Inpatient Notes: Clinical Pearls–Stopping, Starting, and Optimizing Guideline-Directed Medical Therapy in Patients Hospitalized for Heart Failure With Reduced Ejection Fraction

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A 68-year-old woman presents to the emergency department with 1 week of worsening dyspnea on exertion, orthopnea, and leg swelling. She has a history of ischemic cardiomyopathy and heart failure with reduced ejection fraction (HFrEF), with an ejection fraction of 25% on her most recent echocardiogram this past year. Her medications for HFrEF before admission include 10 mg of lisinopril daily, 6.25 mg of carvedilol twice daily, and 40 mg of furosemide twice daily. On physical examination, she is in no acute distress, but her examination is notable for bibasilar crackles, jugular venous distention, and lower extremity edema. Vital signs and laboratories show a blood pressure of 134/69 mm Hg, heart rate of 85 beats/min, estimated glomerular filtration rate of 44 mL/min/1.73 m^2, potassium level of 4.30 mmol/L, and N-terminal pro–B-type natriuretic peptide level of 3141.00 pg/mL.

What Is Contemporary Guideline-Directed Medical Therapy for HFrEF?

Foundational medical therapy for HFrEF consists of comprehensive disease-modifying quadruple medical therapy, including angiotensin receptor–neprilysin inhibitors (ARNIs), β-blockers, mineralocorticoid receptor antagonists, and sodium–glucose cotransporter-2 inhibitors (1). Although an ARNI is preferred and improves survival compared with an angiotensin-converting enzyme inhibitor (ACEI), an ACEI or angiotensin II receptor blocker should otherwise be used among eligible patients if an ARNI is not tolerated or not accessible (for example, out-of-pocket costs) (1).

Quadruple medical therapy is estimated to cumulatively reduce the relative risk for death by 73% over 2 years, with a number needed to treat of 3.9 to save 1 life (2). Framed another way, compared with traditional therapy using an ACEI and a β-blocker, treating a 55-year-old patient with comprehensive disease-modifying quadruple therapy projects to increase life expectancy by more than 6 years (3).

What Are the Goals for This Patient With Respect to Guideline-Directed Medical Therapy During This Hospitalization?

Although the patient requires intravenous diuretics for decongestion, a focus on diuretic therapy and electrolyte monitoring alone during hospitalization leaves the patient with HFrEF at substantial early risk for clinical worsening, rehospitalization, and death after discharge. To improve postdischarge outcomes, hospitalists should ensure that quadruple medical therapy is prescribed before hospital discharge, as tolerated. This patient is eligible for each of the 4 therapies and is already prescribed a β-blocker.

Is It Appropriate to Optimize Chronic HFrEF Medications During the Hospitalization for HF?

Approximately 1 in 4 patients hospitalized for worsening HFrEF die or are rehospitalized within 30 days of discharge (4). For each of the 4 components of quadruple therapy, clinically and statistically significant reductions in death and hospitalization appear early after initiation, within days to weeks (5). Deferring in-hospital initiation is consistently associated with medications never being initiated in the outpatient setting, or initiated after substantial delay (5). Thus, for purposes of improving outcomes after discharge and overall medication use, every effort must be made to discharge patients on quadruple medical therapy, as tolerated. This goal can be achieved safely and without any increase in hospital length of stay.

How Should Guideline-Directed Medical Therapy Changes Be Prioritized? Which Medication Treatments Should Be Started First?

The clinical benefits of all 4 classes of quadruple medical therapy are fully additive, with each therapy offering incremental benefit regardless of background therapy. In clinical trials, there are no instances where the benefit of any of these 4 medications on the primary end point was significantly attenuated among patients receiving other therapies. For example, sodium–glucose cotransporter-2 inhibitors offer consistent relative risk reduction, regardless of whether the patient is already prescribed an ARNI. Likewise, ARNIs offer consistent relative risk reduction, regardless of whether the patient is already prescribed mineralocorticoid receptor antagonists. The emphasis should be on ensuring that all 4 classes of medication are prescribed by time of hospital discharge.

Is It Appropriate to Start Several New Medication Treatments During a Hospitalization? Will This Increase Risk for Adverse Effects?

It is fully appropriate to initiate multiple classes of quadruple therapy during hospitalization for HF, as

tolerated (5). There is no evidence to suggest that "go slow," "one medication change at a time," or "defer to outpatient" approaches improve medication tolerance or accomplish anything beneficial (5). Rather, deferring in-hospital initiation needlessly exposes patients to excess risk for postdischarge clinical events and the possibility of medications never being prescribed at all.

Tolerance during the hospitalization is enhanced by initiating medication treatments at low doses (for example, 24/26 mg of sacubitril–valsartan twice daily or 12.5 mg of spironolactone once daily). Ensuring that the patient is receiving at least low doses of all 4 of these medications should be prioritized ahead of escalating the dose of any 1 therapy. Arranging for early postdischarge follow-up can further enhance a successful transition of care and improved clinical outcomes.

What Specific Changes to Guideline-Directed Medical Therapy Should Occur for This Patient During the Hospitalization?

Patients should be continued on preexisting guideline-directed medical therapy, unless specific contraindications are present. This patient is hemodynamically stable, and continuation of β-blockers during hospitalization for HF has been consistently associated with improved clinical outcomes. Thus, the patient should continue receiving 6.25 mg of carvedilol twice daily. The following medication changes are recommended by time of discharge:

1. The patient should be switched from lisinopril to sacubitril–valsartan. This transition requires a 36-hour washout of the ACEI before initiating 24/26 mg of sacubitril–valsartan twice daily, to decrease risk for angioedema.

2. The patient should be initiated on spironolactone therapy. A starting dose of 12.5 mg once daily is reasonable.

3. The patient should be initiated on a sodium–glucose cotransporter-2 inhibitor, with either 10 mg of dapagliflozin once daily or 10 mg of empagliflozin once daily being approved for treatment of HFrEF.

Of note, sacubitril–valsartan, dapagliflozin, and empagliflozin are newer medications for HFrEF, and insurance coverage, prior authorization requirements, or out-of-pocket costs may be barriers for some patients. Nonetheless, if these barriers arise, the multidisciplinary team and resources routinely available in the hospital (compared with an outpatient clinic) may be optimally positioned to explore all possible strategies for securing patient access to medication.

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