ORIGINAL ARTICLE

Chronic Heart Failure in Argentina. OFFICE IC AR, a joint registry of the Argentine Society of Cardiology and the Argentine Federation of Cardiology

Insuficiencia cardíaca crónica en Argentina. OFFICE IC AR, un registro conjunto de la Sociedad Argentina de Cardiología y de la Federación Argentina de Cardiología

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ABSTRACT

Background: Several Argentine registries on chronic heart failure (CHF) have been generated over the past 25 years, either individually by the Argentine Society of Cardiology (SAC) or the Argentine Federation of Cardiology (FAC), with different representativeness. The last known data are from 2013. The OFFICE IC AR registry was jointly undertaken by the SAC and FAC to know the reality of CHF in Argentina.
Objective: The aim of this registry was to extensively and comprehensively describe the outstanding characteristics of CHF in Argentina, including patient characteristics, use of diagnostic and therapeutic resources, adherence to practice guidelines and mid-and long-term prognosis.
Methods: This was a prospective cohort study of patients with at least 6-month evolution CHF and not hospitalized for at least the past 3 months. Clinical and paraclinical data were collected. Patients were categorized according to left ventricular ejection fraction (LVEF), into HF with reduced EF, HFrEF (≤40 %), HF with midrange EF, now termed HF with mildly reduced EF, HFmrEF (41%-49%), and HF with preserved EF, HFpEF (≥50%). The incidence of hospitalization for HF (HHF), cardiovascular mortality (CVM) and all-cause mortality (ACM) was recorded for at least 1-year follow-up.
Results: Between November 2017 and January 2020, 100 cardiologists from all over the country included 1004 patients with CHF. Mean age was 65.8±12.4 years, 74.6% were men, and 93.8% had known LVEF. In 68.4% of cases, patients had HFrEF, 16% HFmrEF and 15.6% HFpEF. A high prevalence of comorbidities was found, including diabetes and anemia in 30% of cases, and chronic renal failure in 22%. There was high use of neurohormonal antagonists (NHA): 89.5% betablockers, 57.3% renin-angiotensin system inhibitors or antagonists, 28.9% sacubitril-valsartan and 78.6% aldosterone antagonists. Triple therapy was used in 69% of patients, with higher prescription in HFrEF, but elevated even on HFpEF. At a median follow-up of 1.7 years, the annual incidence of CVM/HHF was 12.8%, CVM 6.6% and ACM 8.4%, without statistical differences between the different LVEF categories.
Conclusions: This first SAC-FAC joint CHF registry verified a high prevalence of HFrEF, a high prevalence of comorbidities, frequent use of NHA and prognosis according to international registries.

Key words: Chronic heart failure – Registry – Prognosis.

RESUMEN

Introducción: Diferentes registros argentinos de insuficiencia cardíaca crónica (ICC) fueron generados en los últimos 25 años, en forma individual por la Sociedad Argentina de Cardiología (SAC) y la Federación Argentina de Cardiología (FAC), con diferente representatividad. Los últimos datos conocidos datan de 2013. El Registro OFFICE IC AR fue encarado en forma conjunta por la SAC y la FAC para conocer la realidad de la ICC en Argentina.
Objetivos: Describir en forma amplia y comprensiva las características salientes de la ICC en Argentina, incluyendo las características de los pacientes, el uso de recursos diagnósticos y terapéuticos, la adherencia a las guías de práctica y el pronóstico a mediano y largo plazo.
Material y Métodos: Estudio prospectivo de cohorte, de pacientes con ICC de al menos 6 meses de evolución, alejados de una internación por al menos 3 meses. Se recabaron datos clínicos y paraclínicos. Los pacientes fueron categorizados, de acuerdo a la fracción de eyección ventricular izquierda (FEVI), en IC con FE reducida, ICFER (≤40%); IC con FE en el rango medio, ICFErm, ahora denominada IC con FE levemente reducida, ICFElr (41%-49%), e IC con FE preservada, ICFEP (≥ 50%). En seguimiento de al menos 1 año se registró la incidencia de hospitalización por insuficiencia cardíaca (HIC), muerte cardiovascular (MCV) y muerte de todas las causas (MTC)

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Resultados: Entre noviembre de 2017 y enero de 2020, 100 cardiólogos de todo el país incluyeron 1004 pacientes con ICC; edad media 65,8 ± 12,4 años, 74,6% hombres, FEVI conocida en el 93,8%. El 68,4% tenía ICFER, el 16 % ICFElr y el 15,6% ICFEP. Hubo alta prevalencia de comorbilidades, incluyendo diabetes y anemia en el 30%, e insuficiencia renal crónica en el 22%. Fue elevada la utilización de antagonistas neurohormonales (ANH): 89,5% betabloqueantes; 57,3% inhibidores o antagonistas del sistema renina angiotensina, 28,9% sacubitril valsartán y 78,6 % antialdosterónicos. En 69% se utilizó triple terapia. Su empleo fue mayor en la ICFER, pero elevado incluso en la ICFEP. En una mediana de seguimiento de 1,7 años la incidencia anual de MCV/HIC fue 12,8%, la de MCV 6,6% y la de MTC 8,4%, sin diferencia entre las distintas categorías de FEVI.
Conclusiones: En el primer registro conjunto de ICC SAC-FAC se verificó elevada prevalencia de ICFER, alta prevalencia de comorbilidades, uso frecuente de ANH y pronóstico acorde a los registros internacionales.

Palabras clave: Insuficiencia cardíaca crónica-Registro-Pronóstico

INTRODUCTION

Chronic heart failure (CHF) affects 2-3% of the general population, but more than 10% of people over 70 years of age. It is the final common pathway of most cardiovascular diseases not adequately treated. (1,2) It markedly affects the prognosis, and the related morbidity and mortality is high and increases with age. (3) Acute HF registries have been performed in different countries and contexts, (4,5) the ARGEN IC registry being the most recent and with the largest number of patients in our country. (6) Hospitalizations are very significant; they correspond to the most severe and potentially mortal stages, (7) and determine the greatest part of direct and indirect costs. (8)

However, most of the patient's life is ambulatory; adequate daily behavior, adherence to recommended standards and prompt access to the healthcare system govern the evolution and prevent hospitalizations. In the last years we have known about CHF registries generated in Europe, (9-12) the United States of America, (13,14) and Asia (15). In the Argentine Republic, 6 observational studies on CHF had been published until 2017, (16) including between 389 and 2754 patients. The ones with the largest number of patients were the GESICA, (17) and the OFFICE IC registries from the Argentine Society of Cardiology (SAC), (18) and the HOSPICAL II registry of the Argentine Federation of Cardiology (FAC). (19) To these, we must add the SAC participation in the European Heart Failure Registry between 2012 and 2013, (20) with the inclusion of 370 ambulatory patients. Overall, we considered 9418 patients, 63% men, with mean age 67 years, 62% in FC I-II, and a prevalence of HF with left ventricular ejection fraction (LVEF) ≤40% of 72%, diabetes 22.2%, known coronary artery disease etiology 40%, and treatment with angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARBs) in 82.9% of patients, betablockers (BB) in 53.7% and aldosterone antagonists (AA) in 56.9%. None of the societal registries could be considered to be truly representative of all the Argentine reality, since the geographical area effectively covered by SAC and FAC is different.

Within the framework of other SAC-FAC initiatives, a joint registry of CHF was designed, the OFFICE IC AR, steered from the SAC Heart Failure and Pulmonary Hypertension Council and the FAC Heart Failure and Pulmonary Hypertension Committee. The Registry authorities interacted with those responsible in each district of both Societies. A number of physicians was established in each case, proportional to the district's population. Patient data were collected in an electronic platform. The leaders of each district established the initial contact with the participating physicians of their jurisdiction, and the directors and coordinators of the Registry were in charge of verifying data completeness and monitoring follow-up by the investigators.

The primary objective of the Registry was to describe the present condition of CHF in Argentina, including patient characteristics, use of diagnostic and therapeutic resources, practice guideline adherence and prognosis during a follow-up of at least 1 year. Secondary objectives were the description of diagnostic, therapeutic and prognostic methods according to LVEF. The primary outcome was a composite of cardiovascular mortality (CVM) and hospitalization for heart failure (HHF), and CVM, HHF and all-cause mortality (ACM) were explored separately.

METHODS

Patients with history of CHF diagnosed by signs, symptoms and observed structural or functional cardiac abnormality (preferably, but not exclusively, in an echocardiogram), with at least 6-month evolution, followed-up by the same physician in at least 3 visits, and free from HHF in at least the last 3 months were included in the study. It was stressed that the echocardiogram should be from the past 6 months and that it had not been performed during a hospitalization. Patients were divided according to the 2016 SAC Consensus on CHF, into HF with reduced LVEF, HFrEF (LVEF ≤40%), HF with mid-range LVEF, HFmrEF (LVEF 41-49%) and HF with preserved LVEF, HFpEF (LVEF ≥50%). (21) For this presentation we adopted the Universal Definition of Heart Failure categories, that employs the same cut-off values that the SAC Consensus, but replaces HF with mid-range LVEF denomination for HF with mildly reduced LVEF. (22)

Prior to incorporation, patients signed an informed consent approved by the Ethics Committees of both Societies. Sex, age, geographical area, socioeconomic and educational history, medical coverage, medical history (HF, other relevant cardiovascular or non-cardiovascular conditions) physical examination, ECG, chest X-ray, laboratory tests, echocardiogram and other complementary studies, etiology, pharmacological and non-pharmacological treatment data were collected. Patients were contacted either personally or by telephone for at least 1 year follow-up, and death, HHF

or any other cause of hospitalization were recorded (see protocol in Supplementary Material).

Statistical analysis

Quantitative variables are presented as mean and standard deviation or median and interquartile range, according to normal or non-normal distribution. Means were compared using Student's t test or ANOVA and medians with the Wilcoxon or Kruskal Wallis tests. Qualitative variables are presented as percentages and compared using the chi-square test or Fisher test.

The association of predictive variables with the dependent variable are expressed as odd ratio (OR) and their corresponding 95% confidence interval (95% CI). Event-free survival was explored in a Cox proportional hazards model, and is graphically represented with Kaplan-Meier curves and compared with the logrank test. The association of each variable with evolution is expressed as hazard ratio (HR) with its corresponding 95% CI. In all cases, the independent association of each variable with the dependent variables was established by means of multivariate analysis. A value of $p < 0.05$ was considered as statistically significant.

Stata 10.0 software (StataCorp 4905Lakeway Drive College Station, Texas 77845, USA) was used for the statistical analysis.

RESULTS

One hundred cardiologists from all over the country participated in the Registry (the complete list is presented at the end of this report). Between November 2017 and January 2020, they included 1004 patients, almost half of them from the Buenos Aires Province (24.3%) or Autonomous City of Buenos Aires (23.2%), with >5% participation of Corrientes (9.1%), Córdoba (7.4%), Santa Fe (6.8%), Tucumán (6.2%) and Mendoza (6%) provinces. In 74.6% of cases, patients were men, and mean age was 65.8±12.4 years. Table 1 presents baseline characteristics and treatment of the global population. The predominant etiologies were ischemic and idiopathic, and only 5.9% had Chagas etiology. There was ample prevalence of NYHA functional class I-II; 61.7% had history of HHF (14% in the last year). Slightly more than two-thirds of patients were hypertensive and almost a third had diabetes; more than half of patients also had other significant comorbidities. Almost 70% of patients were in sinus rhythm, and 25% had left bundle branch block (LBBB). The LVEF was known in 942 patients (93.8%), with a mean of 36.5±12.6%. Natriuretic peptide levels were known in one third of cases, and a coronary artery disease etiology had been searched in 75.2% of cases. Two-thirds of patients depended on Social Security.

In 68.5% of cases, patients were receiving loop diuretics or thiazides. Use of neurohormonal antagonists (NHA) was high and 69% of patients were receiving a combination of 3 of them (triple therapy): BB, ACEI/ARBs or sacubitril/valsartan (SV) and an AA. Use of digoxin, ivabradine and hydralazine-nitrates was low. Only 15 patients were receiving gliflozins, all of them with diabetes. In 21.3% of cases, patients had an implantable cardioverter defibrillator (ICD), alone or combined with cardiac resynchronization therapy.

Differences between patients according to LVEF

In 68.4% of cases, patients had HFrEF, 15% HFmrEF and 16.5% HFpEF (Figure 1). Table 2 presents baseline characteristics and therapeutic treatment according to LVEF category. Higher LVEF category was accompanied by older ager, prevalence of female sex, and higher systolic and diastolic blood pressure; the prevalence of LBBB was lower and that of FC III-IV and atrial fibrillation was greater. There were no differences in the prevalence of hypertension or diabetes, and a trend to greater global prevalence of the rest of the aforementioned comorbidities. At higher LVEF, there was decreased coronary heart disease and Chagas disease and increased hypertensive and valvular etiologies. Natriuretic peptide levels determination did not differ, but the search for a coronary etiology was more frequent with lower LVEF. Use of NHA decreased with higher LVEF, but was high even in HFpEF. Use of SV, as well as electrical therapy was logically focused in patients with HFrEF.

Follow-up and long-term prognosis

Median follow-up [available data from 974 patients (97%)] was 21.2 (IQR 16-25.6) months; the study was definitively closed for patients still in follow-up on January 20 2021. The incidence of the composite of CVM/HHF was 22.2% (annual incidence of 12.8%); that of HHF 16.9% (annual 9.8%), CVM 11.5% (annual 6.6%) and ACM 14.6% (annual 8.4%). There were not significant differences between the three LVEF categories (Figure 2). In the multivariate analysis, the independent predictors of the composite endpoint of CVM/HHF were age, FC III-IV, prior hospitalization for HF, LBBB, systolic blood pressure and use of diuretics (Table 3). Cardiovascular death represented 78% of overall deaths, 77% in HFrEf, 82% in HFmrEF, but only 65% in HFpEF. On March 20, 2020, social preventive and compulsory isolation was declared in Argentina due to the COVID-19 pandemic. In mid-term follow-ups of 17.6 and 4.4. months before and after this date, the annualized incidence of CVM/HHF was 13.2% and 11%, that of HHF 10.1% and 8.4%, of CVM 6.5% and 7.2% and of ACM 8.3% and 8.4%, respectively. None of these differences was statistically significant.

DISCUSSION

The OFFICE IC AR Registry is the first CHF registry carried out jointly by the SAC and the FAC, and the first of both societies to have long-term follow-up data. Compared with the Argentine cohort that participated in the 2012-2013 European Society of Cardiology registry, the OFFICE IC AR cohort had a higher prevalence of men, a similar prevalence of FC I-II, and age almost 3 years older, coinciding with a slightly higher LVEF (median 35% vs. 31%) and greater presence of comorbidities. There were some differences in treatment, with slightly lower BB and higher AA use, and, logically, the presence of SV (the PARADIGM-HF

Table 1. Baseline characteristics of the total population

	Total population n=1004
Age, (years)	65.8 ± 12.4
Male gender (%)	74.6
Hypertension (%)	66.6
Diabetes (%)	29.9
Atrial fibrilation(%)	22.6
Comorbidities (%)	57.4
Renal failure(%)	22.7
COPD (%)	13.4
Anemia (%)	30.5
FC I-II (%)	82.1
Previous hospitalization for HF (%)	61.8
Etiology	
Ischemic (%)	36.7
Hypertensive (%)	7.4
Chagas (%)	6
Valvular (%)	9.1
Idiopathic (%)	13.9
Other (%)	21.8
Non-filed (%)	5.1
Coverage	
None (%)	10.9
SS (%)	65.3
Prepaid/Private (%)	23.8
Heart rate (beats/min)	70 ± 10.6
SBP (mmHg)	115.6 ± 16.6
DBP (mmHg)	71.8 ± 10.3
Left Bundle Branch Block (%)	25.5
LVEF	36.5 ± 12.6
Glomerular filtration rate according to the MDRD equation; ml/min/1.73 m^2 (n=884)	75.1 ± 32.5
NP measurement (%)	32.2
Coronary etiology search (%)	75.2
Treatment	
Diuretics (%)	68.5
Beta blockers (%)	89.5
ACEI (%)	33.8
ARBs (%)	23.5
SV (%)	28.9
ACEI/ARBs/SV (%)	86.2
Aldosterone antagonists (%)	78.6
Triple therapy (%)	69
Digoxin (%)	11.2
Ivabradine (%)	5.3
Statins (%)	57.9
OAC (%)	36.1
DOAC (%)	6.3
Amiodarone (%)	24.7
ICD (%)	13.1
CRT (%)	1.5
ICD-CRT (%)	8.2

COPD: chronic obstructive pulmonary disease. **FC:** functional class. **HF:** heart failure. **SS:** social security. **SBP:** systolic blood pressure. **LVEF:** left ventricular ejection fraction. **MDRD:** Modification of Diet in Renal Disease. **NP:** natriuretic peptides. **ACEI:** angiotensin converting enzyme inhibitors. **ARBs:** angiotensin receptor blockers **SV:** sacubitril/valsartan. **OAC:** oral anticoagulantion. **DOAC:** direct-acting oral anticoagulants. I**CD:** implantable cardioverter-defibrillator. **CRT:** cardiac resynchronization therapy.
Continuous variables are presented as mean ± standard deviation

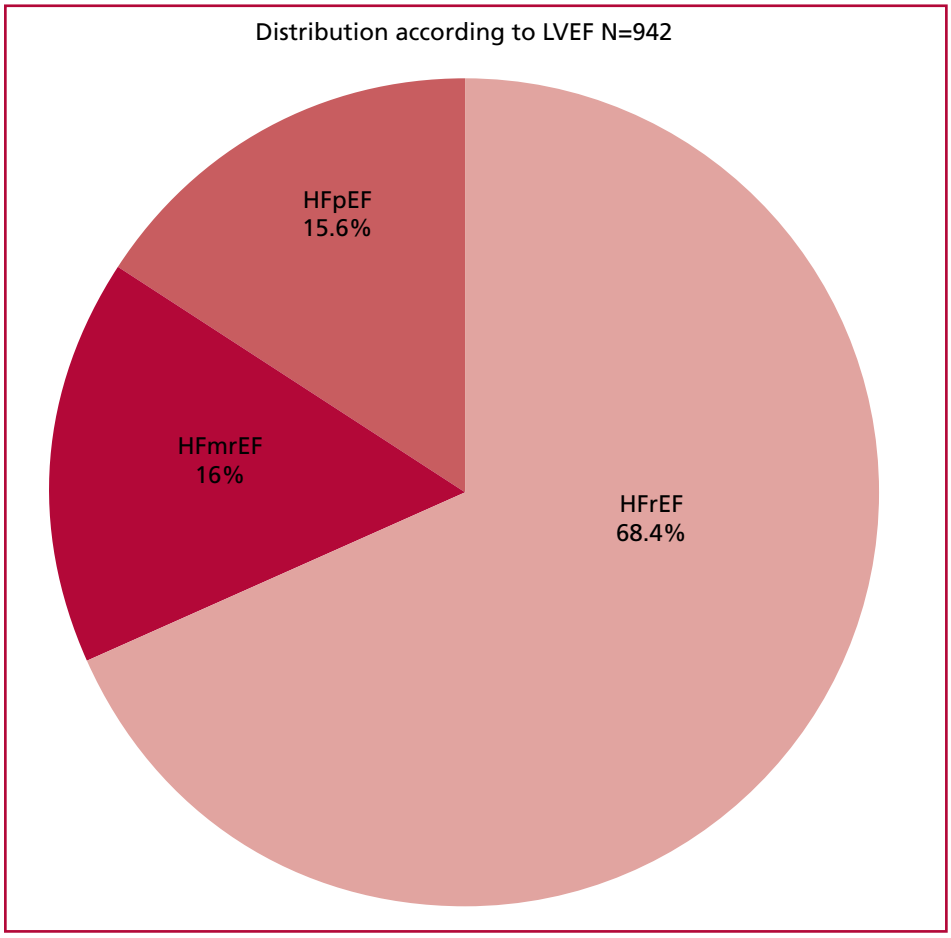


Fig. 1. Heart failure categories according to LVEF in 942 patients with known LVEF

LVEF: Left Ventricular Ejection Fraction. **HFrEF:** Heart failure with reduced EF. **HFmrEF:** Heart failure with mildly reduced EF. **HFpEF:** Heart failure with preserved EF

study was published in 2014) (23). The differences between the 3 LVEF categories fully coincide with those seen in a meta-analysis of 12 studies and 109 257 patients (24) that includes, among others, the Japanese CHART-2 registry (25), the European ESC-HF-LT Registry (10), and an extensive Swedish registry (26); as well as results reported by the American PINNACLE registry (13). The point at which the records diverge is in the proportion of each of the LVEF categories. Our registry shows a patent predominance of HFrEF (just over 2 out of 3 patients); in this sense it is close to the ESC-HF-LT registry (HFrEF in 59.8% of patients) and clearly differs from the CHART-2 (21%), the Swedish (54.8%) and the PINNACLE (45.4%) registries, a phenomenon that might be explained because a large proportion of participating physicians were HF specialists.

The registry confirms the almost universal use of echocardiography in the evaluation of patients with CHF. Natriuretic peptides were used in only one third of cases in the diagnostic or prognostic assessment. It should be noted that the indication for its use was IIa B for the 2016 SAC consensus, (21) and IIa C for the European Society guideline of the same year (27) In fact, the SAC consensus proposed its use when there were doubts about CHF diagnosis, severity and prognosis. The lack of an imperative indication must be added to the notable difficulty or direct impossibility of accessing to the resource in the outpatient context for a large part of the participating physicians, (remember that three quarters of the patients had no coverage, or depended on Social Security).

The high use of NHA is striking, clearly indicated by the guidelines at the start of the Registry in patients with HFrEF, but not in HFmrEF or HFpEF. (21,27,28) The use of triple NHA therapy in almost 80% of cases in HFrEF (Table 2) demonstrates remarkable adherence to the guidelines. In the United States CHAMP-HF registry, (29) with 3518 patients with HFrEF, contemporary to the OFFICE IC AR, 66.8% were receiving BB, 12.8% SV, 72.1% SV, ACEI or ARBs, 33.1% AA and less than 25% triple therapy. Our data compare very favorably with those reported.

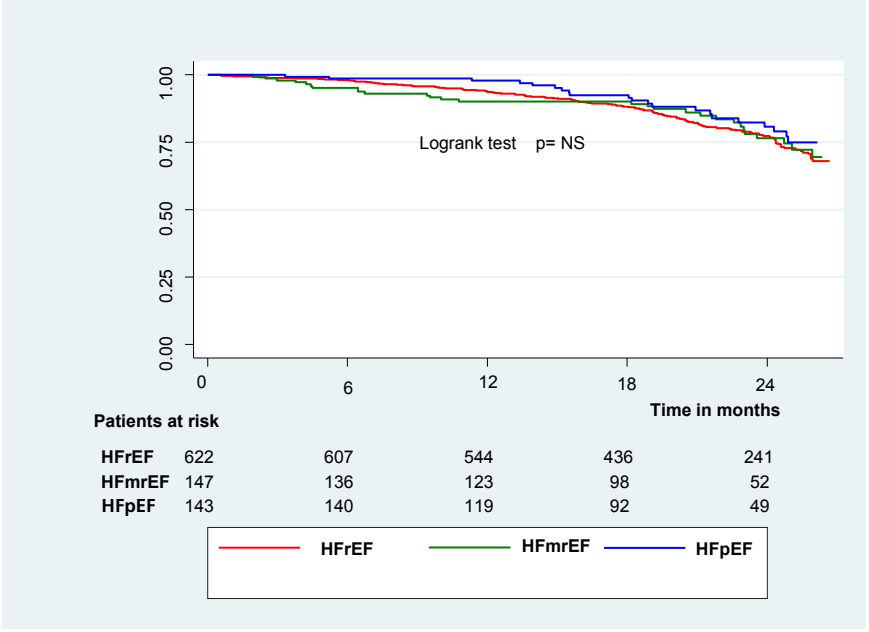
But, similarly, and beyond the guidelines, when it comes to HFpEF, BB are used in just over 80%, ACEI, ARBs, and even sometimes SV in almost 80%, AA in 48% and triple therapy in just over a third of cases. This phenomenon is not exclusive to our country, it is repeated in other registries, although with fairly lower values. (9,10,15) We can partly attribute it to

Table 2. Baseline characteristics of the population according to LVEF category

	HFrEF n=644	HFmrEF n=151	HFpEF n=147	p
Age (years)	64.6 ± 12.3	66.7 ± 12.2	70.5± 12.9	<0.001,001
Male gender (%)	77.8	77.5	54.4	<0.001
Hypertension (%)	66.2	70.8	71.4	0.31
Diabetes (%)	30.3	27.1	33.3	0.51
Atrial fibrillation (%)	18.8	27.8	36.7	<0.001
Comorbidities (%)	56.1	62.9	63.9	0.101
Kidney failure (%)	22.5	21.8	24.5	0.84
COPD (%)	11.8	17.2	17	0.085
Anemia (%)	30.8	34.4	32	0.67
FC I-II (%)	82.3	87.4	71.4	0.001
Previous hospitalization for HF (%)	64.9	61.6,6	58.55	0.31
Etiology				<0.001
Ischemic (%)	42.6	37.1	16.3	
Hypertensive (%)	6.8	6	13.6	
Chagas (%)	6.5	6.6	4.8	
Valvular (%)	6.5	12.5	19.1	
Idiopathic (%)	18.2	9.9	2	
Other (%)	14.6	25.9	34.7	
Non-filed (%)	4.8	2	9.5	
Coverage				0.36
None (%)	11.6	8.7	8.3	
SS (%)	65.9	67.3	62.5	
Prepaid/Private (%)	22.5	24	29.2	
Heart rate (beats/min)	70 ± 10.4	68.6 ± 10.9	70.7±11.2	0.22
SBP (mmHg)	113.9 ± 16.2	116.6 ± 16.6	122.1± 18.8	<0.001
DBP (mmHg)	71.1 ± 10.2	71.1 ± 10.6	74.9 ± 10.9	<0.001
Left Bundle Branch Block (%)	30.6	19.9	14.3	<0.001
LVEF	29.6 ± 6.9	44.8 ± 2.3	58.4 ± 6.2	<0.001
Glomerular filtration rate (MDRD); ml/min/1.73 m^2	74.5 ± 31.5	77.7 ± 33.3	75.8 ± 37.3	0.59
NP measurement (%)	34.3	37.8	27.9	0.18
Coronary etiology search (%)	82.3	75.5	62.6	<0.001
Treatment				
Diuretics (%)	73.6	61.6	68.7	0.011
Betablockers (%)	93.5	93.4	84.4	0.001
ACEI (%)	35.6	35.1	29.3	0.34
ARBs (%)	17.4	32.5	45.6	<0.001
SV (%)	37.9	21.2	4.7	<0.001
ACEI/ARBs/SV (%)	90.8	88.7	78.9	<0.001
Aldosterone antagonists (%)	88.8	76.8	48.3	<0.001
Triple therapy (%)	79.7	66.2	36.7	<0.001
Digoxin (%)	11.5	10.6	11.6	0.95
Ivabradine (%)	7	3.3	1.4	0.011
Statins (%)	62	68.2	40.8	<0.001
OAC (%)	34.5	42.4	42.9	0.055
DOAC (%)	5.6	7.3	10.9	0.065
Amiodarone (%)	28.3	23.2	17	0.014
ICD (%)	17.7	5.3	3.4	<0.001
CRT (%)	1.8	0	1.4	0.23
ICD-CRT (%)	10.7	4.6	2.7	0.001

HFrEF: heart failure with reduced EF. **HFmrEF:** heart failure with mildly reduced EF. **HFpEF:** heart failure with preserved EF. **COPD:** chronic obstructive pulmonary disease. **FC:** functional class. **HF:** heart failure. **SS:** social security. **SBP:** systolic blood pressure. **LVEF:** left ventricular ejection fraction. **MDRD:** Modification of Diet in Renal Disease. **NP:** natriuretic peptides. **ACEI:** angiotensin converting enzyme inhibitors. **ARBs:** angiotensin receptor blockers. **SV:** sacubitril valsartan. **OAC:** oral anticoagulation. **DOAC:** direct-acting oral anticoagulants. **ICD:** implantable cardioverter-defibrillator. **CRT:** cardiac resynchronization therapy.
Continuous variables are presented as mean ± standard deviation

Fig. 2. Survival free of cardiovascular mortality/hospitalization for heart failure according to LVEF category



LVEF: Left Ventricular Ejection Fraction. **HFrEF:** Heart failure with reduced EF. **HFmrEF:** Heart failure with mildly reduced EF. **HFpEF:** Heart failure with preserved EF.
Follow-up data on 97% of patients with known LVEF

Table 3. Independent predictors of cardiovascular mortality/hospitalization for heart failure

	HR	95% CI	p
Age	1.014	1.001-1.028	0.025
FC III-IV	1.998	1.471-2.713	<0.001
Previous hospitalization for HF	1.758	1.247-2.479	0.001
Left bundle branch block	1.376	1.028-1.843	0.032
SBP (mmHg)	0.990	0.981-0.998	0.025
Diuretics	1.658	1.130-2.432	0.010

FC: functional class. **HF:** heart failure. **SBP:** systolic blood pressure

the presence of comorbidities often treated with NHA: hypertension, diabetes, and kidney failure, especially with microalbuminuria. (30,31) It is also possible that, given the lack of indication for specific drugs to treat HFmrEF and HFpEF, cardiologists resort, by analogy, to those effective in HFrEF.

Just over a quarter of HFrEF patients had an ICD, a number that was significantly lower than that of similar patients in the ESC-LT-HF Registry (57%), or the CHAMP-HF Registry (42%), but similar to that in the Spanish LINX registry. (11) A detailed analysis on the use of ICD will be the subject of a specific publication.

Regarding the prognosis, the Argentine cohort patients of the European Registry had a worse evolution than ours: 10.3% annual incidence of ACM and 18.2% of HHF, perhaps expression of a lower LVEF, and a treatment that did not know SV. The lack of difference in the different endpoints according to LVEF is noteworthy in the OFFICE IC AR registry. However, in all cases the outcomes were somewhat less incidental in HFpEF. The almost universal use of NHA in HFrEF may have mitigated the expected worse prognosis, and sample size may have reduced the power to find a difference. In fact, in larger registries (10,25) and in meta-analyses, the prognosis is worse for patients with HFrEF (24,32). Another point to highlight is that the annual incidences of HHF (9.8%); CVM (6.6%) and ACM (8.4%) did not differ greatly from those of the ESC-HF-LT Registry (10.9%; 4.2% and 8.3%, respectively), perhaps because the proportion of the different LVEF categories was not so dissimilar. The different proportion of CVM according to LVEF expresses the different mechanisms involved. (33,34).

Finally, the independent predictors of CVM/HHF are the usual ones. The ones we found have been indicated in previous registries, and are alternately part of different prognostic models, including the one derived from the PARADIGM study, (35) the Barcelona Bio-HF calculator (36) and the MAGGIC score (37).

Among the strengths of the Registry, we want to highlight that due to its joint nature its territorial rep-

resentation is greater than that of any previous societal registry, and the median follow-up of 21 months with a loss rate of only 3% lends greater certainty to the findings. Regarding the limitations, like any initiative not based on mandatory data reporting, it depends on the willingness to participate. The inclusion bias is inevitable: the predominant participation of members of the Heart Failure Councils means that the reported treatment and evolution may be better than those of patients not treated by cardiologists, or cardiologists who are not specialists in HF. The measurement of natriuretic peptides was not uniform, but that is a true reflection of reality. Regarding the minimal use of gliflozins, suffice it to remember that even when the follow-up concluded, it had been only a few months since the DAPA-HF trial had been published, (38) the EMPEROR Reduced trial (39) had not seen the light, and even the imperative indication of these drugs in diabetes with heart failure was recent (40). The last months of the follow-up coincided with the first months of the COVID 19 pandemic; however, we have no indication that it has influenced the evolution of our patients. But logically, we must bear in mind the short period considered, that the moment of greatest epidemiological severity was after the end of follow-up, and that an exhaustive investigation of the relationship between the evolution and the pandemic had not been prospectively defined.

CONCLUSIONS

The OFFICE HF AR registry reflects the reality of patients treated by cardiologists interested in HF and associated to leading societies of National Cardiology. It confirms the usefulness of Registries to know what we are facing, and raise opportunities for improvement.

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Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material.)

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