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Why Ischemia Matters When It Comes to Iron Deficiency in Heart Failure

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Dr. Metra:
Hello, my name is Marco Metra. I am full professor of cardiology at the University of Brescia, Italy. And it's my extreme pleasure to meet here Professor Ponikowski. I don't know if you want to introduce yourself yet.

Dr. Ponikowski:
Piotr Ponikowski, cardiologist, Wroclaw, Poland. Great pleasure to be with Marco today.

Dr. Metra:
Yeah, he is an eminent expert in heart failure. He is the director of his university; he's a major authority, also, with respect to iron therapy. So who best than him to try to solve this issue?

We have had a major improvement in the treatment of the patients with heart failure, and namely those with heart failure with a reduced ejection fraction. We now have patients like the one that we may discuss today, who are 65 years old with a reduced ejection fraction, on medical treatment with sacubitril/valsartan, dapagliflozin, low dose of furosemide, spironolactone, and beta-blockers – bisoprolol – so on optimal medical treatment. Despite this, she still complains of breathlessness with the stairs, walking in a block, and she has a poor quality of life. And what can we do in this case? We took the laboratory exams. We found a hemoglobin of 13.4. But serum ferritin was 65. And also, the TSAT [transferrin saturation] was abnormal.

So who better than you to tell us what to do in this patient?

Dr. Ponikowski:
Marco, I'm very glad that you mentioned this case, because this lady's optimally treated. She received 4 major classes of therapies which tend to prolong her life and tend to prevent hospital admission and tend also to make her life better. Despite this she, as I understand, is in a Class III. So I'm very glad that you mentioned it in these cases of potentially optimally treated patient, you need to seek for some additional factors. And iron deficiency is indeed another factor which may deteriorate the patient condition and, on the top of it, may lead to poorer survival and the greater risk of higher risk of hospital readmission. So in the time, I am very glad that you mentioned that iron deficiency, which is present in this case – which is present in this case, because you can easily detect it.

Marco is the chair of 2021 guidelines. And in these guidelines, there is a very precise statement: consider iron deficiency to be proactively screened in everyone and use only very simple biomarkers, as Marco said, ferritin and transferrin saturation to make sure that you detect it.

So, this lady fulfills the criteria of iron deficiency. Well, apart on this, please remember that she has a 13 hemoglobin, so it's not anemia yet. But if there is a little bit lower level in these elderly patients, please consider as well a diagnosis of some additional causes of

anemia, like malignancy, for example. But for today, let's push this aside. So iron deficiency as a target of therapy, I fully agree that you're good to mention this.

Dr. Metra:
The first thing which is important is to look for iron deficiency. And in our guidelines – but it was already written in the guidelines that you co-chaired in 2016. Despite the similar age, he preceded me in many things. But it was already written in the 2016 guidelines. It's a class 1 recommendation to measure serum ferritin level and TSAT in addition to more symptomatic parameters in all the patients with chronic heart failure. And we will come back to this maybe later, also in the patients hospitalized for acute heart failure. So detect iron deficiency. And we know that the correction of iron deficiency can improve significantly the quality of life for the patient.

Another thing that I didn't mention is that this patient has had a previous myocardial infarction, so she has coronary artery disease. I don't know if, in your opinion, this may have an impact or no. So question regarding the etiology of heart failure. And the question regarding how to treat this patient.

Dr. Ponikowski:
Well, it's a very intriguing area now whether – where the underlying etiology of heart failure may have additional impact on iron deficiency. We still do not quite understand why iron deficiency develops in patients with heart failure, number one; we only know that we should treat it, number two, but potentially ischemia. Well, first of all, we had this analysis based on AFFIRM-AHF study, which we will most likely discuss in a second, showing us that perhaps ischemic etiology patients are a little bit more prone not really to develop anemia, but to be with better chance of benefit with IV [intravenous] iron therapy. It may well be just chance finding. There is post hoc analysis from the AFFIRM-AHF. But still very, very intriguing data. It may well be that ischemia itself somehow affects the myocardium and makes the myocardium prone to develop iron deficiency. Many different hypotheses.

But to make long story short, in my humble opinion, iron deficiency in HFrEF [heart failure with reduced ejection fraction] is about impaired energetics. So I think that regardless of the underlying etiology, we need to consider iron deficiency as a relevant comorbidity, and you need to treat it. With time, we will get more and more information whether ischemia itself, as the, as I said, etiology would be relevant to consider in the diagnostic and therapeutic process in this area.

But for today, I think we would be safe saying consider iron deficiency in patients also stable but also the stabilized and admitted and treat them with IV iron, with ferric carboxymaltose, to make sure that we follow the guidelines.

Dr. Metra:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Marco Metra and I'm here today with Dr. Piotr Ponikowski. We are discussing the significance of ischemic etiology and iron deficiency in the management of patients with heart failure.

Of course, AFFIRM-AHF, and you were the first author of the study of the main trial and the coordinator, was the first trial published with the ferric carboxymaltose assessing outcomes as a primary endpoint. So we now, we are moving from a perspective of studies like CONFIRM, that you authored, and FAIR-HF, which was by Stefan Anker, focused on quality of life, exercise capacity, symptoms, 2 studies which are focused on the outcome. And AFFIRM-HF is the first of these ones showing a reduction in heart failure hospitalizations with ferric carboxymaltose versus placebo. And these data were already shown also in the previous trials, but here, it was the primary outcome of the study. And the problem is that the patients with non-ischemic heart disease at the lower rate of rehospitalizations and events, and therefore the study was surely underpowered to show a result in these patients.

So I think that regardless the etiology, but of course, more if we have more data in patients with coronary artery disease. If the patient has left ventricular dysfunction, even mild because we go up to 50%, and there is no reason – also this is another interesting aspect, if there is a reason to think that patients with preserved ejection fraction may have a different response. I don't think. So I mean, if we detect iron deficiency in a patient with symptoms of heart failure, there is a clear indication to ferric carboxymaltose therapy.

Dr. Ponikowski:
I fully agree about what Marco alluded to: AFFIRM-AHF was the first trial planned to finally answer the question whether correction of iron deficiency with intravenous ferric carboxymaltose would translate in better outcome. So we provided the evidence of reduction in hospitalization. This study was among patients with acutely decompensated heart failure, but as Marco said, reducing – it might be reduced, yes? So it's not only for better quality of life, but also for reduction of the rate of hospitalization. And I fully concur with Marco that we do need that study. Ongoing trials will tell us more about HFpEF [heart failure with preserved ejection fraction], but I agree with you that we do not have any evidence whatsoever to believe that HFpEF would be in a different category. So we are awaiting more evidence. And I'm sure that within 2, 3 years we'll have this evidence.

Dr. Metra:
So I think it's now time to summarize, to give take-home messages. And so, Piotr, which are your take-home messages? Do you have

something to add?

Dr. Ponikowski:
Well, Marco, as we said, very few, but pretty relevant, clinically important take-home messages. Number one, please remember that iron deficiency in heart failure affects around 60% to 70% of patients. And please remember, proactively screen for it using only 2 simple biomarkers: ferritin and transferrin saturation.

Number two, if detected, please consider treating it with IV ferric carboxymaltose. Please remember that we have the evidence that oral iron, sorry to say, doesn't work in this population. Oral iron doesn't work, although we intuitively think it works; it doesn't. So IV iron. And please remember that it is not only for quality of life, but also to reduce the rate of rehospitalization in patients with reduced and mildly reduced ejection fraction. And I think the case you alluded to is the best example, that this lady may benefit of adding IV therapy with ferric carboxymaltose to her standard therapy.

That would be my final message unless you want to add something.

Dr. Metra:
No, I think, yes. Look for iron deficiency and treat it with IV ferric carboxymaltose, because this is the only treatment shown as effective and with a significant improvement in quality of life, symptoms, and rehospitalizations, which is what we want in our patients.

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