radcliffe cardiology

Title: HFA 24 Late-Breaker Discussion: The TITRATE-HF Study
Faculty: Dr Jasper Brugts and Dr Harriette Van Spall
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Harriette Van Spall:

I'm Harriette Van Spall, clinical trialist, and I'm here with Jasper Brugts from the Netherlands at HFA 2024, where he is presenting his registry of heart failure, GDMT optimization. Welcome, Jasper.

Jasper Brugts:

Thank you. It's a pleasure to be here.

Harriette Van Spall:

Tell us about your registry. Why did you initiate it and what were you hoping to achieve with the data?

Jasper Brugts:

So we initiated the TITRATE HF trial two years ago, after the publication of the ESC guidelines for heart failure with the class one, a recommendation for four types of drugs, and we wanted to study how those drugs are implemented in real world. And we developed a rather large study to study de novo heart failure and chronic heart failure and worsening heart failure altogether.

Harriette Van Spall:

Okay, so three patterns of heart failure. What were your inclusion criteria for the registry?

Jasper Brugts:

So for the de novo, it must be a new diagnosis of heart failure without previous heart failure. And we only studied patients with ejection fraction below 50%, so no preserved ejection fraction. And the same is true for chronic, that should be at least six months of heart failure. And for worsening heart failure, there must be a heart failure admission

during the past six months. So we identified, according to the ESC definitions, the three relevant groups in heart failure.

Harriette Van Spall:

Sure. And tell us how you went about engaging clinicians to participate in this registry. That's often a barrier to these registries. So how did you mobilise the energy and the resources required for this?

Jasper Brugts:

It's a correct point. It is always difficult to provide enough attitude to do a registry, and we managed to include 48 hospitals, which is nearly 70% of all Dutch hospitals in our country, through partnerships. We had many partnerships with the Dutch Cardiac Society and the Cardiovascular Alliance and our Netherlands Heart Institute to really boost this registry for a national prospective effort in optimising heart failure care together with each other. And we managed to do that in about 1.5 years. We included 4000 patients.

Harriette Van Spall:

That's fantastic. What were the baseline characteristics of these patients?

Jasper Brugts:

So the mean age was around 70 years of age, which is slightly younger than expected in a real world population. I think the mean age is about 75 in our country, and about 30% was female. And the average duration of heart failure was four to five years of chronic and worsening heart failure. With all the de novo heart failures were, of course, new in their diagnosis.

Harriette Van Spall:

Okay, and what were some of the comorbidities that your patients had?

Jasper Brugts:

Many had diabetes and renal insufficiency and atrial fibrillation. About 30% to 40% had multiple comorbidities, three or more.

Harriette Van Spall:

And what were some of the leading causes of the heart failure?

Jasper Brugts:

So we observed for the de novo category that 60% had non-ischemic and 40% had ischemic. And in the chronic heart failure, it was more balanced, 50% of both categories.

Harriette Van Spall:

And did you look at any sex differences in the baseline characteristics?

Jasper Brugts:

Not yet. At this stage, it is only a cross-sectional first data from TITRATE HF, but in the coming years we will really dive into elderly female comorbidity to really unravel the gaps of knowledge in current heart failure care.

Harriette Van Spall:

Sure. So tell us about your findings on the uptake of guideline-directed medical therapies across the four classes of treatment.

Jasper Brugts:

So for chronic heart failure patients, 85% were on renin-angiotensin system inhibitors and beta blockers, and about 75 were on a mineral receptor antagonist and 65% on SGLT2 inhibitors. So that's quite an appropriate level of guideline-directed medical therapy. And we also assessed difference between hospitals. And if you look at quadruple therapy, this is all four drugs at once, you see quite some variation between hospitals from 25% to 75%. And if you study how those patients were treated at the outpatient clinics, you saw a quite remarkable difference between general outpatient clinic versus heart failure dedicated outpatient clinics where in the general it was about 37% quadruple therapy, and in the heart rate outpatient cares, it was 47. So clearly, I

think the level of dedication in outpatient care also helps implementing guideline-directed medical therapy as well.

Harriette Van Spall:

Sure. And are your outpatient clinics multidisciplinary or do they tend to have physician predominant services?

Jasper Brugts:

In the Netherlands, we have a nurse-led heart outpatient clinic. It's not multidisciplinary, it is a supervisor, heart failure specialist, and a nurse. It's how we are organised in the Netherlands.

Harriette Van Spall:

Got it. So the uptake of therapies was better in that type of care setting. Fantastic. Now tell us some of the barriers or limitations to the implementation of these therapies.

Jasper Brugts:

So what we really observed was also side effects were really relevant and intolerance of drugs, but also reasons not to titrate, like the blood pressure and the pulse and the side effects that patients encountered. That's something that we managed to describe in detail for those patients where it was marked in the electronic healthcare records. One of the pitfalls of retrospect, but also in general, is that usually it is not even reported why patients are not all titrated to target those that the electronic healthcare records is not giving you that information. So we encountered the same problem as well.

Harriette Van Spall:

Sure. So there were real limitations to the uptake of these therapies. Did you find that patients with those limitations were more prevalent in the generalised settings versus the specialised settings, though, or did you look at that? Did you look at setting versus limitations?

Jasper Brugts:

Not yet, but that will be up for the upcoming analysis, for sure. Where we also have prospective data. This is only the cross-sectional first part of the data, but for the coming periods, we have long term prognosis, look at side effects, especially in the de novo category. We follow them for six months with every titration step, and every dose needs to be recorded in a log file. So that will unravel new data on the upcoming medical congresses in the coming period.

Harriette Van Spall:

So, across the world, we see variation in the uptake of certain classes of therapy. Which class would you say had the most adverse effects or intolerable side effect profiles that limited therapy, and which one was the easiest to deliver, or adopt?

Jasper Brugts:

Yeah. What we see for the data that was available in a small set of patients, that you see that in the ACE inhibitors and beta blockers, most of the intolerances occurring, and I think the easiest is by far the SGLT2 inhibitor. And what we really see is that at this moment in the Netherlands, about 50% of the patient is on sacubitril/valsartan and already 65% is on SGLT2 inhibitor. So the uptake of the SGLT2 inhibitor has gone faster. Well, it is only recommended for a few years now. And the sacubitril/valsartan is from the 2016 guideline, of course. And there are other issues about cost access when dosing versus need to up titrate, and then the side effect profile as well.

Harriette Van Spall:

And then, MRAs, you had quite a high prevalence of hyperkalemia with the use of steroidal MRAs? Tell us about that.

Jasper Brugts:

So what we encountered is that about 30% of all side effects that were noted. So that's, of course, the limitation were due to immersing renal function or hyperkalemia, and that's really real world evidence and the practise that we encounter with spironolactone or eplerenone. And for these patients, it was the reason to stop the drug. And I think that's relevant, practical data, that it is a problem in real world as well.

Harriette Van Spall:

Okay. So across these settings, you found greater uptake of medical therapies in specialised centres that were nurse-led, and you found that side effects were a limitation to the uptake of therapies. Overall, what have you learned that could be actionable in the care of heart failure and what are your next steps? What do you plan to do as a next step with this data?

Jasper Brugts:

Yeah, I think that is really essential data that we have. Also for the upcoming analysis, we will check what happens in time. This was one snapshot in time, but we will see how the implementation is going in those patients with de novo heart failure, and we will learn what are the implementation barriers for or the new drugs to those patients with de novo heart failure. And I think that will also be a lesson that the first initiation is where the most important steps are made. So in the first few weeks, just rapid up titration with all four drugs at a relatively low dose is the way to go forward. And I think the best strategy would be to do a test or an implementation randomization within the Novo Heart failure group to see how we can facilitate and improve GDMT up titration in those patients within the registry itself right when they're earlier on in the disease stage and they have more reserve, less likelihood to have intolerable side effects.

Harriette Van Spall:

Thank you so much for being here and for sharing the results of your registry with us.

Jasper Brugts:

Thank you.