current symptoms of chronic HFrEF who are intolerant to ACEi's because of cough or angioedema.	
NEW	I.	ARNI: B-R	In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.	
NEW	III: Harm	B-R	ARNI should not be administered concomitantly with ACEi's or within 36 hours of the last dose of an ACEi.	
NEW	III: Harm	C-EO	ARNI should not be administered to patients with a history of angioedema.	
NEW	lla	Iva: B-R	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF \leq 35%) who are receiving GDMT, including a β -blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.	

Iva, ivabradine; LOE, level of evidence.

Yancy CW, et al. Circulation. 2013;128(16):e240-e327.

17

Treatment of Stage C HF*p***EF**

	COR	LOE	Recommendation
	L	В	Systolic and diastolic blood pressure should be controlled in patients with HF <i>p</i> EF in accordance with published clinical practice guidelines to prevent morbidity.
	I.	С	Diuretics should be used for relief of symptoms due to volume overload in patients with HFpEF.
	lla	С	Coronary revascularization is reasonable in patients with CAD in whom symptoms (angina) or demonstrable MI is judged to be having an adverse effect on symptomatic HF <i>p</i> EF despite GDMT.
	lla	С	Management of AF according to published clinical practice guidelines in patients with HFpEF is reasonable to improve symptomatic HF.
	lla	с	The use of β -blockers, ACEi's, and ARBs in patients with hypertension is reasonable to control blood pressure in patients with HFpEF.
NEW	lib	B-R	In appropriately selected patients with HF <i>p</i> EF, aldosterone receptor antagonists might be considered to decrease hospitalizations.
	llb	В	The use of ARBs might be considered to decrease hospitalizations for patients with HFpEF.
NEW	III: No Benefit	B-R	Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QoL in patients with HF <i>p</i> EF is ineffective .
	III: No Benefit	С	Routine use of nutritional supplements is not recommended for patients with HFpEF.

AF, atrial fibrillation; QoL, quality of life.

Yancy CW et al. Circulation. 2013;128(16):e240-e327.

18

Recommendations for Hypertension

	COR	LOE	Recommendation
NEW	I	B-R	In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be <130/80 mm Hg .
NEW	I	C-EO	Patients with HFrEF (stage C) and hypertension should be prescribed GDMT titrated to attain systolic blood pressure <130 mm Hg .
NEW	I	C-LD	Patients with HFpEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure <130 mm Hg.

Use of RAAS Inhibitors & COVID-19

 Previous treatment with ACEi/ARB in patients with COVID-19 has <u>no</u> <u>effect</u> on mortality, HF, hospitalization, or ICU admission



SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Son M, et al. Hypertension. 2020;76:742–749; Lopez-Otero D, et al. Rev Esp Cardiol (Engl Ed). 2020 Jun 5; Sriram K, et al. Clin Pharmacol Ther. 2020 Aug;108(2):236-241

20

CV Society Recommendations on RAAS Antagonists in the COVID-19 Patient

Society	Pub Date	Recommendation
		Continuation of ACEis/ARBs in COVID-19 patients with preexisting indications (HF, HTN, CAD)
AHA/HFSA/ACC	Mar 17, 2020	Careful consideration prior to addition/ discontinuation of any CVD treatments in COVID-19 patients
Canadian CV Society	Mar 20, 2020	Continuation of ACEi/ARB/ARNi unless clinically contraindicated (symptomatic hypotension, shock, AKI, hyperkalemia)
ESC Council on HTN	Mar 13, 2020	Continue antihypertensive treatment
		Stable COVID-19 patients should continue ACEi/ARB treatment according to 2018 ESC/ESH guidelines
European Society of HTN	Apr 15, 2020	Assess COVID-19 patients with severe symptoms, sepsis, or hemodynamic instability on a case-by-case basis for the discontinuation of blood pressure lowering drugs, with consideration for current guidelines
HTN Canada	Mar 13, 2020	Continue antihypertensive treatment
International Society of HTN	Mar 16, 2020	Routine use of ACEi's/ARBs in hypertensive patients despite COVID-19 concerns

New Indications for HFpEF

- Sacubitril/valsartan
 - FDA advisory committee voted 12-1 to approve for treatment of HFpEF
 - PARAGON-HF trial
- Spironolactone
 - FDA advisory committee voted 8-4 to approve for reduction of HF hospitalization
 - HF with mildly-reduced or midrange EF: LVEF of 40% to 57%
 - TOPCAT Trial

Keown A. Novartis' Entresto on track for new FDA approval following successful AdComm. Biospace. Dec 16, 2020. https://www.biospace.com/article/novartis-entresto-clears-fda-adcomm-for-hfpef Buzby S. FDA advisory panel endorses spironolactone for HF hospitalization reduction HFpEF. Healio. Dec 16, 2020. https://www.healio.com/news/cardiology/20201216/fda-advisory-panel-endorses-spironolactone-for-hf-hospitalization-reduction-in-hfpef

New Indications for HFpEF

	CHARM-P	TOPCAT	PARAGON-HF
	N = 3023	N = 3445	N = 4800
Treatment Arms	Candesartan vs Placebo	Spironolactone vs Placebo	Sacubitril/Valsartan vs Placebo
LVEF Inclusion Criteria	LVEF > 40%	LVEF ≥ 45%	LVEF > 45%
Endpoint	First of either CVD or HFH	First of either CVD, HFH, or RSD	CVD and total HFH (first and recurrent)
Hospitalizations	HR 0.78	HR 0.98	HR 0.85
HR (95% CI)	(0.59–1.03)	(0.74–1.30)	(0.72–1.00)
LVEF Subgroup	LVEF 40–49%	LVEF <50%	LVEF <57%
	HR 0.48 (0.33-0.70)	HR 0.76 (0.46-1.27)	HR 0.78 (0.64-0.95)

HFH, heart failure hospitalization.

Gronda E, et al. Eur Heart J Suppl. 2020;22(suppl):L77-L81.



DAPA-HF Trial

- Phase 3 placebo-controlled trial
- First to examine benefit of SGLT2 inhibitors in patients with HF
 - Regardless of DM status
- 4744 patients with HFrEF
 - NYHA Class II, III, or IV HF and LVEF ≤40%
- Dapagliflozin (10 mg once daily) or placebo
- Primary outcome: composite of worsening HF* or CV death

*Hospitalization or an urgent visit resulting in intravenous therapy for HF. DM, diabetes mellitus; SGLT2, sodium-glucose transport protein 2. McMurray JJV, et al. *N Engl J Med*. 2019;381(21):1995-2008.

DAPA-HF: Primary Outcome



EMPORER-Reduced Trial

- Results announced at ESC 2020
- Empagliflozin 10 mg daily vs placebo in 3730 patients
 - HFrEF
 - With or without diabetes
 - Already receiving standard of care for HF
- Median follow-up: 16 months
- Primary endpoint: CV death or HHF
 - HR 0.75, 95% CI 0.65-0.86, P < .0001
- Total risk of hospitalizations for HF reduced by 30%
- Adverse renal outcomes reduced by 50%

European Society of Cardiology. Hot line: not just in diabetes – empagliflozin improves outcomes in patients with heart failure in the EMPEROR-Reduced trial. Aug 29, 2020. https://www.escardio.org/Congresses-&-Events/ESC-Congress/Congress-resources/Congress-news/hot-line-not-just-indiabetes-empagliflozin-improves-outcomes-in-patients-with-heart-failure-in-the-emperor-reduced-trial

Expanding Opportunities for SGLT2 Inhibitors in HF 2018 ACC Expert Consensus

Considerations for Drug Initiation and Monitoring in Patients Starting an SGLT2 Inhibitor With Demonstrated CV Benefit

- If A1c well-controlled at baseline, or known history of frequent hypoglycemic events, reduce dose of sulfonylurea by 50% or basal insulin dose by 20% when starting therapy
- Avoid hypovolemia. May need to reduce thiazide or loop diuretic dose
- Educate patients regarding symptoms of low blood pressure (light headedness, orthostasis, weakness)
- Instruct patients to more closely monitor glucose at home for the first 4 weeks of therapy
- Educate patients regarding symptoms of diabetic ketoacidosis and that diabetic ketoacidosis can occur even if blood glucose readings are in the 150–250 mg/dL range
- Educate patients regarding foot care and follow-up foot pulse examination (particularly canagliflozin)
- Monitor kidney function
- Educate patients regarding potential for genital mycotic infections

Das SR, et al. J Am Coll Cardiol. 2018;72(24):3200-23.







Increased Risks of Severe Illness

- Study of 6439 patients admitted for COVID-19
 - 422 (6%) had history of HF
- Compared to those without HF and independent of LVEF and RAASi treatment, patients with HF had increased:
 - mLOS: 8 vs 6 days, P<0.001
 - Frequency of ICU care: OR 1.52, 95% CI 1.20-1.92, P=0.001
 - Intubation/mechanical ventilation: OR 2.18, 95%
 CI 1.71-2.77, P<0.001
 - Mortality: OR 2.02, 95% CI 1.65-2.48, P<0.001

mLOS, minimum length of stay. Alvarez-Garcia J, et al. J Am Coll Cardiol. 2020;76(20):2334-2348.





A Dangerous Cycle

Growing evidence suggests that *patients* who contract COVID-19 are at increased risk of developing CV-related comorbidities <u>as a</u> <u>result of infection</u>.

VF, ventricular fibrillation; VT, ventricular tachycardia. Nishiga M, et al. *Nat Rev Cardiol*. 2020;17(9):543-558.







Telemedicine: CMS & How We Got Here

- To reduce transmission of COVID-19, healthcare systems have transitioned to noncontact care delivery
- In early March 2020, CMS broadened access to telehealth services
 - Coronavirus Preparedness and Response Supplemental Appropriations Act
- Through telehealth, physicians can
 - Maintain face-to-face interactions with their patients
 - Gain familiarity with patients' domestic circumstances
 - Obtain vital sign measurement through home blood pressure cuffs, pulse oximeters, and scales
 - Perform limited physical examinations for jugular venous distention, peripheral edema, peripheral catheter and driveline site integrity, and functional capacity
 - Reconcile medications through direct visualization of pill containers
 - Interact with caregivers

Centers for Medicare & Medicaid Services (CMS). Medicare telemedicine health care provider fact sheet. Mar 17, 2020. https://www.cms.gov/newsroom/fact-sheets/medicare-telemedicine-health-care-provider-fact-sheet





Telemedicine Is an Effective Care Component



Implementation Guide for Rapid Integration of an Outpatient Telemedicine Program amidst the COVID-19 Pandemic

"Telemedicine should be considered whenever possible to provide medical advice and follow up of stable HF patients."

-ESC Guidance on Management of CVD During the COVID-19 Pandemic



The European Society for Cardiology. ESC guidance for the diagnosis and management of CV disease during the COVID-19 pandemic. Updated June 10, 2020. https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance Adapted from Smith WR, et al. *J Am Coll Surg.* 2020;231(2):216-222.e2. Available at: https://www.eurekalert.org/multimedia/pub/230767.php

40



Effective Transitions of Care

"The goal of management of HF is to provide a <u>'seamless' system of care</u> that embraces both the community and hospital throughout the health care journey."





Patient Case Scenario

- Aubrey is a 52-year-old obese woman (BMI 31.3) with a history of HFrEF and T2DM. Last year, she had an MI and was hospitalized for 2 weeks. Today, she presents to your practice with flu-like symptoms and a fever of 103.2, and she mentions she was unable to smell her coffee this morning. Aubrey is currently taking lisinopril and metformin and tolerating both agents well. Her recent HbA1c was 8.5%.
 - What concerns do you have about Aubrey's use of lisinopril given she might have COVID-19?
 - What modifications (if any) do you make to her medications?

Summary

- Echocardiography is key to the diagnosis of HF
- Therapy initially relies on the use of ACE inhibitors and beta blockers
- Patients with NYHA class II or III HF and on ACE inhibitors should be transitioned to ARNI
 - ARNI further reduces morbidity and mortality
 - Must have 36-hour washout period between ACE inhibitor and ARNI
 - Sacubitril/valsartan and spironolactone are now approved for HFpEF
 - No established risk to patients with RAAS inhibitors/COVID-19
- SGLT2 inhibitors have evolved into cardiovascular risk reduction therapies independent of glycemic control

Summary

- COVID-19 has radically altered the world, particularly healthcare
- Dangerous cycle: COVID-19 infection increases risk of CV comorbidities, and CV comorbidities increase risk of COVID-19 infection
 - Maintaining GDMT more important now than ever
- Telemedicine
 - CMS broadened telehealth in wake of pandemic
 - Should be used whenever possible
 - Important implementation takeaways
 - Patient information

