

Title: HFA 23: Diagnosis of Heart Failure in Women

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Prof John Cleland

"I'm John Cleland, I'm professor of cardiology at the University of Glasgow in the UK.

What is the background of this study?

So, we've long been intrigued when we've looked at clinical trials of atrial fibrillation and type two diabetes, that there seem to be many more patients treated with loop diuretics than have a diagnosis of heart failure. And what we've noticed consistently in these clinical trials is that the patients taking loop diuretics seem to have a prognosis very similar to the patients with heart failure. And indeed, patients with heart failure who are not taking loop diuretics seem not to have a particular problem. So, it seems that the problem associates more with the use of loop diuretics than with the diagnosis of heart failure. So, we wanted to look at this in a larger epidemiological data set. So, we took population data from the greater Glasgow area. So about 1.1 million people, we identified everybody who had ischemic heart disease or who was taking ace inhibitors, loop diuretics, beta-blockers. So common treatments for cardiovascular disease. Turns out that between a quarter, perhaps a third of the adult population of the region is being treated for cardiovascular disease or has problems such as ischemic heart disease. And so then we started to segment this into patients who had a diagnosis of heart failure, patients taking loop diuretics and the patients to whom both applied. And it works out that there are in that population about 24,000 patients who are taking loop diuretics but without a diagnosis of heart failure, roughly about another 8000 who were taking loop diuretics and had a diagnosis of heart failure. So, you can see that out of all the people taking loop diuretics, only one in four had a diagnosis of heart failure. And we also had a group of patients who had the diagnosis of heart failure but were not taking loop diuretics. Looking at the differences in these populations, there seemed to be many more women given loop diuretics only without a diagnosis of heart failure. It's about 50% of the patients taking loop diuretics and with a diagnosis of heart failure were women, but 70% of those just treated with loop diuretics were women. On the other

hand, those with just a diagnosis of heart failure and not taking loop diuretics tended to be predominantly men, and they looked like post-infarction left ventricular dysfunction rather than true heart failure. We then looked for reasons why the loop diuretics were being given in this large loop diuretic-only population. And we honestly didn't find that much evidence of end-stage renal disease. We didn't find that much evidence of resistant hypertension. We didn't find much evidence of taking medicines like amlodipine, et cetera, that would cause ankle swelling. We had echocardiograms for a subset, and it looked like they had dilated left atria but normal ejection fraction, but this would be consistent with the diagnosis of HFpEF. We then followed the patients for the next five years, and in doing that, they had a substantial mortality, their mortality. And usually these patients, they didn't get a diagnosis of heart failure, they died without transitioning to a diagnosis of heart failure. Over the five-year follow-up, without getting a diagnosis of heart failure, 40% of the men died and 30% of the women died. So bad prognosis. And when we looked at this in multivariable analysis, there was a weak association between the diagnosis of heart failure and outcome, but a very strong association between loop diuretic and outcome. And it didn't matter an awful lot whether you had a diagnosis of heart failure or not. It was a rather similar outcome. So, it seems that the prognosis associates not with the diagnosis of heart failure so much. There may be a small signal there, but a big signal coming from the use of loop diuretics. And the question is, how much undiagnosed heart failure do we have in that population? Because there are three potential explanations for the finding. One is we are concealing diagnosis of heart failure using loop diuretics. Second possibility is they have some other bad disease, and the loop diuretics is just a marker that they have some other bad disease. But the third and possibly most worrying possibility is that inappropriate use of loop diuretics is killing some of these patients. And so, we really ought to find out the reasons why these patients are taking loop diuretics, sort the problem out. And I think it's not quite a public health crisis, but maybe well, I think that maybe it is a public health crisis.

What is the definition of heart failure in 2023?

So, the definition of heart failure as it stands now is that you must have symptoms and signs of congestion, for which loop diuretics, of course, are the class one indicated drug.

According to the guidelines, you then must have objective evidence of cardiac dysfunction and that might either be from an echocardiogram or for measurement of natriuretic peptides. So basically, it is symptoms of symptoms or signs of congestion associated with objective evidence of cardiac dysfunction. Now, there are some of us who believe that that is problematic. And one of the reasons why so many patients the diagnosis is delayed, because the symptoms and signs are not recognised as belonging to heart failure, til the patient is so sick that they need to be hospitalised. 80% of first diagnosis of heart failure in the UK patients are hospitalised. So, we have a problem, and we need to, I think, make an earlier diagnosis. I think there are two ways that we could do this. One is by picking up on all these people who are being initiated on loop diuretics, largely in primary care, and saying that they need investigation. The second possibility is to use natriuretic peptides for screening. Anybody with an elevated natriuretic peptide should have cardiac imaging. If the cardiac imaging shows a dilated left atrium, then that patient almost certainly has heart failure. And I think we need to have a new definition of heart failure, which basically is cardiac dysfunction with congestion. And the markers of congestion area raised natriuretic peptide, dilated atrium. And we should move away from symptoms because patients can control their symptoms just by watching TV every day until, of course, they develop symptoms at rest and need to be admitted to hospital. And I think that's what's happening in a lot of cases.

To what extent can these findings be generalised or applied to patients in different healthcare systems?

So, I suspect that this is a widespread clinical practice, although I'm sure there are cultural variations in the use of loop diuretics. So, we can't be sure that this is true for other parts of the world. Indeed, it might be worse in some parts of the world than what we see. We have looked at some data from England with one of my colleagues, Rosita Zakiri. We looked at a large population of patients with atrial fibrillation in England, and that showed well the same findings that there were just as many people treated with loop diuretics without a diagnosis of heart failure as had a diagnosis of heart failure with their atrial fibrillation. But the prognosis was the same, really. Their loop diuretics seemed to be a signal that something bad is going on and we need to sort it out.”

