

Effect of Gender in Echocardiographic Parameters in Dilated Cardiomyopathy in Angola

Ana Feijão¹, Savarino Victória Pereira¹, Mário Fernandes¹ and Humberto Morais^{2*}

¹Serviço de Cardiologia, Hospital Américo Boavida, Avenida Hoji Ya Henda, Luanda, República de Angola

²Departamento de Cardiologia, Hospital Militar Principal, Rua D. Manuel I, Luanda, República de Angola

*Corresponding Author: Humberto Morais, Departamento de Cardiologia, Hospital Militar Principal, Rua D. Manuel I, Luanda, República de Angola.

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Abstract

Introduction: Data addressing gender-based differences in dilated cardiomyopathy are scarce.

Purpose of the Study: This study was aimed to report the effect of gender in demographic and echocardiographic characteristics of patients with dilated cardiomyopathy (DMC) in Angola.

Patients and Method: We conducted a retrospective analysis of the echocardiograms of all consecutive patients with DCM presented to the echocardiographic laboratory of Hospital Américo Boavida from 2011 to 2018. Echocardiographic procedures and measurements were made according to the American Society of Echocardiography guidelines. Characteristics including age, sex, and echocardiographic parameters including left atrial area, septal and left ventricle posterior wall thickness; left ventricular diameters, and left ventricular ejection fraction, tricuspid anterior systolic excursion and E/e' ratio were analyzed. Results: We enrolled 1431 patients with a mean age of 35,4 ($\pm 10,0$) years. 776 (54,2%) were female. Women had significantly smaller LV cavity size ($67,59 \pm 5,26$ mm vs $70,65 \pm 6,51$ mm, $p < 0,001$), higher LVEF ($28,00\% \pm 4,89\%$ vs $21,52\% \pm 5,28\%$, $p < 0,001$), lower E/e' ratio ($14,10 \pm 2,88$ vs $18,47 \pm 4,48$, $p < 0,001$) and lower left atrial (LA) area ($23,68 \pm 2,65$ cm² vs $24,26 \pm 2,74$ cm², $p < 0,001$).

Conclusion: Our results suggest that women with dilated cardiomyopathy have smaller left ventricles, better left ventricular systolic and diastolic function than men.

Keywords: Dilated Cardiomyopathy; Heart Failure; Echocardiography; Sex Hormones

Introduction

Heart failure (HF) is a major public health problem worldwide [1], in sub-Saharan Africa (SSA), the predominant causes have traditionally been ascribed to rheumatic heart disease, hypertensive heart disease and cardiomyopathy [2]. Dilated cardiomyopathy (DMC) a primary disorder of heart muscle, which is characterized by dilatation and impaired contraction of the chambers of the heart, accounts for 10-17% of cardiac conditions encountered at necropsy and for 20% of patients who are admitted to hospital for heart failure [2].

Gender-based differences in the management and outcomes of cardiovascular disease have been established in humans and in animal models [3-8]. In women, heart failure (HF) is associated more with left ventricular (LV) diastolic dysfunction than in men with an increased incidence of cardiovascular disease in postmenopausal suggesting that ovarian hormones may play a role in this cardioprotection [9], whereas LV systolic dysfunction is the predominant cause of HF in men [10].

Data addressing the differences between genders in dilated cardiomyopathy are scarce [11-14].

Aim of the Study

The aim of this study was to report the effect of gender in demographic and echocardiographic characteristics of patients with dilated cardiomyopathy in an SSA country.

Patients and Methods

Here, we conducted a retrospective analysis of the echocardiograms of all consecutive patients with DCM presented to the echocardiographic laboratory of Hospital Américo Boavida from 2011 to 2018. Institutional review board permission was obtained.

Demographic variables including age, sex, and echocardiographic parameters such as left atrial area, ventricular septal and left ventricle posterior wall thickness, left ventricular diameters, left ventricular ejection fraction, tricuspid anterior systolic excursion and E/e' ratio were analyzed. Echocardiography was performed using commercially available equipment (Mindray DC-T6 Diagnostic Ultrasound System, with a P4-2 transducer).

Echocardiographic procedures and measurements were performed according to the American Society of Echocardiography (ASE) guidelines. M-mode echocardiograms were derived from two-dimensional (2D) images. The M-mode cursor on the 2D scan was moved to specific areas of the heart to obtain measurements, according to the recommendation of the committee on M-mode standardization of the ASE. From the M-mode measurements, left ventricular end-diastolic diameter (LVDD), left ventricular end-systolic diameter (LVSD), posterior wall thickness (PWT) and ventricular septal thickness (VST) (in tele-diastole) were measured. Ejection fraction was calculated by using the Simpson's method. Maximal left atrial area (LAA) was measured using the planimetry using 2D images from the apical 4- and 2-chamber views. For assessing RV function, tricuspid anterior plane systolic excursion (TAPSE) was used.

Pulsed wave Doppler imaging of mitral inflow and tissue Doppler imaging (TDI) of mitral annular motion at the septum were also performed to assess LV diastolic function. Peak velocities of early (E) and late (A) diastolic flow, E/A ratio, and early flow deceleration time were measured from pulsed wave Doppler imaging of mitral inflow. Early (e') and late (a') diastolic annular velocities were measured from TDI. The ratio of mitral E to TDI e' was also calculated using these measurements. Echocardiography examinations also included assessment of valvular architecture, a semi-quantitative estimate of the severity of valvular regurgitation, and determination of the presence of pericardial effusion. Other abnormalities, such as evidence of pulmonary arterial hypertension, intraventricular spontaneous contrast and thrombus were also noted [15,16].

Exclusion criteria: Patients with history of hypertension, diabetes mellitus, ischemic heart disease and valvular heart disease were excluded.

Statistical analysis

Descriptive statistics were expressed as absolute and relative frequencies, averages and respective standard deviations (SD). To analyze the gender differences, the Student's t-test was used for independent samples when the dependent variables were of the quantitative type, and the Qui-square tests of independence or the Fisher's test when the variables were qualitative. P value is considered significant if it is found to be < 0.05. The data were analyzed using the SPSS (Statistical Package for the Social Sciences) version 25.0 for Windows.

Results

Demographic and echocardiographic characteristics are illustrated in table 1. We enrolled 1431 patients the average age was 35,41 ($\pm 10,0$) years. 655 (45,8%) were male and 776 (54,2%) were female. No statistical differences in average age between the genders was found (35,38 \pm 9,73 years in men 35,43 \pm 10,24 years in women; $p = 0.925$).

Regarding left chambers, in women, left atrial (LA) area (23,68 \pm 2,65 cm² vs 24,26 \pm 2,74 cm², $p < 0,001$) and the E/e' ratio (14,10 \pm 2,88 vs 18,47 \pm 4,48, $p < 0,001$), a surrogate of left ventricular filling pressure value was significantly lower, as well as the left ventricular

	Total (n -1431)	Male (n - 655)	Female (n -776)	p Value
Age (Y) range (Mean ± SD)	15 - 67 (35,41 ± 10,0)	15 - 67 (35,38 ± 9,73)	18 - 66 (35,43 ± 10,24)	.925
LVDD* (mm)	69,99 ± 6,06	70,65 ± 6,51	67,59 ± 5,26	.001**
IVST* (mm)	8,77 ± 1,23	8,83 ± 1,15	8,72 ± 1,30	.094
PWT* (mm)	8,71 ± 1,25	8,76 ± 1,16	8,67 ± 1,33	.151
LVEF* (%)	25,03 ± 6,00	21,52 ± 5,28	28,00 ± 4,89	.001**
LA* (cm ²)	23,95 ± 2,70	24,26 ± 2,74	23,68 ± 2,65	.001**
E/e' *	16,10 ± 4,28	18,47 ± 4,48	14,10 ± 2,88	.001**
RVDD* (mm)	35,55 ± 3,63	36,00 ± 3,15	35,18 ± 3,97	.001**
TAPSE* (mm)	14,65 ± 1,73	14,68 ± 1,82	14,63 ± 1,65	.611
Mitral regurgitation N (%)				.985
Mild	16 (1,1%)	7 (1,1%)	9 (1,2%)	
Moderate	171 (11,9%)	78 (11,9%)	93 (12,0%)	
Severe	1244 (86,9%)	570 (87,0%)	674 (86,9%)	
Tricuspid regurgitation N (%)				.442
Moderate	64 (4,5%)	26 (4,0%)	38 (4,9%)	
Severe	1367 (95,5%)	629 (96,0%)	738 (95,1%)	
Pulmonary hypertension N (%)				.649
Mild	48 (3,4%)	25 (3,8%)	23 (3,0%)	
Moderate	1032 (72,1%)	468 (71,5%)	564 (72,7%)	
Severe	351 (24,5%)	162 (23,7%)	189 (24,4%)	
Spontaneous contrast N (%)	70 (4,9%)	27 (4,1%)	43 (5,5%)	.222
Thrombus N (%)	127 (8,9%)	56 (8,5%)	71 (9,1%)	.710

Table 1: Demographic and echocardiographic characteristics of the studied patients (n-1431). LVDD - left ventricular diastolic diameter, LVEF: Left Ventricular Ejection Fraction; IVST: Interventricular Septal Thickness, PWT: Posterior Wall Thickness; LA: Left Atrium; RVDD: Right Ventricular Diastolic Diameter; TAPSE: Tricuspid Anterior Plane Systolic Excursion. *Value are expressed in Mean ± SD **Significant p value.

diastolic diameter (67,59 ± 5,26 mm vs 70,65 ± 6,51 mm, $p < 0,001$). The left ventricular ejection fraction was significantly higher (28,00% ± 4,89%; vs 21,52% ± 5,28%, $p < 0,001$). Regarding right chambers the RVDD was also significantly lower in women (35,18 ± 3,97 mm vs 36,00 ± 3,15 mm, $p < 0,001$). No statistical differences were observed in other echocardiographic parameters between genders such as TAPSE, IVST and PWT.

The present study was lacking to show any difference, between the genders, regarding the presence of severe mitral regurgitation, severe tricuspid regurgitation, severe pulmonary hypertension, and presence of intra-ventricular thrombi or spontaneous contrast, in patients with dilated cardiomyopathy.

Discussion

According to the last classification of the cardiomyopathies, dilated cardiomyopathy (DMC) is defined by the presence of left ventricular dilatation and left ventricular systolic dysfunction in the absence of abnormal loading conditions such as hypertension, valve disease

or coronary artery disease sufficient to cause global systolic impairment. Right ventricular dilation and dysfunction may be present but are not necessary for the diagnosis [17].

We studied the effect of gender in echocardiographic parameters in patients with DMC. In this study, the average age (35 years) is significantly lower than those reported in most studies. Halliday, *et al.* [13] and Vitali-Serdoz, *et al.* [14] reported a median age of 52 and 45 years respectively. This difference may be related to the demographic characteristics of the country that has a predominantly young population. According to Angolan census of 2014, 65.5% of the population are less than 25 years of age.

In the present study the predominance of women with a female:male ratio (1:0,8) was higher than those reported by other authors. Halliday, *et al.* [13] concluded that women were more likely to present with heart failure (64.0% vs. 54.5%; $P = 0.007$), Fairweather, *et al.* [12] and Vitali-Serdoz, *et al.* [14] reported a slightly greater prevalence in men than in women with a female/male ratio between 1:1.3 and 1:1.5. Moreover, in a review published in 2018 Pelliccia, *et al.* [18] described that DCM primarily affects males (1:1,5).

Regarding parameters of left ventricular dimensions, in our study women presented smaller LVDD. This finding was in agreement with that reported by Halliday, *et al.* [13] in patients with dilated cardiomyopathy and by Mejhert, *et al.* [19] in patients with systolic heart failure. Moreover, in a review published in 2016 [20] regarding gender differences in left ventricular adaptations to essential hypertension and premenopausal, the authors referred that women had smaller left ventricular diameter but the difference tended to disappear after the menopause. In the other hands, De Maria, *et al.* [11], concluded that women had a longer duration of disease before diagnosis and consequently presented with a greater LV dilatation. Vitali-Serdoz, *et al.* [14] showed a significantly greater left ventricular end diastolic indexed diameter in women compared with men, but a slight smaller end-diastolic volume index, expressing a different left ventricular remodeling and reshaping in women with DCM.

In our study, women presented significant higher left ventricular ejection fraction. This findings is in agreement with that reported by Daimon, *et al.* in healthy subjects [10], by Halliday, *et al.* [13] in patients with CMD, by Duca, *et al.* [21] in patients with heart failure and preserved systolic function. However, Vitali-Serdoz, *et al.* [14] found no significant difference in ejection fraction between genders.

E/e' ratio is probably the most extensively used parameter for estimation of left ventricular filling pressure (LVFP) in daily practice and its prognostic value is widely recognized [22]. Moreover, in healthy subjects no gender related differences in E/e' has been reported [10] An interesting finding that we found is that women had a lower E/e' ratio, and a lower LA area than men. We do not know whether this difference is due to a lower ejection fraction observed in men or, whether if it represents a better diastolic function in women. On the other hand, the fact that these parameters (E/e' ratio and LA area) are higher in men could justify the worse prognosis observed in these group of patients (further studies addressing this issue should be done).

Several factors have been pointed out to justify the differences found between men and women in cardiomyopathies. First, increased levels of estradiol reduce myocyte apoptosis, while increased testosterone levels potentiate it [9,23-27]. Other studies have demonstrated sex differences in gene expression in patients presenting with HF secondary to DCM and these may be responsible for differences in phenotype and outcome. It is also proved that some genetic mutations generate adverse events significantly earlier in males than in females [26] and that it induces a greater prevalence of adverse events and higher mortality in men [27].

Another possible interpretation for different sex related differences can be found in the inflammatory and biochemical remodeling process. A recent study by Meyer, *et al.* that evaluated serum biomarkers related to inflammation, extracellular matrix remodeling, cardiomyocyte stretch, angiogenesis and oxidative stress found that female patients had a better prognosis and their levels of biomarkers related to inflammation and remodeling were significantly lower [28].

Regarding the dimension and function of the right ventricle in our study, we found a significant difference in the RVDD in contrast; there was no difference in TAPSE. This latter finding agrees with that reported by Duca, *et al.* [21], in patients with heart failure and preserved ejection fraction concluded that men had no differences in TAPSE in spite of significant lower left ventricular ejection fraction.

Martínez-Sellés, *et al.* [29] found that RV dysfunction is unusual in patients with dilated cardiomyopathy but RV systolic dysfunction was found almost exclusively in patients with a very low LVEF especially in men. No gender differences in age-related changes in RV parameters were also observed by Daimon, *et al.* in healthy subjects [10].

Finally, Vitali-Serdoz, *et al.* [14] found that women had more moderate to severe mitral regurgitation at Doppler than men, while our study showed no significant difference between the genders regarding the presence of severe mitral regurgitation, severe pulmonary hypertension or intraventricular thrombi.

Limitations of the Study

This cohort, although large, were enrolled in a single centre. It is possible that this reflects a degree of selection bias. We also recognize that other markers like body surface, other echocardiographic diastolic function parameters, exercise performance and natriuretic peptides were not available for the current analysis but would provide interesting insights. Another important limitation was the fact that we base the diagnostic guarantee of exclusion of ischemic heart disease on the patient's history, electrocardiogram and echocardiographic signs, and a diagnostic guarantee is required with greater sensitivity.

Conclusion

Our results suggest that women with dilated cardiomyopathy have smaller left ventricles, better left ventricular systolic and diastolic function than men. In spite of these differences between the genders in left ventricular function, we didn't find any differences, between the genders, regarding right ventricular function, presence of severe mitral and tricuspid regurgitation, severe pulmonary hypertension, presence of intra-ventricular thrombi and spontaneous contrast.

Conflict of Interests

None to declare.

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