MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2022; 28: e934804
DOI: 10.12659/MSM.934804

Received: 2021.09.15
Accepted: 2021.10.28
Available online: 2021.12.18
Published: 2022.01.02

Retrospective Study of 573 Patients with Heart Failure Evaluated for Coronary Artery Disease at Toulouse University Center, France

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Statistical Analysis C
Data Interpretation D
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Financial support: Funding for this study was provided by Toulouse University Hospital
Conflict of interest: None declared

Background: Heart failure (HF) most commonly occurs due to ischemic heart disease from stenotic coronary artery disease (CAD). HF is classified into 3 groups based on the percentage of the ejection fraction (EF): reduced (HFrEF), mid-range (HFmrEF), and preserved (HFpEF). This retrospective study included 573 patients who presented with HF based on the evaluation of EF and were evaluated for CAD by coronary angiography before undergoing coronary angioplasty at a single center in Toulouse, France.

Material/Methods: This retrospective observational study included patients recently diagnosed with HF or acute decompensation of chronic HF and referred for coronary angiography at Toulouse University Hospital between January 2019 and May 2020.

Results: Significant CAD was found in 55.8%, 55%, and 55% of the whole population, HFpEF, and HFrEF groups, respectively. Older age, male sex, and diabetes mellitus were the main risk factors for ischemic HF. Except for age and sex, patients with ischemic HFpEF were comparable to those with non-ischemic HFpEF, unlike the ischemic HFrEF group, which had more common cardiovascular risk factors than the non-ischemic HFrEF group. The ischemic HFpEF group had an older age and higher rate of dyslipidemia than the ischemic HFrEF group.

Conclusions: At our center, CAD was diagnosed in more than half of patients who presented with heart failure with preserved or reduced EF. Older age and male sex were the common risk factors in patients with HFpEF and HFrEF.

Keywords: Coronary Artery Disease • Heart Failure • Heart Failure, Diastolic • Heart Failure, Systolic

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/934804

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Background

Heart failure (HF) is a major medical concern accounting for a huge number of hospitalizations, emergency department visits, and cardiovascular deaths [1,2]. The growing prevalence of HF is the consequence of increased life expectancy, hypertension, obesity, aging of the population, prolonged HF survival, and advancement in diagnostic and therapeutic strategies [3,4]. Neuro-humoral activation is the cornerstone of the complex pathophysiology of HF syndrome. HF is currently classified into 3 categories based on the percentage of left ventricular ejection fraction (LVEF): reduced (HFrEF, LVEF ≤40%), mid-range (HFmrEF, 40%< LVEF <50%), and preserved (HFpEF, LVEF ≥50%) [5]. Unlike HFpEF, for which medical therapy is limited to diuretics, the treatment of HFrEF has been extensively investigated in research studies and clinical trials. Treatment includes different drug classes (β-blockers, angiotensin converting enzyme inhibitor/angiotensin II receptor blocker, angiotensin receptor-neprilysin inhibitor, mineralocorticoid receptor antagonist, ivabradine, SGLT2 inhibitors, and vericiguat), devices (implantable cardiac defibrillator), stem cell transplantation, and gene therapy [6,7].

While coronary artery disease (CAD) has been long recognized as a major cause and therapeutic target of HF, the beneficial role of percutaneous intervention for coronary revascularization in patients with HF remains controversial [8]. Indeed, the presence of hibernating myocardium is crucial to predict improvement in cardiac function after coronary revascularization [9]. The role of CAD is not limited to HFrEF but is also implicated in HFpEF [10], and a prevalence of 80% of significant CAD in patients with HFpEF was reported in a study using the coronary angiography approach [11]. Moreover, CAD and HFpEF share several common risk factors, such as age and hypertension [12]. It is worth mentioning that HFpEF is more common in women, and HFrEF is more common in men [12,13], which is explained by the fact that much HF in men is provoked by myocardial infarction [12,13]. Guidelines recommend the careful search of CAD in patients with HF [5], but in general, the prevalence of CAD is underestimated in patients with HF because noninvasive tests are commonly used for screening. Therefore, this retrospective study conducted at a single center in Toulouse, France, included 573 patients who presented with HF based on the evaluation of reduced EF and were evaluated for CAD by coronary angiography before undergoing coronary angioplasty.

Material and Methods

Study Design and Population

This observational retrospective study included 573 patients with HF who presented for coronary angiography at the Interventional Cardiology Department at the University Hospital of Toulouse, France, between January 2019 and May 2020. The indications of coronary angiography in the included patients were a recent diagnosis of HF or acute decompensation of chronic HF. Then, patients were divided into 2 groups, HFpEF and HFrEF, which were subsequently divided into 2 subgroups of those with ischemic HF (IHF) and those without IHF, according to the presence or absence of significant CAD (**Figure 1**). All patients were informed at admission that their clinical data could be used for research purposes and gave their informed consent. The cohort was registered by the Ministry of Research and the Regional Health Agency Occitanie (no. DC-2017-298).

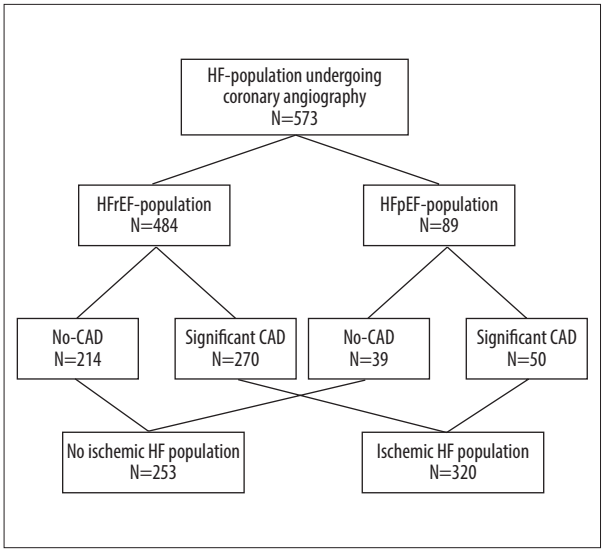

Figure 1. Study flowchart.

Data Collection and Endpoints

The baseline and demographic characteristics of the study participants, including age, sex, cardiovascular risk factors, medical treatment, prior medical history, and concomitant comorbidities, were collected by the study investigators. Also, transthoracic echocardiography parameters (left ventricular EF and valvulopathies), biological markers (troponin and NT-proBNP), and coronary angiography results were collected. All of these data were collected from the Orbis and Hemolia database used in our center. Significant CAD was defined as a ≥50% reduction in luminal coronary diameter. The purpose of this retrospective study was to assess the prevalence of significant CAD in the 573 patients who presented with HF and underwent coronary angiography at our center.

Statistical Analyses

Numbers and percentages were used to describe categorical variables, while means±standard deviations were used to describe continuous variables. Continuous variables were

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Table 1. Characteristics of the studied population stratified by type of heart failure.

	Studied population N=573	HFpEF N=89	HFrEF N=484	P-value
Age	68.28±12.25	72.53±9.72	67.50±12.51	<0.05
Male sex	438 (76.44%)	63 (70.78%)	375 (77.48%)	0.171
BMI	27.89±18.104	27.65±6.565	27.93±19.501	0.893
Coronary artery disease	320 (55.84%)	50 (56.18%)	270 (55.78%)	0.945
Atrial fibrillation	174 (30.37%)	25 (28.09%)	149 (30.78%)	0.611
Cardiovascular risk factors				
Chronic kidney disease	266 (46.42%)	45 (50.56%)	221 (45.66%)	0.500
Dyslipidemia	164 (28.62%)	39 (43.82%)	125 (25.83%)	0.001
Diabetes mellitus	171 (29.84%)	29 (32.58%)	142 (29.34%)	0.711
Hypertension	309 (53.93%)	61 (68.54%)	248 (51.24%)	0.006
Smoking	144 (25.13%)	11 (12.36%)	133 (27.48%)	0.001
Family history	89 (15.53%)	11 (12.36%)	78 (16.12%)	0.289
Echocardiographic parameters				
Valvulopathy	224 (39.09%)	29 (32.58%)	195 (40.29%)	0.181
Right ventricular dysfunction	110 (19.20%)	6 (6.74%)	104 (21.49%)	0.535
TAPSE	16.77±4.45	16.45±3.488	16.78±4.50	0.811
PAPSE	41.38±13.30	40.62±10.26	41.46±3.63	0.829
Implanted devices				
Pacemaker	41 (7.16%)	6 (6.74%)	35 (7.23%)	0.858
Defibrillator	38 (6.63%)	1 (1.12%)	37 (7.64%)	0.023
NYHA class				
1	23 (4.01%)	0	4 (0.82%)	0.433
2	143 (24.96%)	17 (19.10%)	126 (26.03%)	
3	149 (26.00%)	20 (22.47%)	129 (26.65%)	
4	47 (8.20%)	4 (4.49%)	43 (8.88%)	
Baseline hemodynamics				
Systolic blood pressure	128.86±22.80	137.72±22.43	127.37±22.55	0.001
Diastolic blood pressure	75.27±15.84	72.92±20.56	75.67±14.90	0.197
Heart rate	82.07±20.79	77.91±17.95	82.76±21.16	0.081
Laboratory biomarkers				
Troponin	143.87±543.08	112.13±212.21	149.21±580.79	0.726
NT-ProBNP	5535.15±8523.84	4073.81±7245.54	5770.14±8697.02	0.140

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Table 1 continued. Characteristics of the studied population stratified by type of heart failure.

	Studied population N=573	HFpEF N=89	HFrEF N=484	P-value
Baseline treatment				
β-blockers	324 (56.54%)	41 (46.06%)	283 (58.47%)	0.030
Diuretics	328 (57.24%)	50 (56.18%)	278 (57.44%)	0.809
Mineralocorticoids	95 (16.58%)	11 (12.36%)	84 (17.35%)	0.277
ACE/ARA	289 (50.44%)	51 (57.30%)	238 (49.17%)	0.164
ARNI	45 (7.85%)	3 (3.37%)	42 (8.68%)	0.087
Ivabradine	7 (1.22%)	0	7 (1.45%)	0.603
SAPT	172 (30.02%)	36 (40.45%)	136 (28.10%)	0.041
DAPT	47 (8.20%)	8 (9.00%)	39 (8.05%)	0.893
DOAC+AVK	165 (28.79%)	27 (30.33%)	138 (28.51%)	0.799
AAP+OAC	35 (6.11%)	6 (6.74%)	29 (6.00%)	0.893
Discharge treatment				
β-blockers	480 (83.77%)	58 (65.17%)	422 (87.19%)	<0.05
Diuretics	439 (76.61%)	62 (69.66%)	377 (77.89%)	0.067
Mineralocorticoids	231 (40.31%)	19 (21.35%)	212 (43.80%)	<0.05
ACE/ARA	332 (57.94%)	65 (73.03%)	267 (55.16%)	0.002
ARNI	137 (23.90%)	4 (4.49%)	133 (27.48%)	<0.05
Ivabradine	19 (3.32%)	2 (2.25%)	17 (3.51%)	0.752
SAPT	120 (20.94%)	33 (37.08%)	87 (17.97%)	<0.05
DAPT	215 (37.52%)	29 (32.58%)	186 (38.43%)	0.256
DOAC+AVK	217 (37.87%)	31 (34.83%)	186 (38.43%)	0.480
AP+OAC	82 (14.31%)	11 (12.36%)	71 (14.67%)	0.569

BMI – body mass index; APT – single anti-platelet therapy; DAPT – dual anti-platelet therapy; DOAC – direct oral anti-coagulant; AP+OAC – anti-platelet +oral anti-coagulant.

Table 2. The distribution of significant coronary artery disease.

	Ischemic heart failure population (N=320)	IHFrEF group (N=270)	IHFpEF group (N=50)
Left anterior descending coronary artery	214 (66.88%)	182 (67.40%)	32 (64.00%)
Right coronary artery	169 (52.81%)	146 (54.07%)	23 (46.00%)
Circumflex coronary artery	179 (55.94%)	152 (56.30%)	27 (54.00%)
Single vessel coronary disease	145 (45.31%)	118 (43.70%)	27 (54.00%)
Two-vessel coronary disease	106 (33.13%)	92 (34.07%)	14 (28.00%)
Triple-vessel coronary disease	68 (21.25%)	59 (21.85%)	9 (18.00%)

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Table 3. Characteristics of heart failure with preserved ejection fraction (HFpEF) group stratified by the presence of coronary artery disease.

	HFpEF population N=89	No CAD N=39	Significant CAD N=50	P-value
Age	72.53±9.722	70.59±10.43	74.04±8.95	0.097
Male sex	63 (70.78%)	21 (53.85%)	42 (84.00%)	0.002
BMI	27.65±6.56	27.99±7.66	27.39±5.63	0.668
Atrial fibrillation	25 (28.09%)	14 (35.89%)	11 (22.00%)	0.148
Cardiovascular risk factors				
Chronic kidney disease	45 (50.56%)	18 (46.15%)	27 (54.00%)	0.538
Dyslipidemia	39 (43.82%)	14 (35.89%)	25 (50.00%)	0.237
Diabetes mellitus	29 (32.58%)	10 (25.64%)	19 (38.00%)	0.267
Hypertension	61 (68.54%)	25 (61.10%)	36 (72.00%)	0.596
Smoking	11 (12.36%)	3 (7.69%)	8 (16.00%)	0.338
Family history	11 (15.53%)	4 (10.25%)	7 (14.00%)	0.751
Echocardiographic parameters				
Valvopathy	29 (32.58%)	12 (30.77%)	17 (34.00%)	0.697
Right ventricular dysfunction	6 (6.74%)	3 (7.69%)	3 (6.00%)	0.182
TAPSE	16.45±3.48	12.67±2.31	17.88±2.70	0.016
PAPSE	40.62±10.26	41.43±10.29	39.67±11.11	0.772
Implanted devices				
Pacemaker	6 (6.74%)	0	6 (12.00%)	0.033
Defibrillator	1 (1.12%)	0	1 (2.00%)	1
NYHA class				
1				0.115
2	17 (19.10%)	4 (10.26%)	13 (26.00%)	
3	20 (22.47%)	6 (15.38%)	14 (28.00%)	
4	4 (4.49%)	3 (7.69%)	1 (2.00%)	
Baseline hemodynamics				
Systolic blood pressure	137.72±22.43	134.52±24.00	139.73±21.45	0.367
Diastolic blood pressure	72.92±20.56	71.48±29.31	73.83±12.76	0.658
Heart rate	77.91±17.95	83.48±14.39	74.43±19.21	0.047
Laboratory biomarkers				
Troponin	112.13±212.21	184.82±344.36	72.15±62.86	0.307
NT-ProBNP	4073.81±7245.54	4523.32±7943.45	3724.19±6747.79	0.665

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Table 3 continued. Characteristics of heart failure with preserved ejection fraction (HFpEF) group stratified by the presence of coronary artery disease.

	HFpEF population N=89	No CAD N=39	Significant CAD N=50	P-value
Baseline treatment				
β-blockers	41 (46.07%)	17 (43.59%)	24 (48.00%)	0.679
Diuretics	50 (56.18%)	21 (53.85%)	29 (58.00%)	0.695
Mineralocorticoids	11 (12.36%)	4 (10.26%)	7 (14.00%)	0.749
ACE/ARA	51 (57.30%)	24 (61.54%)	27 (54.00%)	0.476
ARNI	3 (3.37%)	3 (7.69%)	0	0.080
SAPT	36 (40.45%)	11 (28.21%)	25 (50.00%)	0.031
DAPT	8 (8.98%)	1 (2.56%)	7 (14.00%)	0.075
DOAC+AVK	27 (30.34%)	11 (28.21%)	16 (32.00%)	0.699
AAP+OAC	6 (6.74%)	1 (2.56%)	5 (10.00%)	0.225
Discharge treatment				
β-blockers	58 (65.17%)	26 (66.66%)	32 (64.00%)	0.894
Diuretics	62 (69.66%)	25 (64.10%)	37 (74.00%)	0.314
Mineralocorticoids	19 (21.35%)	9 (23.07%)	10 (20.00%)	0.725
ACE/ARA	65 (73.03%)	28 (71.79%)	37 (74.00%)	0.816
ARNI	4 (4.49%)	3 (7.69%)	1 (2.00%))	0.315
Ivabradine	2 (2.23%)	1 (2.56%)	1 (2.00%)	1
SAPT	33 (37.08%)	11 (28.21%)	22 (44.00%)	0.126
DAPT	29 (32.58%)	2 (5.13%)	27 (54.00%)	<0.05
DOAC+AVK	31 (37.87%)	16 (34.83%)	15 (38.43%)	0.279
AAP+OAC	11 (14.31%)	2 (12.36%)	9 (14.67%)	0.103

BMI – body mass index; APT – single anti-platelet therapy; DAPT – dual anti-platelet therapy; DOAC – direct oral anti-coagulant; AP+OAC – anti-platelet +oral anti-coagulant.

analyzed with the *t* test, as appropriate, and categorical variables were analyzed with the χ^2 or Fisher's exact test, as appropriate. Stepwise logistic regression analyses were used on all variables with a *P* value <0.2 in the bivariate analysis comparing the IHFrEF subgroup with the non-IHFrEF subgroup, IHFpEF subgroup with the non-IHFpEF subgroup, and the IHF group with the non-IHF group. Comparisons were conducted to assess the baseline characteristics associated with IHFrEF, IHFpEF, and IHF. A 2-sided *P* value <0.05 was considered statistically significant. All statistical analyses were carried out using SPSS version 20 (IBM Corp, Armonk, NY, USA).

Results

The mean age of the 573 study participants was 68.3±12 years. HFrEF was significantly more prevalent than HFpEF (84.5% vs 15.5%). Patients with HFpEF were older and had more cardiovascular risk factors than the other groups; there was no difference in smoking. Significant CAD was detected in 55.8% of patients, and 76.4% of patients were men. **Tables 1 and 2** show the characteristics of the study population.

Compared with the non-IHFpEF subgroup (n=39), patients with IHFpEF (n=50) were older (74 vs 70.5 years), predominantly men (84% vs 53.8%), and had a lower mean baseline heart rate (74 vs 83 beats/min), New York Heart Association class, prevalence of associated atrial fibrillation (22% vs 35.9%),

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Table 4. Characteristics of heart failure with reduced ejection fraction (HFrEF) group stratified by the presence of coronary artery disease.

	HFrEF population N=484	No CAD N=214	Significant CAD N=270	P-value
Age	67.50±12.51	63.86±13.79	70.38±10.57	<0.05
Male sex	375 (77.48%)	148 (69.16%)	227 (84.41%)	<0.05
BMI	27.89±19.50	30.27±28.72	26.08±4.69	0.036
Atrial fibrillation	149 (30.78%)	65 (30.37%)	84 (31.11%)	0.861
Cardiovascular risk factors				
Chronic kidney disease	221 (45.66%)	66 (30.84%)	155 (57.41%)	<0.05
Dyslipidemia	125 (25.82%)	44 (20.56%)	81 (30.00%)	0.080
Diabetes	142 (29.34%)	48 (22.43%)	94 (34.81%)	0.020
Hypertension	248 (51.24%)	86 (40.18%)	162 (60.00%)	0.001
Smoking	133 (27.48%)	56 (26.17%)	77 (28.52%)	0.906
Family history	78 (16.12%))	38 (17.76%)	40 (14.81%)	0.164
Echocardiographic parameters				
Valvopathy	195 (40.29%)	81 (37.85%)	114 (42.22%)	0.317
RVD	104 (21.49%)	49 (22.89%)	55 (20.37%)	0.244
TAPSE	16.78±4.50	16.15±4.36	17.26±4.55	0.053
PAPSE	41.46±13.63	41.53±12.75	41.41±14.30	0.963
Implanted devices				
Pacemaker	35 (7.23%)	15 (7.10%)	20 (7.41%)	0.860
Defibrillator	37 (7.64%)	12 (5.61%)	25 (9.26%)	0.133
NYHA				
1	23 (4.75%)	10 (4.67%)	13 (4.81%)	1
2	126 (26.03%)	56 (26.17%)	70 (25.93%)	
3	129 (26.65%)	56 (26.17%)	73 (27.04%)	
4	43 (8.88%)	19 (8.89%)	24 (8.88%)	
Baseline hemodynamics				
Systolic blood pressure	127.37±22.55	126.62±22.02	127.95±22.99	0.566
Diastolic blood pressure	75.67±14.90	77.02±15.53	74.62±14.35	0.118
Heart rate	82.76±21.16	86.13±20.99	80.13±20.97	0.005
Laboratory biomarkers				
Troponin	149.21±58.78	87.71±269.36	186.97±705.82	0.262
NT-ProBNP	5770.14±8697.02	5341.15±8308.36	6135.28±9017.84	0.365

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Table 4 continued. Characteristics of heart failure with reduced ejection fraction (HFrEF) group stratified by the presence of coronary artery disease.

	HFrEF population N=484	No CAD N=214	Significant CAD N=270	P-value
Baseline treatment				
β-blockers	283 (58.47%)	113 (52.80%)	170 (62.96%)	0.024
Diuretics	278 (57.44%)	116 (54.20%)	162 (60.00%)	0.184
Mineralocorticoids	84 (17.35%)	36 (16.82%)	48 (17.77%)	0.783
ACE/ARA	238 (49.17%)	90 (42.05%)	148 (54.81%)	0.006
ARNI	42 (8.67%)	18 (8.41%)	24 (8.89%)	0.853
Ivabradine	7 (1.45%)	2 (0.93%)	5 (1.85%)	0.471
SAPT	136 (28.10%)	33 (15.42%)	103 (38.15%)	<0.05
DAPT	39 (8.06%)	3 (1.40%)	36 (13.33%)	<0.05
DOAC+AVK	138 (28.51%)	59 (27.57%)	79 (29.26%)	0.683
AAP+OAC	29 (5.99%)	4 (1.87%)	25 (9.26%)	0.001
Discharge treatment				
β-blockers	422 (87.19%)	187 (87.38%)	235 (87.03%)	0.748
Diuretics	377 (77.89%)	169 (78.97%)	208 (77.04%)	0.837
Mineralocorticoids	212 (43.80%)	105 (49.06%)	107 (39.63%)	0.047
ACE/ARA	267 (55.16%)	122 (57.01%)	145 (53.70%)	0.545
ARNI	133 (27.48%)	68 (31.77%)	65 (24.07%)	0.064
Ivabradine	17 (3.51%)	7 (3.27%)	10 (3.70%)	0.774
SAPT	87 (17.97%)	30 (14.02%)	57 (21.11%)	0.037
DAPT	186 (38.43%)	12 (5.61%)	174 (64.44%)	<0.05
DOAC+AVK	191 (39.46%)	90 (42.06%)	101 (37.41%)	0.299
AAP+OAC	71 (14.67%)	3 (1.40%)	68 (25.18%)	<0.05

and right ventricular dysfunction (6% vs 7.7%). Except for the anti-thrombotic regimen, there were no differences in the received medical treatments (diuretics, β-blockers, mineralocorticoid, and ACEi/ARAII) (**Table 3**). Positive correlations between age (odds ratio [OR] 1.1, 95%CI 1.01-1.2, *P*=0.02), male sex (OR 26.9, 95%CI 4.7-152.8, *P*<0.001), and IHFpEF were revealed by the adjusted multivariate analysis.

Compared with the non-IHFrEF subgroup (n=214), the IHFrEF subgroup (n=270) had significantly higher age (70.3 vs 63.8 years), male sex (84.1% vs 69.2%) cardiovascular risk factors (chronic kidney disease [59.4% vs 31.9%], dyslipidemia [32.5% vs 24.7%], arterial hypertension [65.1% vs 48.3%], and diabetes mellitus [37.8% vs 27%]), implantable cardiac devices (7.4% vs 4.2%), and prescribed medical treatment (diuretics, β-blockers, ACEi/ARAII, and anti-thrombotic regimen). By contrast, mean baseline heart rate (80 vs 86 beats/min), diastolic blood pressure (74 vs 77 mmHg), and body mass index (BMI) (26.1 vs 30.3 kg/m^2) were lower in IHFrEF subgroup (**Table 4**). The adjusted multivariate logistic regression on the previously cited confounding variables showed that IHFrEF was positively correlated with age (OR 1.02, 95%CI 1-1.05, *P*=0.02), male sex (OR 2.7, 95%CI 1.4-5.2, *P*=0.002), chronic kidney disease (OR 2.3, 95%CI 1.2-4.3, *P*=0.006), diabetes mellitus (OR 1.9, 95%CI 1.1-3.4, *P*=0.01), and arterial hypertension (OR 1.7, 95%CI 1.02-2.9, *P*=0.04), while it was inversely correlated with BMI (OR 0.9, 95%CI 0.88-0.99, *P*=0.04).

Male sex was more common in IHF (n=320) than in non-IHF (n=253) groups. The following were also more common in

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Table 5. Characteristics of the study population stratified by the presence of coronary artery disease.

	Studied population N=573	No-CAD N=253	Significant CAD N=320	P-value
Age	68.28±12.25	64.90±13.532	70.95±10.404	<0.05
Male sex	438 (76.44%)	169 (66.80%)	269 (84.06%)	0.171
BMI	27.89±18.104	29.92±26.581	26.28±4.864	0.033
Atrial fibrillation	174 (30.37%)	79 (31.23%)	95 (29.69%)	0.691
HFrEF	484 (84.47%)	214 (84.58%)	270 (84.37%)	0.945
Cardiovascular risk factors				
Chronic kidney disease	266 (46.42%)	84 (33.20%)	182 (56.87%)	<0.05
Dyslipidemia	164 (28.62%)	58 (22.92%)	106 (33.13%)	0.041
Diabetes	171 (29.84%)	58 (22.92%)	113 (35.31%)	0.010
Hypertension	309 (53.93%)	111 (43.87%)	198 (61.87%)	0.001
Smoking	144 (25.13%)	59 (23.32%)	85 (26.56%)	0.802
Family history	89 (15.53%)	42 (16.60%)	47 (14.69%)	0.261
Echocardiographic parameters				
Valvulopathy	224 (39.09%)	93 (36.76%)	131 (40.93%)	0.284
RVD	110 (19.20%)	52 (20.55%)	58 (18.13%)	0.535
TAPSE	16.77±4.45	16.05±4.35	17.29±4.48	0.026
PAPSE	41.38±13.30	16.05±4.347	17.29±4.472	0.026
Implanted devices				
Pacemaker	41 (7.16%)	15 (5.93%)	26 (8.13%)	0.307
Defibrillator	38 (6.63%)	12 (4.74%)	26 (8.13%)	0.106
NYHA class				
1	23 (4.01%)	10 (3.95%)	14 (4.38%)	0.964
2	143 (24.96%)	60 (23.72%)	83 (25.94%)	
3	149 (26%)	62 (24.51%)	87 (27.19%)	
4	47 (8.20%)	22 (8.70%)	25 (7.81%)	
Baseline hemodynamics				
Systolic blood pressure	128.86±22.80	127.64±22.37	129.77±23.12	0.325
Diastolic blood pressure	75.27±15.84	76.30±17.90	74.50±14.09	0.233
Heart rate	82.07±20.79	85.79±20.26	79.25±20.78	0.001
Laboratory biomarkers				
Troponin	143.87±543.08	100.90±280.22	1169.84±652.32	0.368
NT-ProBNP	5535.15±8523.84	5232.62±8247.12	5789.47±8758.01	0.485

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Table 5 continued. Characteristics of the study population stratified by the presence of coronary artery disease.

	Studied population N=573	No-CAD N=253	Significant CAD N=320	P-value
Baseline treatment				
β-blockers	324 (56.54%)	130 (51.38%)	194 (60.63%)	0.027
Diuretics	328 (57.24%)	137 (54.15%)	191 (59.69%)	0.169
Mineralocorticoids	95 (16.58%)	40 (15.81%)	84 (17.19%)	0.663
ACE/ARA	289 (50.44%)	114 (45.06%)	175 (54.69%)	0.025
ARNI	45 (7.85%)	21 (8.30%)	24 (7.50%)	0.724
Ivabradine	7 (1.22%)	2 (0.79%)	5 (1.56%)	0.472
SAPT	172 (30.02%)	44 (17.39%)	128 (40.00%)	<0.05
DAPT	47 (8.20%)	4 (1.58%)	43 (13.44%)	<0.05
DOAC+AVK	164 (28.62%)	70 (27.67%)	94 (29.37%)	0.637
AAP+OAC	35 (6.11%)	5 (1.977%)	30 (9.38%)	0.05
Discharge treatment				
β-blockers	480 (83.77%)	213 (84.19%)	267 (83.44%)	0.851
Diuretics	439 (76.61%)	194 (76.68%)	245 (76.56%)	0.810
Mineralocorticoids	231 (40.31%)	114 (45.06%)	117 (36.56%)	0.048
ACE/ARA	332 (57.94%)	150 (59.29%)	182 (56.88%)	0.643
ARNI	137 (23.90%)	71 (28.06%)	66 (20.62%)	0.041
Ivabradine	19 (3.32%)	8 (3.16%)	11 (3.44%)	0.833
SAPT	120 (20.94%)	41 (16.20%)	79 (24.68%)	0.011
DAPT	215 (37.52%)	14 (5.53%)	201 (62.81%)	<0.05
DOAC+AVK	217 (37.87%)	106 (41.89%)	111 (34.69%)	0.480
AAP+OAC	82 (14.31%)	5 (1.98%)	77 (24.06%)	<0.05

the IHF than in the non-IHF groups: implantable cardiac devices (8.1% vs 4.7%) and cardiovascular risk factors, including chronic kidney disease (58.5% vs 34.3%), dyslipidemia (35.8% vs 27.2%), diabetes mellitus (38.2% vs 27.2%), and arterial hypertension (66.9% vs 52.1%). Also, diuretics, β-blockers, ACEi/ARAII, and anti-thrombotic agents were used more often in patients with IHF. However, the prevalence of associated RVD (47.3% vs 38.4%), mean baseline heart rate (85.8 vs 79.2 bpm/min), and BMI (29.9 vs 26.3 kg/cm^2) were higher in the non-IHF than IHF groups (**Table 5**). Lastly, the adjusted multivariate logistic regression showed a positive correlation between age (OR 1.05, 95%CI 1.02-1.09, *P*=0.003), male sex (OR 3, 95%CI 1.2-7.2, *P*=0.01), and diabetes mellitus (OR 2.4, 95%CI 1.06-5.37, *P*=0.03) and IHF, which was inversely associated with BMI (OR 0.9, 95%CI 0.85-0.98, *P*=0.02).

Lastly, patients with IHFpEF were older (74 vs 70.4 years) with a lower mean baseline heart rate (74 vs 80 beats/min) and higher systolic blood pressure (139.7 vs 127.9 mmHg), BMI (27.4 vs 26.1 kg/cm^2), and rate of cardiovascular risk factors, including dyslipidemia (50% vs 30%) and arterial hypertension (72% vs 60%) than those with IHFrEF, which had more smokers (28.5% vs 16%) and higher NT-proBNP levels (6135 vs 3724) (**Table 6**). Compared with IHFrEF, the multivariate analysis showed that age and dyslipidemia were associated to IHFpEF (**Figure 2**).

Discussion

This study showed that more than half of patients referred for coronary angiography for a recent diagnosis of HF or acute decompensation of chronic HF presented with significant CAD. Age,

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Table 6. Characteristics of ischemic heart failure (IHF) group stratified by type of heart failure.

	CAD-population N=320	HFpEF N=50	HFrEF N=270	P-value
Age	70.95±10.404	74.04±8.949	70.38±10.567	0.022
Male sex	269 (84.06%)	42 (84.00%)	227 (84.07%)	0.990
BMI	26.28±4.86	27.39±5.63	26.08±4.69	0.081
Atrial fibrillation	95 (29.69%)	11 (22.00%)	84 (31.11%)	0.195
Cardiovascular risk factors				
Chronic kidney disease	182 (56.87%)	27 (54.00%)	155 (57.41%)	0.479
Dyslipidemia	106 (33.13%)	25 (50.00%)	81 (30.00%)	0.007
Diabetes	113 (35.31%)	19 (38.00%)	94 (34.81%)	0.729
Hypertension	198 (66.9%)	36 (72.00%)	162 (60.00%)	0.123
Smoking	85 (26.56%)	8 (16.00%)	77 (28.52%)	0.053
Family history	47 (14.69%)	7 (14.00%)	40 (14.81%)	0.840
Echocardiographic parameters				
Valvopathy	131 (40.93%)	17 (34.00%)	114 (42.22%)	0.305
RVD	58 (18.13%)	3 (6.00%)	55 (20.37%)	0.1
TAPSE	17.29±4.47	17.88±2.69	17.26±4.55	0.706
PAPSE	41.38±14.01	39.67±11.11	41.41±14.30	0.772
Implanted devices				
Pacemaker	26 (8.13%)	8 (12.00%)	20 (7.41%)	0.268
Defibrillator	26 (8.13%)	1 (2%)	25 (9.26%)	0.096
NYHA				
1	13 (4.06%)	0	13 (4.81%)	0.339
2	83 (25.94%)	13 (26.00%)	70 (25.93%)	
3	87 (27.19%)	14 (28.00%)	73 (27.04%)	
4	25 (7.81%)	1 (2.00%)	24 (8.89%)	
Baseline hemodynamics				
Systolic blood pressure	129.77±23.12	139.73±21.452	127.95±22.99	0.003
Diastolic blood pressure	74.50±14.09	73.83±19.76	74.62±14.35	0.742
Heart rate	79.25±20.78)	74.43±19.21	80.13±20.97	0.110
Laboratory biomarkers				
Troponin	169.84±652.32	72.15±62.86	186.97±705.82	0.470
NT-ProBNP	5889.47±8758.00	3724.19±6747.79	6135.28±9017.84	0.127

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Table 6 continued. Characteristics of ischemic heart failure (IHF) group stratified by type of heart failure.

	CAD-population N=320	HFpEF N=50	HFrEF N=270	P-value
Baseline treatment				
β-blockers	194 (60.63%)	24 (48.00%)	170 (62.96%)	0.047
Diuretics	191 (59.69%)	29 (58.00%)	162 (60.00%)	0.768
Mineralocorticoids	55 (17.19%)	7 (14.00%)	48 (17.78%)	0.552
ACE/ARA	175 (54.69%)	27 (54.00%)	148 (54.81%)	0.915
ARNI	24 (7.50%)	0	24 (8.89%)	0.016
Ivabradine	5 (1.56%)	0	5 (1.85%)	1
SAPT	128 (40.00%)	25 (50.00%)	103 (38.15%)	0.189
DAPT	43 (13.44%)	7 (14.00%)	36 (13.33%)	0.958
DOAC+AVK	1 (0.31%)	0	1 (0.37%)	1
AAP+OAC	30 (9.37%)	5 (10.00%)	25 (9.26%)	0.677
Discharge treatment				
β-blockers	267 (83.43%)	32 (64.00%)	235 (87.04%)	<0.05
Diuretics	245 (76.56%)	37 (74.00%)	208 (77.04%)	0.514
Mineralocorticoids	117 (36.56%)	10 (20.00%)	107 (39.63%)	0.007
ACE/ARA	182 (56.87%)	37 (74.00%)	145 (53.70%)	0.011
ARNI	66 (20.62%)	1 (2.00%)	65 (24.07%)	<0.05
Ivabradine	11 (3.43%)	1 (2.00%)	10 (3.70%)	1
SAPT	79 (24.69%)	22 (44.00%)	57 (21.11%)	0.001
DAPT	201 (62.81%)	27 (54.00%)	174 (64.44%)	0.115
DOAC+AVK	111 (34.69%)	15 (30.00%)	96 (35.55%)	0.398
AAP+OAC	77 (24.06%)	9 (18.00%)	68 (25.18%)	0.281

BMI – body mass index; APT – single anti-platelet therapy; DAPT – dual anti-platelet therapy; DOAC – direct oral anti-coagulant; AP+OAC – anti-platelet +oral anti-coagulant.

male sex, and diabetes mellitus were independent predictors of IHF. Aside from age and sex, there were no differences between the IHFpEF and non-IHFpEF groups, unlike patients with IHFrEF, who had more cardiovascular risk factors, such as arterial hypertension, diabetes mellitus, and chronic kidney disease, than those with patent coronary arteries. Regardless, age and dyslipidemia, which were baseline characteristics of patients with HFpEF, were comparable to patients with HFrEF with CAD.

The literature has reported a similar rate of CAD in patients with HF after a systematic angiography approach, especially in those presenting with HFpEF [14-16]. Despite the known implications of CAD in the pathophysiology and development of HF, the effect of coronary revascularization on lowering the associated mortality and morbidity remains controversial [8]. Indeed, the co-existence of CAD in patients with HF was linked with poor long-term prognosis. CAD is usually underestimated in patients with HF, particularly in patients with HFpEF, in whom the role of CAD is under-recognized [17]. In agreement with our study result, Hwang et al showed that patients with HFpEF and those without CAD are comparable in medical treatment, laboratory markers, echocardiographic parameters, and baseline characteristics except for age and sex [10]. By contrast, cardiovascular risk factors in addition to older age and male sex were significantly more expressed in patients with IHFrEF compared with those with normal or near-normal coronary arteries. Regardless, this finding was included in a study conducted by Drissa et al [18]. It is well known that women

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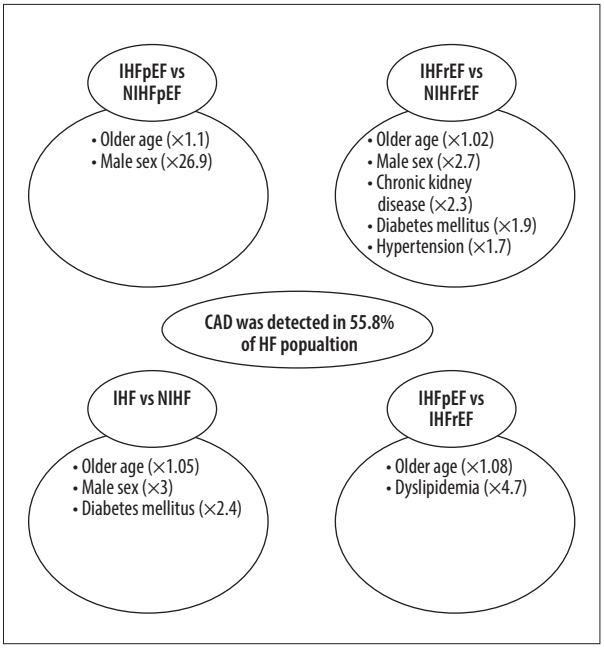

Figure 2. Illustration of the independent predictors of ischemic heart failure with preserved ejection fraction (IHFpEF), ischemic heart failure with reduced ejection fraction (IHFrEF), and ischemic heart failure (IHF).

are more predisposed to HFpEF, while men are more predisposed to HFrEF [12,19]. However, the present study showed that these sex differences vanished when comparing IHFpEF and IHFrEF. In view of the high prevalence of CAD in patients with HFpEF, absence of a difference in the distribution of cardiovascular risk factors, and poor outcomes attributed to the presence of CAD, searching for CAD in older men with HFpEF may improve prognosis and patient quality of life by preventing future ischemic heart events.

Compared with studies of HF in patients with non-obstructive CAD, the present study revealed that IHFpEF and IHFrEF share just 2 risk factors: older age and male sex. The relationship of sex and the development of ischemic cardiac diseases during the whole lifetime are well established in the literature. Furthermore, a recently published study investigated the role of sex in affecting the importance of risk factors for CAD [20]. Prospective trials based on the angiographic approach to screen and manage CAD in patients with HF and to evaluate the long-term impact on survival and quality of life are needed.

The main limitations of this study were the retrospective observational design and the lack of long-term follow-up data. Also, data concerning revascularization were not provided because we were interested in assessing the differences between various categories of HF according to the presence of significant CAD. The mean age of our study population was lower than that of the large registries of patients with HF, therefore explaining the ratio of HFrEF to HFpEF in these study participants from a tertiary referral hospital.

Conclusions

At our center, CAD was diagnosed in more than half of patients who presented with HF with preserved or reduced EF. Older age and male sex were the common risk factors in patients with HFpEF and HFrEF. Therefore, screening for CAD in patients recently diagnosed with HF or presenting with acute decompensation of HF is warranted. Future prospective studies investigating the impact of revascularization on long-term prognosis in patients with ischemic HFrEF and HFpEF compared with those without CAD are needed.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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