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Hugo Ricardo Leal Teixeira
Characterization of patients with heart failure and
reduced ejection fraction attending two Heart
Failure clinics in Portugal and in Mozambique

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Mestrado Integrado em Medicina

Área: Cardiologia

Trabalho efetuado sob a Orientação de:
Prof. Doutor José Carlos de Magalhães Silva Cardoso
E sob a Coorientação de:
Prof. Doutor Albertino António Moura Damasceno

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Characterization of patients with heart failure and reduced ejection fraction attending two Heart Failure Clinics in Portugal and in Mozambique

Caracterização de pacientes com insuficiência cardíaca e fração de ejeção reduzida em duas Clínicas de Insuficiência Cardíaca em Portugal e Moçambique

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Resumo

Introdução e objetivos: A insuficiência cardíaca é um problema de saúde comum, incapacitante e relacionado a elevada morbidade e mortalidade. A patogenia varia nos diferentes países africanos, sendo a mais prevalente a não isquémica, enquanto em Portugal são a hipertensão arterial e doença isquémica. O nosso objetivo foi comparar doentes Moçambicanos e Portugueses para identificar possíveis diferenças clínicas, etiológicas e terapêuticas.

Métodos: Recolheu-se informação do processo clínico hospitalar (história, exame físico, meios complementares de diagnóstico e terapêutica, relativa à consulta inicial na clínica de insuficiência cardíaca e à primeira consulta no período entre 1 de Maio e 30 de Julho de 2012. Foi realizada análise estatística e os resultados apresentados em tabelas.

Resultados: Estudaram-se 242 doentes, 187 Portugueses e 55 Moçambicanos. Globalmente, os Portugueses apresentaram classes NYHA menos graves na admissão ($p < 0.001$), mas mais comorbilidades (exceto insuficiência renal e infeção HIV). As etiologias mais frequentes foram a isquémica, familiar e alcoólica nos Portugueses, e a valvular, hipertensiva e peri-parto nos Moçambicanos. Não se encontraram diferenças estatisticamente significativas relativas à associação com infeção HIV ($p = 0.085$).

Em ambos, os inibidores da enzima de conversão da angiotensina/inibidores do recetor da angiotensin foram prescritos num elevado número de doentes, tendo globalmente os bloqueadores beta sido os mais prescritos em Portugal e os diuréticos em Maputo, estando a terapêutica não-farmacológica indisponível para Moçambicanos.

Conclusões: Num estudo observacional sem precedentes, explicitámos algumas diferenças entre estas populações, podendo contribuir para melhorar a abordagem da insuficiência cardíaca nas respetivas clínicas.

Palavras-chave: insuficiência cardíaca; epidemiologia; fração de ejeção; África.

Abstract

Background and objectives: Heart failure is a common and disabling health problem, associated with high morbidity and mortality. The pathogenesis varies between African countries, with the most prevalent pathogenesis being non-ischemic disease, whereas on Portugal hypertension and ischemic disease are the most prevalent. We aimed to compare Mozambican and Portuguese patients to identify possible clinical, etiological and therapeutic differences.

Methods: We collected information from patient's clinical file (history, physical examination, complementary diagnostic tests and therapeutic, from the first appointment ever on the heart failure clinic and the first appointment between May 1st and July 30th 2012. Statistical analysis was performed and the results presented as tables.

Results: We studied 242 patients, 187 Portuguese and 55 Mozambicans. Overall, Portuguese presented with less severe NYHA class at admission ($p < 0.001$), but had higher proportion of co-morbidities (except renal insufficiency and HIV infection). Ischemic, familial and alcoholic etiologies were more prevalent on Portuguese patients, whereas valvular, hypertensive and peripartum etiologies were more frequent on Mozambicans. No statistical difference was found regarding HIV-associated heart failure ($p = 0.085$). On both populations the angiotensin converting enzyme inhibitor/angiotensin receptor blocker were prescribed to a high percentage of patients, and on a global perspective beta-blockers were the most prescribed drugs in Oporto and diuretics the most prescribed in Maputo, with non-pharmacological treatment unavailable for Mozambicans.

Conclusions: In an unprecedented cross-sectional study we made clear some differences between these two populations that may contribute to improve the approach to heart failure on both clinics.

Keywords: heart failure; epidemiology; ejection fraction; Africa.

Abbreviations / Abreviaturas

	English	Português
ACE	Angiotensin converting enzyme	Enzima de conversão da angiotensina
AF	Atrial fibrillation	Fibrilação auricular
ARB	Angiotensin receptor blocker	Antagonista do recetor da angiotensin
BMI	Body mass index	Índice de massa corporal
BNP	B-type natriuretic peptide	Peptídeo natriurético tipo B
CABG	Coronary artery bypass graft	Cirurgia de pontagem aorto-coronária
CAD	Coronary artery disease	Doença das artérias coronárias
DM	Diabetes mellitus	Diabetes mellitus
ECG	Electrocardiogram	Eletrocardiograma
ESC	European Society of Cardiology	Sociedade Europeia de Cardiologia
GFR	Glomerular filtration rate	Taxa de filtração glomerular
HF	Heart failure	Insuficiência cardíaca
LMCA	Left main coronary artery	Tronco coronário comum
LV-EF	Left ventricle ejection fraction	Fração de ejeção do ventrículo esquerdo
MRA	Mineralocorticoid receptor antagonist	Antagonista do recetor mineralocorticóide
NYHA	New York Heart Association	<i>Sem tradução</i>
PCI	Percutaneous coronary intervention	Intervenção coronária percutânea
VF	Ventricular fibrillation	Fibrilação ventricular
VT	Ventricular tachycardia	Taquicardia ventricular

Introduction

Heart failure (HF) is a major health problem as it is common, disabling and associated with high morbidity and mortality, despite being highly treatable¹⁻³. It can be defined as an abnormality of cardiac structure, function or both, leading to the inability of the heart to pump enough blood to meet the body's demand of oxygen, despite normal filling pressures (or only at the expense of increased filling pressures)^{4,5}. According to the European Society of Cardiology (ESC), HF can be clinically defined as a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function⁶.

The aging population, the increasing prevalence of co-morbidities such as Diabetes Mellitus (DM) and obesity, the decrease in sudden death due to device therapy, and the increasing proportion of patients surviving acute myocardial infarction with substantial left ventricular damage that predisposes to post-infarction HF^{7,8}, all contribute to an epidemiological trend of increasing prevalence of chronic HF during the coming decades^{9,10}.

The diagnosis of HF can be difficult. Many of the symptoms of HF are non-discriminating and, therefore, of limited diagnostic value¹¹⁻¹⁵. Many of the signs of HF result from sodium and water retention and resolve quickly with diuretic therapy, i.e. may be absent in patients receiving such treatment. Demonstration of an underlying cardiac cause is therefore central to the diagnosis of HF. This is usually myocardial disease causing systolic ventricular dysfunction. However, abnormalities of ventricular diastolic function or of the valves, pericardium, endocardium, heart rhythm and conduction can also lead to HF (and more than one abnormality can be present). Identification of the underlying cardiac problem is also crucial for therapeutic reasons, as the precise pathology determines the specific treatment used⁶.

Up to 80% of first-diagnoses of heart failure occur at the time of hospitalisation, over 40% of patients in the community with heart failure have been hospitalised within the previous year and one-third of patients with heart failure will be hospitalised within any given year, reflecting the more severe end of the disease spectrum in terms of morbidity and mortality. In-hospital mortality is approximately 20% and many patients with heart failure will die or be re-hospitalised (10-30% or more) within the following 6 months¹⁶⁻¹⁹.

Although the causes of heart failure vary within and between African countries, the pathogenesis remains largely nonischemic (98%), with hypertension, rheumatic heart disease and cardiomyopathy accounting for 65% of cases, whereas tuberculous pericarditis and pulmonary heart disease account for the remainder. In the study performed by Mayosi BM²⁰, the diagnosis of myocardial infarction was made in only 2% of cases, which confirms the observation that coronary artery disease (CAD) remains uncommon in black Africa. Unlike other parts of the world in which cardiomyopathies are rare, dilated cardiomyopathy is a major cause of heart failure throughout Africa. Similarly, peripartum cardiomyopathy is ubiquitous on the continent, with an incidence ranging from 1 in 100 to 1 in 1000 deliveries²¹⁻²³. Nowadays, cardiovascular diseases account for 7-10% of all medical admissions to hospital, with heart failure contributing to 3-7%^{24,25}.

In Portugal, the EPICA study showed a HF prevalence of 4.4% amongst adults older than 25 years old, with a mean age of 65 years old, a preponderance among women (63.3%), 1.3% had left ventricular systolic dysfunction and 1.7% didn't have. EPICA studied also estimated that nearly 36% of Portuguese patients older than 60 years old had HF. This study also made clear that hypertension is the leading cause of HF in Portugal (66%), followed by CAD (40%) and major valvular disease (26%)²⁶.

Our aim was to compare two populations of HF patients, one from an European country and other from Africa, in order to understand their clinical, etiological and treatment differences.

Methods

This is an observational retrospective study that intends to evaluate on two different moments of time the clinical characteristics of the patients from two HF clinics, one from Maputo (outpatient clinic of the Cardiac Department of the Maputo Central Hospital, Mozambique) and the other from Oporto (outpatient clinic of the Cardiac Department of the Hospital São João, Portugal). The first moment corresponds to the patient's first appointment on the HF clinic on the period between May 1st and July 30th 2012, and those patients' clinical files were studied to gather information about the second moment studied (their first appointment on the HF clinic from all time). All the information was obtained from the patient's clinical file after the appointment on HF Clinic. If a patient came to an appointment twice or more on the period between May 1st and July 30th 2012 only the first appointment was considered and the subsequent ones excluded.

Nearly 100 variables were collected from history, physical examination, Electrocardiogram (ECG), echocardiography, myocardial perfusion scintigraphy, coronary angiography, stress ECG, blood tests and pharmacological or non-pharmacological treatment.

Regarding the statistical analysis, continuous variables are described as median values and corresponding 25th and 75th percentiles. Dichotomous variables are reported as absolute numbers and percentages. To evaluate the characteristics of differences between the populations studied, Chi-square tests, Mann Whitney U tests or Fischer tests were applied as appropriate. All calculations were performed using IBM SPSS Statistics version 21.0 software package. For all tests a p value of 0.05 or less (two-sided) was considered statistically significant.

Ethical approval for the study was sought from the local Ethical Committee and permission confirmed through the relevant administrative bodies. The study conformed to the principles outlined in the Declaration of Helsinki.

Results

Demographic profile

There were more individuals from Portugal (147 – 72%), generally older than the ones from Mozambique (median: 60, 25-75 percentile: 49-67 vs. median: 53, 25-75 percentile: 38.5-61, respectively), with a high proportion of male patients in Portugal (131 – 70.1%) and similar gender distribution in Mozambique.

Co-morbidities

Overall, Portuguese individuals were found to have a higher proportion of co-morbidities, as shown in Table 1, except from renal insufficiency (35 – 63.6% in Mozambique vs. 50 – 30.5% in Portugal; $p<0.001$) and HIV infection (8 – 15.1% in Mozambique vs. 3 – 1.8% in Portugal; $p<0.001$) whose proportion was found to be greater in Mozambique. From the co-morbidities studied, no statistical difference was found on hypertension ($p=0.894$), hepatic dysfunction ($p=1.000$), presence of actual or past atrial fibrillation (AF) or flutter ($p=0.641$), previous episodes of emboli ($p=0.338$) and previous hospital admissions ($p=0,087$). No statistical inference was possible to be made regarding myocardium ischemia (on stress electrocardiogram or myocardium perfusion scintigraphy) and CAD

(on coronary angiography), as none of the individuals from Mozambique was submitted to the clinical test to evaluate so.

Heart failure etiology

Table 2 summarizes the differences found regarding HF etiology. Ischemic (46 – 28.9% in Portugal vs. 1 – 2.0% in Mozambique; $p<0.001$), familial (26 – 16.4% in Portugal vs. 0 – 0% in Mozambique; $p=0.002$) and alcoholic (17 – 10.7% in Portugal vs. 0 – 0% in Mozambique; $p<0.015$) etiologies were more prevalent on Portuguese patients, whereas valvular (10 – 19.6% in Mozambique vs. 3 – 1.9% in Portugal; $p<0.001$), hypertensive (13 – 25.5% in Mozambique vs. 2 – 1.3% in Portugal; $p<0.001$) and peripartum (5 – 9.8% in Mozambique vs. 0 – 0% in Portugal; $p<0.001$) etiologies were more frequent on Mozambican patients. Regarding HIV-associated HF no significantly statistical difference was found ($p=0.085$).

Clinical aspects

Table 3 summarizes the clinical aspects gathered from physical examination, echocardiography 2D and ECG. In what concerns New York Heart Association (NYHA) class, the most used classification for clinical categorizing of HF, we demonstrated that there were a significantly statistical difference between the populations on presentation to HF clinic ($p<0.001$) but that difference ceased to exist when the patients were evaluated on their last appointment ($p=0.342$). It is also possible to see that while in Oporto most patients were on NYHA class I and II (141 – 58.3% vs. 14 – 5.8% on classes III or IV) on their first appointment, on Maputo the majority of patients presented on NYHA class III or IV (39 – 70.9% vs. 9 – 16.4% on classes I or II).

The blood pressure profile of this groups showed that the Portuguese population has globally better control over this risk factor, as they had lower systolic (median: 110, 25-75 percentile: 100-130 in Oporto vs. median: 120, 25-75 percentile: 110-139, in Maputo; $p=0.006$) and diastolic (median: 70, 25-75 percentile: 60-80 in Oporto vs. median: 80, 25-75 percentile: 70-89, in Maputo; $p<0.001$) blood pressures.

Mitral regurgitation was also a situation more frequent in Maputo than in Oporto, both on auscultation of the respective murmur (25 – 46.3% vs. 7 – 3.9%; $p<0.001$, respectively) and on the evaluation by echocardiogram (28 – 51.9% vs. 24 – 15.2%; $p<0.001$, respectively).

Regarding blood tests, it was not possible to establish a comparison of B-type natriuretic peptide (BNP) values between the populations as this was not evaluated in none of the patients from Maputo.

Pharmacological treatment

In what concerns pharmacological treatment (Table 4), on presentation to HF clinic most patients had already some treatment prescribed by other doctors, being the most prescribed drugs in Oporto beta-blockers (73.8%), angiotensin converting enzyme (ACE) inhibitors (61.0%) and diuretics (56.1%), in opposition to Maputo where the most prescribed drugs before presentation to HF clinic were diuretics (72.2%), ACE inhibitors (50.0%) and digitalis (42.6%).

On the last appointment, we were able to show a different pattern on drugs prescribed, with beta-blockers (84.6%), ACE inhibitor/angiotensin receptor blocker (ARB) (81.2%), diuretics (72.4%) and statins (67.4%) being the most prescribed drugs to patients in Oporto, in opposition to diuretics (92.7%), ACE inhibitors/ARB (81.8%), digitalis (54.5%) and beta-blockers (47.3%) which were the ones most prescribed in Maputo.

Non-pharmacological treatment

The most prominent aspect on Table 5 is that none of the patients from Maputo had undergone any of the non-pharmacological treatments studied. In Oporto, it was frequent that patients had resynchronizing devices (46 – 26.0%) or defibrillators (48 – 27.3%) implanted, and there were more patients who have been submitted to heart transplant surgery (12 – 6.8%) than the ones submitted to coronary artery surgery (11 – 6.3%) and valvular surgery (7 – 4.0%).

Discussion

In an unprecedented cross-sectional study, we aimed to compare the characteristics of HF patients between an African and an European HF clinic, considering characteristics of the disease itself, the patient's co-morbidities and clinical status and the approach used on diagnosis and treatment of these patients. A total of 242 patients were studied, 187 from Oporto and 55 from Maputo. In Portugal the patients were older and 70.1% were man, while in Maputo there was a more homogenous distribution regarding gender.

We also found a higher prevalence within the Portuguese population of risk factors and co-morbidities (with the exception of HIV infection and renal insufficiency that are more prevalent in Maputo), which may be related to economic and social development of Mozambique, one of the poorer countries in the world.

While our data did not provide a complete picture of the etiology of the HF, it is conceivable that we made clear some differences between these populations. A similar amount of patients was categorized as having idiopathic HF, but there was a clear preponderance of ischemic, familial and alcoholic causes on Portuguese population in opposition with valvular and hypertensive heart diseases in Mozambicans, as expected²⁷, and peripartum etiology was also more common among Mozambicans. HIV-related HF was more prevalent in Mozambique but this result lacks statistical significance.

Differences have also been made clear when it comes to the first appointment on the HF clinic, as only 1 (0.6%) Portuguese patient presented with NYHA class IV in opposition to 23 (47.9%) Mozambican patients and 54 (34.8%) Portuguese patients presented with NYHA class I in opposition to Mozambique where none of the patients presented with such NYHA class. This may be the reflex of both clinical follow-up for patients with risk factors and co-morbidities, and to a better access to health care services in Portugal. On the other hand no significant difference was found on the NYHA class on the last appointment, meaning that even with limited resources Mozambican patients become as little symptomatic as the Portuguese ones.

However, Mozambican patients showed a more accentuated left ventricle ejection fraction (LV-EF) recovery. This may be related to the institution of the correct treatment for HF, namely increased use of beta-blockers and also to the fact that peripartum cardiomyopathy frequently shows EF recovery. However, in the absence of a central validation of the echocardiograms performed at

each center, caution is needed in the interpretation of this parameter. Even so, other variables suggest that the population from Portugal has a more severe disease, as the more prolonged QRS interval, and higher percentage of patients with left bundle brunch block.

A curious finding was that even though there were a similar percentage of patients with actual or past AF/flutter, with higher usage of hypocoagulants and antiaggregants on the Portuguese population, there were a similar number of embolic events. Probably, that can be related with a lower CHA2DS2-VASc Score for Atrial Fibrillation Stroke Risk, with lower embolic risk, as the population is younger, with lower incidence of DM and CAD.

It also became clear the difference of approaches used with patients before and after being evaluated on a HF clinic. We observed that prior to first appointment on HF clinic both populations were on a drug therapy with similar proportion of ACE inhibitors prescribed but with ARB, beta-blocker and mineralocorticoid receptor antagonists (MRA) being more used in Portugal and diuretic and digitalis being more used in Maputo (all differences are statistically significant). When it comes to the drugs prescribed on last appointment, the proportion of ACE inhibitor/ARB was high and similar on both clinics, but there were significantly differences on other drugs: diuretics and digitalis were still more prescribed to Mozambican patients, while beta-blockers, MRA, statins, hypocoagulants, antiaggregants and nitrates were more prescribed to Portuguese patients. The higher prevalence of ischemic heart disease among the Portuguese patients may explain some of these differences. Oral antidiabetics were also more prescribed on Oporto, but we must have in consideration that in our study the prevalence of DM on Oporto was superior to Maputo's prevalence. No difference was found on the use of calcium channel blockers, antiarrhythmic or insulin, with low percentages of use of these drugs.

Besides pharmacological treatment, when it comes to HF there is also the possibility to use non-pharmacological approaches, and in the setting of this study the use of these other approaches revealed that none of the Mozambican patients studied have ever been submitted to a non-pharmacological way of treatment, as these techniques are expensive and therefore are not available for Mozambican patients, who live in one of the poorer countries in the world.

This study has several limitations, starting with the size of the samples, especially the one from Maputo that may not be representative of the populations. Both clinics are situated on central

hospitals which, especially on Mozambique may lead to selection bias on the patients involved. The absence of a core lab for validation of the Echocardiograms is also a significant limitation.

Conclusion

We consider that the purpose of this study was achieved as it was possible to make clear the differences between these two populations.

Mozambican patients generally presented to the HF clinic with more severe NYHA class, usually III and IV, while the Portuguese patients usually presented with NYHA class I and II. Despite this, Mozambican patients were able to become as little symptomatic as the Portuguese ones with fewer resources, which may be explained by the fact that they had higher EF and better recovery of the LV-EF.

The difference between HIV-related HF on both populations did not prove to be as higher as expected, as no statistical difference was found.

Different approaches are used regarding pharmacological treatment, as even though the similar proportion of ACE inhibitors/ARB prescribed by both clinics, in Portugal beta-blockers, MRA, statins, hypocoagulants, antiaggregants and nitrates were more prescribed, whereas on Maputo there was a higher percentage of prescription of diuretics and digitalis. We also noticed that non-pharmacological approaches are still unavailable for Mozambican patients.

However, considering the limitations mentioned, it would be of greater interest to repeat this study, with bigger samples of the population for a longer period time, as it may help to clarify if some results are real or derived from biases.

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Tables

Table 1 – Co-morbidities and risk factors

	Population of origin		<i>p</i> value	Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)		
Hypertension, n (%)	80 (47.3)	25 (46.3)	0.894	19 (7.9)
Diabetes mellitus, n (%)	50 (29.2)	1 (1.9)	<0.001	17 (7.0)
Renal insufficiency, n (%)	57 (30.5)	35 (63.6)		73 (30.2)
Stage 1, n (%)	0 (0)	0 (0)		73 (30.2)
Stage 2, n (%)	39 (68.4)	18 (51.4)	<0.001	73 (30.2)
Stage 3, n (%)	12 (21.1)	16 (45.7)		73 (30.2)
Stage 4, n (%)	3 (5.3)	1 (2.9)		73 (30.2)
Stage 5, n (%)	3 (5.3)	0 (0)		73 (30.2)
Hepatic dysfunction, n (%)	1 (0.8)	0 (0)	1.000	61 (25.2)
Dyslipidemia, n (%)	109 (59.6)	3 (5.6)	<0.001	5 (2.1)
Weight				
Overweight, n (%)	53 (37.3)	12 (22.6)	<0.001	47 (19.4)
Obesity, n (%)	45 (31.7)	10 (18.9)	<0.001	47 (19.4)
Smoke, n (%)	74 (43.5)	0 (0)	<0.001	20 (8.3)
Alcohol abuse, n (%)	55 (33.1)	-	-	92 (35.7)
HIV, n (%)	3 (1.8)	8 (15.1)	<0.001	20 (8.3)
AF/flutter -actual or past, n (%)	48 (27.3)	13 (24.1)	0.641	12 (5.0)
VT/VF – history of, n (%)	35 (19.8)	0 (0)	0.001	11 (4.5)
Emboli, n (%)	13 (7.4)	2 (3.7)	0.338	12 (5.0)
Myocardium ischemia, n (%)	144 (81.4)	-	-	65 (26.9)
Coronary artery disease, n (%)	36 (14.9)	-		173 (71.5)
Disease of 1 artery, n (%)	15 (22.1)	-		173 (71.5)
Disease of 2 arteries, n (%)	9 (13.2)	-	-	173 (71.5)
Disease of 3 arteries, n (%)	9 (13.2)	-		173 (71.5)
Disease of LMCA, n (%)	3 (4.4)	-		173 (71.5)

Table 1 – Co-morbidities and risk factors (cont.)

	Population of origin		<i>p</i> value	Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)		
Hospital admissions				
1 admission, n (%)	39 (76.5)	15 (88.2)		190 (73.6)
2 admissions, n (%)	10 (19.6)	0 (0)	0.087	190 (73.6)
≥ 3 admissions, n (%)	2 (3.9)	2 (11.8)		190 (73.6)

AF: atrial fibrillation; LMCA: Left main coronary artery; VF: ventricular fibrillation; VT: ventricular tachycardia.

Renal insufficiency stages are defined by the Glomerular Filtration Rate (GFR): stage 1 – GFR ≥ 90mL/min/1.73m²; stage 2 – GFR between 60-89mL/min/1.73m²; stage 3 – GFR between 30-59mL/min/1.73m²; stage 4 – GFR between 15-29 mL/min/1.73m²; stage 5 – GFR < 15mL/min/1.73m² or patient on dialysis.

Overweight is defined by the World Health Organization as having a BMI ≥ 25,00kg/m².

Obesity is defined by the World Health Organization as having a BMI ≥ 30,00kg/m².

Table 2 – Heart failure etiology

	Population of origin			Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)	<i>p</i> value	
Idiopathic, n (%)	48 (30.2)	17 (33.3)	0.673	32 (13.2)
Ischemic, n (%)	46 (28.9)	1 (2.0)	<0.001	32 (13.2)
Familial, n (%)	26 (16.4)	0 (0)	0.002	32 (13.2)
Alcoholic, n (%)	17 (10.7)	0 (0)	0.015	32 (13.2)
Neuromuscular, n (%)	2 (1.3)	0 (0)	0.421	32 (13.2)
Valvular, n (%)	3 (1.9)	10 (19.6)	<0.001	32 (13.2)
Hypertensive, n (%)	2 (1.3)	13 (25.5)	<0.001	32 (13.2)
HIV, n (%)	1 (0.6)	2 (3.9)	0.085	32 (13.2)
Peripartum, n (%)	0 (0)	5 (9.8)	<0.001	32 (13.2)
Other etiologies, n (%)	14 (8.8)	3 (5.9)	0.506	32 (13.2)

Table 3 – Clinical aspects

	Population of origin		<i>p</i> value	Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)		
<i>First appointment</i>				
NYHA class				
Class I, n (%)	54 (34.8)	0 (0)	<0.001	39 (16.1)
Class II, n (%)	87 (56.1)	9 (18.8)		39 (16.1)
Class III, n (%)	13 (8.4)	16 (33.3)		39 (16.1)
Class IV, n (%)	1 (0.6)	23 (47.9)		39 (16.1)
Ecocardiography 2D				
LV-EF, % median (P25 - P75)	30.0 (24-42)	35.0 (28-42)	0.261	66 (29.7)
<i>Last appointment</i>				
NYHA class				
Class I, n (%)	67 (39.9)	20 (37)	0.342	20 (8.3)
Class II, n (%)	86 (51.2)	25 (46.3)		20 (8.3)
Class III, n (%)	14 (8.3)	9 (16.7)		20 (8.3)
Class IV, n (%)	1 (0.6)	0 (0)		20 (8.3)
LV-EF, % median (P25 - P75)	33.0 (26.0-45.0)	45.2 (34.3-59.2)	0.003	69 (28.5)
Systolic blood pressure, mmHg median (P25 - P75)	110 (100-130)	120 (110-139)	0.006	16 (6.6)
Diastolic blood pressure, mmHg median (P25 - P75)	70 (60-80)	80 (70-89)	<0.001	16 (6.6)
Heart rate, bpm median (P25 - P75)	70 (62-79)	80 (70-90)	<0.001	43 (17.8)
Pulmonary congestion, n (%)	23 (12.6)	2 (3.7)	0.061	6 (2.5)
Systemic congestion, n (%)	23 (12.6)	11 (20.4)	0.155	6 (2.5)
Cold extremities, n (%)	0 (0)	0 (0)	-	8 (3.3)

Table 3 – Clinical aspects (cont.)

	Population of origin		<i>p</i> value	Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)		
Murmur of mitral regurgitation, n (%)	7 (3.9)	25 (46.3)	<0.001	7 (2.9)
Other murmurs, n (%)	31 (17.1)	10 (18.5)	0.813	7 (2.9)
<i>ECG</i>				
Sinus rhythm, n (%)	138 (77.5)	45 (84.9)	0.245	11 (4.5)
QRS duration, ms	128.5	86.0	p<0.001	15 (6.2)
median (P25 - P75)	(102.0-159.0)	(80.0-112.0)		
Left bundle branch block, n (%)	89 (51.1)	10 (18.2)	<0.001	13 (5.4)
<i>Ecocardiography 2D</i>				
Left auricle diameter in parasternal long axis, mm	46.0 (42.0-49.0)	45.5 (37.8-51.0)	0.817	36 (14.9)
median (P25 - P75)				
Left ventricular end diastolic diameter, mm	60.0 (52.0-65.0)	62.0 (54.1-67.5)	0.115	29 (12.0)
median (P25 - P75)				
Left ventricular end systolic diameter, mm	44.0 (31.5-55.5)	50.0 (36.9-57.3)	0.248	151 (62.4)
median (P25 - P75)				
Shortening fraction, %	25.2 (17.7-39.4)	23.0 (16.0-29.8)	0.087	169 (69.8)
median (P25 - P75)				
Preserved right ventricle function, n (%)	140 (89.7)	38 (70.4)	<0.001	32 (13.2)
Deteriorated right ventricle function, n (%)	16 (10.3)	16 (29.6)	<0.001	32 (13.2)
Moderate to severe mitral regurgitation, n (%)	24 (15.2)	28 (51.9)	<0.001	30 (12.4)

Table 3 – Clinical aspects (cont.)

	Population of origin		<i>p</i> value	Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)		
<i>Blood tests</i>				
Hb, mg/dL median (P25 - P75)	13.8 (12.9-14.9)	12.3 (10.5-13.3)	<0.001	40 (16.5)
Na, mEq/L median (P25 - P75)	139.0 (137.0 – 140.0)	139.0 (136.3 – 143.8)	0.324	30 (12.4)
K, mEq/L, median (P25 - P75)	4.5 (4.2 – 4.83)	4.4 (4.1- 4.7)	0.097	33 (13.6)
Uric acid, mg/dL median (P25 - P75)	6.4 (5.4-7.8)	6.8 (5.3-9.8)	0.305	94 (38.8)
Urea, mg/dl median (P25 - P75)	43.0 (34.5-54.5)	33.0 (22.5-51.0)	<0.001	40 (16.5)
Creatinine, mg/dL median (P25 - P75)	0.9 (0.8-1.1)	1.1 (0.9-1.4)	0.006	47 (19.4)
Creatinine clearance, mL/min median (P25 - P75)	91.0 (71.7-121.0)	71.2 (55.3-84.5)	<0.001	73 (30.2)
Liver dysfunction, n (%)	1 (0.8)	0 (0)	0.536	77 (29.8)
BNP, pg/mL median (P25 - P75)	139.8 (51.3 – 457.6)	- ^a	-	75 (31.0) ^b

BNP: B-type natriuretic peptide; ECG: Electrocardiogram; LV-EF: Left ventricle ejection fraction; NYHA: New York Heart Association.

^a – the test was not performed on any patient; ^b – only considering patients from Oporto

Table 4 – Pharmacological treatment

	Population of origin		<i>p</i> value	Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)		
<i>Before first appointment</i>				
ACE inhibitor, n (%)	100 (61.0)	27 (50.0)	0.156	24 (9.9)
ARB, n (%)	25 (15.2)	0 (0)	0.002	24 (9.9)
Beta blocker, n (%)	121 (73.8)	6 (11.1)	<0.001	24 (9.9)
Diuretic, n (%)	92 (56.1)	39 (72.2)	0.036	24 (9.9)
MRA, n (%)	45 (27.4)	0 (0)	<0.001	24 (9.9)
Digitalis, n (%)	19 (11.6)	23 (42.6)	<0.001	24 (9.9)
<i>Prescribed on last appointment</i>				
ACE inhibitor/ARB, n (%)	147 (81.2)	45 (81.8)	0.920	6 (2.5)
Beta blocker, n (%)	154 (84.6)	26 (47.3)	<0.001	5 (2.1)
Diuretic, n (%)	131 (72.4)	51 (92.7)	0.002	6 (2.5)
MRA, n (%)	82 (45.3)	1 (1.8)	<0.001	6 (2.5)
Digitalis, n (%)	26 (14.4)	30 (54.5)	<0.001	6 (2.5)
Ivabradine, n (%)	12 (6.6)	0 (0)	0.050	6 (2.5)
Statin, n (%)	122 (67.4)	3 (5.5)	<0.001	6 (2.5)
Hypocoagulants, n (%)	52 (28.7)	2 (3.6)	<0.001	6 (2.5)
Antiaggregants, n (%)	63 (34.8)	4 (7.3)	<0.001	6 (2.5)
Nitrates, n (%)	27 (14.9)	0 (0)	0.002	6 (2.5)
Calcium channel blockers, n (%)	25 (13.8)	8 (14.5)	0.891	6 (2.5)
Antiarrhythmic, n (%)	13 (7.2)	1 (1.8)	0.140	6 (2.5)
Insulin, n (%)	8 (4.4)	0 (0)	0.113	6 (2.5)
Oral antidiabetics, n (%)	38 (21.0)	1 (1.8)	0.001	6 (2.5)
ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; MRA: mineralocorticoid receptor antagonist.				

Table 5 – Non-pharmacological treatment

	Population of origin		<i>p</i> value	Patients not in the analysis (n)
	Oporto (n=187)	Maputo (n=55)		
Pacing, n (%)	46 (26.0)	0 (0)	-	10 (4.1) ^a
Defibrillator, n (%)	48 (27.3)	0 (0)	-	11 (4.5) ^a
PCI, n (%)	26 (14.9)	0 (0)	-	12 (5.0) ^a
CABG, n (%)	11 (6.3)	0 (0)	-	12 (5.0) ^a
Valvular surgery, n (%)	7 (4.0)	0 (0)	-	12 (5.0) ^a
Transplant, n (%)	12 (6.8)	0 (0)	-	10 (4.1) ^a

CABG – coronary artery bypass graft; PCI – percutaneous coronary intervention.

^a – only considering patients from Oporto

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Imagem	TIFF	.tif	Tamanho máximo 10MB
Audio	MP3	.mp3	Tamanho máximo 10MB
Video	WMV	.wmv	Tamanho máximo 30MB

ANEXO I

DECLARAÇÃO

Declaro que autorizo a publicação do manuscrito:

Ref.^a

Título

.....

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do qual sou autor ou c/autor:

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Do mesmo modo, este tipo de material deverá cumprir também todos os requisitos e responsabilidades éticas gerais descritas nessas normas.

O Corpo Redactorial reserva-se o direito de recusar o material electrónico que não julgue apropriado.

ANEXO II

Símbolos, abreviaturas de medidas ou estatística

Designação	Português	Inglês
Ampere	A	A
Ano	ano	yr
Centímetro quadrado	cm ²	cm ²
Contagens por minuto	cpm	cpm
Contagens por segundo	cps	cps
Curie	Ci	Ci
Electrocardiograma	ECG	ECG
Equivalente	Eq	Eq
Grau Celsius	°C	°C
Grama	g	g
Hemoglobina	Hb	Hb
Hertz	Hz	Hz
Hora	h	h
Joule	J	J
Litro	L ou l	l ou L
Metro	m	m
Minuto	min	min
Molar	M	M
Mole	mol	mol
Normal (concentração)	N	N
Ohm	Ω	Ω
Osmol	osmol	osmol
Peso	peso	WT
Pressão parcial de CO ₂	pCO ₂	pCO ₂
Pressão parcial de O ₂	pO ₂	pO ₂
Quilograma	kg	kg
Segundo	s	sec
Semana	Sem	Wk
Sistema nervoso central	SNC	CNS
Unidade Internacional	UI	IU
Volt	V	V
Milivolt	mV	mV
Volume	Vol	Vol
Watts	W	W
Estatística:		
Coefficiente de correlação	r	r
Desvio padrão (standard)	DP	SD
Erro padrão (standard) da média	EPM	SEM
Graus de liberdade	gl	df
Média	X	X
Não significativa	NS	NS
Número de observações	n	n
Probabilidade	p	p
Teste «t» de Student	teste t	t test