Although the failed matches are the main limitation of our study, we achieved considerably greater matching (71.7% vs 60.8%) than a previous study[6] of acute coronary syndrome (ACS) that used the DIOCLES clinical registry as reference; while our sensitivity (67.5% vs 85.1%) and concordance (κ = .7 vs κ = .86) were lower, our specificity was similar (97.1% vs 98.3%). These results indicate that the validity and concordance of the variables relevant for the adjustment of risk of HF events recorded in the RSHCA-MDS are generally reasonable and are in line with the expected results in ADs,[5] although somewhat lower than those found for ACS.

Our consideration of variables with very low incidence rates could partly explain the slightly lower validity and concordance for HF than previously found for ACS. However, independently of this factor, adjustments by risk of in-hospital mortality and readmission are usually worse for HF than for ACS. Accordingly, measures should be adopted to improve the recording and coding of HF events in the RSHCA-MDS, particularly for comorbidities with lower incidences.

FUNDING

This work has not received any external funding.

AUTHORS' CONTRIBUTIONS

Study design and manuscript drafting: J.L. Bernal, J. Elola, and M. Anguita. Data revision and statistical analysis: J.L. Bernal and N. Rosillo. Revision, editing, and manuscript approval: all authors.

CONFLICTS OF INTEREST

The authors report no conflicts of interest associated with this work.

ACKNOWLEDGMENTS

We thank the Spanish Ministry of Health for granting access to the MBDS database and the Institute of Health Information of the Spanish National Health System for the facilities provided to the Spanish Society of Cardiology to undertake the RECALCAR project.

José L. Bernal,[ab,*] Juan Luis Bonilla-Palomas,[c] Nicolás Rosillo,[b,d] Clara Bonanad,[c,e,f] Javier Elola,[b] and Manuel Anguita[g,h]

[a]*Servicio de Análisis de Información y Control de Gestión, Hospital Universitario 12 de Octubre, Madrid, Spain*
[b]*Fundación Instituto para la Mejora de la Asistencia Sanitaria, Madrid, Spain*
[c]*Servicio de Cardiología, Hospital San Juan de La Cruz, Úbeda, Jaén, Spain*
[d]*Servicio de Medicina Preventiva, Hospital Universitario 12 de Octubre, Madrid, Spain*
[e]*Facultad de Medicina y Odontología, Universidad de Valencia, Valencia, Spain*
[f]*Instituto de Investigación Sanitaria del Hospital Clínico Universitario de Valencia, Valencia, Spain*
[g]*Servicio de Cardiología, Hospital Universitario Reina Sofía, Córdoba, Spain*
[h]*Instituto Maimónides de Investigación Biomédica (IMIBIC), Córdoba, Spain*

[*] Corresponding author.
E-mail address: Jluis.bernal@movistar.es (J.L. Bernal).

Available online 16 July 2023

REFERENCES

1. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021;42:3599–3726.
2. Bonilla-Palomas JL, Anguita-Sanchez MP, Elola-Somoza FJ, et al. Thirteen-year trends in hospitalization and outcomes of patients with heart failure in Spain. *Eur J Clin Invest.* 2021;51.
3. McCormick N, Lacaille D, Bhole V, Avina-Zubieta JA. Validity of Heart Failure Diagnoses in Administrative Databases: A Systematic Review and Meta-Analysis. *PLoS ONE.* 2014;9:e104519.
4. Registro de Insuficencia Cardiaca. SEC Excelente. Available in: https://secardiologia.es/institucional/reuniones-institucionales/sec-calidad/sec-excelente/registro-ic Consulted 27 Apr 2023.
5. Anguita Sánchez M, Lambert Rodríguez JL, Bover Freire R, et al. Classification and Quality Standards of Heart Failure Units: Scientific Consensus of the Spanish Society of Cardiology. *Rev Esp Cardiol.* 2016;69:940–950.
6. Bernal JL, Barrabés JA, Íñiguez A, et al. Clinical and Administrative Data on the Research of Acute Coronary Syndrome in Spain Minimum Basic Data Set Validity. *Rev Esp Cardiol.* 2019;72:56–62.

https://doi.org/10.1016/j.rec.2023.05.007

Home exercise intervention with the Vivifrail program in frail older patients with heart failure with reduced ejection fraction. The ExFRAIL-HF randomized trial

Intervención con ejercicio domiciliario con Vivifrail para ancianos frágiles con insuficiencia cardiaca y fracción de eyección reducida. El ensayo aleatorizado ExFRAIL-HF

To the Editor,

Frailty is a common syndrome in older patients with heart failure (HF) and is characterized by decreased functional reserve and associated risks of disability, hospitalization, and death.[1] Exercise rehabilitation programs have been demonstrated to improve the functionality of patients with HF.[2,3] However, the implementation of these structured programs is hindered by certain barriers. The REHAB-HF trial[2] improved Short Physical Portable Battery (SPPB) scores in 349 frail patients randomized after an acute HF episode. In the trial, patients attended 3 in-person weekly sessions for 12 weeks.

Although this protocol might seem ideal, its implementation in the real world is hampered by the resources needed. Another obstacle to the implementation of in-person treatments is the need for patients to travel from home, especially in older patients in suburban or rural areas. Furthermore, the patients studied were significantly younger than those in usual clinical practice in cardiogeriatrics and therefore the results of these clinical trials cannot be directly extrapolated to frail older patients.

Some exercise programs have been adapted to frail older patients, such as the Vivifrail program.[4] These programs have been shown to improve outcomes in these patients,[5] but have not been studied in patients with HF with reduced ejection fraction (HFrEF).

The Vivifrail program individualizes the type, frequency, and intensity of exercises to the functional characteristics and estimated risk of falls in each patient and can be performed at home, with 5 sessions per week, overcoming the limitations of conventional cardiac rehabilitation in frail older patients.

The Ex-FRAIL-HF randomized controlled single-blind intervention trial analyzed the benefit of Vivifrail in elderly patients with HFrEF and frailty criteria during a 6-month period. The flowchart for the study is shown in figure 1. After approval from the regional ethics committee of Galicia, the study was conducted by the Cardiology Department and Geriatric Medicine Department of the *Complexo Hospitalario Universitario de Vigo*. This is a parallel group study with a 1:1 ratio between the intervention and control groups and with blind evaluation of the outcome variables. Included patients were aged at least 75 years, with SPPB < 10 points, and had a diagnosis of HFrEF. Following other experiences in the literature,[6] we included 60 patients in this pilot study. After signing the informed consent form, patients were recruited between May 2021 and May 2022 and the last follow-up was in November 2022. All patients underwent a comprehensive geriatric assessment, which was carried out again at 6 months. The effects of the Vivifrail program on functional status, quality of life and frailty were analyzed. As a safety and exploratory analysis, we also analyzed clinical variables.

Patients randomized to the intervention group were offered the possibility of following the Vivifrail program. The assignment of the individualized exercise (included in each different Vivifrail "passport" document: "A", "B" or "C", with Vivifrail passport A including the most frail patients) was selected according to the findings of the baseline assessment. After a short information and training session, the patients were given the Vivifrail "passport" document. Like the control group, patients in the intervention group also received standard self-management guidelines for HF, including general advice on physical activity. The intervention was performed for 6 months, with patient re-evaluation and reinforcement at 2 months. Adherence to the exercise prescribed in the Vivifrail group was monitored using the diary of activities included with the Vivifrail passport as well as patients' self-reports. Patients were considered nonadherent when the diary of activities was completely empty and they self-reported that they did not follow the program at all. Both criteria were necessary.

A total of 60 patients (30 from each group) were included in the study; 2 patients died before the 6-month visit (both from the control group) and another 2 patients (1 from each group) refused to attend the 6-month visit because of the COVID-19 pandemic and were excluded from the analysis. Of the remaining 56 patients, 27 were in the control group and 29 were in the intervention group. Of the latter, 8 patients reported that they never followed the Vivifrail exercises. They were considered nonadherent and were excluded from the analysis as per protocol.

Finally, we analyzed 27 patients in the control group and 21 in the intervention group. The baseline characteristics and 6 month follow-up evaluation are summarized in table 1. Patients allocated to the Vivifrail exercise program significantly improved their New York Heart Association (NYHA) class compared with control group (improved NYHA by at least 1 point 47.6% vs 22.2% respectively; $P = .04$) and physical activity scale for the elderly (PASE) score (+6.4

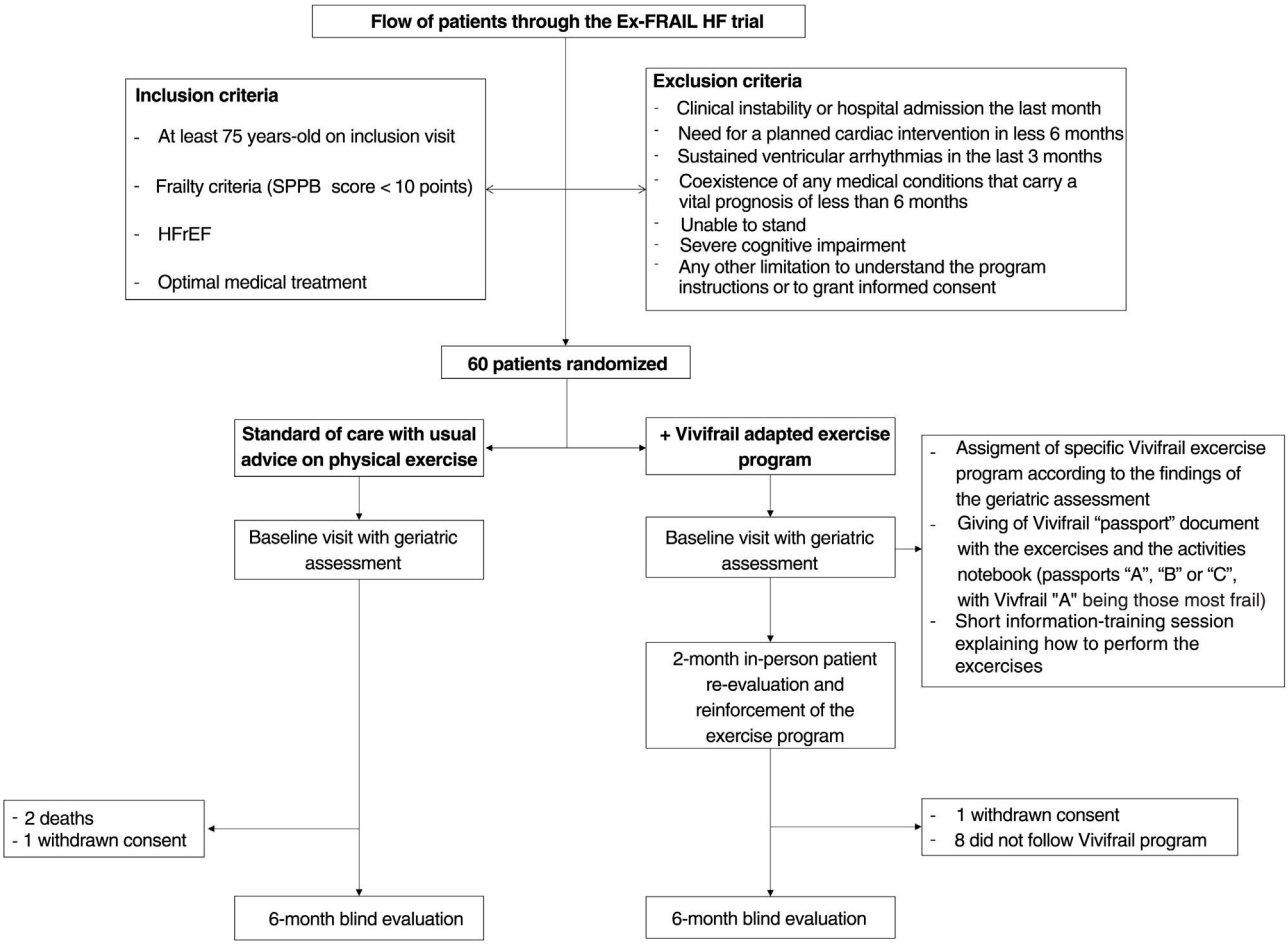

Figure 1. Flowchart of the ExFRAIL-HF trial. HFrEF, heart failure with reduced ejection fraction. SPPB, short physical performance battery.

vs − 12.5; *P* = .004). Of those who improved NYHA class, most had NYHA III at baseline compared with NYHA II (60% vs 40%; *P* = .037). The Vivifrail group showed no statistically significant improvements in the other functional indicators measured compared with standard treatment, although some indicators were more numerically favorable in the Vivifrail group: nonfrail status with SPPB higher than 9 points (Vivifrail 38.1% vs 22.2% control; *P* = .13), improved Katz index (Vivifrail 23.8% vs 18.5% control; *P* = .65), 6-minute walk test (6MWT) change compared with baseline (% change; Vivifrail + 3.24% vs − 4.98% control; *P* = .37), and quality of life as indicated by the Minnesotta Living with Heart Failure (MLWHF) questionnaire (Vivifrail − 3.81 vs − 1.33 control; *P* = .45). Clinical events were also recorded for the exploratory analysis. In addition to the 2 deaths due to HF progression in the control group, 2 patients in the control group and another 2 patients in the Vivifrail group required hospital admission or an unplanned visit due to HF progression during the study period. No falls requiring medical assistance were reported in the Vivifrail or control groups.

Patients who reported they were nonadherent to the Vivifrail program did not have more advanced HF nor were they more frail: the proportion of patients with A and B Vivifrail passports was the same in the 2 groups (87.5% in nonadherent vs 85.7% in adherent; *P* = .77), as was functional class III (25% vs 28.6%; *P* = .48), left ventricular ejection fraction (32.6% ± 6.9 vs 31.1 ± 7.4%; *P* = .61), SPPB (7.4 ± 2.3 vs 6.5 ± 2.1; *P* = .21), PASE score (40.1 ± 31.9 vs 28.1 ± 17.9; *P* = .34), Barthel score (90.6 ± 17.8 vs 92.1 ± 10.7; *P* = .77), and 6MWT (308 ± 128 vs 269 ± 112; *P* = .44). Nonadherent patients showed worse depression (Geriatric Depression Scale, 6.0 ± 1.9 vs 3.7 ± 2.2; *P* = .01) and quality of life scores (MLWHF, 20.7 ± 14.2 vs 11.2 ± 11.0; *P* = .07), which might have hampered adherence to the exercise prescribed.

Table 1
Baseline characteristics of the EX-FRAIL HF population and 6-month re-evaluation

Baseline characteristics	Control group	Intervention group	*P*
Baseline evaluation			
Age, y	82.6 ± 5.7	83.2 ± 5.1	.72
Hypertension	25 (92.6)	16 (76.2)	.11
Diabetes	9 (33.3)	12 (57.1)	.10
Dyslipidemia	18 (66.7)	12 (57.1)	.49
LVEF, %	34.5 ± 5.1	31.1 ± 7.4	.07
Treatment on inclusion			
Beta-blockers	22 (81.5)	17 (81)	.96
ACE inhibitor/ARB	6 (22.2)	3 (14.3)	.79
ARNI	20 (74.1)	18 (85.7)	.32
iSGLT2	10 (37)	9 (42.9)	.68
MRA	11 (41)	9 (43)	.74
Loop diuretics	20 (74.1)	12 (57.1)	.21
Oral anticoagulants	23 (85.2)	15 (71.4)	.24
ICD	4 (14.8)	1 (4.8)	.25
CRT	4 (14.8)	3 (14.3)	.96
Pacemaker	2 (7.4)	4 (19)	.22
Examination			
SBP, mmHg	121.7 ± 17.8	122.7 ± 17.0	.85
Heart rate, bpm	68.8 ± 11.2	67.7 ± 10.8	.72
Body mass index	28.4 ± 4.7	29.9 ± 5.3	.30
Blood tests			
Hemoglobin, g/dL	13.6 ± 2.1	13.8 ± 1.6	.67
GFR, mL/min/m^2	50.4 ± 1.6	38.8 ± 28.5	.16
Sodium, mEq/L	140.8 ± 2.2	140.5 ± 2.0	.68
NT-ProBNP, pg/mL (median)	1409	1257	.97
Total cholesterol, mg/dL	150.3 ± 45.6	161.0 ± 35.9	.41
Functionality on inclusion			
SPPB, points	6.3 ± 1.9	6.5 ± 2.1	.75
NYHA I	9 (33)	3 (14)	.24
NYHA II	14 (52)	12 (57)	.24
NYHA III	4 (15)	6 (29)	.24
PASE score, points	38.5 ± 23.6	28.1 ± 3.5	.11
Katz index A	19 (70.4)	11 (52.4)	.50
Katz index B	4 (14.8)	6 (28.6)	.50
Katz index C	1 (3.7)	2 (9.5)	.50
Katz index D	3 (11.1)	2 (9.5)	.50
Barthel index, points	93.7 ± 11.2	92.1 ± 10.7	.63
Frield frail/prefrail	18/9 (66.7/33.3)	12/9 (57/43)	.64

Table 1 *(Continued)*
Baseline characteristics of the EX-FRAIL HF population and 6-month re-evaluation

Baseline characteristics	Control group	Intervention group	*P*
Lawton-Brody index, points	5.1 ± 2.4	4.67 ± 2.4	.53
Geriatric Depression Scale, points	3.9 ± 2.1	3.7 ± 2.2	.69
MLWHF, points	11.6 ± 12.2	11.2 ± 11.0	.91
6MWT, m	246 ± 106	269 ± 112	.49
Functionality at 6 months of follow-up			
SPPB, points	7.27	7.71	.64
SPPB above 9	6 (22.2)	8 (38.1)	.13
NYHA I	11 (41)	7 (33)	.82
NYHA II	13 (48)	12 (57)	.82
NYHA III	3 (11)	2 (10)	.82
NYHA improvement	6 (22.2)	10 (47.6)	.04
PASE score*	− 12.5	6.4	.004
Katz index A	16 (61.5)	12 (57.1)	.60
Katz index B	6 (23.1)	3 (14.3)	.60
Katz index C	1 (3.8)	2 (9.5)	.60
Katz index D	2 (7.7)	3 (14.3)	.60
Katz index E	1 (3.8)	1 (4.8)	.60
Katz improvement	18.5	23.8	.65
Barthel,* points	− 3.14	− 3.1	.98
Lawton-Brody,* points	− 0.4	− 0.52	.77
Geriatric Depression Scale,* points	0.04	− 0.14	.78
MLWHF,* points	− 1.33	− 3.81	.45
6MWT,* m	− 14.2	2.26	.55
6MWT change, m	− 4.98	3.24	.37

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers; ARNI, angiotensin receptor-neprilysin inhibitors; CRT, cardiac resynchronization therapy; GFR, glomerular filtration rate; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MLWHF, Minnesotta Living with Heart Failure; 6MWT, 6-minute walk test; MRA, mineralocorticoid receptor antagonist; NT-ProBNP, N-Terminal probrain natriuretic peptide; NYHA, New York Heart Association; PASE, physical activity scale for the elderly; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitor; SPPB, short physical performance battery.
Data are expressed as No. (%), mean ± standard deviation or median [interquartile range] unless otherwise indicated.
* Mean change from index scores.

This pilot study shows that the Vivifrail program improved NYHA and PASE score in frail older patients with HFrEF in 6 months. A multicenter study would be desirable to confirm these findings as well as testing Vivifrail in a larger sample to better understand its effect on the other functional and quality of life parameters analyzed. The Ex-FRAIL-HF approach could be considered more pragmatic and easier to implement in the real world of constrained resources than other in-hospital programs. Another finding is that one-third of the patients randomized to the exercise program did not perform the exercises prescribed. These patients did not have a worse HF profile, but showed significantly worse depression scores, which has also been linked to worse HF drug adherence and prognosis. This finding highlights that depression should be actively investigated and adequately addressed to improve patient adherence to treatments.

FUNDING

This study was funded with an unconditional grant from the Spanish Society of Cardiology (SECAINC-INV-ICC 20/002).

AUTHORS' CONTRIBUTIONS

Study design: D. Dobarro, M. Cordeiro-Rodríguez, and C. Rodríguez-Pascual. Inclusion and study procedures: A. Costas-Vila and M. Melendo-Viu. Analysis and writing: D. Dobarro and M. Melendo-Viu. Proofreading: C. Rodríguez Pascual and A. Íñiguez-Romo.

CONFLICTS OF INTEREST

None.

David Dobarro,[a,*] Ana Costas-Vila,[b] María Melendo-Viu,[a] Mónica Cordeiro-Rodríguez,[b] Andrés Íñiguez-Romo,[c] and Carlos Rodríguez-Pascual[b]

[a]*Unidad de Insuficiencia Cardiaca e Hipertensión Pulmonar, Servicio de Cardiología, Hospital Álvaro Cunqueiro, Complexo Hospitalario Universitario de Vigo, Vigo, Spain*
[b]*Unidad de Cardiogeriatría, Servicio de Geriatría, Hospital do Meixoeiro, Complexo Hospitalario Universitario de Vigo, Vigo, Spain*
[c]*Servicio de Cardiología, Hospital Álvaro Cunqueiro, Complexo Hospitalario Universitario de Vigo, Vigo, Spain*

* Corresponding author.
E-mail address: david.dobarro.perez@sergas.es (D. Dobarro).
@DrDavidDobarro @maria_viu

Available online 12 June 2023

REFERENCES

1. Jiménez-Méndez C, Díez-Villanueva P, Bonanad C, et al. Frailty and prognosis of older patients with chronic heart failure. *Rev Esp Cardiol.* 2022;75:1011–1019.
2. Kitzman DW, Whellan DJ, Duncan P, et al. Physical Rehabilitation for Older Patients Hospitalized for Heart Failure. *N Engl J Med.* 2021;385:203–216.
3. Pandey A, Segar MW, Singh S, et al. Frailty Status Modifies the Efficacy of Exercise Training Among Patients With Chronic Heart Failure and Reduced Ejection Fraction: An Analysis From the HF-ACTION Trial. *Circulation.* 2022;146:80–90.
4. The Vivifrail project. Available at https://www.vivifrail.com, Accessed 28 Apr 2023.
5. Martínez-Velilla N, Valenzuela PL, Sáez de Asteasu ML, et al. Effects of a Tailored Exercise Intervention in Acutely Hospitalized Oldest Old Diabetic Adults: An Ancillary Analysis. *J Clin Endocrinol Metab.* 2021;106:e899–e906.
6. Wielenga RP, Huisveld IA, Bol E, et al. Exercise training in elderly patients with chronic heart failure. *Coron Artery Dis.* 1998;9:765–770.

https://doi.org/10.1016/j.rec.2023.06.001

SGLT2i and loop diuretic withdrawal or downtitration in heart failure

iSGLT2 y retirada o reducción de diurético de asa en insuficiencia cardiaca

To the Editor,

Loop diuretics are the cornerstone of the treatment of fluid overload in heart failure (HF) but have possible deleterious effects on intravascular depletion and subsequent activation of the renin-angiotensin-aldosterone and sympathetic nervous systems. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) reduce glucose and sodium resorption in the proximal tubule, causing natriuresis and osmotic diuresis due to glucosuria. Differences between the diuretic effects of SGLT2i vs loop diuretics suggest that SGLT2i may selectively reduce interstitial fluid, thereby avoiding deleterious reflex neurohumoral stimulation.[1] The effect of SGLT2i on the diuretic regimen in real-world ambulatory HF patients is not yet fully understood.

This study aimed to investigate diuretic use after the introduction of SGLT2i in outpatients with HF. As a secondary endpoint, lung ultrasound and HF biomarkers were assessed to monitor congestion status.

This prospective single-center study included ambulatory patients with nondecompensated HF and type-2 diabetes, irrespective of left ventricular ejection fraction (LVEF). The patients were receiving treatment with loop diuretics, and had an estimated glomerular filtration rate (eGFR) > 45 mL/min/1.73 m^{2*}. The study was performed in a HF clinic. All participant-sprovided written informed consent, and the protocol was approved by the local ethics committee (PI-18-163).

Study visits were performed at baseline and at 3 months of follow-up. At the initial visit, empagliflozin or dapagliflozin 10 mg/d were added to the HF treatment. As per the treatment protocol, clinicians were encouraged to reduce or withdraw diuretic treatment in accordance with their clinical assessment and were blinded to biomarker values. Neurohormonal HF medication could be adjusted, if clinically indicated.

Lung ultrasound was performed with a pocket device (V-scan, General Electric, United States) scanning 2 upper and 2 lower areas of each hemithorax, and images were analyzed offline.

The biomarker panel included N-terminal pro-B-type natriuretic peptide (NT-proBNP), cancer antigen 125 (CA125), and interleukin-1 receptor-like 1 (ST2).

The sums of B-lines and biomarker levels were compared between baseline and the 3-month follow-up.

From November 7, 2018 to March 25, 2021, 66 consecutive patients were included (mean age 67 years, predominantly male, with ischemic etiology, and mainly in New York Heart Association [NYHA] class II) (table 1). The mean LVEF was 43.7 ± 11.4 (30.2 ± 9.8 at admission to the HF clinic). The mean dose of furosemide or equivalent (10 mg torsemide = 40 mg furosemide) was 44.5 ± 29.6 mg/d.

After the introduction of SGLT2i, the number of patients treated with loop diuretics decreased by 50% ($P < .001$) (figure 1). Among the 33 patients who continued to receive loop diuretics, the mean dose was significantly reduced ($P < .001$) (figure 1); of note, these patients were receiving a higher dose of diuretics at baseline (61 ± 5 mg/d) than patients able to discontinue diuretic therapy (27.6 ± 11.1 mg/d), $P = .001$, and had a higher prevalence of chronic kidney disease and a history of previous HF hospitalization. The groups receiving empagliflozin (n = 29) vs dapagliflozin (n = 37) treatment did not differ in the percentage of patients with loop diuretic withdrawal ($P = .46$) or diuretic dose downtitration ($P = .63$). Only 1 patient returned to his previous dose of diuretic after withdrawal upon SGLT2i introduction.

There were no significant differences in the percentage of patients able to discontinue diuretic treatment based on etiology ($P = .08$). The percentage of these patients was higher in patients in NYHA functional class II (50%) than in those in NYHA III (28.5%), but this difference was not statistically significant, probably due to the small number of patients in class III ($P = .29$).

There were no significant changes in eGFR at 3 months of follow-up ($P = .20$) or in HF treatment at 3 months of follow-up. Indeed, only the percentage of angiotensin receptor-neprilysin inhibitors (ARNI) increased slightly from 48.9% to 53.4% ($P = .22$). Among treatment doses, only the ARNI dose increased statistically significantly from 233.3 ± 119.5 mg/d to 254.2 ± 114.3 mg/d, $P = .04$.

No significant changes were observed in the sum of B-lines ($P = .59$) or in biomarker concentrations (figure 1). There were no HF hospitalizations or deaths during follow-up.

Despite the limitation of the small sample size, our present results suggest that the introduction of SGLT2i treatment might facilitate withdrawal or dose-reduction of loop diuretics among ambulatory patients with HF, without evidence of worsening congestion, and assessed by either lung ultrasound or biomarkers of congestion.

In the pivotal clinical trials with SGLT2i in chronic HF, diuretic management was left to the investigators' discretion, and was rarely modified. In DAPA-HF,[2] the mean diuretic dose did not differ between groups after randomization, although a decrease in diuretic dose was more frequent with dapagliflozin. In EMPEROR-Reduced, patients in the empagliflozin group were less likely to require diuretic intensification.[3] Recently, a retrospective study of both empagliflozin and diuretics[4] showed that diuretics were reduced in 21% of patients and the mean dose of furosemide by about half.

In the current study, we evaluated additional information on fluid overload. Our results showed that SGL2i initiation and simultaneous dose reduction of loop diuretic did not significantly increase the number of B-lines or biomarker values.