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CLINICAL MEDICINE | JULY 27, 2022 | FREE


Use your window into heart failure

A new guideline and experts urge hospitalists to maximize heart failure therapies, but also to be aware of their costs.

By Charlotte Huff

6-min read

Admission of a heart failure patient provides both a window of vulnerability and a pivotal opportunity, according to experts.

“Every heart failure hospitalization should be considered a sentinel event that can portend worse outcomes,” said Michelle Kittleson, MD, PhD. She cited evidence from the [2019 American College of Cardiology expert consensus decision pathway on heart failure](#)  showing that a patient's risk of death increases by 20% to 30% in the year following admission.

Recent data have also highlighted the patients most at risk. Black adults are more likely to be hospitalized than White adults; the highest hospitalization rates are among Black men.

On the brighter side, hospitalists are well situated to intervene and improve outcomes by revisiting the specifics of a patient's heart failure diagnosis, watching out for underdiagnosed conditions, and tapping the expertise of pharmacists and other resources to reduce the cost of treatment, said Dr. Kittleson, director of heart failure research and director of postgraduate education in heart failure and transplantation at Cedars-Sinai's Smidt Heart Institute in Los Angeles.

Advice on how best to do this was offered by the latest [American College of Cardiology](#) [/American Heart Association](#) [/Heart Failure Society of America](#) guideline on heart failure, published April 1 by the societies' journals. Dr. Kittleson was an author of the recommendations.

The guideline places significant emphasis on the benefits of multidrug medication therapy, recommending consideration of quadruple therapy, which newly includes sodium-glucose cotransporter-2 (SGLT-2) inhibitors, noted Gregg Fonarow, MD, also an author on the 2022 guideline and interim chief of the University of California, Los Angeles, division of cardiology.

“In the past, many of these patients would just get their intravenous diuretics and would be continued on whatever oral medications they happened to be on when they presented to the hospital,” Dr. Fonarow said. “What has evolved is the clear evidence that a key determinant of what that patient's outcome will be in the next 30 days after discharge from the hospital is whether they received each of these therapies or not.”

Updated prescribing

Along with SGLT-2 inhibitors, the recommended quadruple-therapy regimen for heart failure with reduced ejection fraction ($\leq 40\%$) includes an angiotensin receptor-neprilysin inhibitor (ARNi) preferentially over an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB), along with a beta-blocker and a mineralocorticoid receptor antagonist (MRA).

Subgroup analyses of medication trials show that the survival benefits of these drugs start to appear within four to eight weeks after initiation, said Dr. Kittleson, whose [clinician's guide to the new guideline](#) was published in the *Journal of Cardiac Failure* in May.

“There's no reason for delay,” Dr. Kittleson said. “For the hospitalist admitting a patient, the question should be ‘Why is this patient not on these four therapies?’ And if you can't justify a contraindication, then they should be started prior to discharge.”

There are differences of opinion about whether to begin needed heart failure medications all at once or sequentially, said Dr. Kittleson, who described herself as falling into the latter camp. “Every time you give a patient a medicine, you are giving some of your trust and credibility to that patient. ‘Take this pill and you will feel better,’” she said.

If medications are started together, it's more difficult to identify the cause of any side effects that develop, Dr. Kittleson said. She prefers to introduce the drugs sequentially over a series of days. As she titrates the medications, she monitors a patient's heart rate, blood pressure, potassium, and creatinine, along with any reactions or side effects, which is easier to do in a hospital setting, she noted.

The new focus on SGLT-2 inhibitors was motivated in part by evidence such as a [meta-analysis, cited frequently in the 2022 guideline](#) and published in *The Lancet* in 2020, which found that dapagliflozin and empagliflozin produced a 26% relative reduction in the combined risk of cardiovascular death or first hospitalization for heart failure.

A more recent [subgroup analysis of the industry-funded EMPULSE study](#), looking specifically at hospitalized patients taking empagliflozin and published online April 4 in *Circulation*, found that improvements in heart failure-related symptoms and physical limitations began to emerge as early as 15 days and continued through the 90 days studied.

The patients, who either had newly diagnosed or decompensated chronic heart failure, improved regardless of the presence of diabetes, their ejection fraction, or the initial severity of their symptoms, said lead author Mikhail Kosiborod, MD, a cardiologist at Saint Luke's Mid America Heart Institute and professor of medicine at University of Missouri-Kansas City.

“We're talking about a patient population that's at very high risk for recurrent events, like repeat hospitalizations,” Dr. Kosiborod said. “And we already see a symptomatic benefit within 15 days. ... You can tell patients that within a short period of time of getting started on this medication, they can feel better and be able to do more.”

In addition to recommending SGLT-2 inhibitors for patients with reduced ejection fraction, the 2022 guideline also gave the class a weaker recommendation (class 2A) as a treatment for patients with preserved ejection fraction or mildly reduced ejection fraction of 41% to 49%. “In some ways that simplifies it, right?” said Dr. Fonarow. “Any patient with heart failure who is hospitalized should really be started on an SGLT-2 inhibitor regardless of ejection fraction.”

Diagnosis and other considerations

The 2022 guideline also delineated some new classifications of symptomatic heart failure. For instance, the new category of improved ejection fraction describes someone with a reading that was initially 40% or below but has increased to above 40%.

Notable improvement doesn't mean treatment should be halted, said Clyde W. Yancy, MD, MACP, a 2022 guideline author and chief of the division of cardiology at Northwestern University Feinberg School of Medicine in Chicago.

A small study that tested withdrawal of therapy in patients with ejection fraction improvement [↗](#) (defined as increasing from 40% or lower to 50% or greater) found that some relapsed within eight weeks, according to results published by *The Lancet* in 2019. “It's pretty evident that therapies need to continue,” said Dr. Yancy.


Even so, improvement represents an opportunity to motivate patients to stick with medications and other measures, according to Dr. Yancy. “I say, “This means that your expectations for this condition have fundamentally changed. You are much less likely to die. You are much less likely to need hospitalization. You are much less likely to have overt symptoms.”

Along with reviewing the heart failure diagnosis to determine if the classification should be adjusted, other steps to take during hospitalization include looking for other conditions, such as cardiac amyloidosis, Dr. Kittleson said. “It's far more common than we used to think,” she said, pointing to a study published in 2015 in the *European Heart Journal*.

That study determined that 13% of patients admitted for decompensated heart failure with preserved ejection fraction actually had a form of amyloidosis called wild-type transthyretin [↗](#). In 2019, FDA officials approved a medication, tafamidis [↗](#), for the condition. The drug does not reverse the amyloids that have

already been deposited but can slow further damage, with the survival difference appearing after 18 months, Dr. Kittleson said. “So the sooner you start it, the sooner the benefit can accrue.”

Of course, none of the drugs are effective if patients can't afford them, Dr. Yancy said. Given the cost of some, and variations in insurance coverage, “Every bedside physician should de facto assume that the patient in front of that physician is at risk for financial toxicity, regardless of the apparent social class,” he said.

For example, tafamidis got a strong clinical recommendation from the guideline for patients with heart failure with wild-type or variant transthyretin cardiac amyloidosis, but its cost is steep. Dr. Kittleson cited a study published in 2020 in *Circulation* finding that the manufacturers would have to reduce the drug's price tag by 92.6% for it to be considered cost-effective .

The guideline assessed whether medications are of high, intermediate, or low value where cost-effectiveness data were available, an addition in this update that Dr. Yancy touted. “Yes, we have a lot of therapies that work very well, but some of these therapies are quite expensive,” he said. “What's the benefit of that therapy versus the cost?”

Tafamidis was classified as a treatment of low economic value, with the guideline noting the list cost worked out to \$180,000 per quality-adjusted life-year gained. For patients with reduced ejection fraction symptoms, the guideline judged SGLT-2 inhibitors to be of intermediate value. Replacing an ACE inhibitor with an ARNi in the same patients was assessed as providing high value.

Even if the patient doesn't request help with medication costs, physicians should work with the hospital's pharmacy team to see if they can identify discounts, such as coupons, to make heart failure drugs more affordable, Dr. Yancy recommended.

As hospitalists discuss the treatment plan with patients and their loved ones, they should also seize on the “teachable moment” to boost awareness about the risks of skimping on medication and other measures, Dr. Yancy said. The very terminology of heart failure carries a “certain heft, certain gravity” that catches people's attention, he noted.

“But in that same breath, that hospital physician should also say, “This is a new era. And there are more things that can be done for this condition than ever before. So what you read on the internet is not necessarily applicable to you,”” Dr. Yancy said.



Charlotte Huff is an independent medical journalist in Fort Worth, Texas.



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