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Clinical Champion Update

Date: 10/23/23 Subject: Congestive Heart Failure

Getting meds optimized in HFrEF with CKD

Guideline-directed medical therapy (GDMT) recommends getting patients on quadruple therapy:

- ARB, ACE, or ARNI
- BB (e.g. carvedilol, metoprolol ER)
- SGLT2i (e.g. Farxiga or Jardiance)
- Mineralocorticoid antagonist (MCA, e.g. spironolactone or eplerenone)

This cocktail has been proven to reduce mortality and rehospitalization, while addition of a loop diuretic is often helpful for symptoms of fluid overload.

However, I personally have few patients on optimized doses of meds based on GDMT, or even on all the recommended meds at any dose, and data suggest that well under 1% of patients nationwide reach target doses. Reasons for this include cost, adverse effects, "I just don't want to be on all these meds", and difficulty with uptitration due to comorbidities.

One particularly tricky situation is the delicate balance needed to get patients with CKD on optimized meds for HFrEF. Hyperkalemia can occur with an ACEI or ARB, *Entresto* (sacubitril/valsartan), or an aldosterone antagonist. Plus these meds or SGLT2 inhibitors can cause an initial bump in creatinine. But at the same time, suboptimal HFrEF treatment can worsen kidney function.

In a change from prior recommendations, a recent study suggests that rapid titration of HFrEF meds over a couple of weeks reduces hospitalizations at 6 months. But rapid titration requires very close monitoring since it increases the risk of adverse effects like hypotension, hyperkalemia, and kidney injury.

Some patients are not able or willing to follow up closely enough for this, but selected patients can be started on low-dose combo therapy. For example, prescribe *Entresto* 24/26 mg bid, carvedilol 3.125 mg bid, spironolactone 12.5 mg qd, and Farxiga 2.5mg qd. This can be tailored to individual needs if necessary. For instance, wait to add a beta-blocker for a week or so in patients with fluid overload since beta-blockers may initially worsen fluid retention or other symptoms.

As long as labs and vitals are stable and patients don't have symptomatic low BP or bradycardia, it's acceptable to uptitrate multiple meds at once. For example, if eGFR hasn't decreased by more than 30%,

potassium is under 5.5, systolic BP is above 95, and HR is over 60, try doubling the doses of an ACEI, ARB, or ARNI plus a beta blocker after 1 to 2 weeks.

Our nephrologist colleagues (e.g. Despina Hoffman DO) are available and responsive on TigerConnect. It's a good idea to run any changes by them when in doubt, especially when eGFR is below 30 or potassium is above 5, because studies exclude patients with these low eGFRs. But it's often okay to use an ACEI or ARB with close monitoring even in patients on dialysis. Meanwhile, beta-blockers are okay at any eGFR. SGLT2 inhibitors are expensive and the cost of $550/month may be a barrier. But these improve HFrEF and CKD outcomes regardless of diabetes and can be started down to an eGFR of 20. Consider lowering diuretic doses when starting an SGLT2 inhibitor due to the risk of hypovolemia and acute kidney injury.

Monitor electrolytes and kidney function closely especially when adding or titrating meds. Make sure you have baseline labs and check again 1 to 2 weeks after making changes. Even if meds are at stable doses, check BMP at least quarterly.

If creatinine bumps up over 50%, hold SGLT2 inhibitors and halve doses of other meds except for BBs. Hold meds that raise potassium for levels above 5.5. Try retitrating meds in 2 to 4 weeks once labs improve.

Avoid clinical inertia. A couple months is often long enough to get to target—e.g. *Entresto* 97/103 mg bid, carvedilol 25 mg bid, spironolactone 25 mg qd, and Farxiga 10mg qd.

See the "HF Meds Table" from my April 2022 blog post for details on target doses and monitoring.

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