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

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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

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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 (HFrmEF, 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 Clinical Research department at a single center in 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).

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

|                                | Studied population N=573 | HfP-EF N=89 | HfR-EF 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±18.10              | 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%)    |         |
| 2                              | 143 (24.96%)             | 17 (19.10%) | 126 (26.03%) | 0.433   |
| 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   |
### 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%)   |
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                            |                         |             |                       |         |
| 2                            | 17 (19.10%)            | 4 (10.26%)  | 13 (26.00%)           | 0.115   |
| 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   |
analyzed with the \( t \) test, as appropriate, and categorical variables were analyzed with the \( \chi^2 \) 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 HFrEF 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.

### 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** |                        |             |                       |                |
| \( \beta \)-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%)              | 1 (2.56%)   | 0 (0.00%)             |                |
| SAPT                   | 36 (40.45%)            | 11 (28.21%) | 25 (50.00%)           | 0.031          |
| DAPT                   | 8 (8.98%)              | 2 (5.13%)   | 6 (12.00%)            | <0.05          |
| 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

|                        | HFpEF population N=89 | No CAD N=39 | Significant CAD N=50 | \( P \)-value  |
|------------------------|------------------------|-------------|-----------------------|----------------|
| \( \beta \)-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 (43.83%) | 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.
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%)             |         |
| 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   |
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 1.01-1.03, \( P = 0.02 \)), 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

| Table 4 continued. Characteristics of heart failure with reduced ejection fraction (HFrEF) group stratified by the presence of coronary artery disease. |
|---|---|---|---|---|
| **Baseline treatment** | **HFrEF population N=484** | **No CAD N=214** | **Significant CAD N=270** | **P-value** |
| 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 |
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 (85.58%) | 270 (84.37%)           | 0.945    |
| Cardiovascular risk factors          |                          |              |                        |          |
| Chronic kidney disease               | 266 (46.42%)             | 84 (33.20%)  | 182 (56.87%)           | <0.05    |
| Diabetes                             | 164 (28.62%)             | 58 (22.92%)  | 106 (33.13%)           | 0.041    |
| Hypertension                         | 171 (29.84%)             | 58 (22.92%)  | 113 (35.31%)           | 0.010    |
| 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%)             |          |
| 2                                    | 143 (24.96%)             | 60 (23.72%)  | 83 (25.94%)            | 0.964    |
| 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    |
Table 5 continued. Characteristics of the study population stratified by the presence of coronary artery disease.

| Characteristic           | 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 (1.97%)    | 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   |

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/m²), 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,
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%)  |         |
| 2                        | 83 (25.94%)           | 13 (26.00%)| 70 (25.93%) | 0.339   |
| 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   |
Table 6 continued. Characteristics of ischemic heart failure (IHF) group stratified by type of heart failure.

| Characteristic                     | CAD-population | 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 HfP EF, 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 HfP EF [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 HfP EF, in whom the role of CAD is under-recognized [17]. In agreement with our study result, Hwang et al showed that patients with HfP EF 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
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 HFrEF 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 HFrEF 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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