Title page:

Title: The prevalence, profile, and prognosis of heart failure with preserved ejection fraction: A South African tertiary hospital experience.

Student: David Nshuti Shema
Student number: NSHDAV001
Supervisor: Professor Mpiko Ntsekhe

Submitted to the University of Cape town in partial fulfilment of the requirements of the Masters in Medicine Degree (MMED)

Faculty of Health Sciences
UNIVERSITY OF CAPE TOWN

DECLARATION

I, *David Nshuti Shema* hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature: …… Signed by candidate.

Date: ……28/08/2022…….

Background

Heart failure with preserved ejection fraction (HFpEF) is a heterogeneous disorder characterized broadly by a combination of symptoms and signs of heart failure (HF), the absence of reduced left ventricular ejection fraction (LVEF ≤50%), evidence of left ventricular (LV) diastolic dysfunction, abnormal LV and/or left atrial structure and elevated levels of natriuretic peptides.[1, 2] HFpEF is currently recognized as a distinct HF phenotype driven by unique pathophysiological mechanisms.[3] Although the pathophysiology is poorly understood, data from available studies suggest that the syndrome of HFpEF is associated with increasing age, hypertension, diabetes, obesity, microvascular disease and left ventricular hypertrophy (LVH), and is more common in women.[4-7] There are also suggestions that the clinical phenotype of HF in patients with well treated HIV is predominantly HFpEF.[8]

HFpEF is a major public health issue globally.[9] Both community and hospital based epidemiology studies, conducted mainly in Western countries, have reported a prevalence varying from 40% to 71% amongst populations with heart failure.[10, 11] [12, 13] Many of the same studies suggest that the prognosis and quality of life of patients with HFpEF is not dissimilar to those with other forms of heart failure.

Despite the growing volume of information on this condition globally, there is limited data on the prevalence, profile, and outcomes of HFpEF in Sub-Saharan Africa (SSA). Published data from Nigeria and Ghana suggest that the proportion of heart failure admissions due to HFpEF

is between 35 and 60%,[14, 15] and that the condition is driven predominantly by hypertension. [14, 15]

There is little information on prognosis from these regions.[14, 15] Given the differences in population profiles with regards to the age structure, [16] and underlying prevalence of co-morbidities associated with HFpEF (diabetes, obesity, hypertension and HIV), [17-19] it is important not to assume that information obtained elsewhere is locally applicable, especially in light of the potential implications on local practice and prevention strategies.

We report the results of a single South African Urban Centre experience of the proportion of heart failure admissions with HFpEF over a 24-month period and describe their clinical and demographic profile, as well as one-year outcomes.

Methods

Study design and participants.

We conducted a retrospective review of the hospital records of all consecutive adult patients (≥18 years old) admitted to the general medical wards at Groote Schuur Hospital (GSH) (a 900-bed tertiary and quaternary referral hospital in Cape Town) with a clinical diagnosis of de novo acute heart failure during the period of January 2016 to December 2017. Patients were identified from the Western Cape electronic discharge database for the period of the study using the international classification of diseases 10th revision (ICD 10) code and key words such as congestive heart failure, diastolic heart failure and de novo heart failure as primary diagnosis. Patient folders were subsequently retrieved and reviewed to identify participants with incident heart failure and a diagnosis of HFpEF.

For the purpose of the study, patients were considered to have HFpEF if the following criteria were met:

1. Admission to hospital with clinical diagnosis of heart failure confirmed by the attending physician
2. A left ventricular ejection fraction of ≥ 50% as determined by echocardiography within three months of the diagnosis
3. No evidence of valvular heart disease, a history of myocardial infarction or constrictive pericarditis as the primary HF aetiology.

The study was formally approved by the Faculty of Health Sciences' Human Research Ethics Committee (HREC) at the University of Cape Town (UCT) (ref. no. 384/2018).

Data collection

Information on the socio-demographic profile (age, gender), medical history (comorbidities), clinical examination findings and laboratory investigations (electrolytes, renal function, haematological parameters) were recorded on all patients who fulfilled the HFpEF criteria. Additional investigations which were collected for analysis included the admission chest radiograph (CXR), admission 12-lead electrocardiogram (ECG), and echocardiography (echo) performed within 3 months of admission. During the time period in question, natriuretic peptides (NT-proBNP and BNP) were not available for routine measurement in the public sector of the Western Cape Province.

Participant discharge prescriptions were reviewed for the following anti-failure, and anti-hypertensive agents: thiazide diuretics, loop diuretics, mineralocorticoid antagonist (MRA), angiotensin converting enzyme inhibitor (ACE-i), angiotensin receptor blocker (ARB), calcium channel blocker, beta blockers, alpha blocker, aspirin, oral anticoagulant (warfarin), statin therapy and nitrate was recorded. The outcome of interest was the composite of readmission to hospital or death within one year of index admission for HFpEF.

Statistical analysis

Data were captured on Research Electronic Data Capture (REDCap Version 9.5.13), a secure electronic database hosted by the University of Cape Town, before being exported to Stata (Version 14.2, StataCorp, College Station, Texas, USA) for statistical analysis. The period prevalence of HFpEF was calculated by dividing the number of patients with HFpEF by the total number of patients with new onset of heart failure over the review period. Continuous variables were summarized as means with standard deviations (SD) for parametric data or median with interquartile range (IQR) for non-parametric data. Categorical

variables were expressed as frequencies and percentages. Variables were compared between outcome measures at follow-up using either the Student's t-test (parametric data) or Wilcoxon rank-sum test (non-parametric data). Fisher's exact or Chi-squared test was used to compare categorical variables, as appropriate. A p value of < 0.05 was interpreted as statistically significant. For descriptive purposes, a Kaplan-Meier curve was used to illustrate event-free survival for death and readmission to hospital during the study period.

Results

Prevalence and profile of HFpEF participants

A total of 315 potential cases of de novo heart failure were identified for the study period (2016 and 2017), of which 42 patients (13.3%) had HFpEF and met the eligibility criteria to be included in the study (Fig. 1). Table 1 summarises baseline socio-demographic and clinical characteristics of the study population. The median age of the cohort was 55.5 years (IQR 47-66), with a female preponderance (81.0%). The most common comorbidities were hypertension (85.7%), CKD (40.5%) and diabetes (40.5%). Of these, 27.7 % of patients in this cohort had all three co-morbidities and 38.8% had two out of the three. All patients presented to hospital with shortness of breath, with 45.2% and 40.5% of the cohort presenting with New York Heart Association (NYHA) functional class III or IV respectively. The most common finding on physical examination was respiratory crackles (83.3%).

As shown in Table 2, the majority of patients (61.9%) had at least one major abnormal finding on the ECG. This included LVH by Sokolow-Lyon criteria and Cornell criteria (both 16.7%), LBBB (11.9 %) and abnormal T wave inversion (38.1%). Atrial fibrillation (2.4%) and atrial flutter (2.4%) were rare. On echo, 81.0% of patients had evidence of concentric LVH and 45.2 % had left atrial enlargement. The majority of participants had evidence of diastolic dysfunction (92.9%).

Treatment

Participants were discharged on the following medication with descending frequency (table 3): loop diuretics (85.7%), statin (61.9%), calcium channel blocker (57.1%), beta blockers (54.8%), ACE-i (42.9%), aspirin (40.5%), alpha blocker (23.8%), ARB (19.0%), MRA

(14.3%), thiazide diuretics (11.9%), nitrates (4.8%) and oral anticoagulant (2.4%). Less than 25% of the patients with HFpEF were referred to Cardiology for review during the admission.

Outcomes

During the follow up period of the first year after the index admission for de novo heart failure, there were 20 patients (47.6%) who had poor outcome. Of these, fifteen patients (35.7%) were readmitted to hospital with decompensated heart failure and five patients (11.9%) died. Event free survival during the first year after index presentation is illustrated in Fig. 2.

Discussion

There were three main findings from the study. These were: 1) the prevalence of HFpEF in patients admitted to our hospital with heart failure over the study period was 13.3%, which was lower than expected. 2) Participants with HFpEF were on average middle-aged (median age 55.5 years, IQR 47-66 years), predominantly female (81.0%) with hypertension, diabetes, and CKD as most common comorbidities. 3) Almost half (47.6%) of those with HFpEF either demised (11.9 %) or required readmission with heart failure (35.7%) within 12 months post discharge.

The prevalence of HFpEF in our study was low (13.3%) compared to other recent studies from Africa which found prevalence rates varying between 39.5% and 59%.[14, 15] Our finding was also much lower than global estimates of HFpEF of between 40 to 71% .[13] The reason for this marked difference in the prevalence of HFpEF between our study and the rest of the world is unclear. However, it is possible that the lack of the availability of NT-pro BNP testing and access to routine echocardiography in the community may have led to significant under diagnosis of the condition in patients with appropriate symptoms and under referral to our facility.[20, 21]

When compared to other studies, our study revealed a relatively young population with a median age of 55.5 years (IQR 47-66 years) which is similar to other African studies[14, 15] and to the African American HFpEF ARIC cohort[4]. This is in contrast to the much older population (median age of 71 to 77 years) described in studies with predominantly Caucasian [22-25] and Asian cohorts.[26] This highlights that HFpEF may present in younger participants of African descent in whom important co morbidities associated with HFpEF such as

diabetes, hypertension, obesity and CKD are more frequent, and more often poorly treated.[21, 27] Similar to many international HFpEF studies, our population included a much higher proportion of females with hypertension (85.7%), diabetes and CKD. [4, 14, 15, 23, 26, 28]

Our HFpEF population had a poor prognosis. This was much worse than anticipated based on comparative studies from Ghana, [14] and elsewhere with a similar age profile.[26] This poor outcome despite a young age may be explained by socio-economic factors and inadequate access to healthcare in our settings, factors which have previously been found to have a significant impact on heart failure outcomes in low and middle income countries.[29, 30]

Our study had a number of limitations. This was a single centre study with a retrospective design. Medical records may have been inaccurate, with missing results and reliance on ICD-10 codes for accuracy of diagnosis has been shown to be unreliable.[31] The lack of availability of natriuretic peptides and access to routine advanced echo in the clinical service environment were also important limitations. Finally, the small number of patients with HFpEF limited capacity for any detailed analysis. In view of this, our results may not be generalizable to all medical centres in South or sub-Saharan Africa. However, we believe the study was important because it may serve to highlight the fact that this important condition may be underrecognized and under diagnosed in the community. Furthermore, our study suggests that admission for heart failure may be a harbinger of a poor natural history. Large prospective studies of heart failure in the community and in hospital across Africa are needed to better understand the characteristics of the condition locally. This will be important to improve recognition, diagnosis, and treatment, and encourage implementation of targeted prevention strategies in groups identified as high risk.

Conclusion

This study provides important insights into the proportion, profile, and outcome of heart failure admissions with HFpEF in a tertiary care centre in SA. It confirms prior observations from sub-Saharan Africa which suggest that HFpEF is a disorder of middle-aged women with a history of hypertension, diabetes, and CKD. The study further suggests that HFpEF occurs in a relatively low proportion (13.3%) of patients with heart failure requiring hospital admission. However, this could potentially be explained by referral bias and the absence of diagnostic tools in the community. Finally, our study finding suggest that patients requiring admission with HFpEF have poor outcome (high readmission and mortality rates over the first 12 months). Although these findings may have implications for local awareness and practice, the study limitations are such that a larger prospective study is warranted to better understand this condition in a South African context.

Acknowledgements.

We would like to thank Prof Peter Raubenheimer for his tremendous assistance in data extraction, and the Records Department of Groote Schuur hospital for assisting with acquiring patient folders to collect data.

Contributions.

DNS developed the study protocol, collected, and assisted in data analysis and wrote the first draft of manuscript. MN and CAV contributed to the study design, data analysis, reviewing and editing of the manuscript. KM contributed to the study design and data analysis. ES, HJL contributed to data collection and analysis.

Funding.

None.

Conflicts of interest.

None to declare

References:

1. Komajda M, Lam CSP. Heart failure with preserved ejection fraction: a clinical dilemma. European Heart Journal. 2014;35(16):1022-1032.
2. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016;18(8):891-975.
3. Lupón J, Gavidia-Bovadilla G, Ferrer E, et al. Heart Failure With Preserved Ejection Fraction Infrequently Evolves Toward a Reduced Phenotype in Long-Term Survivors. Circulation: Heart Failure. 2019;12(3):e005652.
4. Gupta DK, Shah AM, Castagno D, et al. Heart failure with preserved ejection fraction in African Americans: the ARIC (Atherosclerosis Risk In Communities) study. JACC: Heart Failure. 2013;1(2):156-163.
5. Magana-Serrano JA, Almahmeed W, Gomez E, et al. Prevalence of heart failure with preserved ejection fraction in Latin American, Middle Eastern, and North African Regions in the I PREFER study (Identification of Patients With Heart Failure and PREserved Systolic Function: an epidemiological regional study). Am J Cardiol. 2011;108(9):1289-1296.
6. Nanayakkara S, Patel HC, Kaye DM. Hospitalisation in patients with heart failure with preserved ejection fraction. Clinical Medicine Insights: Cardiology. 2018;12:1179546817751609.
7. Pepine CJ, Merz CNB, El Hajj S, et al. Heart failure with preserved ejection fraction: Similarities and differences between women and men. International Journal of Cardiology. 2020;304:101-108.
8. Freiberg MS, Chang C-CH, Skanderson M, et al. Association Between HIV Infection and the Risk of Heart Failure With Reduced Ejection Fraction and Preserved Ejection Fraction in the Antiretroviral Therapy Era: Results From the Veterans Aging Cohort Study. JAMA Cardiology. 2017;2(5):536-546.
9. Shah SJ, Borlaug BA, Kitzman DW, et al. Research Priorities for Heart Failure With Preserved Ejection Fraction: National Heart, Lung, and Blood Institute Working Group Summary. Circulation. 2020;141(12):1001-1026.
10. Fonarow GC, Stough WG, Abraham WT, et al. Characteristics, treatments, and outcomes of patients with preserved systolic function hospitalized for heart failure: a report from the OPTIMIZE-HF Registry. J Am Coll Cardiol. 2007;50(8):768-777.
11. Yancy CW, Lopatin M, Stevenson LW, De Marco T, Fonarow GC. Clinical presentation, management, and in-hospital outcomes of patients admitted with acute decompensated heart failure with preserved systolic function: a report from the Acute Decompensated Heart Failure National Registry (ADHERE) Database. J Am Coll Cardiol. 2006;47(1):76-84.
12. Hogg K, Swedberg K, McMurray J. Heart failure with preserved left ventricular systolic function; epidemiology, clinical characteristics, and prognosis. J Am Coll Cardiol. 2004;43(3):317-327.
13. Lam CS, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. European journal of heart failure. 2011;13(1):18-28.
14. Adebayo AK, Adebiyi AA, Oladapo OO, et al. Characterisation of heart failure with normal ejection fraction in a tertiary hospital in Nigeria. BMC cardiovascular disorders. 2009;9(1):52.
15. Bonsu KO, Owusu IK, Buabeng KO, Reidpath DD, Kadirvelu A. Clinical characteristics and prognosis of patients admitted for heart failure: a 5-year retrospective study of African patients. International journal of cardiology. 2017;238:128-135.
16. National Research Council Committee on P. The National Academies Collection: Reports funded by National Institutes of Health. In: Cohen B, Menken J, editors. Aging in Sub-Saharan Africa: Recommendation for Furthering Research. Washington (DC): National Academies Press (US) Copyright © 2006, National Academy of Sciences.; 2006.
17. Trends in obesity and diabetes across Africa from 1980 to 2014: an analysis of pooled population-based studies. Int J Epidemiol. 2017;46(5):1421-1432.
18. Gómez-Olivé FX, Ali SA, Made F, et al. Regional and Sex Differences in the Prevalence and Awareness of Hypertension: An H3Africa AWI-Gen Study Across 6 Sites in Sub-Saharan Africa. Glob Heart. 2017;12(2):81-90.
19. Mayosi BM, Flisher AJ, Lalloo UG, et al. The burden of non-communicable diseases in South Africa. The lancet. 2009;374(9693):934-947.
20. Banerjee P. Heart failure with preserved ejection fraction: A clinical crisis. Int J Cardiol. 2016;204:198-199.

21. Clark AM, Flynn R, Hsu ZY, Haykowsky M. Heart failure with preserved ejection fraction: health services implications of a stealth syndrome. Eur J Cardiovasc Nurs. 2013;12(4):316-317.
22. Failure M-aGGiCH. The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. European heart journal. 2012;33(14):1750-1757.
23. Fonarow GC, Stough WG, Abraham WT, et al. Characteristics, treatments, and outcomes of patients with preserved systolic function hospitalized for heart failure: a report from the OPTIMIZE-HF Registry. Journal of the American College of Cardiology. 2007;50(8):768-777.
24. Solomon SD, McMurray JJV, Anand IS, et al. Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction. New England Journal of Medicine. 2019;381(17):1609-1620.
25. West R, Liang L, Fonarow GC, et al. Characterization of heart failure patients with preserved ejection fraction: a comparison between ADHERE-US registry and ADHERE-International registry. European journal of heart failure. 2011;13(9):945-952.
26. Nagai T, Yoshikawa T, Saito Y, et al. Clinical Characteristics, Management, and Outcomes of Japanese Patients Hospitalized for Heart Failure With Preserved Ejection Fraction―A Report From the Japanese Heart Failure Syndrome With Preserved Ejection Fraction (JASPER) Registry―. Circulation Journal. 2018;82(6):1534-1545.
27. White MA, O'Neil PM, Kolotkin RL, Byrne TK. Gender, race, and obesity-related quality of life at extreme levels of obesity. Obes Res. 2004;12(6):949-955.
28. Solomon SD, Rizkala AR, Lefkowitz MP, et al. Baseline Characteristics of Patients With Heart Failure and Preserved Ejection Fraction in the PARAGON-HF Trial. Circulation: Heart Failure. 2018;11(7):e004962.
29. Dokainish H, Teo K, Zhu J, et al. Global mortality variations in patients with heart failure: results from the International Congestive Heart Failure (INTER-CHF) prospective cohort study. Lancet Glob Health. 2017;5(7):e665-e672.
30. Agbor VN, Ntusi NAB, Noubiap JJ. An overview of heart failure in low- and middle-income countries. Cardiovasc Diagn Ther. 2020;10(2):244-251.
31. Reeves SL, Freed GL. Problems With Quality Measurement Using International Statistical Classification of Diseases, Tenth Revision, Clinical Modification: The Elephant No One Knows Is in the Room. JAMA Pediatr. 2019;173(6):515-516.

List of tables and figures

Table 1. Baseline characteristics of this HFpEF cohort, as categorised according to outcome.

		All patients N= 42	Good outcome N= 22	Poor outcome N= 20	P value
Age (years)	Median (IQR)	55.5 (47.0-66.0)	52.5 (35.0-63.0)	62 (55.0-68.5)	0.018
Sex (Female)	N (%)	34 (81.0)	19 (86.4)	15 (75.0)	0.294
Comorbidities					
Hypertension	N (%)	36 (85.7)	17 (77.3)	19 (95.0)	0.115
Diabetes	N (%)	17 (40.5)	5 (22.7)	12 (60.0)	0.016
Smoking	N (%)	16 (38.1)	9 (40.9)	7 (35.0)	0.470
Dyslipidaemia	N (%)	13 (30.9)	5 (22.7)	8 (40.0)	0.191
Chronic Kidney Disease	N (%)	17 (40.5)	7 (31.8)	10 (50.0)	0.188
Atrial fibrillation	N (%)	3 (7.1)	2 (9.1)	1 (5.0)	0.537
Symptoms					
Dyspnoea	N (%)	42 (100)	22 (100)	20 (100)	
Orthopnoea	N (%)	32 (76.2)	16 (72.7)	16 (80.0)	0.426
PND	N (%)	28 (66.7)	12 (54.5)	16 (80.0)	0.077
Chest pain	N (%)	19 (45.2)	9 (40.9)	10 (50.0)	0.390
Palpitations	N (%)	4 (9.5)	1 (4.5)	3 (15.0)	0.267
Syncope	N (%)	3 (7.1)	3 (13.3)	0 (0)	0.134
Functional class					
NYHA I	N (%)	1 (2.4)	1 (4.6)	0	0.256
NYHA II	N (%)	5 (11.9)	3 (13.6)	2 (10.0)	
NYHA III	N (%)	19 (45.2)	12 (54.6)	7 (35.0)	
NYHA IV	N (%)	17 (40.5)	6 (27.3)	11 (55.0)	
Clinical presentation					
SBP (mmHg)	Mean (SD)	151.0 (37.1)	153.6 (35.6)	148.2 (39.4)	0.644
DBP (mmHg)	Mean (SD)	87.0 (22.8))	88.0 (27.8)	86.2 (16.3)	0.797
Heart rate (bpm)	Median (IQR)	93 (81-106)	94 (85-106)	93 (81-108)	0.740
Oedema	N (%)	28/41 (68.3)	15/21 (71.4)	13 (65.0)	0.457
Raised jugular venous pressure	N (%)	29/41 (70.7)	13/21 (61.9)	16 (80.0)	0.177
Crackles	N (%)	35 (83.3)	19 (86.4)	16 (80.0)	0.444

DBP, diastolic blood pressure; IQR, interquartile range; NYHA, New York Heart Association; PND, paroxysmal nocturnal dyspnoea; SBP, systolic blood pressure; SD, standard deviation.

Table 2. Special investigations, as categorised according to outcome.

		All patients N= 42	Good outcome N= 22	Poor outcome N= 20	P value
Laboratory findings					
Na (mmol/L)	Mean (SD)	137.1 (3.7)	137.6 (3.1)	136.5 (4.2)	0.367
K (mmol/L)	Median (IQR)	4.2 (3.8-5.0)	4.0 (3.6-4.6)	4.4 (3.8-5.0)	0.262
Urea (mmol/L)	Mean (SD)	12.4 (10.4)	10.3 (10.1))	14.8 (10.4)	0.172
Creatinine (µmol/L)	Mean (SD)	206.8 (281.1)	211.3 (355.4)	201.9 (175.9)	0.915
Haemoglobin (g/dL)	Median (IQR)	11.3 (8.2-12.9)	11.4 (8.4-12.7)	10.7 (8.1-12.9)	0.970
White cell count (cells/L)	Mean (SD)	10.9 (5.4)	11.0 (5.6)	10.9 (5.4)	0.954
Troponin T (ng/L)	Mean (SD)	135.6 (231.9)	98.3 (183.4)	176.1 (277.9)	0.414
Chest radiography					
Cardiomegaly	N (%)	29 (69.0)	11 (50.0)	18 (90.0)	0.006
Pleural effusion	N (%)	23 (57.1)	13 (59.1)	11 (55.0)	0.517
Pulmonary oedema	N (%)	34 (80.9)	18 (81.8)	16 (80.0)	0.594
ECG					
Heart rate	Mean (SD)	94 (21.0)	96 (14.2)	91 (26.8)	0.460
Sinus rhythm with normal rate	N (%)	24 (58.5)	10 (47.6)	14 (70.0)	0.098
Sinus tachycardia	N (%)	15 (36.6)	10 (47.6)	5 (25.0)	0.145
Atrial fibrillation	N (%)	1 (2.4)	1 (4.8)	0	0.524
Atrial flutter	N (%)	1 (2.4)	0	1 (5.0)	0.524
Heart rate variability	N (%)	17 (41.5)	6 (28.6)	11 (55.0)	0.08
QRS width (ms)	Mean (SD)	94.9 (30.5)	86.2 (9.0)	104.6 (41.6)	0.049
QRS axis	Median (IQR)	41.5 (0-70)	55 (38-70)	5.5 (-35.5-46.5)	0.008
LVH by Sokolow-Lyon criteria	N (%)	7 (16.7)	4 (18.2)	3 (15.0)	0.556
LVH by Cornell's criteria	N (%)	7 (16.7)	3 (13.6)	4 (20.0)	0.444
LVH in lead 1	N (%)	10 (23.8)	6 (27.3)	4 (20.0)	0.426
LVH in V2	N (%)	1 (2.4)	0	1 (5.0)	0.476
LBBB	N (%)	5 (11.9)	1 (4.5)	4 (20.0)	0.144
T wave inversion	N (%)	16 (38.1)	8 (36.4)	8 (40.0)	0.53
QT interval (ms)	Mean (SD)	374.26 (90.6)	360.14 (102.2)	389.8 (75.5)	0.295
Echocardiogram					
Ejection fraction (%)	Median (IQR)	62 (58-69)	66.5 (58-70)	60.5 (56.5-66.0)	0.251
LVDd (mm)	Median (IQR)	45 (41-53)	47.5 (42-53)	44.5 (40.5-52.5)	0.301
LVDs (mm)	Median (IQR)	30 (25-35)	30 (25-36)	29.5 (25-34.5)	0.686
IVSd (mm)	Mean (SD)	13.7 (4.6)	14.1 (5.9)	13.2 (2.9)	0.543
LVPWd (mm)	Median (IQR)	13 (11-14)	12 (11-13)	13 (11-16)	0.252
LVH	N (%)	34 (81.0)	15 (68.2)	19 (95.0)	0.032
Left atrial diameter (mm)	Median (IQR)	40 (36-43)	39 (36-41)	40.5 (35.0-48.5)	0.165
Left atrial area (ml/m²)	Median (IQR)	24.3 (20.1-29)	22.7 (19.5-26.4)	27 (20.8-30)	0.071
Mitral E	Median (IQR)	0.875 (0.6-1.1)	0.855 (0.6-1.1)	0.9 (0.6-1.1)	0.7914
Deceleration time(ms)	Mean (SD)	215 (86.9)	231.73 (105.8)	196.6 (57.1)	0.195
Mitral A	Mean (SD)	2.46 (11.0)	4.06 (15.2)	0.71 (0.3)	0.331
E/A ratio	Mean (SD)	1.49 (1.1)	1.39 (1.1)	1.59 (0.9)	0.545
E/e'	Mean (SD)	15.18 (11.1)	15.51 (13.8)	14.84 (7.6)	0.86
TR velocity (m/s)	Mean (SD)	4.8 (12.4)	1.88 (0.9)	7.1 (16.4)	0.305
Diastolic dysfunction					
Grade 1	N (%)	29 (74.4)	16 (80.0)	13 (68.4)	0.418
Grade 2	N (%)	3 (7.7)	0	3 (15.8)	0.099
Grade 3	N (%)	7 (17.9)	4 (20.0)	3 (15.8)	0.556

ECG, electrocardiogram; IVSd, interventricular septum thickness at end-diastole; IQR, interquartile range; LBBB, left bundle branch block; LVDd, left ventricular dimension at end-diastole; LVDs, left ventricular dimension at end-systole LVH, left ventricular hypertrophy; LVPWd, left ventricular posterior wall thickness at end-diastole; SD, standard deviation; TR, tricuspid regurgitation.

Table 3. Treatment on discharge, as categorised according to outcome.

		All patients N= 42	Good outcome N= 22	Poor outcome N= 20	P value
Loop diuretic	N (%)	36 (85.7)	18 (81.8)	18 (90.0)	0.380
Thiazide diuretic	N (%)	5 (11.9)	3 (13.6)	2 (10.0)	0.547
ACE-i	N (%)	18 (42.9)	10 (45.4)	8 (40.0)	0.483
ARB	N (%)	8 (19.0)	3 (13.6)	5 (25.0)	0.294
CCB	N (%)	24 (57.1)	13 (59.1)	11 (55.0)	0.517
Beta-blocker	N (%)	23 (54.8)	12 (54.6)	11 (55.0)	0.976
Alpha-blocker	N (%)	10 (23.8)	5 (22.7)	5 (25.0)	0.574
MRA	N (%)	6 (14.3)	4 (18.2)	2 (10.0)	0.380
Aspirin	N (%)	17 (40.5)	6 (27.3)	11 (55.0)	0.065
Statin	N (%)	26 (61.9)	10 (45.4)	16 (80.0)	0.023
Nitrate	N (%)	2 (4.8)	0 (0)	2 (10.0)	0.221
Oral anticoagulant	N (%)	1 (2.4)	1 (4.5)	0 (0)	0.524

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; MRA, mineralocorticoid antagonist.

Figure 1. Study flow. *EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction.*

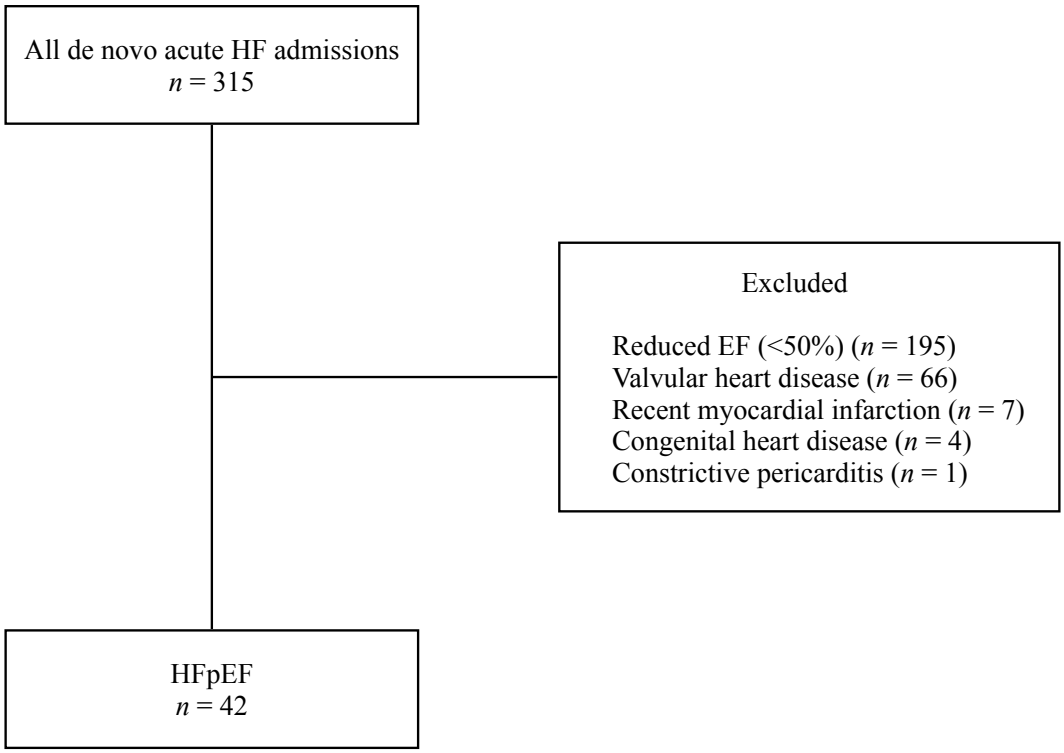

Figure 2. Kaplan-Meier curve showing event free survival (death or readmission to hospital) in the first 12 months after diagnosis.