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Clinical Profile of Afro-Caribbean Patients with Angiographycally-proven Non-ischemic Dilated Cardiomyopathy: A Case Series Discussion and Review of the Literature

***Felix Nunura[1], Edwin Tulloch-Reid[1,2], Joel Brooks[1,2], Dainia S Baugh[3] and Ernest C Madu[1]**

[1]*Division of Cardiovascular Medicine*

[2]*Department of Interventional Cardiology*

[3]*Department of Medicine, Heart Institute of the Caribbean, Kingston, Jamaica*

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***Corresponding author:** Felix Nunura, University of Technology, Adjunct Associate Professor of Medicine, 1 Brumalia Rd Unit 7, Manchester, Jamaica, West Indies, Tel: 1 876 8797031; Email: fnunura@caribbeanheart.com

Abstract

It has been reported that in Afro-Caribbean patients, the most common cause of heart failure (HF) is non-ischemic dilated cardiomyopathy (NIDCM). The clinical profile of patients with angiographycally diagnosed NIDCM in this population is however, not very well known. We undertook a cases control study to determine which clinical characteristics and traditional cardiovascular risk factors are associated or not with the outcome of angiographycally-proven NIDCM in a population of Afro Caribbean patients utilizing a sample of our Heart Failure with reduced EF (HFrEF) patient's data base. Among 16 cases with HFrEF (mean age 62 years old) we randomly determined 8 cases with angiographycally -proven NIDCM (Group 1) and compare them with 8 controls with angiographycally-proven ischemic dilated cardiomyopathy -IDCM (Group 2) . The subsequent analysis indicated that although male sex was more frequent in Group 2 and Obesity in Group 1, a history of Hypertension or Diabetes were not different in both groups. The cases (Group 1) showed more reduced EF and more dilated Left ventricle than the controls, but a history of old myocardial infarction in Group 2 turned out to be the statistically most significant variable. We conclude that the presence or the absence of the most important traditional cardiovascular factors (Hypertension and Diabetes) , which have been described as strongly correlated with coronary artery disease , are not necessarily predictive of angiographycally-proven NIDCM in an Afro Caribbean population with HFrEF.

Keywords: Non-ischemic dilated cardiomyopathy; Cardiovascular risk factors; Afro Caribbean community

Abbrevations: HF: Heart Failure; NIDCM: Non-Ischemic Dilated Cardiomyopathy; HFrEF: Heart Failure with reduced EF; PAHO: Pan American Health Organization; CNCDs: Caribbean epidemic of chronic Non-Communicable Diseases; IHD: Ischemic Heart Disease; IDCM: Ischemic Dilated Cardio-Myopathy; EMR: Electronic Medical Records; LVEF: LV Ejection Fraction; LVEDD: LV End Diastolic Dimension; IVS: LV wall thickness; CAD: Coronary Artery Disease; DCM: Dilated Cardio-Myopathy; PET: Position Emission Tomography; DM: Diabetes Mellitus; HOPE: Heart Outcomes Prevention Evaluation; CHF: Congestive Heart Failure

Introduction

Over the past 50 years, countries of the Caribbean Region have experienced an Epidemiological Transition [1-4]. In fact, data from the Pan American Health Organization (PAHO) suggests that the Caribbean epidemic of chronic non-communicable diseases (CNCDs) is the worst in the region of the Americas [5,6]. The overall epidemiology of Diabetes and cardiovascular disease in the Caribbean has reviewed and [7-9] highlights the high prevalence of Hypertension, pre-hypertension, Diabetes Mellitus, Obesity and Dyslypidemia. An update of the prevalence estimates for traditional CVD risk factors in Jamaica, the grater English speaking Caribbean community of the Caribbean, has shown that the prevalence of hypertension is 25%; diabetes, 8%; hypercholesterolemia, 12%; obesity, 25%; smoking 15%. However there are not many studies on the impact, characteristics and risk factors associated in heart failure in the Caribbean.

Laljie [10,11] founded that most of the patients with Heart Failure were over 65 years of age, female, never smoked cigarettes, overweight/obese . About 82 % of this series were hypertensive, 42 % were Diabetics, and 28 % had history of

Ischemic Heart Disease. Based on echocardiography studies the etiology of Heart Failure was classified as hypertensive heart disease (54 %), ischemic heart disease (IHD) (26%), Dilated cardiomyopathy (3%) and Rheumatic heart Disease (2 %) . Systematic literature review among the Afro-Caribbean populations and Caribbean immigrants living in UK, compared to other ethnic groups studies [12] have shown that the prevalence of coronary heart disease and peripheral artery disease is lower in Afro-Caribbean populations: the prevalence of CHD ranged from 0-7 % in Afro-Caribbean compared to 2-22 % in Caucasians.

Moreover between 211 Afro-Caribbean patients [13] the most common cause of heart failure was non-ischemic dilated cardiomyopathy in 27.5% (whites, 19.9%; P<0.001). Lower rates of ischemic cardiomyopathy were observed (13% versus 41%; P<0.001), and the fourth most common cause of heart failure in Afro-Caribbeans was cardiac amyloidosis (11.4%) as 10% of Afro-Caribbean patients attending a heart failure clinic in South London have ATTR V122I cardiac amyloidosis. Currently, there is not information about Caribbean patients with angiographycally defined Non-ischemic Cardiomyopathy, accordingly, we sought to characterize the clinical factors associated with angiographically Non-ischemic cardiomyopathy in an cases series of afro Caribbean population.

Methods

Design

Observational case control study in which a group of cases with angiographycally defined Non-ischemic Dilated Cardiomyopathy (NIDCM) are compared to a group of controls with angiographycally defined Ischemic Dilated Cardiomyopathy (IDCM) with the aim to describe if exposure to traditional cardiovascular risk factors has occurred more or less frequently in cases than controls.

Sample

From our Heart Failure with reduced left ventricular ejection fraction - HFrEF (< 50 %) patients data base, we identify a case series of patients with clinical, echocardiographic and angiographic diagnosis of NIDCM (Group 1, n=8) and compare them with a group of patient with clinical, echocardiographic and angiographic diagnosis of IDCM (Group 2, n=8). All patients underwent coronary angiography at the Heart Institute of the Caribbean Cath Lab. Patients with myocardial infarction within 30 days and patients with primary valvular heart disease were excluded. Patients were considered to have cardiomyopathy secondary to coronary artery disease if a significant coronary stenosis 70% was present in one or more major epicardial coronary arteries associated with a wall motion abnormality in the dependent myocardial territory. Conversely, patients were considered to have nonischemic cardiomyopathy if coronary arteriography failed to reveal significant coronary artery disease.

Data collection

The clinical variables from each patient were obtained from our Electronic Medical Records (smart EMR) including the age, gender, history of Hypertension, Diabetes Mellitus, Dyslipidemia, Smoking, Obesity and history of old myocardial infarction . In addition echocardiographic variables including LV ejection fraction (LVEF), LV end diastolic dimension (LVEDD) and LV wall thickness (IVS) were also collected for the final analysis.

Data analysis

Case series involving a retrospective electronic medical record review using descriptive quantitative and qualitative analysis. Continuous variables were expressed as means ± standard deviation and were compared using the Student's t test. Categoric variables are expressed as percentages.

Results

Table 1: Basal characteristics of the two groups.

Variable	Group 1 (N=8)	Group 2 (N=8)	p
Male sex	4 (50%)	6 (75%)	0.17
Age (years)	61	62	0.79
Hypertension	6 (75%)	6 (75%)	1.00
Diabetes	4 (50%)	4 (50%)	1.00
Obesity	3 (37.5 %)	1 (12.5%)	0.17
Hypercholesterolemia	3 (37.5%)	2 (25%)	0.35
Smoking	1 (12.5%)	0	0.30
LVEF (%)	31	36.80	0.18
IVS (mm)	11	10	0.75
LVEDD (mm)	70	62.5	0.01
old MI	0	5 (62.5%)	0.0042

A total of sixteen patients were evaluated during the study period. After the initial patient evaluation and use of eligibility criteria Eighth patients had angiographycally defined NIDCM and eight patients had angiographycally defined IDCM to be included in the analysis. The clinical characteristics of both groups are shown in (Table 1). There were more females, more obese, more dyslipidemia and slightly more smokers patients in the nonischemic cohort than in the cohort of patients with ischemic cardiomyopathy. More patients with ischemic cardiomyopathy were men and they were slightly older, and had less reduced LVEF than the NIDCM patients but the frequency of the most important risk factors: Hypertension (75%) and Diabetes (50 %), commonly associated with CAD, were similar in both groups. Finally, although patients with NIDCM had more severe heart

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failure with lower LVEF and showed more significant cardiac dilatation. A history of myocardial infarction was more common in the ischemic group.

Discussion

The present cases series study was the first in our country that have investigated the impact of coronary artery risk factors in patients with angiography defined non-ischemic vs ischemic dilated cardiomyopathy One attempts can be made to hypothesize a cause and effect theory in the sense that although both group of patients were exposed over their lifetime to the same strong risk factors for CAD , they , potentially, can develop the same outcome (DCM, dilated cardiomyopathy) but one group can develop DCM with angiographycally normal epicardial coronary arteries and the other DCM with angiographycally abnormal coronary arteries. According to the recommendations of current guidelines for chronic heart failure [14] invasive coronary angiography should be considered in patients with HF and intermediate to high pre-test probability of CAD and the presence of ischemia in non-invasive stress tests (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity. So that an angiographic diagnostic approach to a patient with a high probability for ischemic heart disease and clinical and echocardiographic evidence of dilated cardiomyopathy looks plausible and logical.

Patients with left ventricular systolic dysfunction are commonly divided into two major groups-those with ischemic and non ischemic cardiomyopathy. Ischemic cardiomyopathy, a result of the complications of coronary artery disease (CAD), is one of the most common causes of heart failure in the Western world [15]. It has been reported that 60% of these patients with Heart Failure do have coronary artery disease (CAD) [16], however, in about 40% of cases, the etiology of heart failure remains unclear even after coronary angiography as coronary artery disease was ruled out or its extent could not explain the obvious myocardial dysfunction. As previously mentioned, recent studies have confirmed the clinical impression that in Afro-Caribbean patients, the most common cause of heart failure (HF) is nonischemic dilated cardiomyopathy [13]: Dungu JN et al. reported that in a population of 211 Afro-Caribbean patients, the nonischemic dilated cardiomyopathy was present in 27.5% (whites, 19.9%; P<0.001), also lower rates of ischemic cardiomyopathy were observed (13% versus 41%; P<0.001).

Although other possible etiologies such as cardiac amyloidosis have been proposed and appear to contribute up to 10% of Afro Caribbean patients with heart failure [13], it is interesting to consider in our study group the possibility of abnormalities in coronary flow: Impairment of coronary flow reserve has been shown in patients with dilated cardiomyopathy (DCM) despite normal epicardial coronary arteries [17]. Various methods have been used to measure coronary flow in these patients, [18] including coronary sinus thermo dilution, intracoronary Doppler flow wire, position emission tomography (PET), and trans-esophageal echocardiography. In all these studies, it has been demonstrated that coronary flow reserve is reduced in DCM patients. Besides, it has been reported that reduced coronary blood flow reserve is associated with unfavorable outcome in patients with DCM [19].

Most recently Yasar et al. [20] have shown that patients with idiopathic DCM and angiographically normal coronary arteries have higher TIMI frame counts for all 3 coronary vessels, indicating impaired coronary blood flow, compared to control subjects without DCM. In addition to epicardial disease, microvascular coronary disease is also both widespread and often under-recognized [21]. In our case series 75 % of the both groups of patients were hypertensive and 50 % were diabetics the epidemiology of cardiovascular disease in the black population of the Caribbean is important as attempts are made to understand the reasons for racial disparities in health outcomes in developed countries. Over the past 50 years, the Afro-Caribbean population (i.e., Caribbean people of African descent) has undergone an epidemiologic transition; with cardiovascular disease now ranked as the leading cause of death in the region [22]. The Afro-Caribbean population currently has a prevalence of cardiovascular risk factors between that of African nations and the black population of the United States.

Afro-Caribbean women have a greater burden of cardiovascular risk factors than Afro-Caribbean men. The high prevalence of cardiovascular risk factors and the presence of type 2 diabetes in Afro-Caribbean youth indicate that the current epidemic of cardiovascular disease is likely to remain unabated in the short to medium term [22]. Too few clinical trials of cardiovascular disease or cardiovascular risk factors have been conducted in the region: estimates of prevalence for traditional cardiovascular disease risk factors have shown a prevalence of Hypertension, 25 %; diabetes, 8 %; hypercholesterolemia, 12 %; obesity, 25 %; smoking, 15 % . In addition, 35 % of Jamaican have pre-hypertension, and 3% had impaired fasting glucose [23].

Therefore it is clear from an epidemiological perspective hypertension is the most prevalent cardiovascular risk factor in the Afro Caribbean population but it is also well know that Hypertension is an antecedent of the vast majority of individuals with heart failure in the community, as suggested by data from the Framingham Study [24]. The classic paradigm of the progression of hypertensive heart disease is that hypertension does not lead to dilated cardiac failure unless there is interval myocardial infarction or a preceding phase of concentric hypertrophy (i.e., hypertension does not lead directly to a dilated ventricular chamber). However, this may not be accurate. Blacks who commonly have a non-ischemic cardiomyopathy attributed to hypertension have heart failure onset at a relatively young age, making it less likely that they had progressed from concentric hypertrophy to a burned-out dilated cardiomyopathy during a long latent period.

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In aggregate, these data raise the possibility that hypertensive patients can progress directly to dilated cardiac failure without antecedent concentric hypertrophy [25]. Being that left ventricular mass increases disproportionately in hypertension, relative to the ability of the microvasculature [26] to perfuse the hypertrophied myocardium both at rest and during exercise, thereby proving to be a 'set up' for chronic sub endocardial hypo perfusion. On the other hand it is known that Heart failure (HF) is the most common cardiovascular complication of diabetes mellitus (DM). Heart dysfunction in the diabetic population may develop regardless of typical risk factors such as hypertension and coronary artery disease. The cause of HF in diabetes is certainly multi factorial in nature, but hyperglycemia and insulin resistance seem to be the core factors [27] Studies have suggested the existence of a Diabetic Cardiomyopathy.

Hamby et al. found that diabetes was present in 22% of patients with idiopathic cardiomyopathy compared to 11% in the control group [28] Functional changes occurring in diabetic patients typically involve the impaired diastolic function of the heart, that may precede the systolic dysfunction. There is also a significant association of dilated cardiomyopathy with DM [29]. Accordingly, changes typical for systolic dysfunction may indicate an increased risk for the development of HF, particularly in the presence of coexisting hypertension. Several hypotheses have been proposed to explain the mechanisms responsible for decreased myocardial contractility in the diabetic population. These include metabolic disturbances, accumulation of AGE, myocardial fibrosis, small vessel disease, impaired calcium homeostasis, autonomic neuropathy and insulin resistance. It has been observed that in diabetic patients the endothelium-dependent dilatation of the epicardial coronary arteries is impaired [27].

The results of the Heart Outcomes Prevention Evaluation (HOPE) study indicate that microalbuminuria is associated with significant risk for congestive heart failure (CHF) [30]. That is why it seems reasonable to perform echocardiographic screening for HF in diabetic subjects with micro albuminuria. So in our presented case series the question might be: is this a Coronary Artery Disease Problem or a Hypertension Problem or a Diabetes problem? Thus, even in heart failure patients classified clinically as 'non-ischemic cardiomyopathy,' up to a fourth may have evidence of CAD at autopsy. Also, ischemic changes have been demonstrated on endomyocardial biopsies in such patients. Indeed, such patients with so called 'non-ischemic cardiomyopathy' may develop clinical ischemic events on subsequent follow-up, an observation that suggests that coronary disease may not be just a 'bystander' in these patients.

The frequent presence if micro vascular disease detected with PET scanning or with Doppler flow velocimetry in response to stress in such patients further incriminates CAD as a potential contributor to the ventricular dysfunction [31]. Finally, we found that more obesity patients in the group of NIDCM which brings into consideration the issue of the Metabolic Syndrome. The metabolic syndrome and its components, glucose intolerance, T2DM, hypertension, dyslipidaemia and obesity seem increasingly common in the Afro Caribbean community. The prevalence of LV systolic dysfunction in obese patients with diabetes and hypertension but no overt coronary artery disease may be of the order of 30% [32] with women at slightly lower risk than men. With such a high prevalence, and the availability of successful treatments, it may be time to consider screening initiatives to identify LV systolic dysfunction in diabetic patients, in order to prevent the progression to overt heart failure.

Conclusion

The present cases series study was the first in our country that have investigated the impact of coronary artery risk factors in patients with angiography defined non-ischemic vs ischemic dilated cardiomyopathy in a Afro Caribbean population. One attempts have be made to hypothesize a cause and effect theory in the sense that although both group of patients were exposed over their lifetime to the same strong risk factors for CAD , they, potentially, can develop the same outcome (DCM, dilated cardiomyopathy) but one group can develop DCM with angiographycally normal epicardial coronary arteries and the other DCM with angiographycally abnormal coronary arteries, however, further research is needed to refine the clinical definition of non ischemic cardiomyopathy in the Afro Caribbean population so physicians can appropriately prescribe treatment and accurately predict outcome of Heart Failure in this community.

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