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What You Should Know When Addressing GDMT For ID in Heart Failure

Announcer:
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Dr. Ponikowski:
Iron deficiency is an important and common comorbid condition in patients with heart failure. Iron deficiency independently predicts both morbidity and mortality, and is also associated with reduced exercise capacity and poor quality of life. Unfortunately, despite its clinical significance, iron deficiency still remains underdiagnosed and undertreated. So how can we better identify and treat patients with heart failure suffering from iron deficiency?

This is the question, and this is CME on ReachMD, and I am Dr. Piotr Ponikowski.

Dr. Sindone
And I am Dr. Andrew Sindone.

Dr. Hernandez:
And I'm Dr. Adrian Hernandez.

Dr. Ponikowski:
Let's answer that important question by starting with a discussion on a patient case. Let's say we have a 75-year-old man with a history of heart failure with reduced ejection fraction in the round of 35%-37%, type 2 diabetes mellitus, history of hypertension, and chronic kidney disease with EGFR in the range of 30-35, and now he is admitted to the hospital with an acute exacerbation of his heart failure symptoms. His baseline medication before coming to the hospital included metoprolol, sacubitril/valsartan, eplerenone, empagliflozin, and atorvastatin on pretty optimal doses. He is now decompensated, and he's now in New York Heart Association Class III. Vitals are pretty stable, ECG is unremarkable, but obviously according to the guidelines we included in the lab analysis hemoglobin and ferritin and transferrin saturation. His hemoglobin is 13.6 g/dL, serum ferritin is 120 ng/mL, and TSAT is of 18%.

So, Andrew, what is the most likely cause of this patient's acute exacerbation, decompensation? Please comment.

Dr. Sindone:
So the things we have to exclude is whether he's had micro ischemia or infarction, atrial fibrillation, whether he has an infection like a respiratory infection or endocarditis or urinary tract infection. Maybe if he's got hyperthyroidism or worsening kidney function, or if he's noncompliant with his medications or fluid or salt restriction. Once we've excluded all those things, we've already got evidence that he has iron deficiency, so it's probable that the iron deficiency has caused worsening of his symptoms. Now, it's important to remember that about 50% of patients with heart failure with reduced ejection fraction have iron deficiency, and that's regardless of whether they have anemia or not. In fact, iron deficiency is more important in patients with heart failure in this situation than the anemia.

And so if you have patients with iron deficiency, they actually have poorer outcomes. They have a higher chance of presenting to the

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hospital with emergency presentations, they have higher readmission rates, they have a longer length of stay, and also they have a longer chance of dying in the short term and the long term. So, it's associated with poorer outcomes, and that's, again, irrespective of whether they have anemia or not. So what is the impact of iron deficiency on patients with heart failure? There's many. There's the cellular issues, because they have mitochondrial dysfunction. They also have deranged enzyme activity, like oxidative phosphorylation and abnormal protein functions. Also, there's increased apoptosis, so programmed cell death. There's tissue remodeling, worsened muscle function – we all know the heart is the most important muscle in the body. That all leads to reduced exercise capacity, reduced work efficiency, reduced cognitive performance and behavior, poorer quality of life, and ultimately, as I said before, increased morbidity and mortality. So the long-term outcomes, these patients have these poor quality of life or reduced exercise capacity, they tend to come into hospital more frequently, stay in hospital longer, have a higher chance of dying, and it's going to cost the community more money.

So, in fact, the European Society of Cardiology heart failure guidelines in 2021 suggested that all patients presented at hospital with heart failure and with chronic heart failure should have their ferritin measured and their transferrin saturation, just like this patient, where he was diagnosed with iron deficiency because the ferritin was between 100 and 200, and the transferrin saturation was less than 20%. Or it can also be diagnosed if the ferritin is less than 100. Those are the 2 criteria. And if you have those patients with chronic heart failure it was a Class 1 recommendation. These patients should be tested for heart failure and have periodic testing every 3 to 6 months thereafter. And also, if they have acute heart failure, they should be checked pre-discharge. And this was a recommendation in the guidelines, and now it's been replicated in the Australian guidelines which I helped write just recently.

So the thing is that heart failure is an important condition in the whole continuum of the heart failure with reduced ejection fraction patient journey. So early on, so try and reduce progression of disease and reduce hospitalization, and then later on to improve quality of life. And in all those situations, the guidelines suggest that treating that heart failure with reduced ejection fraction is important, and it's in all of the guidelines – the American Heart Association, American College of Cardiology, Heart Failure Society of America guidelines, as well as the European Society of Cardiology guidelines – all recommend that patients with heart failure should be screened, and if present, they should be treated.

So it's important that we look at these patients, whether they're inpatients or outpatients, it really doesn't matter. We should be looking for iron deficiency, treating iron deficiency, because number 1, you're going to improve their outcomes, but number 2, the patients with iron deficiency are the high-risk patients. They are more likely to have other comorbidities, like chronic renal impairment, chronic lung disease, ischemic heart disease, have worse ejection fraction. So those are the friends that heart failure and iron deficiency keeps, and if you can treat the iron deficiency, hopefully you'll be able to improve their outcomes, and screening for the patients is so important. That's recommended in all of the guidelines.

Dr. Ponikowski:
Andrew, thank you very much, indeed. You have raised very interesting points. Adrian, do you have anything additional to add?

Dr. Hernandez:
It's to hard to add anything to that great summary. But really, 2 take-home points from what you talked about was, one is that heart failure patients who come in, they're likely to have multiple contributing factors to their worsening of their heart failure. And so you can't necessarily always nail it, what's the exact one, and so it's important to be comprehensive. The second thing is actually to test and treat. And so, in this case, you know, this patient was on good medical therapy coming in, but it's important to test for other factors, such as iron deficiency, and also treat it to improve quality of life and hopefully prevent hospitalizations for heart failure.

Dr. Ponikowski:
Well, great. For those just tuning in, you are listening to CME on ReachMD. I am Dr. Piotr Ponikowski, and here with me today are Dr. Andrew Sindone and Dr. Adrian Hernandez. We are discussing the impact of iron deficiency in our patients with heart failure, how to diagnose and how to treat this in our everyday clinical practice.

Now as we have already diagnosed iron deficiency as one of several reasons potentially underlying this deterioration, decompensation in this gentleman, I have a challenging question for Adrian. Adrian, how would you now treat this gentleman?

Dr. Hernandez:
Yes, so I think there are a couple of things to consider in this patient. You know, one, as I was just alluding to is that it is important to look for it. And so testing every time you have an opportunity is really critical. So whether our patient comes in in the hospital like this, it's important to test, even if they have had prior treatment for iron deficiency because it could recur. The second thing is also just imagining this patient in the outpatient arena, again reconsidering whether that patient has iron deficiency as an outpatient is also important. And it's important to consider the basis for these recommendations that the guidelines now have incorporated. Testing is a recommendation for all the guidelines, and then importantly, treating for improving quality of life, as well as considerations of preventing hospitalizations.

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And we're now accumulating really strong evidence for doing so. A number of trials have built up to these recommendations led by you and others that include showing clear evidence in terms of improving patients' well-being, quality of life, 6-minute walk. And then also, the interesting thing now is we're beyond improving functional status, which is really important in this patient. We're also seeing the accumulation of data that suggests that we can prevent hospitalizations here, as well as cardiovascular outcomes such as death.

Certainly, there are other studies that are ongoing that will really cap this all out, but it's important to think about these patients, especially given this patient's very high risk for coming back in the hospital, having recurrent hospitalizations for heart failure. So testing and treating is really critical, and not something that we do in clinical practice, especially now.

Dr. Ponikowski:
I can't agree more, indeed. So as you heard, first of all diagnosing and then correcting, not only to improve quality of life, functional status, but also prevent recurrent hospital admission.

Do you have anything to add, Andrew?

Dr. Sindone:
Yes. So what we do is, when someone comes to the hospital with iron deficiency, we give them intravenous ferric carboxymaltose, 1,000 mg intravenous over 15 minutes, and then we will check it usually every 3-6 months. If they're anemic as well, we will look for the cause of the anemia, but otherwise we don't usually investigate for the cause of the iron deficiency. It's also important to remember that oral iron is out. That was shown in the IRONOUT study. It needs to be intravenous iron to overcome the problems with ferroportin and hepcidin block. And what we should do is remember that it's going to improve their exercise capacity and their 6-minute walk test and reduce hospitalization. That happens probably within 6 weeks, but the quality of life can improve really, really quickly.

Dr. Ponikowski:
Well, great comments. Thank you. I am very glad that you mentioned about oral iron, which people somehow intuitively believe that works very well and is even better. So we need to reiterate it is not very good option, due to our American colleagues, which did excellent study some years ago. So thank you very much for your additional comments.

I think that it has been an excellent conversation. But before we wrap up, Andrew, what is your take-home message for the audience, please?

Dr. Sindone:
Look for iron deficiency, because if you don't look for it, you'll never find it. And if you find iron deficiency during the admission to hospital, or if you're looking for it in an outpatient, treat it with the intravenous iron; ferric carboxymaltose is the preparation which has the data. And we know if you screen for iron deficiency, you have about 50% of the patients with heart failure with reduced ejection fraction who do have iron deficiency, and treating will improve their exercise capacity, their quality of life, and reduce the risk of hospitalization, and it's regardless of anemia. Anemia has nothing to do with this, so it's all about treating iron deficiency.

Dr. Ponikowski:
Adrian, anything to add?

Dr. Hernandez:
Test, retest, treat with IV iron. As you noted, don't do oral iron. We learned that from the IRONOUT trial, and we're humbled by that. And it's important to think about iron deficiency independent of anemia, and that's a critical factor here.

Dr. Ponikowski:
Well, indeed you had a great summary. Again, diagnose, please remember that it is one of the most common comorbidities, coinciding with several other comorbidities. And once diagnosed, then, as Adrian said, treat this, recheck, and please remember ferric carboxymaltose works; oral iron doesn't work.

Unfortunately, sorry to say, that's all the time we have today. So I want to thank our audience for listening and thank you both, Dr. Andrew Sindone and Dr. Adrian Hernandez, for joining me, for joining us, and for sharing all of your valuable insights. It was great, as usual, speaking with you today. Thank you.

Dr. Sindone:
Thank you very much.

Dr. Hernandez:
Thank you. Great to be here.

Announcer:

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