Practical Approach to HF Medication

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- 1. Understand practical tips for initiating and up-titrating Quadruple therapy
- 2. Compare and contrast novel approaches to prescribing Quadruple therapy
- 3. Review tools for counselling patients on safety considerations of therapies

Conflict of interest

- Rodolfo Pike
 - Honoraria/consulting fees
 - Astra Zeneca
 - Boehringer Ingelheim
 - Pfizer
 - Novartis
- Nadia Thomson
 - No conflict of interest

HFrEF VS HFpEF

Ejection fraction: the percent of blood ejected from the ventricle with each beat



Reference: Abraham et al., Eur J Heart Fail 2020 Dec 22: 2175-2186

Body's reaction to inadequate cardiac output with LVEF ≤ 40%



Role of naturetic peptides in heart failure



Need for dual blockade

Sacubitril: Neprilysn Inhibitor

Valsartan: RAAS blockade

Adapted from Langenickel TH, Dole WP. Angiotensin receptor-neprlysin inhibition with LCZ696: a novel approach for the treatment of heart failure. Drug Discovery Today: Therapeutic Strategies 2012;9:e131-e139.

Key: NP = natriuretic peptide; RAAS = renin-angiotensin-aldosterone-system

2021 Heart failure Guidelines



Case study- Mrs. Viola

68 year old female with Non-ischemic cardiomyopathy. Presented to hospital with HX of leg edema, PND, orthopnea and breathlessness with minimal activity. 18 lb weight gain over previous 2 months. Diversed and started on triple therapy prior to discharge. Referred CHF clinic post discharge for patient education and titration of heart failure therapies. Today is first visit to heart function clinic.

PmHx:

- HTN
- Type II DM
- Ex-smoker

- Social ETOH
- Surgical History: Nil
 - Viral infection 6
 months ago

Assessment:

- BP 120/62 sitting,
- 114/58 standing
- HR 68 , RR 18
- Weight: 86 kg

- JVP 4 CM ASA
- S1/S2, no S3/S4, II/VI murmur of MR at apex
- Edema- 2+ midshin
- Lungs- clear
- NYHA Class II

Self-Care

Daily weights Low sodium diet: < 2000 mg

Investigations:

Labs:

Hgb 124, Creatinine 92 umol/L, K+ 4.9 mmol/L, NA 136 mmol/L, NT pro BNP 1650. HbA1C 8.7 <u>CXR</u>: no evidence of congestion <u>Echo:</u> LVEF 28%, LVEDD 6.2cm, Moderate MR, Trace TR. <u>ECG</u>: SR 69 BPM with LBBB Cath: No flow limiting lesions

Medication:

Sacubitril/Valsartan 49/51mg po

Bisoprolol 2.5 mg po daily Aldactone 12.5 mg daily Metformin 1000 mg tid Furosemide 60 mg po bid

POLL QUESTION

- After completing your assessment you decide to make changes to her medical therapies. You will:
 - A. Decrease her Lasix
 - B. Increase her Bisoprolol
 - C. Increase Sacubitril/Valsartan
 - D. Start SGLT2 inhibitor
 - E. A and D

CCS recommendation 2021

1.We recommend that in the absence of contraindications, patients with HFrEF be treated with combination therapy including 1 evidence-based medication from each of the following categories:

a. ARNI (or ACEI/ARB);

b. β -blocker;

c. MRA; and

d. SGLT2 inhibitor.

(Strong Recommendation; Moderate-Quality Evidence).

Medication changes:

- Patient was prescribed an SGLT2 inhibitor: Dapagliflozin 10 mg daily
- Lasix decreased to 40 mg bid

Follow up:

- Repeat blood work to check renal/electrolytes in 1 week
- 2 weeks in clinic for assessment
- Daily weights
- Low sodium diet



SGLT2 Inhibition Reduces Renal Glucose Reabsorption and Increases Glucose Elimination



SGLT2 inhibitors Practical Tips



Abbreviations:

CLI: critical limb ischemia; DKA: diabetic ketoacidosis; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; GMI: genital mycotic infections; HFrEF: heart failure with reduced ejection fraction; SGLT2i: SGLT2 inhibitors; SU: sulfonylurea; UACR: urine albumin to creatinine ratio



Soclété canadienne d'insuffisance cardiaque

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SGLT2 and Sick Day Management



Case Study- Mrs. Viola- 2 weeks later

Assessment:

- BP 102/54 sitting, 88/52 standing,
- HR 72 , RR 18
- Weight 81 kg (5 kg weight loss)
- Light-headed with standing

- JVP 2 CM ASA
- S1/S2, no S3/S4, II/VI murmur of MR at apex
- Edema- none
- Lungs- clear
- NYHA Class II- breathlessness with exertion and fatigue

Investigations:

<u>Labs</u>:

<u>Hgb 124,</u>

Creatinine 152 umol/L,

K+ 4.6 mmol/L, NA 136 mmol/L, GR 7.2- 9

ECG: SR 72 BPM with LBBB

Medication:

Sacubitril/Valsartan 49/51mg po bid Bisoprolol 2.5 mg po daily Aldactone 12.5 mg daily Metformin 1000 mg tid

Last visit:

Started Dapagliflozin 10 mg po daily Decreased Furosemide 40 mg po bid Self-Care Daily weights Low sodium diet: < 2000 mg After completing your assessment you decide to make additional changes to her medical therapies.

You will:

- A. Stop SGLT2 inhibitor due to increased Creatinine
- B. Stop/Decrease Lasix
- C. Decrease Beta Blocker
- D. Start Ivabradine

Management Plan

Medication changes:

- Stop daily Lasix- prn only
- Continue other medications

Follow up:

- Home BP, HR and weight monitoring.
- Call clinic if decreasing BP and worsening light-headedness
- Repeat labs: Lytes, BUN and creatinine in 1 week
- Return to clinic in 2 weeks.

Case Study- Mrs. Viola- 2 weeks later

Assessment:

- BP 110/58 sitting, 104/52 standing,
- HR 68, RR 18
- Brief Light-headed lasting few seconds with standing
- Weight 83 kg (2 kg weight increase)

- JVP 3 CM ASA
- S1/S2, no S3/S4, II/VI murmur of MR at apex
- Edema- none
- Lungs- clear
- NYHA Class II- breathlessness with exertion and fatigue

Investigations:

Labs: Hgb 124, Creatinine 96 umol/L, K+ 4.9 mmol/L, NA 136 mmol/L, GR 7.2- 9 ECG: SR 68 BPM with LBBB

Medication:

Ramipril 2.5 mg po bid Bisoprolol 2.5 mg po daily Aldactone 12.5 mg daily Metformin 1000 mg tid Dapagliflozin 10 mg po daily Last visit: Lasix prn Self-Care Daily weights Low sodium diet: < 2000 mg

CCS recommendation 2021 use of ARNI

3. We recommend that an ARNI be used in place of an ACEI or ARB, in patients with HFrEF, who remain symptomatic despite treatment with appropriate doses of GDMT to decrease CV death, HF hospitalizations, and symptoms (Strong Recommendation; High Quality Evidence).

4. We recommend that patients admitted to hospital for acute decompensated HF with HFrEF should be switched to an ARNI, from an ACEI or ARB, when stabilized and before hospital discharge (Strong Recommendation; Moderate-Quality Evidence).

5. We suggest that patients admitted to hospital with a new diagnosis of HFrEF should be treated with ARNI as first-line therapy, as an alternative to either an ACEI or ARB (Weak Recommendation; Moderate-Quality Evidence).

GDMT CCS 2021

Table 2 Standard therapies and their initial and optimal dose targets for patients with HFrEF

Drug class	Specific agent	Start dose	Target dose
ARNI	Sacubitril-valsartan	50-100 mg BID (dose rounded)	200 mg BID (dose rounded)
ACEI	Enalapril Lisinopril Perindopril Ramipril Trandolapril	1.25-2.5 mg BID 2.5-5 mg daily 2-4 mg daily 1.25-2.5 mg BID 1-2 mg daily	10 mg BID/20 mg BID (NYHA IV) 20-35 mg daily 4-8 mg daily 5 mg BID 4 mg daily
ARB	Candesartan Valsartan	4-8 mg daily 40 mg BID	32 mg daily 160 mg BID
β-Blocker	Carvedilol Bisoprolol Metoprolol (CR/XL)	3.125 mg BID 1.25 mg daily 12.2-25 mg daily	25 mg BID/50 mg BID (> 85 kg) 10 mg daily 200 mg daily
MRA	Spironolactone Eplerenone	12.5 mg daily 25 mg daily	25-50 mg daily 50 mg daily
SGLT2 inhibitor	Dapagliflozin Empagliflozin Canagliflozin	10 mg daily 10 mg daily 100 mg daily	10 mg daily 10-25 mg daily 100-300 mg daily
Sinus node inhibitor	Ivabradine	2.5-5 mg BID	7.5 mg BID
sGC stimulator	Vericiguat	2.5 mg daily	10 mg daily
Vasodilator	Hydralazine and isosorbide dinitrate	10-37.5 mg TID/10-20 mg TID	75-100 mg TID or QID/40 mg TID
Cardiac glycosides	Digoxin	0.0625-0.125 mg daily	Not applicable: monitor for toxicity

Practical tips

The approach to initiation and titration of standard therapies should be directed by clinical and other patient factors including hemodynamic status, renal function, access to medication, adherence, anticipated side effects and tolerability, and patient preference

Every attempt should be made to titrate medications as soon as feasible after the diagnosis. It is reasonable to aim for titration of all standard therapies concurrently to target doses, or maximally tolerated doses, within 3-6 months from diagnosis.

Because of the superiority of ARNI over ACEIs or ARBs in the setting of HFrEF, prescribing ARNI as first-line therapy or before full titration of ACEIs/ARBs might facilitate more rapid optimization of GDMT.

If a drug with proven mortality or morbidity benefits does not appear to be tolerated (eg, low blood pressure [BP], low heart rate, or renal dysfunction), concomitant drugs (eg, diuretics) with less proven benefit should be carefully reevaluated to determine whether their dose can be reduced or the drug discontinued.

Practical tips for initiation and titration of heart failure therapies!

GDMT for HFrEF should be continued at the usual dose during acute intercurrent illness unless they are not tolerated or could potentially worsen severity of illness. Whenever possible, GDMT withheld during a hospitalization should be restarted before discharge.

In the event of a life-threatening complication, GDMT may be discontinued abruptly, but generally, if there is concern about their use, the dose should be decreased by one-half, and the patient should be reassessed. If the dose is reduced, the previous tolerated dose should be resumed as soon as safely possible.

If symptomatic hypotension persists with GDMT, consider separating the administration of the dose from the timing of other medications that could also lower BP.

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Outline



Medication adherence in Heart Failure



Importance of patient-centric communication when discussing quadruple therapy



Educational strategies that may support adherence and safe administration of quadruple therapy



Adherence

• WHO (2003) defines adherence to long-term therapy:

"...the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider".

- Multiple factors affect medication adherence in HF
- Medication adherence is one of the most important self-care behaviours in chronic HF

Medication Adherence in HF

- Medication adherence: Number of days the correct number & prescribed dosages of a medication(s) is taken
 - Cut off in literature for adherence ~ 80-88%
- Medication nonadherence in HF is common
 - Wu & Moser (2018) found that 41% of HF patients were nonadherent; Those with higher medication adherence had fewer HF symptoms

Poor medication adherence in HF is associated with:

- Increased risk of CV hospitalization¹
- Increased risk of all-cause mortality²
- ↑ increased health care costs
- Poorer QOL and health outcomes

^{1,2} Fitzgerald, A. A. et al. (2011). Impact of medication nonadherence on hospitalizations and mortality in heart failure. Journal of Cardiac Failure, 17(8), 664-669. doi:10.1016/j.cardfail.2011.04.011.

Wu, J., & Moser, D. (2018). Medication adherence medicates the relationship between heart failure symptoms and cardiac event-free survival in patients with heart failure. *Journal of Cardiovascular Nursing*, 33(1), 40-46. doi:10.1097/JCN.0000000000427.

Factors Influencing Medication Adherence

- Patient factors (comorbidities)
- Cost-related nonadherence (CRNA)
- Therapy related
- Socio-economic
- Health care system
- Health care provider

Question for Audience:

Are we in need of a standardized tool that can be easily implemented in practice to assess adherence and identify barriers to quadruple therapy?

A. Yes

B. No

C. Uncertain









- Poor communication is associated with increased medication nonadherence
- How can we best discuss with HF patients 'quadruple therapy' and enhance adherence/safety?
- Adopt a patient-centric approach:
 - Patient understanding, knowledge, attitudes & values on treating HF
 - Use open-ended questions:
 - *"What is your understanding about your heart condition?"*
 - "How has heart failure affected your daily life?"
 - "What are your concerns?"
 - Assess cultural beliefs & views on the necessity of medical treatment



- 2. Allow time to clarify misconceptions about diagnosis Many patients may believe HF is curable Understanding of long-term outcomes if HF not treated
- 3. Be clear, specific in describing diagnosis & approach to treatment: Discuss role, benefits, risks of quadruple therapy
- 2. 'Chunking' of information can enhance retention
- 3. Establish a shared treatment plan

- 5. Language used in medical discussions matters:
 - Medical jargon can be frightening to patients
 - Words such as 'common', 'rare', 'stable' can be interpreted differently
 - Patients often prefer terms such as 'side effects' vs. 'adverse effects'



Freeman, A. (2019). How to communicate evidence to patients. British Medical Journal, 57(8). http://dx.doi.org/10.1136/dtb.2019.000008

- 6. Outline an approach ahead of time to medication initiation, titration & follow-up:
 - Introducing drugs in parallel vs. linear
 - ARNI + SGLT2 inhibitor
 - BB + SGLT2 inhibitor
 - Clearly describe goal to titrate to target doses or maximally tolerated
 - Repeat blood work with titration
 - · How to manage 'sick days'

7. Assess known predictors of worse medication adherence:

- Prescription cost(s)
- Complex drug regimens:
 - \uparrow number of medications/day assoc. with \downarrow adherence
 - Polypharmacy (≥ 4 medications/day)
- \downarrow clinic time to clearly explain medications & dosing directions
- Multiple prescribers
- Inconsistent messaging from healthcare team
- Patient work schedules; Multiple jobs
- Managing comorbidities:
 - Depression is associated with increased risk of nonadherence
 - Cognitive function
- Poor social support

- 8. Implement educational interventions to support medication adherence & safety
- 9. Ensure patients have contact information of health care provider
- 10. Regularly assess medication adherence at follow-up visits:
 - Take a non-judgemental, no-blame, approach

How would you describe your daily routine for taking your medications? In the past one week, how often did you forget or skip taking one of your medications? Are you worried about taking your prescribed medications?

- Seek to determine underlying cause of nonadherence
 - Unintentional (drug costs) vs. intentional (perceived lack of benefit)

Bussell, J. K. (2017). Ways healthcare providers can promote better medication adherence. Clinical Diabetes, 35(3): 171-177. doi: <u>https://dx.doi.org/10.2337%2Fcd016-0029</u>.

Drugs don't work in patients who don't take them.

C. Everett Koop

🖌 quotefancy



Question for Audience:

What strategy are you mainly using to educate patients and families about quadruple therapy?

A. In-person counseling

- **B. Written information**
- **C. Web-based resource**
- **D.** None of the above



Health Literacy

• The Canadian Public Health Association defines health literacy as:

"the ability to access, understand, evaluate and communicate information as a way to promote, maintain and improve health in a variety of settings across the life-course".

- ~ 30% of HF patients in Canada have low health literacy¹
- Often under-recognized in practice
- Low health literacy is associated with reduced medication adherence:
 - In patients with admitted with ACS and/or ADHF, 50% had a medication error in days following a hospital admission²
 - Those with low health literacy were at increased risk of medication errors³

Rootman, I., Gordon-El-Bihbety, D. (2008). A vision for a health literate Canada Report of the Expert Panel on Health Literacy. Canadian Public Health Association. <u>https://www.cpha.ca/sites/default/files/uploads/resources/healthlit/report_e.pdf</u>

¹McConnery, J et al. (2018). Impact of health literacy on knowledge, self-care and clinical outcomes in Heart Failure patients. Canadian Cardiovascular Society (CCS) ePosters HF-Abstracts. ^{2,3}Mixon, A.S. et al. (2014). Characteristics associated with post-discharge medication errors. *Mayo Clinic Proceedings*, 89(8), 1042-1051. doi:10.1016/j.mayocp.2014.04.023,

Strategies

- Medication counseling needs to be personalized:¹
 - Assess health literacy
 - Discuss tools to support medication adherence
- Take a team approach with consistent messaging:
 - Physician, nursing, pharmacy, social work, psychologists
 - Collaborative disease management clinics:
 - HF & DM
 - Organizational (HF clinics) implement standardized approach to assessing and improving medication adherence
 - Engage community partners; Home care services

- Provide additional resources:
 - Written
 - Web-base
- Use of technology to support medication titration & adherence:
 - Remote Patient Monitoring (RPM) programs

 medication reminders
 - Telehealth for follow-up

Customized Strategies

Suggest customized strategies to remember pill taking:

- Create a daily routine link pill taking with a daily task
- Calendar, medication logbook
- Phone alarm
- Programmed medication reminders (smart speakers)
- Blister packaging
- Pill box or organizer
 - Pill boxes with alarms
- Apps for pill reminders







Summary

- Quadruple therapy in management of HFREF: BB, ARNI/ACE/ARB, MRA, SGLT2
- Start low and go slow: 3 6 months to titrate to GDMT
- Frequent monitoring of renal function and electrolytes
- Medication nonadherence in HF is common and a 'real world' concern
- Taking a patient-centered approach is essential when discussing quadruple therapy with patients & families
- Interdisciplinary educational approaches work best & should include regular reassessment of medication adherence