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Pulmonary hypertension in patients with heart failure: analysis of the Colombian Registry of Heart Failure

Hipertensión pulmonar en pacientes con falla cardíaca: análisis del Registro Colombiano de Falla Cardíaca

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ABSTRACT. Introduction: the diagnosis of pulmonary hypertension is associated with greater deterioration of heart failure, as well as a risk of adverse outcomes. **Objective:** the objective of this study was to analyze the prevalence of pulmonary hypertension and evaluate its prognosis in patients from the Colombian Registry of Heart Failure-RECOLFACA. **Material and methods:** RECOLFACA included adult outpatients with a diagnosis of heart failure belonging to 60 medical centers in Colombia in the period 2017-2019. The primary outcome was all-cause mortality. A Cox proportional hazards regression model was used to evaluate the factors associated with the primary outcome in patients with HF and pulmonary hypertension. A p value < 0.05 was considered significant. **Results:** of the 2,528 patients included in RECOLFACA, 1,833 were analyzed in this study because they had sufficient echocardiography reports to confirm or rule out the diagnosis of pulmonary hypertension. 48.6% met the diagnostic criteria for pulmonary hypertension. The

RESUMEN. Introducción: el diagnóstico de hipertensión pulmonar se asocia con mayor deterioro de falla cardiaca, así como un riesgo de desenlaces adversos. **Objetivo:** analizar la prevalencia de hipertensión pulmonar y evaluar su pronóstico en pacientes del Registro Colombiano de Falla Cardíaca (RECOLFACA). **Material y métodos:** RECOLFACA incluyó pacientes ambulatorios adultos con diagnóstico de falla cardíaca pertenecientes a 60 centros médicos en Colombia en el período 2017-2019. El desenlace primario fue mortalidad por todas las causas. Se utilizó un modelo de regresión de riesgos proporcionales de Cox para evaluar los factores asociados al desenlace primario en pacientes con falla cardíaca e hipertensión pulmonar. Se consideró significativo un valor de $p < 0.05$. **Resultados:** de los 2,528 pacientes incluidos en RECOLFACA, en este estudio se analizaron 1,833 porque tenían reportes de ecocardiografía suficientes para confirmar o descartar el diagnóstico de hipertensión pulmonar. El 48.6% cumplían con criterios diagnósticos de hipertensión

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diagnoses of chronic obstructive pulmonary disease, atrial fibrillation, valvular heart disease, HF and the use of diuretics and anticoagulants were useful predictors for the identification of those patients with HF with preserved ejection fraction and pulmonary hypertension (AUC-ROC: 0.73). **Conclusions:** pulmonary hypertension is common in patients with heart failure, regardless of their ejection fraction. The differential characteristics of patients with heart failure according to the diagnosis of pulmonary hypertension were highlighted for the first time in a Latin American population. However, additional studies are required evaluating other echocardiographic parameters as predictors of pulmonary hypertension and adverse outcomes in this context.

Keywords: heart failure, pulmonary hypertension, mortality.

pulmonar. Los diagnósticos de enfermedad pulmonar obstructiva crónica, fibrilación auricular, valvulopatías, falla cardíaca y el uso de diuréticos y anticoagulantes fueron predictores útiles para la identificación de aquellos pacientes con falla cardíaca con fracción de eyección preservada e hipertensión pulmonar (AUC-ROC: 0.73). **Conclusiones:** la hipertensión pulmonar es frecuente en pacientes con falla cardíaca, independientemente de su fracción de eyección. Se destacaron por primera vez en una población latinoamericana las características diferenciales de los pacientes con falla cardíaca de acuerdo con el diagnóstico de hipertensión pulmonar. No obstante, se requieren estudios adicionales que evalúen otros parámetros ecocardiográficos como predictores de hipertensión pulmonar y desenlaces adversos en este contexto.

Palabras clave: falla cardíaca, hipertensión pulmonar, mortalidad.

Abbreviations:

AUC = Area Under the Curve.
COPD = chronic obstructive pulmonary disease.
HF = heart failure.
HFpEF = heart failure with preserved ejection fraction.
LVEF= left ventricular ejection fraction.
HR = Hazard Ratio.
PH = pulmonary hypertension.
95% CI = 95% confidence interval.
NT-proBNP = N-terminal pro b-type natriuretic peptide.
NYHA = New York Heart Association.
PASP = pulmonary artery systolic pressure.
Q1 = quartile 1.
Q3 = quartile 3.
RECOLFACA = Colombian Registry of Heart Failure.
ROC = Receiver Operating Characteristic.

INTRODUCTION

Heart failure (HF) represents a chronic non-communicable disease of high prevalence worldwide and is considered one of the most relevant public health problems today.[1,2] Its genesis and evolution of adjacent pathophysiological mechanisms promote the appearance of other conditions such as atrial fibrillation (AF), insulin resistance and pulmonary hypertension (PH). The latter is secondary to the increase in filling pressures of the left ventricle chronically as a consequence of HF, increases pulmonary venous pressures and triggers processes of vasoconstriction and arterial remodeling, resulting in greater pulmonary vascular resistance and, consequently, in pre-capillary PH.[3,4] Previous studies suggest that patients with PH and HF present a worse prognosis than those only diagnosed with HF, highlighting the positive value of pharmacological and mechanical interventions in the reversibility of PH and the prognosis of these patients.[5,6]

The study of PH in the context of patients with HF has shown relevant aspects that represent a high impact on survival; however, further research is still required in understanding the phenomenon.[7] An important focus of attention results from the relationship of PH and preserved ejection fraction (HFpEF) in Latin American population whose characteristics, prevalence and implications may differ with respect to other populations and impact on therapeutic management.[8-10] It is necessary to evaluate this interaction, firstly, because the presence of elevated pulmonary venous pressures in patients with pEF is associated with a differential hemodynamic process, closely related to the severity of diastolic dysfunction, as has been observed in patients with aortic stenosis; secondly, because the factors associated with adverse outcomes in Latin American patients have not been evaluated so far.[3,4,11] For this reason, the objective of this study is to describe and analyze the clinical, echocardiographic and outcome characteristics of patients diagnosed with HF and with PH from the Colombian Registry of Heart Failure (RECOLFACA).

MATERIAL AND METHODS

Study design and population. The RECOLFACA is a prospective cohort study conducted in 60 medical institutions, heart failure clinics and outpatient centers in Colombia. Patient recruitment began in February 2017 and ended in October 2019, including outpatients older than 18 years with a clinical diagnosis of HF who had at least one hospitalization for HF in the 12 months prior to recruitment. The specific inclusion and exclusion criteria, together with the additional methodological characteristics of the registry, were previously described.[12,13] This study was reviewed and approved by the Biomedical Research Ethics Committee of the Valle del Lili Foundation, approval number 174-2017.

Data collection. Information on sociodemographic, clinical, and laboratory variables was recorded at baseline. The severity of HF was assessed using the New York Heart Association (NYHA) classification. In addition, a diagnosis of ischemic disease was recorded if the patient underwent a coronary revascularization procedure or had a history of prior myocardial infarction. The recording of left ventricular ejection fraction (LVEF) ≥ 40% allowed the identification and classification of HF with HFpEF, while those with LVEF < 40% were considered to have HF with reduced

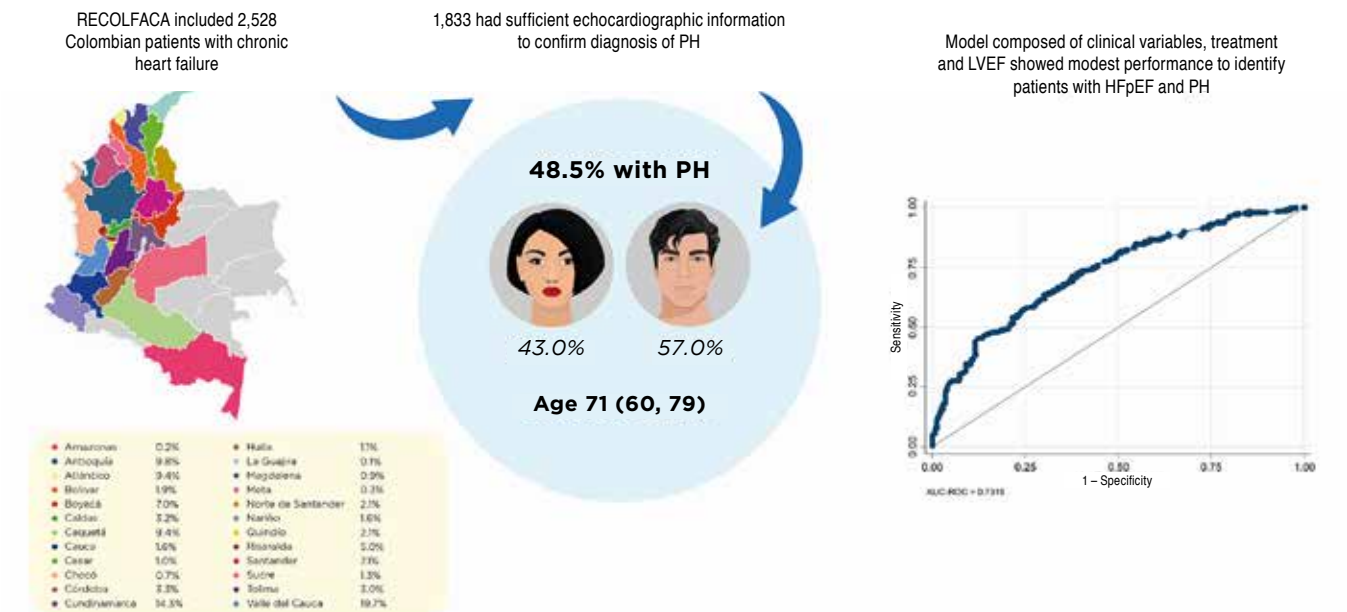
ejection fraction (HFrEF). The diagnosis of PH was defined according to the results of 2D echocardiography and color Doppler, specifically in those patients with a pulmonary artery systolic pressure (PASP) > 35 mmHg. On the other hand, chronic kidney disease was defined as an estimated glomerular filtration rate of < 60 mL/min/1.73 m^2 according to the MDRD formula. Clinical comorbidities evaluated were: arterial hypertension defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, atrial fibrillation (AF) diagnosed based on a 12-lead electrocardiogram (ECG) or documented history of this condition, anemia defined as the presence of a hemoglobin value < 13 g/dL for men and < 12 g/dL for women, and dyslipidemia defined as elevated total cholesterol [≥ 200 mg/dL] or low-density lipoprotein-bound cholesterol [LDL] [≥ 100 mg/dL], or triglycerides ≥ 150 mg/dL, or receiving lipid-lowering medications at enrollment. Other clinical diagnoses such as valvulopathy, chronic obstructive pulmonary disease (COPD), type 2 diabetes, cancer, liver failure, dementia, thyroid disease and Chagas disease were reported, according to how they were completed in the RECOLFACA database.

Outcomes. The main outcome of the study was all-cause mortality. Data on this outcome were collected using a questionnaire applied by each participating institution in an outpatient follow-up conducted six months after recruitment. Each institution also reviewed each patient's clinical records to assess specific data on outcomes.

Statistic analysis. Baseline characteristics were described as medians and quartiles if the variable was continuous. For categorical variables, proportions and percentages were recorded. Differences between patients with HF and PH (HF + PH) and those with HF without PH were assessed using Pearson's χ^2 tests and Fisher's exact test if they were categorical variables. The Mann-Whitney U test was used for continuous variables. The cumulative incidence of mortality events was calculated with their respective 95% confidence intervals (95% CI). Survival analyses were performed using the Kaplan-Meier method, the life table, and Cox proportional hazard models. A univariate and multivariate analysis was performed using Cox proportional regression models to assess the association between PH and mortality. On the other hand, a multivariate logistic regression model was adjusted to evaluate the clinical conditions associated with the diagnosis of PH in patients with pEFHF. For this purpose, we fit a stepwise logistic regression model. A p-value < 0.05 (two-tailed test) was considered statistically significant. All analyses were performed using the STATA statistical package version 15 (Station College, Texas, USA).

RESULTS

The RECOLFACA included a total of 2,528 outpatients with chronic HF between 2017 and 2019. Considering that



Diagnosis of PH was not associated with a differential risk of mortality during follow-up (HR 1.22; 95% CI 0.84-1.76)

Figure 1: Pulmonary hypertension in patients with heart failure in Colombia: an analysis of the Colombian Registry of Heart Failure (RECOLFACA). HFpEF = heart failure with preserved ejection fraction. LVEF = left ventricular ejection fraction. PH = pulmonary hypertension.

Table 1: Characteristics according to the diagnosis of pulmonary hypertension.

	Without PH N = 943, n (%)	With PH N = 890, n (%)	Total N = 1,833, n (%)	p
Male	549 (58.2)	507 (57.0)	1,056 (57.6)	0.588
Age [years]	69 (59.8)	71 (60.8)	70 (59.8)	**0.002**
Arterial hypertension	695 (73.7)	635 (71.3)	1,330 (72.6)	0.259
Alcoholism	33 (3.5)	28 (3.1)	61 (3.3)	0.673
Type 2 diabetes	231 (24.5)	212 (23.8)	443 (24.2)	0.735
Liver disease	1 (0.1)	5 (0.6)	6 (0.3)	0.088
Coronary heart disease	252 (26.7)	258 (29.0)	510 (27.8)	0.279
COPD	110 (11.7)	203 (22.8)	313 (17.1)	**< 0.001**
Atrial fibrillation	164 (17.4)	241 (27.1)	405 (22.1)	**< 0.001**
Thyroid disease	130 (13.8)	168 (18.9)	298 (16.3)	**0.003**
Chronic kidney disease	142 (15.1)	181 (20.3)	323 (17.6)	**0.003**
Valvulopathy	825 (87.5)	698 (78.4)	1,523 (83.1)	**< 0.001**
Coronary revascularization	77 (8.2)	55 (6.2)	132 (7.2)	0.100
Dyslipidemia	240 (25.5)	258 (29.0)	498 (27.2)	0.089
Smoking	150 (15.9)	175 (19.7)	325 (17.7)	**0.035**
Anemia	262 (29.0)	282 (33.4)	544 (31.1)	**0.049**
Chagas disease	29 (3.1)	30 (3.4)	59 (3.2)	0.720
NYHA functional class				**< 0.001**
I	140 (14.8)	87 (9.8)	227 (12.4)	–
II	521 (55.2)	462 (51.9)	983 (53.6)	–
III	253 (26.8)	284 (31.9)	537 (29.3)	–
IV	29 (3.1)	57 (6.4)	86 (4.7)	–
Use of medications				
ACEIs/ARBs-II	699 (74.1)	660 (74.2)	1,359 (74.1)	0.987
Beta-blockers	810 (85.9)	775 (87.1)	1,585 (86.5)	0.459
ARNI	91 (9.7)	88 (9.9)	179 (9.8)	0.864
MRA	534 (56.6)	513 (57.6)	1,047 (57.1)	0.662
Ivabradine	68 (7.2)	54 (6.1)	122 (6.7)	0.326
Diuretics	590 (62.6)	659 (74.0)	1,249 (68.1)	**< 0.001**
Nitrates	41 (4.3)	33 (3.7)	74 (4.0)	0.487
Anti-aggregants	463 (49.1)	394 (44.3)	857 (46.8)	**0.038**
Statins	531 (56.3)	504 (56.6)	1,035 (56.5)	0.890
Anticoagulants	199 (21.1)	268 (30.1)	467 (25.5)	**< 0.001**
SBP (mmHg)*	120 [110-135]	119 [104-131]	120 [107-134]	**0.011**
Heart rate (bpm)*	72 [65-80]	72 [65-84]	72 [65-81]	0.117
LVDD (mm)*	56 [48-65]	57 [48-65]	57 [48-65]	0.257
LVEF*	35 [25-42]	30 [24-42]	33 [25-42]	**0.002**
Hemoglobin (mg dL)*	13 [11.7-14.4]	13 [11.6-14.3]	13 [11.6-14.4]	0.549
NT-proBNP*	1,723.500 [571.3-4,911.5]	3,581 [1,428.3-8,692.3]	2,407.500 [954-6,043.3]	**< 0.001**
Prolonged QRS	171 (30.2)	218 (42.4)	389 (36.0)	**< 0.001**

ACEIs = Angiotensin-converting enzyme inhibitors. ARBs = angiotensin receptor antagonists. ARNI = angiotensin receptor neprilysin inhibitor. bpm = beats per minute. COPD = chronic obstructive pulmonary disease. LVDD = left ventricular diastolic diameter. LVEF= left ventricular ejection fraction. MRA = aldosterone receptor antagonists. NT-proBNP = N-terminal pro B-type natriuretic peptide. NYHA = New York Heart Association. PH = pulmonary hypertension. SBP = systolic blood pressure.
*Median and [interquartile range].

Table 2: Characteristics in the presence of heart failure with preserved ejection fraction (HFpEF) according to the diagnosis of pulmonary hypertension.

	HFpEF		Total N = 605 n (%)	p
	Without PH N = 328 n (%)	With PH N = 277 n (%)		
Male	185 (56.4)	130 (46.9)	315 (52.1)	**0.020**
Age [years]	70 (60.79)	74 (65.82)	72 (62.81)	**< 0.001**
Arterial hypertension	253 (77.1)	220 (79.4)	473 (78.2)	0.497
Alcoholism	8 (2.4)	5 (1.8)	13 (2.1)	0.592
Type 2 diabetes	81 (24.7)	59 (21.3)	140 (23.1)	0.324
Liver disease	0 (0.0)	3 (1.1)	3 (0.5)	0.059
Coronary heart disease	92 (28.0)	73 (26.4)	165 (27.3)	0.641
COPD	40 (12.2)	90 (32.5)	130 (21.5)	**< 0.001**
Atrial fibrillation	52 (15.9)	94 (33.9)	146 (24.1)	**< 0.001**
Thyroid disease	52 (15.9)	66 (23.8)	118 (19.5)	**0.014**
Chronic kidney disease	49 (14.9)	53 (19.1)	102 (16.9)	0.170
Valvulopathy	50 (15.2)	74 (26.7)	124 (20.5)	**< 0.001**
Coronary revascularization	29 (8.8)	23 (8.3)	52 (8.6)	0.814
Dyslipidemia	118 (37.8)	92 (34.6)	210 (36.3)	0.421
Smoking	92 (28.0)	78 (28.2)	170 (28.1)	0.976
Anemia	8 (2.4)	6 (2.2)	14 (2.3)	0.824
Chagas disease	46 (14.0)	54 (19.5)	100 (16.5)	0.071
NYHA functional class				**< 0.001**
I	49 (14.9)	17 (6.1)	66 (10.9)	–
II	194 (59.1)	149 (53.8)	343 (56.7)	–
III	79 (24.1)	95 (34.3)	174 (28.8)	–
IV	6 (1.8)	16 (5.8)	22 (3.6)	–
Use of medications				
ACEIs/ARBs-II	243 (74.1)	225 (81.2)	468 (77.4)	**0.037**
Beta-blockers	255 (77.7)	228 (82.3)	483 (79.8)	0.163
ARNI	15 (4.6)	4 (1.4)	19 (3.1)	**0.028**
MRA	106 (32.3)	97 (35.0)	203 (33.6)	0.483
Ivabradine	171 (52.1)	197 (71.1)	368 (60.8)	**< 0.001**
Diuretics	9 (2.7)	5 (1.8)	14 (2.3)	0.444
Nitrates	11 (3.4)	11 (4.0)	22 (3.6)	0.686
Anti-aggregants	160 (48.8)	130 (46.9)	290 (47.9)	0.650
Statins	181 (55.2)	163 (58.8)	344 (56.9)	0.365
Anticoagulants	65 (19.8)	103 (37.2)	168 (27.8)	**< 0.001**
SBP (mmHg)*	122.5 [110-140]	123.5 [110-140]	123.0 [110-140]	0.683
Heart rate (bpm)*	71 [63-80]	70 [64-81]	70.5 [64-80]	0.299
LVEF*	47 [41.8-56]	50 [45-58]	49 [43-56]	**0.003**
Hemoglobin (mg dL)*	12.9 [11.3-14.0]	12.9 [11.3-14.1]	12.9 [11.3-14.1]	0.675
NT-proBNP*	1,153.5 [571.3-2,401.3]	3,131 [1,187.5-5,308.0]	1,719 [805.0-4,100.0]	**< 0.001**
Prolonged QRS	57 (25.5)	55 (31.9)	112 (28.3)	0.153

ACEIs = angiotensin-converting enzyme inhibitors. ARBs = angiotensin receptor antagonists. ARNI = angiotensin receptor neprilysin inhibitor. bpm = beats per minute. COPD = chronic obstructive pulmonary disease. LVDD = left ventricular diastolic diameter. LVEF = left ventricular ejection fraction. MRA = aldosterone receptor antagonists. NT-proBNP = N-terminal pro B-type natriuretic peptide. NYHA = New York Heart Association. PH = pulmonary hypertension. SBP = systolic blood pressure. *Median and [interquartile range].

1,833 patients had sufficient echocardiographic information to confirm or rule out the diagnosis of PH, this was the population analyzed in the present study *(Figure 1)*.

Socio-demographic and clinical characteristics. The median age of the population was 70 years (Q1: 59; Q3: 78), being mainly male (57.6%). A total of 890 (48.6%) patients had a diagnosis of PH according to echocardiogram at the time of inclusion in the registry. *Table 1* summarizes the baseline characteristics of patients enrolled in the RECOLFACA according to their diagnosis of PH (PH versus Non-PH). Patients with PH had a significantly higher median age and reported a higher prevalence of COPD, atrial fibrillation, thyroid disease, chronic kidney disease, valvular heart disease, and anemia compared to those without this comorbidity. On the other hand, regarding clinical characteristics and pharmacological treatment, it was observed that patients in the HF and PH group had a significantly higher prevalence of patients in functional class NYHA III and IV and a more frequent prescription of diuretics and anticoagulants. In addition, patients diagnosed with PH had a lower median systolic blood pressure and a higher prevalence of QRS segment prolongation on the electrocardiogram. Finally, significantly lower LVEF was observed in those with PH, as well as a higher N-terminal brain natriuretic peptide (NT-proBNP) value *(Table 1)*.

PH in the patient with HFpEF. It was observed that patients with HFpEF and PH were more frequently female, with a median age significantly higher than that of patients with HFpEF without a diagnosis of PH *(Table 2)*. Similar to the results in the general population of RECOLFACA HF patients, individuals with HFpEF and PH had a higher prevalence of COPD, atrial fibrillation, thyroid disease, and valvulopathies compared to those without PH. On the other hand, although the prevalence of patients in functional class NYHA III and IV was similar, relevant differences were observed when analyzing the pharmacological prescription in the population of patients with HFpEF, highlighting a greater use of angiotensin converting enzyme inhibitor/angiotensin II receptor antagonist, diuretics and anticoagulants, as well as a lower use of neprilysin inhibitor (ARNi) compared to those without PH *(Table 2)*.

Despite having a significantly higher median NT-proBNP, patients with HFpEF and PH had a significantly higher value of their LVEF compared to those with HFpEF without PH.

In addition, among the factors that could potentially differentiate those patients with HFpEF and PH from those with HFpEF alone, it was observed that the diagnosis of COPD, atrial fibrillation, valvulopathy, NYHA classification, use of diuretics, use of anticoagulants and LVEF were independently associated with a greater likelihood of presenting both conditions compared to presenting with HFpEF alone *(Table 3)*. Finally, in the logistic regression model including these independent variables, an area value under the ROC curve of 0.73 was obtained.

Table 3: Variables independently associated with PH and HFpEF versus isolated HFpEF.

Factor	Odds ratio	Confidence interval	
		Lower limit	Upper limit
COPD	3.14	2.02	4.87
Atrial fibrillation	1.73	1.05	2.84
Valvulopathy	1.93	1.24	2.98
NYHA II versus I	1.86	0.98	3.51
NYHA III versus I	2.54	1.28	5.01
NYHA IV versus I	6.86	2.16	21.77
Diuretic use	1.66	1.14	2.41
Anticoagulant use	1.60	1.01	2.56
LVEF	1.03	1.01	1.05

COPD = chronic obstructive pulmonary disease. HFpEF = heart failure preserved ejection fraction. LVEF = left ventricular ejection fraction. NYHA = New York Heart Association. PH = pulmonary hypertension.

Mortality. The median follow-up in the present cohort was 215 days (Q1: 188; Q3: 254). In the overall group, a total of 170 patients (6.76%) died during follow-up, for a mortality rate of 0.30 per 1,000 person-years (95% CI 0.26-0.35). On the other hand, patients diagnosed with HF and PH had a mortality rate of 0.32 per 1,000 person-years (95% CI 0.25-0.41), with no statistically significant differences observed with that observed in patients without this comorbidity (0.25 per 1,000 person-years; 95% CI 0.19-0.33). Consequently, the diagnosis of PH was not associated with a differential risk of mortality during follow-up (HR 1.22; 95% CI 0.84-1.76). No significant interactions were found between the diagnosis of PH and sex, age, or LVEF.

DISCUSSION

This study represents the first detailed analysis of the characteristics and outcomes of patients with HF and PH in Latin America. The relevant differences in comorbidities, drug use, echocardiographic parameters, laboratory analysis, and between those patients with HFpEF with and without PH are highlighted presenting a series of factors that allow differentiating both groups with modest performance.

The first studies that evaluated the prevalence of PH in HF were published in the late 1990's, highlighting the study by Butler et al.,[14] in which 320 patients with advanced HF were evaluated, noting that only 28% had normal pulmonary vascular resistance and the remaining 72% had elevated vascular tone, which negatively impacted

their maximum VO_2 value, as well as other ventilatory and hemodynamic parameters. On the other hand, Ghio et al.[6] observed a prevalence of PH of 60% in a cohort of 377 patients with chronic HF. The prevalence observed in the present study was 49%, this probably due to the relative better condition of the patients included compared to those evaluated in the aforementioned studies, since the median LVEF of the present study was 33%, while this value was 22% in the study by Ghio et al.[6] and 23% in that by Butler et al,[14] thus reflecting the close relationship between HF, ventricular function and PH prevalence.

The finding of a higher prevalence of atrial fibrillation and valvulopathies in patients with HF and PH has pathophysiological implications. In the case of mitral or aortic stenosis-type valvulopathies, it is well known that their presence is associated with increased pressures in the left heart chambers, subsequently reflected in increased pulmonary venous pressures.[15] On the other hand, atrial fibrillation may reflect an advanced state of PH, a product of the overload of the right atrium, which progresses into fibrosis and eventually leads to conduction disorders such as atrial fibrillation or atrial flutter.[16]

The finding of a higher prevalence of thyroid disease in patients with PH has been reported in other studies, mainly relating PH to the diagnosis of hyperthyroidism.[17] The mechanisms behind this association are not yet fully understood; however, it is believed that greater sensitivity to catecholamines may lead to greater vasoconstriction at the pulmonary level, in addition, a faster metabolism of vasodilator substances such as prostacyclin and nitric oxide, coupled with an alteration in the metabolism of vasoconstrictor molecules (serotonin, thromboxane and endothelin 1) may explain the higher prevalence of PH in this population.[18]

This study highlights the differences that can help in the clinical differentiation of patients with HFpEF with and without PH; taking into account the high prevalence found in the latter group in our study population and considering that complications and similar symptoms occur in both,[19] these results allow us to suspect early of those patients who, despite having a preserved LVEF, may present elevated pulmonary pressures and, therefore, to seek an optimized therapeutic treatment.[20] The model presented here consists of clinical variables (COPD, atrial fibrillation, valvulopathies and NYHA), treatment (use of diuretics and anticoagulants) and LVEF, obtained a modest performance to discriminate patients with HFpEF with PH from those without this condition (AUC-ROC 0.73). This fact potentially highlights the importance of other echocardiographic parameters in differentiating these two conditions, such as right ventricular pressures, aortic systolic pressure, and cardiac output.[21]

Finally, multiple studies have reported a wide variety of risk factors for adverse outcomes in the context of PH; however, the evidence evaluating these factors in patients with HF and PH is scarcer.[22-24] Among these factors, age, right ventricular function, functional class, LVEF, and kidney disease diagnosis have been highlighted.[25] Moreover, the finding of an increased risk of mortality in patients who are receiving nitrates may be due to the severity of PH rather than the effect of the medication. Unfortunately, no information was recorded in the RECOLFACA regarding PH severity markers such as PASP, among others.

Limitations. The present study has several limitations. One of them is participation in the registry, which was voluntary between the different centers, therefore, there may be a selection bias. On the one hand, there was no additional information regarding echocardiographic parameters relevant in the context of PH, such as end of diastole pressure of the aorta, right atrial pressure and pulmonary vascular resistances, among others. There was also no information available about the classification of PH in the patients evaluated, thus limiting the possibility of making additional adjustments by specific groups. On the other hand, it should be noted that RECOLFACA did not include information on pharmacological and non-pharmacological therapy of the evaluated comorbidities, limiting the possibility of including these relevant factors in the analyses of risk factors. Finally, no information was available on the severity and duration of the comorbidities evaluated, which limited a more detailed assessment of the impact of these conditions.

CONCLUSIONS

PH represents a condition frequently observed in patients with HF, regardless of their LVEF. There are important differences in the profiles of comorbidities when comparing patients with HF with and without PH, mainly related to the multiple pathophysiological mechanisms related to the development of the latter. This study highlights for the first time in a Latin American population the differential characteristics of patients with HF according to the diagnosis of PH, highlighting the subgroup of patients with HFpEF. Additional studies are required to evaluate other echocardiographic parameters as predictors of PH and adverse outcomes in this context.

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