PERSPECTIVES ON **Comanaging Diabetes & Heart Failure**

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Diabetes mellitus (DM) & heart failure (HF) are closely linked. Individuals with DM are at increased risk of developing HF, and those with HF are at increased risk of developing DM. Furthermore, individuals with both DM & HF are at **increased risk of cardiovascular (CV) death & HF hospitalizations.**

HF medication selection is essentially the same, whether an individual has diabetes or not.

- Use diuretics to manage HF signs & symptoms due to fluid retention. Titrate to minimum effective dose to maintain euvolemia.
- For individuals with **HF with a reduced ejection fraction** (HF-rEF, i.e. left ventricular ejection fraction [LVEF] ≤40%), strive for HF quadruple therapy as these agents have been shown to reduce CV death & HF hospitalizations:
  1) an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) or angiotensin receptor neprilysin inhibitor, i.e. **ENTRESTO** (ARNI), and
  2) a HF beta-blocker (i.e. bisoprolol **MONOCOR**, carvedilol **COREG**, or metoprolol **LOPRESOR**), and
  3) a mineralocorticoid receptor antagonist (MRA, i.e. eplerenone **INSPRA**, or spironolactone **ALDACTONE**), and
  4) **SGLT2 inhibitors** (i.e. dapagliflozin **FORXIGA**, or empagliflozin **JARDIANCE**)
- For individuals with HF and an ejection fraction (EF) above 40%:
  1) **SGLT2 inhibitor** (i.e. dapagliflozin **FORXIGA**, or empagliflozin **JARDIANCE**) to reduce the risk of HF hospitalizations
  2) select other medications to optimally treat risk factors / associated conditions (e.g. antihypertensives for high blood pressure, rate or rhythm control agents for atrial fibrillation); may consider spironolactone

Other Medication Considerations

- **Metformin** remains a 1st line agent in type 2 DM & HF in individuals with eGFR >30mL/min. Risk of lactic acidosis is rare; however, metformin should be dose adjusted for CKD and held during HF exacerbation or acute decline in renal function. Guidelines suggest avoiding metformin if eGFR significantly & persistently remains <30mL/min. However, given outcome benefits and rare risk of lactic acidosis, metformin is sometimes used cautiously (e.g. 500mg daily) with stable renal function between 15-30mL/min.
- There is no strong evidence to guide the sequence of initiating / titrating HFrEF medications. As such, **the order of HFrEF quadruple therapy can be tailored to the individual**. For example, option of adding SGLT2 inhibitors early in individuals with HF and DM.
- **Diabetes medications to AVOID in individuals with HF**:
  - Thiazolidinediones (i.e. rosiglitazone **AVANDIA**, pioglitazone **ACTOS**) are contraindicated in HF due to the increased risk of causing / exacerbating HF & fluid retention.
  - Two of the four DPP4 inhibitors (i.e. saxagliptin **ONGLYZA**, alogliptin **NESINA**) increase the risk of HF hospitalizations.

FREQUENT MONITORING IS REQUIRED FOR INDIVIDUALS WITH DM & HF

RENAL FUNCTION

- Uncontrolled DM increases the risk of renal impairment (see page 8).
- Renin angiotensin aldosterone system (RAAS) HF medications (e.g. ACEI, ARB, ARNI) & SGLT2 inhibitors can increase SCr. Check renal function at baseline, & 7 to 14 days after starting or titrating these medications. Start HF medications at lower doses & titrate slowly.
- If SCr increases >30% for RAAS inhibitors or >15-20% for SGLT2 inhibitors after starting or titrating, reassess fluid status. If hypovolemic, decrease or discontinue diuretics.
- The initial decline in renal function with SGLT2 inhibitors usually resolves in 1 to 3 months. These agents can help preserve renal function over time.

BLOOD PRESSURE

- SGLT2 inhibitors can cause hypovolemia, & therefore can lower BP. Other HF medications will also lower BP (e.g. ACEI, ARB, ARNI, beta-blockers).
- There is no target BP for individuals with HF; doses of HF medications should be reassessed if symptomatic hypotension (e.g. dizziness, lightheaded) occurs. **Consider**: spacing medication administration times (e.g. give some in the morning & others at bedtime), and / or split once daily regimens into BID regimens before reducing the dose.
- If possible, reduce or discontinue diuretics to preserve other HF medications.

POTASSIUM

- Check serum K^+ at baseline, and 7 to 10 days after starting or titrating medications.
- Individuals with diabetes, particularly elderly &/or those with renal impairment, are at increased risk of hyperkalemia.
- RAAS HF medications (e.g. ACEI, ARB, ARNI, MRA) increase serum K^+.
- Hypovolemia, which can be caused by diuretics, ARNI & SGLT2 inhibitors, can increase serum K^+.
- Remember to discontinue or decrease the dose of K^+ supplements.
- **If serum K^+ > 5.5mmol/L**: reassess dose / therapy. If serum **K^+ >5mmol/L**: avoid foods high in K^+.

FLUID STATUS / HEART FAILURE SYMPTOMS

- HFrEF quadruple therapy reduce mortality; diuretics do not. Titrate diuretics to the lowest effective dose to maintain euvolemia → this will reduce the risk of hypovolemia.
- In euvolemic individuals, consider reducing a loop diuretic by 25-50% when starting an SGLT2 inhibitor.
- Caution with starting an SGLT2 inhibitor in an individual who is hypovolemic; wait until volume depletion is corrected.
- Instruct individuals to temporarily hold SADMANS medications (e.g. ACEI / ARB / ARNI, diuretics, metformin, SGLT2 inhibitors) during acute illness with diarrhea, vomiting and / or fever. See RxFiles SADMANS handout pg 37.

See also RxFiles Heart Failure for additional information on therapeutic management.

ACEI=angiotensin converting enzyme inhibitor **ARB=**angiotensin II receptor blocker **BID=**twice daily **BP=**blood pressure **CKD=**chronic kidney disease **CV=**cardiovascular **DM=**diabetes mellitus
DPP4=dipeptidyl peptidase-4 **eGFR**=estimated glomerular filtration rate **HF=**heart failure **K^+=**potassium **RAAS=**renin-angiotensin-aldosterone system **SCr**=serum creatinine **SGLT2=**sodium-glucose cotransporter-2

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