Asymptomatic Coronary Artery Disease in Chagasic Patients with Heart Failure: Prevalence and Risk Factors

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Abstract

Background: Concomitant asymptomatic coronary artery disease in patients with Chagas cardiomyopathy in heart failure is controversial in the medical literature, as both diseases are prevalent in some regions of Brazil.

Objetive: To determine the prevalence of coronary artery disease (lesions > 50%) in a specific population of patients with Chagas cardiomyopathy in HF functional class III and IV, who had no previous coronary events.

Methods: Coronary angiography was performed in 61 consecutive patients with Chagasic cardiomyopathy, in heart failure functional class III and IV, to exclude coronary artery disease. These patients were part of the Cell Therapy Study in Heart Diseases protocol, which required the coronary angiography to be carried out before stem cells were injected. Risk factors for atherosclerosis also analyzed in this population were: age, arterial hypertension, diabetes, dyslipidemia, smoking and overweight.

Results: mean age was 51.6 + 9.6 years and 65.5% (n = 40) of them were males. The prevalence of coronary disease in this population was 1.6% (1). The prevalence of risk factors were: arterial hypertension 18% (11), smoking 59% (36), diabetes 1.6% (1) and dyslipidemia, 6.5% (4).

Conclusion: The prevalence of asymptomatic coronary artery disease in patients with severe heart failure due to Chagas disease is low and among the risk factors for coronary heart disease, smoking was the most prevalent. (Arq Bras Cardiol 2011;97(5):408-412)

Keywords: Coronary artery disease/complications; heart failure; chagas disease; risk factors; prevalence.

Introduction

In Brazil, the main etiology of heart failure (HF) is ischemic heart disease associated with arterial hypertension[1]. However, in regions of low socioeconomic status, Chagas' disease has endemic characteristics and is an important cause of dilated cardiomyopathy and HF, accounting for high morbimortality rates[1-3].

In patients with HF, early diagnosis and treatment, as well as prognostic stratification, are very important to promote improved survival and quality of life and, sometimes, total or partial reversal of the HF picture. In this context, the ischemic and Chagasic etiologies are important markers of poor prognosis[1,4-6].

Although many patients with Chagasic cardiomyopathy have a premature death due to complications, the current treatment for HF has substantially improved longevity and quality of life of these individuals[1].

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However, it is reasonable to consider the possibility of an overlap of etiologies responsible for chronic cardiomyopathy, mainly in areas of endemic Chagas disease, where the population is exposed to risk factors for coronary artery disease[1]. It is worth mentioning that in cases of left ventricular dysfunction due to ischemia, systolic function may be improved or normalized, if patients are adequately revascularized[6-8].

Therefore, in Chagasic patients with HF unresponsive to optimized medical therapy, one should take into account not only situations such as the inappropriate use of medication, pulmonary thromboembolism, infections and arrhythmias[1], but also the coexistence of myocardial ischemia caused by coronary disease[1]. This association may be more deleterious to the ventricular function and its specific treatment would positively influence patient survival[6].

Although the coronary angiography is the gold standard procedure for the diagnosis of coronary disease, it is an invasive diagnostic method capable of causing complications, in which left ventricular dysfunction and functional class IV are predictors of mortality[9]. In such cases, the use of angiotomography is an interesting method for the diagnosis of coronary artery disease in patients with HF, as it is a noninvasive test, in addition to having high negative predictive value[10-13]. However, its applicability is still limited by the low availability and high cost[13].

Documentation of coronary disease frequency in Chagasic patients with severe heart failure is important in order to help, in a safe and effective manner, the clinical stratification, treatment and prognosis of this pathology[1,10-13].

Methods

This study was approved by the Ethics and Research Committee of Hospital das Clinicas, Universidade Federal de Goiás, registration number 01/2010.

The study is an investigation[14] that performed a cross-temporal assessment in a population of Chagasic patients in functional class NYHA III and IV, with severe left ventricular systolic dysfunction. This was a population of patients participating in the Cell Therapy Multicenter Randomized Study in Heart Disease (EMRTCC), in which a coronary angiography had to be performed to rule out the possibility of coronary artery lesions (> 50%) and that included only pure Chagasic patients in this arm of the study. The procedures were performed by the same medical team.

The medical records of 61 adult patients with Chagasic cardiomyopathy in heart failure included in the EMRTCC were analyzed. The patients' data included in the study were sex, age, presence of obstructive coronary disease, as well as risk factors for coronary heart disease: smoking, diabetes, arterial hypertension, dyslipidemia and overweight.

Obstructive coronary artery disease was considered present when, by visual estimate, an obstruction ≥ 50% was found in the coronary angiography in an epicardial coronary artery. Although lesions with lower degrees of stenosis can eventually cause angina, these have a lower prognostic significance[7,8].

Only patients that currently smoked cigarettes were considered smokers, as recorded in medical files. Diabetic patients were those using insulin or oral hypoglycemic agents, or those whose fasting glucose > 126 mg/dL[15].

Hypertensive patients were those using antihypertensive drugs or with systolic blood pressure ≥ 140 mmHg and diastolic pressure ≥ 90 mmHg[16]. Overweight was considered when the body mass index (BMI) was > 25 kg per m^2 (kg/m^2)[17]. Dyslipidemia was verified when patients were taking lipid-lowering drugs or when total cholesterol was > 200 mg/dL[18].

The analysis of the coefficient of prevalence (frequency) of coronary artery disease was determined by the formula[14]:

$$\text{Coefficient of Prevalence} = \frac{\text{Number of cases of severe coronary disease cases x 100}}{\text{Studied population}}$$

The Kolmogorov-Smirnov test was performed to determine the distribution of the studied sample. In case of normal distribution, means and standard deviation were used; in cases of abnormal distribution, the median was used.

The comparison between frequencies of categorical variables was performed using the X^2 (Chi-square) test or the "T" test of the difference of proportions. The latter was used when one of the analyzed frequencies was < 5. Student's *t* test was performed to compare the frequencies of continuous variables. Univariate and multivariate regression analyses were performed to determine predictors of coronary heart disease.

The margins of error for the results were given by the formula of standard error for infinite population.

The software SPSS-15.0 was used for statistical calculations, with a 95% confidence interval and p values < 0.05 being considered significant.

Results

The data obtained from the sample of 61 Chagasic patients with HF and normal distribution are shown in Table 1.

The only case of coronary artery disease observed in the studied sample was an obstruction of 90% in the mid-third of the circumflex branch of the left coronary artery (Figure 1). Univariate analysis (logistic regression) of the variables in relation to coronary artery disease is shown in Table 2.

In this analysis, tobacco use was considered the only predictor of coronary heart disease in the studied sample, with OR = 5.696, representing a 5,000-fold higher chance of smokers to develop coronary artery disease. Therefore, this risk factor for coronary artery disease was analyzed in the multivariate regression, not being considered an independent predictor, as for this analysis a p value of 0.089 was obtained, which was not statistically significant.

Discussion

This study analyzed 61 patients with Chagas cardiomyopathy and severe LV systolic dysfunction, with no clinical signs of coronary disease, submitted to a study protocol for intracoronary stem cell implant, and only one patient had coronary artery disease (1.6%).

The low prevalence of coronary heart disease in this specific group of patients with Chagas disease is possibly due to the fact that the mean age of the subjects is low, a fact that should be taken into account, as age is a risk factor for cardiovascular events[5].

Moreover, Chagasic cardiomyopathy affects younger people, in whom the risk factors have not acted significantly for the development of coronary disease[1-5].

Smoking was the most prevalent risk factor in this population. Considering as smokers only those patients currently smoking cigarettes, tobacco use was higher than that found in the general population [59% *versus* 20.1%, p <0.001][19-21]. It is worth noting that tobacco smoke load was not evaluated. None of the other risk factors analyzed was considered a predictor of coronary heart disease (Table 2).

Arterial hypertension, as well as diabetes and dyslipidemia were less prevalent among Chagasic patients when compared to the general population[1,16,18,21].

No BMI > 25kg/m^2 is due to the fact that the studied patients had some degree of cardiac cachexia, due to severe heart failure chronic ventricular systolic dysfunction[1].

In this sense, the low prevalence of arterial hypertension, diabetes and dyslipidemia, in association with the low age range of the Chagasic patients in this study, would favor this group of patients, as shown by the low prevalence of coronary heart disease.

Patients with heart failure of both Chagasic and ischemic etiologies have poor prognosis, and these causes are considered independent predictors of cardiovascular mortality[1,22]. Moreover, in cases where there is early detection of heart failure symptoms, the approach of the predictors of poor prognosis that can be controlled provides better survival, especially when specific therapeutic techniques and effective drug treatment are promptly implemented[23-26].

Marin-Neto et al[27] demonstrated, in a recent publication, that in Chagasic cardiomyopathy, even in the absence of obstructive lesions in epicardial coronary arteries, perfusion deficit areas can be observed when assessed by thallium scintigraphy, and also that these are viable areas[27]. This fact was explained by changes in platelet homeostasis and microcirculation of these patients[27-29]. Some authors admit, however, that the concomitance of the microcirculatory dysfunction of Chagasic patients can add to the epicardial atherosclerotic coronary obstruction, which could have a synergistic effect toward myocardial perfusion worsening, further aggravating cardiac function[27-30].

Table 1 – Chagasic patient sample data

Analyzed Data	Results
Number of patients	61
Age – years	51.6 ± 9.6
Sex	
Male	65.5% (n = 40)
Female	34.5% (n = 21)
Functional Class (NYHA)	
III	78.6% (n = 48)
IV	21.4% (n = 13)
Echocardiogram	
End diastolic diameter – millimeters	78.8 + 8.5
End systolic diameter – millimeters	67.3 + 7.6
LVEF – %	26.4 + 5.3
Mild mitral regurgitation	78.7% (n = 48)
Moderate mitral regurgitation	19.6% (n = 12)
Risk factors for coronary artery disease	
Systemic arterial hypertension	18% (n = 11)
Smoking	59% (n = 36)
Diabetes	1.6% (n = 1)
Overweight	0
Dyslipidemia	6.5 % (n = 4)
Coronary artery disease	1.6% (n = 1)
Men	100% (n = 1)
Women	0

Categorical variables shown as percentages and frequencies; continuous variables as means and standard-deviations.

The performance of the coronary angiography in asymptomatic patients is not routine and there are limitations to its indication[1,31]. Coronary artery angiography is an invasive procedure capable of causing complications and left ventricular systolic dysfunction is a predictor of mortality[9].

In literature, there are no similar groups of Chagasic patients in whom this procedure has been carried out to determine coronary artery disease[22,32].

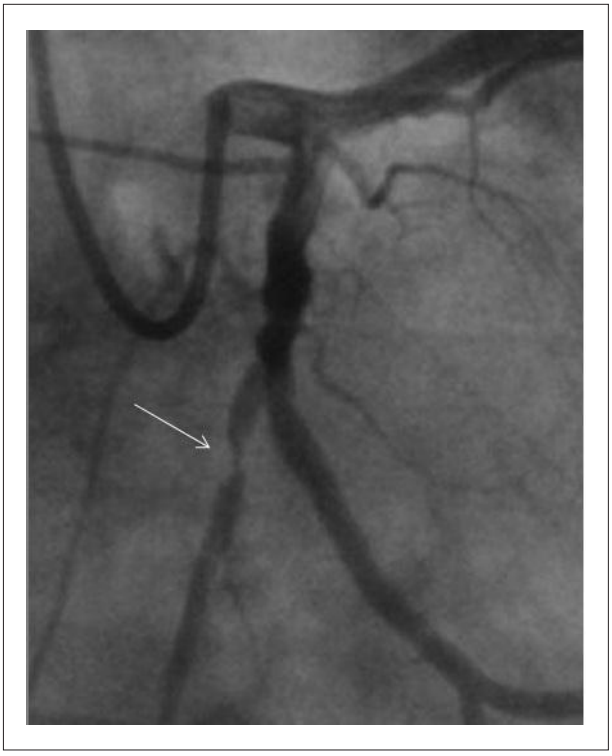

Figure 1 – *Coronary artery disease identified. The arrow shows a 90% lesion in the circumflex branch of the left coronary artery.*

Table 2 – Logistic regression univariate analysis of risk factors for coronary disease in Chagasic patients with HF

Variables	Univariate Analysis		Confidence Interval (95%)	
	P	OR	Min	Máx
Age	0.801	1.031	0.911	1.150
Male	0.300	0.06	-1.013	1.013
Female	0.930	0.007	-3.54	2.35
Dyslipidemia	0.940	0.002	-82.135	82.139
Systemic Arterial Hypertension	0.929	0.001	-81.661	81.662
Diabetes	0.946	0.016	-60.423	60.456
Smoking	0.009	5696.110	5604.962	5787.258

Non-invasive diagnostic methods, such as the angiotomography, have good accuracy in diagnosing coronary artery disease and could be safer for the population of Chagasic patients in this study[10-13]. However, access to this diagnostic method is still limited for most patients with Chagas' disease, as they must be treated by the public health system, which does not subsidize this examination. Moreover, we do not have this equipment in our institution.

In spite of the limited reproducibility of the logistic regression analysis results, mainly due to the small sample size, only smoking was a risk factor for coronary artery disease and it was not considered an independent outcome predictor.

Therefore, even though the increasing presence of coronary disease in the aging general population is known, the real prevalence of coronary disease in asymptomatic patients is uncertain[18]. In Chagasic patients with severe HF, as long as there are no signs or symptoms of coronary insufficiency, cardiac catheterization to rule out coronary artery disease in the presence of clinical treatment failure, in addition to exposing patients to the risks of an invasive procedure[9] not would bring additional benefits, as the prevalence of coronary heart disease in this specific group of individuals appears to be low.

Conclusion

The present study showed low prevalence of obstructive coronary disease in a specific group of patients with Chagas cardiomyopathy in severe heart failure with no signs or symptoms of coronary disease, even though these individuals were exposed to risk factors for cardiovascular events, in which smoking was very prevalent.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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