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Obesity in the Development of Premature Coronary Artery Disease

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Abstract

Objective: To explore the relationship between cardiovascular risk factors and coronary artery disease (CAD) severity in young Puerto Rican adults who have suffered a myocardial infarction.**Methods:** A cross-sectional study examined adults aged 21 to 35 years who underwent left cardiac catheterization in the Cardiovascular Center for Puerto Rico and the Caribbean during 2008-2012 due to myocardial infarction. Demographic characteristics, clinical risk factors, and the extent of CAD were documented. Chi-square statistic or Fisher's exact test was used to compare the distribution of demographic, clinical, and lifestyle characteristics across CAD extent. Polytomous logistic regression models were fitted to estimate the prevalence odds ratios (POR) with 95% confidence intervals (CI) for non obstructive and obstructive coronary disease (OCD) compared with normal coronary anatomy. Statistical analyses were performed using Stata 11.0.**Results:** Sixty-three (n=63) adults were evaluated (81% were men). The mean age was 31 ± 4 years. The most frequent clinical risk factors were history of tobacco use, hyper tension, and dyslipidemia. Obesity was present in 45.9% of subjects and OCD was present in 52.38% of subjects. Obesity and family history of CAD were significantly associated with OCD when adjusted by age. Obese patients had 5.94 times the possibility of having OCD than normal weight patients.**Conclusion:** Obesity was the most important treatable predictor of premature obstructive CAD in our young adult population.**Keywords:** Myocardial infarctions; Obesity; Coronary disease; Inflammation; Young; Premature CAD

Introduction

Coronary heart disease (CHD) is the leading cause of death in Puerto Rico and the United States. In 2010, the prevalence of CHD in Puerto Rico was 8% [1]. Many predictors have shown to confer a greater mortality in the setting of CHD and myocardial infarction. In particular, angiographic severity of coronary artery disease (CAD) has been shown to be a predictor of long-term adverse cardiovascular events and mortality as well as treatment costs [2,3]. Exploring the association between cardiovascular risk factors and angiographic severity or extent of CAD in young Puerto Rican adults who have suffered a myocardial infarction could elucidate which factors have the most impact on the progression of premature CHD in this unique population. The objective of this study was to evaluate the association between the cardiovascular risk profile and angiographic characteristics of young Puerto Rican adults who have suffered a myocardial infarction.

Methods

This was a cross-sectional study which reviewed the medical records of young adults aged 21 to 35 years who underwent left cardiac catheterization in the Cardiovascular Center of Puerto Rico and the Caribbean during 2008 to 2012 due to myocardial infarction. Myocardial infarction was defined as hospital or physician records confirming a definite history of myocardial infarction and cardiac enzyme elevation. Patients without cardiac enzyme elevation documented on record were excluded from the study. Within the variables collected were age, gender, BMI, history of systemic hypertension, diabetes mellitus,

dyslipidemia, tobacco use, and family history of CHD and the use of drugs such as cocaine. The BMI was used to classify patients into three weight categories: obese, which have a BMI of 30 or more; overweight, which includes BMI of 25 to 29.9; and normal weight which consisted of patients with a BMI of 24.9 or less. In addition, angiographic data was retrieved and it was categorized into 3 groups corresponding to the extent of CAD. Obstructive coronary artery disease (OCD) was defined as 70% or more occlusion in the right, left anterior descending or left circumflex artery, or a 50% or more occlusion of the left main artery. Non-obstructive coronary artery disease (NOCD) was defined as less obstruction than that of OCD, or any degree of obstruction in minor vessels. Normal coronary anatomy was defined as angiographically normal coronary arteries.

IRB approval was attained for the performance of this study. Data from study participants was recorded in a database designed with the use of Research Electronic Data Capture (REDCap) software developed and supported by the Puerto Rico Clinical and Translational Research Consortium (PRCTRC). Chi-square statistic or Fisher's exact test was used to compare the distribution of demographic, clinical, and lifestyle characteristics across CAD extent. Polytomous logistic regression models were fitted to estimate the prevalence odds ratios (POR) with 95% confidence intervals (CI) for non-obstructive and obstructive coronary disease compared with normal coronary anatomy. Statistical analyses will be performed using Stata for Windows release 11.0 (Stata Corporation, College Station, Texas).

Results

Data chart review consisted of 63 medical records. An 81 % of the subjects were male and a 46% was obese (Table 1). The mean age was 31 years. The most frequently present risk factors other than obesity were a history of hypertension, tobacco use and dyslipidemia (Table 2). Interestingly, a 30% of the subjects had a normal coronary anatomy and a 52% of the patients had OCD (Table 3).

Results adjusted to polytomous logistic regression model demonstrated with statistical significance that patients 30 to 35 years of age were 7.71 times more likely to have OCD than patients from 21 to 29 years of age (Table 4). Table 5 shows statistically significant associations between clinical and demographic factors and the coronary artery disease severity adjusted by age. Obese patients were 5.94 times more likely to have OCD than those with a normal BMI (p=0.04). In addition, patients with family history of CHD were 19.48 times more likely to have OCD than patients without family history of CHD (p=0.02). There were no statistically significant associations between hypertension, diabetes mellitus, dyslipidemia and tobacco use, and the extension of coronary artery disease.

Discussion

Ethnicity and premature CAD

Our patients had a markedly higher frequency of normal coronary arteries (30%) upon index myocardial infarction than in other comparable studies, including the Coronary Artery Surgery Study Registry (16% men and 21% women) [4], a study performed in Pakistan (6.7%) [5] and another in Poland (20%) [6]. Myocardial infarctions with normal coronary arteries usually occur in patients where risk factors for CHD are absent [7]. The young Puerto Rican adult population or Hispanics in general, as suggested by this study, may have a higher incidence of myocardial infarction with normal coronary arteries due to increased predisposition for coronary vasospasm, micro vascular disease or enhanced thrombolytic mechanisms. Whichever the reason, it is known

	Frequency (%)
Gender	
Male	51 (80.95)
Female	12 (19.05)
Age	
<30	23 (36.51)
≥30	40 (63.49)
BMI	
normal	14 (22.95)
overweight	19 (30.15)
obese	28 (45.90)

Tables 1: Patient Demographics

	Present (%)	Absent (%)	Not Documented (%)
Hypertension	21 (33.33)	23 (36.51)	19 (30.16)
Diabetes Mellitus	13 (20.63)	44 (69.84)	6 (9.52)
Dyslipidemia	15 (23.81)	31 (49.21)	17 (26.98)
History of tobacco	21 (33.33)	38 (60.32)	4 (6.35)
History of alcohol	12 (19.05)	27 (42.86)	24 (38.10)
Family History of CVD	14 (22.22)	18 (28.57)	31 (49.51)

Table 2: Patient Clinical Risk Factors

	Frequency (%)
Normal Coronary Anatomy	19 (30.16)
Non-obstructive Coronary Disease (NOCD)	11 (17.46)
Obstructive Coronary Diseases (OCD)	33 (52.38)

Table 3: Angiographic Characteristics

Characteristic	NOCD Unadjusted POR (95% CI)	OCD Unadjusted POR (95% CI)
Age		
<30 yrs	1.00	1.00
≥ 30 yrs	2.06 (0.45-9.30)	7.71 (2.13-27.89) P=0.002

Table 4: Prevalence odds ratio (POR) estimation for the association of age for NOCD and OCD compared with normal coronary anatomy
NOCD: Non-obstructive coronary disease; OCD: Obstructive coronary disease

Characteristic	NOCD (n=11)	OCD (n=33)
	Age-Adjusted POR (95% CI)	Age-Adjusted POR (95% CI)
Sex		
Female	1.00	1.00
Male	0.28 (0.02-3.66)	0.17 (0.02-1.62)
BMI		
Normal	1.00	1.00
Overweight	0.47 (0.03-6.66)	2.03 (0.41-10.20)
Obese	6.01 (0.78-46.38)	5.94 (1.09-32.45) p=0.04
Diabetes Mellitus	0.73 (0.05-9.66)	2.88 (0.52-15.96)
Dyslipidemia	2.23 (0.28-18.10)	3.34 (0.57-19.63)
Hypertension	0.40 (0.05-3.13)	1.68 (0.34-8.26)
Smoking	2.54 (0.44-14.60)	1.34 (0.35-5.13)
Family history of CVD	4.60 (0.19-112.96)	19.48 (1.60-236.88) p=0.02

Table 5: Prevalence odds ratio (POR) estimation for the association of risk factors for NOCD and OCD compared with normal coronary anatomy
NOCD: Non-obstructive coronary disease; OCD: Obstructive coronary disease

that there is ethnic variation in the expression of cardiovascular diseases. We have recently reviewed the studies that support the idea of a milder phenotype of the metabolic syndrome and CHD in Hispanic versus non-Hispanic populations [8]. Similarly, it has been shown that black and Hispanic patients in the United States have a lower prevalence of CAD than their white, non-Hispanic counterparts when referred for evaluation of stable and unstable chest pain symptoms [9].

Cocaine and CAD

It is probable that the use of cocaine in our subjects was underreported. The prevalence of myocardial infarctions induced by cocaine is likely higher, especially in view of the high frequency of normal coronary anatomy found in these patients. The self-reported history of cocaine and marijuana use was present in 6.3% and 3.2% of our subjects, respectively. Toxicology was positive for cocaine in 3% of subjects; however, only 14.3% of the total subjects underwent drug toxicology. Furthermore, cocaine is cleared from the urine and blood in approximately 3 and 7 days respectively. Thus, the fact that cocaine use is not biochemically confirmed in an acute setting does not indicate that chronic use of the drug has not taken a toll on the cardiovascular system. The abuse of cocaine has been associated to serious coronary ailments of both an acute (i.e vasospasm) and chronic (i.e. atherosclerosis) nature, as well as to heart failure, cardiomyopathies, arrhythmias, aortic dissection, and endocarditic [10]. All these facts should be of particular concern in Puerto Rico, where the prevalence of this illicit drug use is high. Cocaine abuse may be placing a heavier burden on the cardio metabolic profile of our country than is traditionally perceived and further research into drug use and its association with cardiovascular disease in our population is imperative from a public health and economic standpoint.

Obesity and premature obstructive CAD

Obesity adversely impacts cardiovascular hemodynamics, structure and function [11], as well as increases the prevalence of most cardiovascular diseases. However, an “obesity paradox” has been noted in a variety of cardiovascular ailments, wherein a higher BMI has been reported as protective against cardiovascular events [12]. It has been shown that despite the fact that obesity increases the risk for developing CHD, at least overweight and mild obesity do not seem to adversely affect prognosis in older patients with established CHD [13]. It is currently unknown if obesity itself is a marker of improved nutrition in older populations or whether a low BMI is confounded by unexplained factors that promote mortality, such as frailty. It has also been documented that obese people tend to receive a more aggressive medical intervention. On the other hand, the risk of dying overall and from most major health causes has been associated to increasing BMI within the class III obesity group [14].

In our study, obesity was the only statistically significant “treatable or modifiable” predictor of premature obstructive CAD in young adults upon index myocardial infarction. Obesity is more prevalent than diabetes mellitus, hypertension, tobacco use and dyslipidemia in adolescent and pre-adolescent populations [15]. Thus, it is more than plausible that obesity holds a heavier and more detrimental cumulative burden on the coronary vasculature of our subjects than do the other risk factors that may have developed later in time. Indeed, obesity, especially central or abdominal obesity, is associated with augmented neuro-hormonal activation, inflammation, pro-thrombosis and insulin resistance that may lead to high blood pressure, dyslipidemia, impaired glucose metabolism and endothelial dysfunction. This natural history of obesity may explain why obesity is more prevalent in our subjects than the other risk factors. Similarly, a recent study has shown that younger patients with heart failure are more likely to be obese than have other co morbidities such as diabetes mellitus, hypertension and stroke, like wise reflecting that these conditions occur beyond middle age [16].

In the United States, the total excess cost related to the current prevalence of adolescent overweight and obesity is estimated to be \$208 billion in lost productivity secondary to premature morbidity and mortality [17]. The first large-scale data on body mass index (BMI) and cardiovascular disease risk factors among U.S. Hispanic/Latino adult populations demonstrated that the most severe class of obesity, a BMI greater than 40, was most common among young adults between 25 and 34 years of age [18]. In Puerto Rico, an alarmingly high prevalence of obesity has been estimated at 26.8% in elementary school children [19]. It is imperative that risk factor management, especially lifestyle changes, exercise and healthy dietary habits be implemented at an early age, when the effects of obesity may be most damaging.

Obesity and inflammation

Systemic inflammation is a fundamental process in the development of cardiovascular disease in patients with the metabolic syndrome and obesity, and this process starts with the activation of the neurohormonal system. Adipose tissue is a hormonally active endocrine tissue, producing cytokines, which influence other body tissues. Adiponectin is one such adipocytokine that protects cardiovascular tissue from ischemic injury and increases insulin sensitivity by stimulating fatty acid oxidation, decreasing plasma triglycerides and improving glucose metabolism [20,21]. On the other hand, tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) are insulin-antagonizing adipocytokines [22] that are associated to augmentation of inflammation and insulin resistance. As seen, inflammation is a complicated issue in obesity that has to be stopped due to the deleterious effects produced in the cardiovascular system. Insulin resistance is also a fundamental mechanism underlying central obesity and the metabolic syndrome. Abnormalities in fat storage

and mobilization have been implicated in the pathogenesis of insulin resistance [23]. Systemic chronic inflammation, on the other hand, paints the most complete picture of insulin resistance as it is the result of all altered cytokine production and signaling pathways in the body [24]. A more accessible marker for this inflammation can be obtained by measuring C-reactive protein (CRP). Clinically, each of the diagnostic component criteria of the metabolic syndrome has been associated with increased levels of CRP [25], elevation of which bears a negative prognostic implication in the population involved-this biomarker has been associated to the development of heart disease, although this observation is not totally clear. CRP production is located in the liver, a process induced by pro-inflammatory cytokines; this non-specific marker of inflammation has an important role in the host innate defense mechanism, but also regulates the amount of inflammatory response by activating the complement system. CRP can be used to monitor the status of the inflammatory system, and has been used to monitor the effect of stains in the inflammatory process of the metabolic syndrome [26]. In the Jupiter trial, rosuvastatin (20 mg/day) reduced the systemic marker of CRP.

Limitations

Due to the infrequent nature of myocardial infarctions at a young age, an inherent limitation of our study naturally is a poor sample size. In addition, because the exposure and outcome were simultaneously assessed, there is generally no evidence of a temporal relationship between exposure and outcome. Thus, it is difficult to infer about causality. Thirdly, there was a limit to the detail to which the information on CHD risk factors was collected. Tobacco use, for example, was classified as positive if the medical record stated a history of chronic use as described by the patients. However, data regarding the number of pack-years, exposure duration and whether tobacco use was recent or not was not available. Similarly, duration of other risk factors such as hypertension, diabetes and dyslipidemia was not available in the medical records. Moreover, CRP as a measure of inflammation was not included as a variable to be assessed in the study since it has no widespread indications as a marker for stratifying patients who are already known to be high risk, as those in our study who suffered myocardial infarctions. Lastly, results of this study cannot be generalized to all subjects in Puerto Rico with CHD.

Conclusion

The fight against the obesity epidemic should always remain a cornerstone in the prevention of cardiac disease. It may prove to be the best placed effort to ameliorate the rampant nature of CHD in the island of Puerto Rico. In addition, more resources should be spent in the exploration of cardiovascular disease in Puerto Ricans as it provides important and unique information for understanding the interrelationship between genetics, environment and culture in the modification of cardiovascular health.

Conflict of Interest

The authors have no conflict of interest to disclose

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