

# RESEARCH LETTER

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## Differences between heart failure specialists and non-specialists regarding heart failure drug implementation and up-titration

Following the 2021 heart failure (HF) European guidelines,<sup>1</sup> an extensive web-based international survey questioning more than 600 cardiologists about their perception of HF sequencing and titrating approach of therapy in HF with reduced ejection fraction (HFrEF) was published.<sup>2</sup>

This study raises queries about the optimal sequencing approach and how to apply a simple algorithm for the cardiology community, keeping in mind that the therapeutic HF arsenal continues to increase and considering individual patients' particularities. Indeed, since HF prevalence is rising worldwide,<sup>3</sup> 'HF specialists' cannot manage all HFrEF patients. Given a certain amount of overlap in pathophysiology, it is not uncommon for interventional cardiologists to manage these patients, while managing HF is a specialty in its own right.

In this context, a post hoc analysis of this web-based international survey limited to the population of HF specialists versus non-specialists (excluding cardiologists in training and medical students) was performed in order to assess the differences in perception of HF therapies between these two groups.

Briefly, this survey was drafted within the HF working group of the French Society of Cardiology (FSC), affiliated with the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Afterward, it was revised and approved by several board members of the HF group from the FSC, the Young Cardiologist Community from the FSC, alums of the Zurich Post-Graduate Course in HF (PCHF) task and task force members from the ESC Academy. After validation, the survey was available for a month in 2022 on the SurveyMonkey platform. It was shared with several international cardiologists'

groups via email and posted on multiple social networks, with three successive invitations sent. The questions asked in the survey have been detailed elsewhere.<sup>2</sup> For this study, we compared the answers from the cardiologists who answered 'Heart failure' versus 'Other' to the question: 'What is your primary subspecialty in cardiology?', excluding cardiologists in training or students (Question 5). Statistical analysis was performed with R (R Project for Statistical Computing, Vienna, Austria, version 4.0.2), using bilateral tests with  $p < 0.05$  considered statistically significant.

Among the 615 cardiologists who completed the survey, 167 HF specialists and 393 non-specialists were included in this analysis. Compared to the HF specialists, non-specialists were younger (38 vs. 42 years,  $p < 0.001$ ), less likely to work in University Hospital (53% vs. 64%,  $p = 0.012$ ), and to have attended a previous ESC academy course (21% vs. 41%,  $p < 0.001$ ).

The left ventricular ejection fraction (LVEF) threshold to define HFrEF differed significantly between the two groups ( $p = 0.01$ ; Figure 1) since non-specialists were more likely to use 50% as the threshold. Regarding HF drug sequencing, non-specialists tended to start more frequently with beta-blockers (25% vs. 18%). In contrast, specialists would prefer to start with angiotensin-converting enzyme inhibitor (ACEi)/angiotensin receptor–neprilysin inhibitor (ARNi) first (80% vs. 74%; ANOVA  $p = 0.064$ ). For most participants, it was possible to introduce the four major drugs during initial hospitalization (84% vs. 85%,  $p = 0.9$ ), and the most realistic timing for titration was 1 month for half of the participants (47% vs. 42%,  $p = 0.11$ ).

Interestingly, 44% of non-specialists thought that titration is more important than adding another HF drug, whereas a majority (64%) of HF specialists thought otherwise, and this difference tended to be significant ( $p = 0.063$ ).

The same proportion of cardiologists would start ARNi in a treatment-naive patient with HFrEF (56% vs. 54%,  $p = 0.6$ ). Yet, non-specialists were less likely to start mineralocorticoid receptor antagonist (MRA) when estimated glomerular filtration rate (eGFR) is  $< 30$  ml/min/1.73 m<sup>2</sup> (52% vs. 69%;  $p < 0.001$ ) to achieve complete titration ( $p < 0.001$ ),

modify or optimize HF drugs ( $p = 0.003$ ), and to monitor iron deficiency during hospitalization ( $p = 0.003$ ) or outpatient visits ( $p < 0.001$ ; Figure 1).

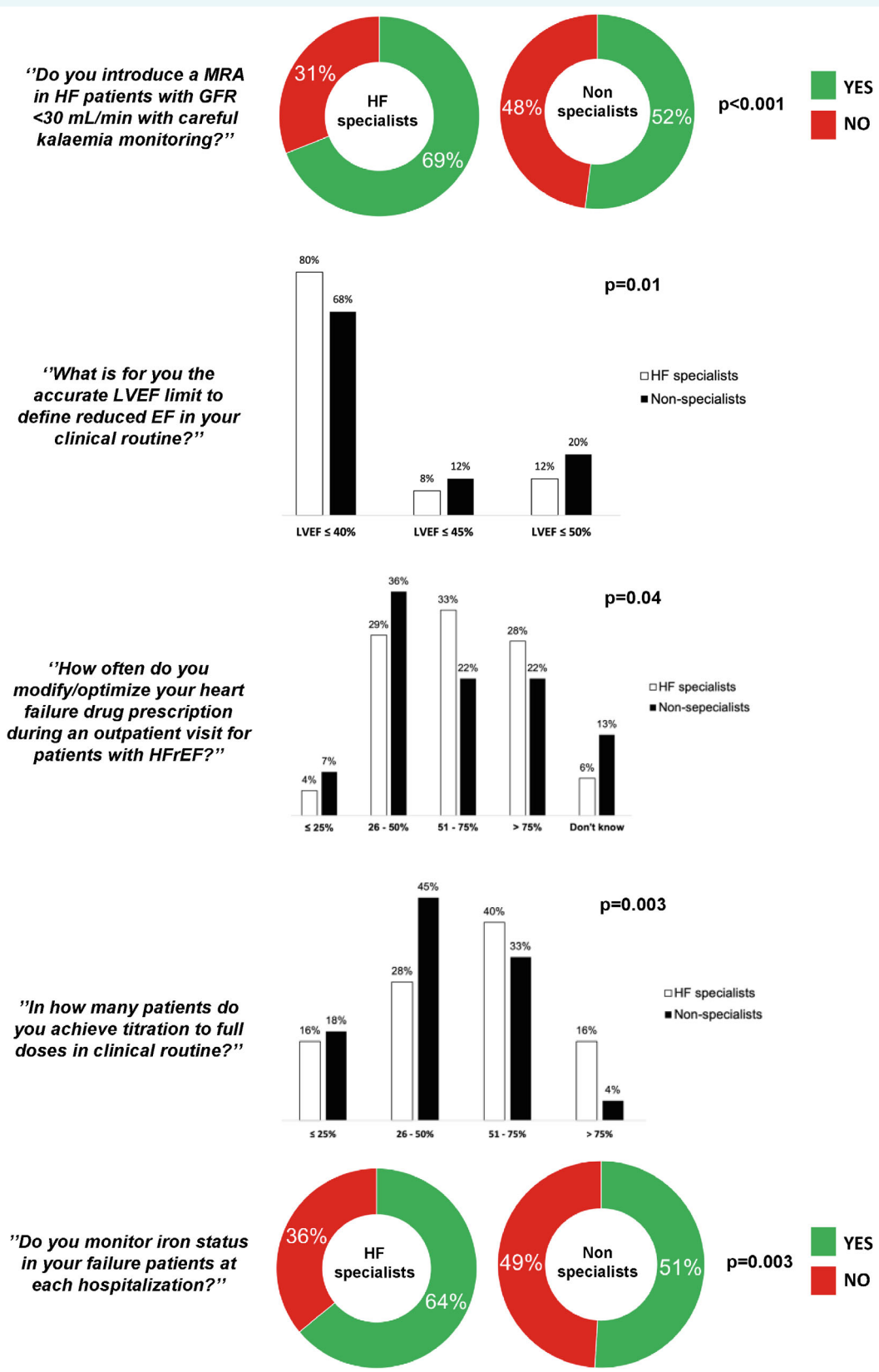
Compared to secondary care centres, cardiologists in tertiary care centres were more likely to start titration by beta-blockers (27% vs. 19%,  $p = 0.004$ ) and to start ARNi in a treatment-naive patient (61% vs. 50%;  $p = 0.006$ ). However, there were no differences regarding the more realistic timing titration ( $p = 0.20$ ), the proportion believing that titrating is more important than adding another HF drug ( $p = 0.8$ ), HF drug optimization frequency ( $p = 0.12$ ), and the percentage of achieving complete titration ( $p = 0.7$ ).

Not surprisingly, this analysis shows that HF specialists and non-specialists have different perceptions of HF titration and, more widely, management.

First of all, it is interesting to stress that almost half of non-specialists consider titration to be more important than adding another HF drug. In contrast, in the HF community, there is a clear shift to targeting all the pathologically activated pathways in HFrEF by introducing a new class rather than titrating a single class to a maximally tolerated dose.<sup>4,5</sup>

Secondly, and as already discussed,<sup>2</sup> HF specialists seem more open about introducing MRA when eGFR  $< 30$  ml/min/1.73 m<sup>2</sup>, for instance. It emphasizes the importance of the 'risk treatment paradox' concept in non-HF specialists,<sup>6</sup> leading to a non-prescription of potentially required treatment. Interestingly, these results suggest that non-specialists are less likely to fully titrate, modify or optimize HF drugs, thus participating in the known therapeutic inertia in HF.<sup>6</sup> Yet, we cannot exclude the possible self-perception bias of HF specialists in overestimating their patients' guideline-directed medical therapy (GDMT) adherence. For instance, Adamo *et al.*<sup>7</sup> recently showed low real-life GDMT adherence before transcatheter mitral valve edge-to-edge repair in patients with secondary mitral regurgitation, which is consistent with a COAPT trial post-hoc analysis.<sup>8</sup>

Thirdly, HF management cannot be reduced to initiating and titrating the four major therapeutic classes. Among others, addressing iron deficiency is an essential part of HF management.<sup>1,9</sup> Again, non-specialists



**Figure 1** Discrepancies between heart failure (HF) specialists and non-specialists regarding the survey responses. EF, ejection fraction; GFR, glomerular filtration rate; HF rEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist.

were less prone to seek and thus treat this condition, increasing the risk of rehospitalization for acute HF.<sup>10</sup>

Fourthly, even if HF specialists are less cautious about introducing and fully titrating HF drugs, only 16% achieve >75% of target treatment dose in clinical routine and 36% still believe titration is more important than adding another drug. It emphasizes that, even in the HF community, several aspects must be improved to achieve GDMT. Of note, this low adherence seems equivalent between secondary and tertiary care centres.

Finally, we must acknowledge that, even if international, this survey still represents a limited part of the cardiology community. Moreover, since it was an open-access survey, we cannot affirm that all the responders were physicians which may have induced selection bias. Yet, the results are consistent.


Knowing that HFrEF mortality remains high with a deleterious impact on quality of life, these data reinforce the critical value of dedicated HF programmes and specialized HF clinics staffed by HF experts, including physicians and nurses.<sup>6</sup> Limited access to HF expertise is a significant driver of therapeutic inertia and lower drug implementation, while dedicated HF clinics improve HF management.<sup>6</sup> Furthermore, specific courses, such as those endorsed by the HFA of the ESC (i.e. PCHF courses), may also improve physicians' knowledge and ultimately benefit patients. Just as cardiovascular imaging or interventional cardiology are specialties in their own right, these findings emphasize the importance of HF specialization.

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