Correlation between Carotid Atherosclerosis and Left Ventricular Dysfunction at Echocardiography

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Abstract

Introduction: **Cardiovascular diseases are the leading cause of morbidity and mortality worldwide. Primary prevention, through early diagnosis, is necessary to enable proper treatment and control disease progression, reducing mortality and public health expenditures.**

Objective: **Correlate carotid artery atherosclerosis (evaluated by Doppler echocardiography) and left ventricular dysfunction (evaluated by echocardiography) and to correlate the findings with the patients' cardiovascular risk.**

Method: **A total of 286 medical records of patients who underwent carotid Doppler echocardiography and transthoracic echocardiography were analyzed. The data analyzed were: presence of atherosclerotic plaque and degree of stenosis, left ventricular ejection fraction and presence of diffuse or segmental left ventricular contractile disorders.**

Results: **Of the 238 reports of carotid Doppler echocardiography, 18 had stenosis greater than 70% in the carotid artery and 14 of those had left ventricular contractile disorders ($p = 0.045$). Of the patients with very high cardiovascular risk, 61 had carotid artery stenosis ($p < 0.001$); 51 patients with very high cardiovascular risk had contractile disorders ($p < 0.001$). Of the 266 echocardiography reports, 37 had reduced left ventricular ejection fraction. Of these, 25 had very high cardiovascular risk ($p < 0.001$).**

Conclusion: **There was a positive relationship between carotid artery stenosis, reduced left ventricular ejection fraction and left ventricular (diffuse or segmental) contractile disorder with very high cardiovascular risk. It was also possible to correlate carotid stenosis with contractile disorder, although this study did not demonstrate any correlation between carotid stenosis and reduced left ventricular ejection fraction. (Arq Bras Cardiol: Imagem cardiovasc. 2019;32(1):6-13)**

Keywords: **Aterosclerotic Plaque; Carotid Stenosis; Systolic Volume; Left Ventricular Dysfunction; Echocardiography.**

Introduction

Cardiovascular diseases are the major cause of morbidity and mortality worldwide, with increasing importance as population aging occurs. There is also an increase in the prevalence of obesity, overweight, hypertension and diabetes – important conditions when speaking of cardiovascular risk.[1]

In Brazil, cardiovascular diseases are also the main cause of mortality, accounting for about 30% of deaths. In Western European countries and in the United States, death from coronary artery disease (CAD) is about three times more frequent than from cerebrovascular diseases. In Brazil, we observed a similar trend, where CAD deaths also exceed those from cerebrovascular diseases. However, mortality from cardiovascular diseases in Brazil is still considered high compared to European and North American countries.[1]

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The most serious consequence of CAD is acute myocardial infarction (AMI), resulting from myocardial ischemia. This can be attributed to the difficulties in patient access to intensive care therapy, reperfusion methods and the clinical measures established for AMI. Besides, the repercussions are considerable when it comes to impacts on public health costs, expenditures with hospitalizations, percutaneous interventions and coronary artery bypass grafting (CABG) surgeries. There are also indirect social impacts, such as loss of productivity associated with patients who were away from their jobs or who died as a result of cardiovascular events.[1,2]

Primary prevention in cardiovascular diseases on asymptomatic patients is necessary. Follow-up of patients with risks for CAD and early diagnosis of atherosclerosis and myocardial ischemia, when asymptomatic, enable proper treatment and control the evolution of cardiovascular disease, reducing mortality and public health expenditures.[2]

It is believed that patients who have atherosclerotic plaque in the carotid arteries also have atherosclerotic plaque in the coronary arteries (directly evaluated only by cardiac catheterization). As the condition of myocardial ischemia primarily results from CAD, we can observe segmental contractile disorders, diffuse contractile disorders and even a decrease in left ventricular ejection fraction (LVEF). These findings are easily detected by conventional transthoracic echocardiography (TTE). It is important to

note that, in some situations, left ventricular dysfunction may be sub-clinical (asymptomatic).

Since Doppler (or Doppler echocardiography) of carotid and vertebral arteries (CVD) analyzes atherosclerotic plaque in these vessels, and TTE evaluates global and segmental systolic ventricular dysfunction (reduced LVEF), it was hypothesized that, from the analysis of both tests, associated with clinical criteria, the presence of atherosclerosis in carotid arteries associated with left ventricular dysfunction could be analyzed.

The purpose of this study was to correlate cardiovascular risk with atherosclerosis in carotid arteries and left ventricular dysfunction.

Method

This was a retrospective study conducted at Hospital de Clínicas de Curitiba da Universidade Federal do Paraná, approved by the Research Ethics Committee of the same institution, under number 2,399,009. Supported by the IT department of Hospital de Clínicas de Curitiba, individuals who underwent CVD and TTE at the Cardiology and Pneumology Unit over the past 4 years were selected from the database of medical records.

One of the exclusion criteria applied in the study was age. From the list of medical records, patients under the age of 18 or over 80 were selected and excluded using *Microsoft Excel*®. Patients with time greater than 6 months between the performance of CVD and TTE, who had moderate and severe valvular heart diseases, restrictive heart diseases, congenital diseases, pericardiopathies or patients who had already undergone carotid artery surgery (endarterectomy) were also excluded. The record of each of the individuals selected to make up the sample of our research was thoroughly evaluated.

The medical records analysis was performed in the Archiving Department of Hospital de Clínicas de Curitiba, and all the data were transcribed into a *Microsoft Excel*® worksheet. The data collected were age, sex, data to stratify the patient's cardiovascular risk, and relevant CVD and TTE anatomical and hemodynamic findings.

Cardiovascular risk

The patients' classification regarding cardiovascular risk was performed throughout the analysis of each medical record, and the final classification was then recorded. The criteria for risk stratification were not recorded one by one, due to the large number of variables, making it difficult to correlate them later in the statistical analysis.

These criteria are addressed by D'Agostino et al.,[3] authors of the Framingham study, and Faludi et al.,[2] who were responsible for latest update of the Brazilian Guidelines on Dyslipidemias and Prevention of Atherosclerosis. The stratification of cardiovascular risk in patients who do not receive lipid modifying therapy can be: very high, high, intermediate and low risk. It takes into account factors such as significant or subclinical atherosclerotic disease, chronic kidney disease, diabetes mellitus, high levels of low-density lipoprotein cholesterol (LDL-c), etc.

According to this guideline, when patients make use of statins or do not fall under the classification of very high or high CVR, they have their risk stratified by the Global Risk Score, a tool that estimates the risk of myocardial infarction, stroke, fatal or nonfatal heart failure or peripheral vascular disease in 10 years. The Global Risk Score criteria include age, high density-lipoprotein cholesterol (HDL-c) and total cholesterol (CT), treated and untreated systolic blood pressure (SBP), smoking and diabetes.

Carotid and vertebral Doppler

In the analysis of the CVD findings, special attention was given to plaque location and luminal stenosis of the carotid arteries, which are divided into right and left and internal and external, from the common carotid arteries. The portion of the division is called carotid bulb. Atherosclerotic plaques ≥ 70% are considered critical for carotid disease.

According to Freire et al.,[4] carotid plaque is defined as a protrusion of at least 0.5 mm for the vessel lumen, and/or measuring more than 50% of the intima-media thickness (IMT) and/or IMT > 1.5 mm. Therefore, values of IMT greater than 1,5 mm were considered as plaques. Values of IMT lower than 1.5 mm represented intima-media thickening.

Transthoracic echocardiography

The echocardiographic variable studied during the TTE was LVEF. Left ventricular segmental and global contractile analysis was performed carefully in the search of findings that indicate disorders in systolic parietal thickening, described as hypokinesia, akinesia and dyskinesia.

According to the American Society of Echocardiography (ASE), the lower limit of normality for LVEF is 52% for men and 54% for women. In order to facilitate the analysis, this study used 55% for all patients, a value suggested by the ASE before its update, in 2015. LVEF ≥ 55% were considered left ventricular dysfunction. The model used was two-dimensional imaging (Simpson's method).[5,6]

Selection of medical records

We analyzed information from 341 medical records, but only 286 met the inclusion criteria. We found 20 medical records that included valvular heart diseases with moderate to major mitral or tricuspid valve reflux; five patients had carotid artery endarterectomy performed; one patient had anatomical variation of the coronary vessels and one had pericardiopathy. Besides, 28 had performed the tests with more than 6 months of difference between them. After excluding these 55 records, the data underwent statistical analysis.

Of the total population analyzed, 48 did not have CVD reports available and 20 had no TTE reports (two of them only had the LVEF percentage recorded), although they had done both tests according to the hospital's internal system. However, the medical records of these patients were considered for statistical analysis, as they included information about age, sex and cardiovascular risk.

Descriptive analysis and inferential statistics were performed. In the inferential statistics, chi-square, Fisher's exact, Kruskal-Wallis and Mann-Whitney tests were used. In this study, $p < 0.05$ was considered statistically relevant.

Results

Descriptive analysis

Of the 286 patients analyzed, the youngest one was 31 and the oldest one was 80. The mean age was 65.59. Most of them were females, accounting for 67% of the population analyzed.

With regard to cardiovascular risk, half of the patients were classified as high risk, while 10% as intermediate risk and only 1.7% as low risk. Very high cardiovascular risk was found in 103 (37%) patients.

Regarding carotid stenosis, 34% did not have stenosis, 58% had stenosis < 70% and only 18 patients had stenosis > 70%. The most common location of plaques with stenosis > 70% was originating in the right internal carotid artery (39%), followed by left internal carotid artery (28%). The prevalence of stenosis percentages in patients with stenosis < 70% is shown in figure 1.

In respect of carotid stenosis, only 13% had reduced LVEF, while the rest had normal LVEF. Regarding left ventricular contractility disorder and previous CABG surgery, 73% of the patients had normal contractility, only 7% had diffuse hypokinesia and the remainder (19%) had left ventricular segmental disorders and/or had previous CABG. Of the segmental or regional disorders, most had hypokinesia (32%), followed by hypokinesia and akinesia, in different segments (17%) and akinesia (9%).

Inferential statistics

Through the chi-square test, information on the presence of carotid stenosis and reduced LVEF was cross-referenced, as well as the presence of carotid stenosis and abnormal contractility. Figure 2 shows the correlation found between carotid stenosis and LVEF. Of the patients with stenosis > 70% in carotid arteries, 31% also had reduced LVEF (p = 0.1602). Of the 18 patients with stenosis > 70% in the carotid artery, 14 (77%) presented diffuse or segmental abnormality of the left ventricle, or had performed CABG (p = 0.045), as shown in figure 3.

Using Fisher's exact test, information regarding CVR was correlated with carotid stenosis, CVR was correlated with reduced LVEF, and CVR was correlated with abnormal contractility, as shown in Figures 4 to 6, respectively. Of the patients who had very high CVR, 70% had carotid artery stenosis (15% with stenosis greater than 70%). Of the 37 echocardiographic reports with reduced LVEF, 25 had very high CVR (67.5%). Of the patients with very high CVR, 53% had abnormal contractility (diffuse or segmental) or had CABG done. These three tests had p < 0.001.

Using the Kruskal-Wallis test, information of age and presence of carotid stenosis; age and reduced LVEF; age and abnormal contractility; and age and CVR were cross-referenced. Figure 7 (boxplot) shows the distribution of the variable age according to the categories without carotid stenosis, stenosis < 70% and stenosis > 70%. Patients with carotid stenosis, whether smaller or greater than 70%, are generally older than those whithout carotid stenosis (p = 0.0023).

Also using the Kruskal-Wallis test, it was found that there was no significant difference in age between patients with segmental disorders or CABG and those who did not present any contractility disorders. However, patients with diffuse disorders were, in general, older (p = 0.77).

Using the same statistical test, age was distributed for the categories of very high, high, intermediate and low cardiovascular risk, as shown in figure 8. In this boxplot, it is clearly seen that patients with low cardiovascular risk are younger, while those who are at very high or high risk are older. In this test, the p value was < 0.001.

It was found that there was no significant difference in age between patients presenting normal LVEF and those with reduced LVEF. The test used for this correlation was the Mann-Whitney test, with p = 0.2089.

Regarding sex, the chi-square test was used in the correlation with the presence of carotid stenosis, LVEF reduction and contractility disorder. In women, 88.2% had normal LVEF; and in men, 81% (p = 0.1569). Only 4.6% of the women had carotid stenosis > 70%, while men accounted for 14% (p = 0.0021). Regarding abnormal contractility, 77.6% of the women had none, and 65% of the men were in the same situation (p = 0.0394).

Finally, using Fisher's exact test, sex was compared to CVR. Of the women, 85.5% had very high or high CVR, while in men, this percentage was 91%. Only five were women (out of 187) and no men (p = 0.2068) had low CVR.

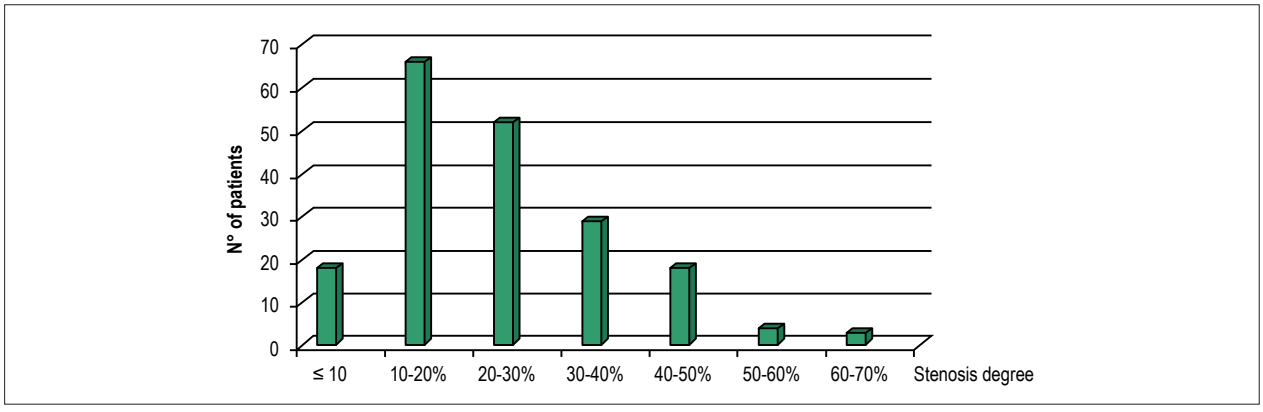

Figure 1 – *Distribution of the prevalence of carotid stenosis degrees < 70%.*

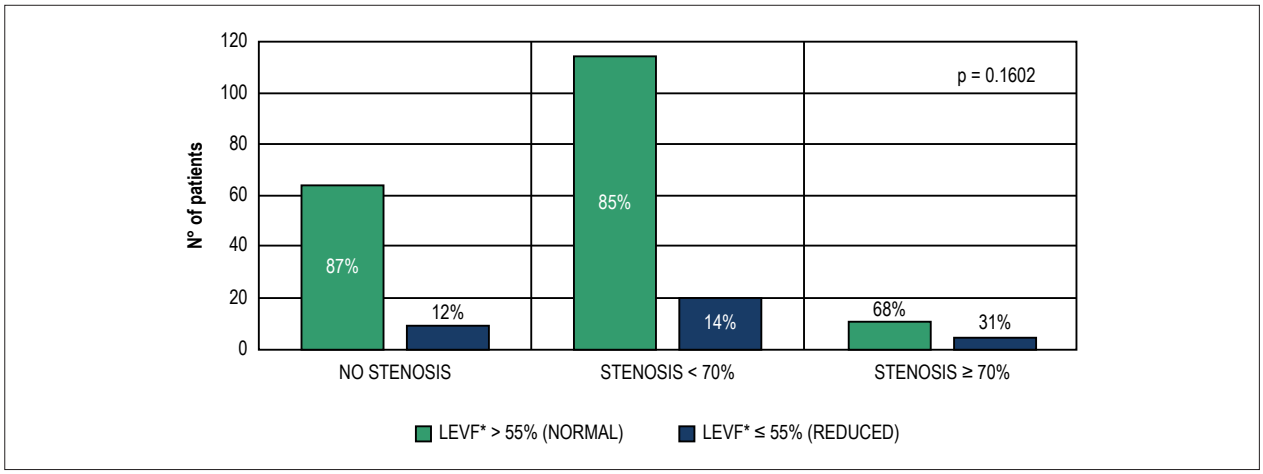

Figure 2 – *Distribution of patients with and without carotid stenosis and normal or reduced left ventricular ejection fraction (LVEF).*

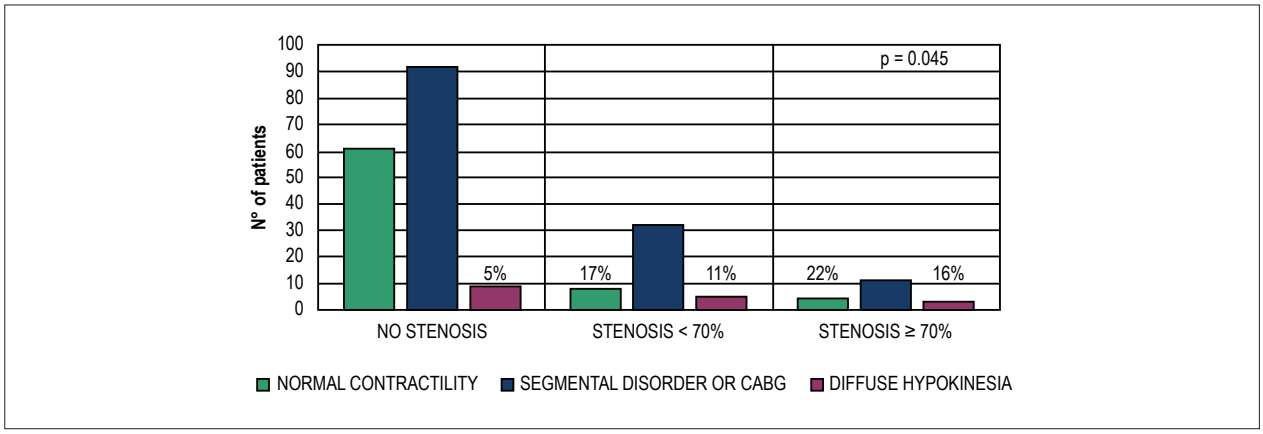

Figure 3 – *Distribution of patients with and without carotid stenosis and myocardial contractility disorders. CABG: coronary artery bypass grafting.*

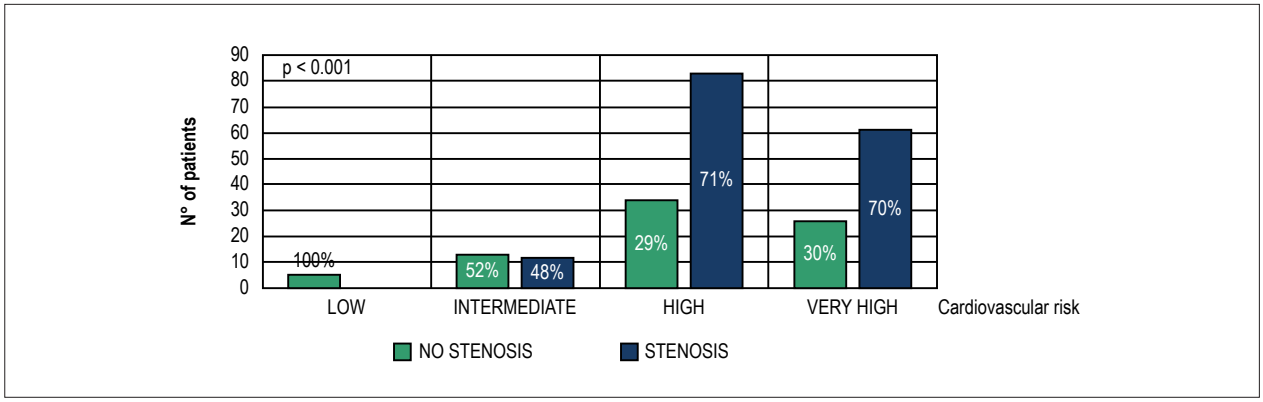

Figure 4 – *Distribution of patients for low, intermediate, high and very high cardiovascular risk, and presence or absence of carotid stenosis.*

Discussion

This study reported important information. Firstly, it was clear that most patients who underwent CVD and TTE were elderly and had high or very high CVR. These patients come to tertiary care to do tests that should have been done previously, evidencing difficulties in the public primary prevention. In other words, the hospital's medical team investigates clinical conditions in hospitalizations and outpatient follow-ups, but not in a preventive way – otherwise, most patients analyzed in this study would be younger. This relationship is built by finding, in this study, that the greater the age the greater the cardiovascular risk.

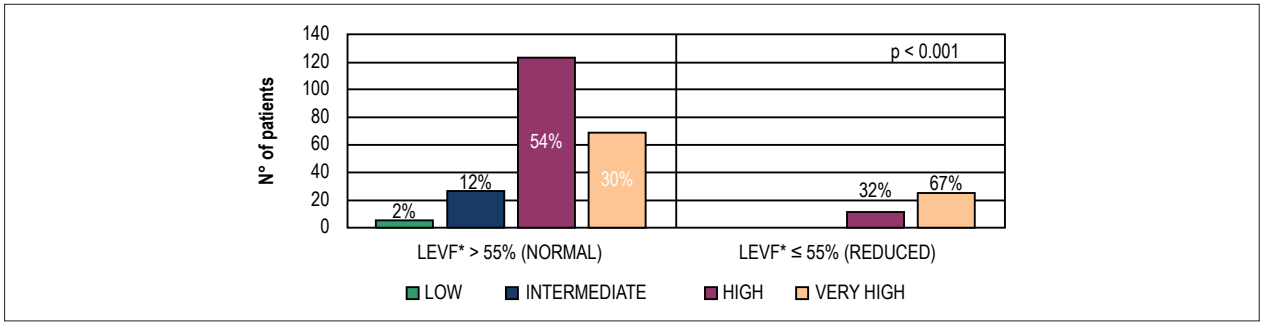

Figure 5 – *Distribution of patients for low, intermediate, high and very high cardiovascular risk, and normal or reduced left ventricular ejection fraction (LVEF).*

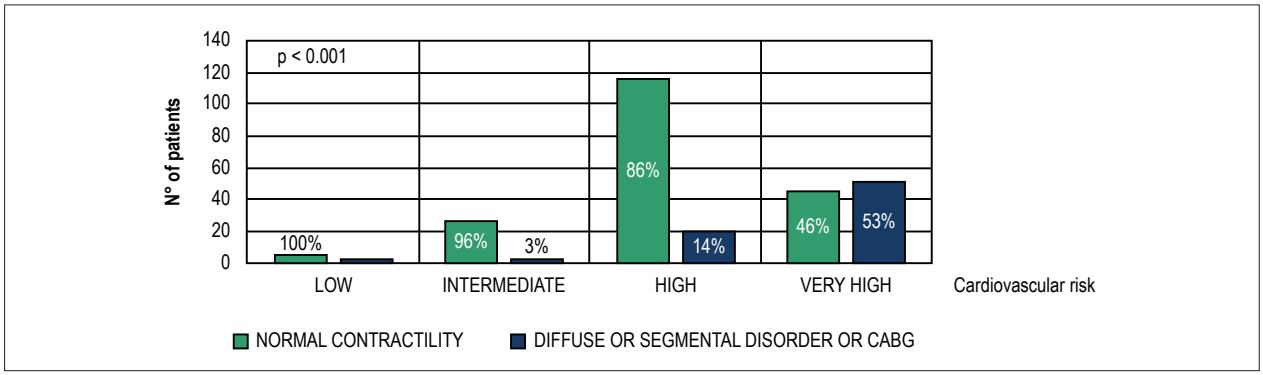

Figure 6 – *Distribution of patients for low, intermediate, high and very high cardiovascular risk, and contractile myocardial disorders. CABG: coronary artery bypass grafting.*

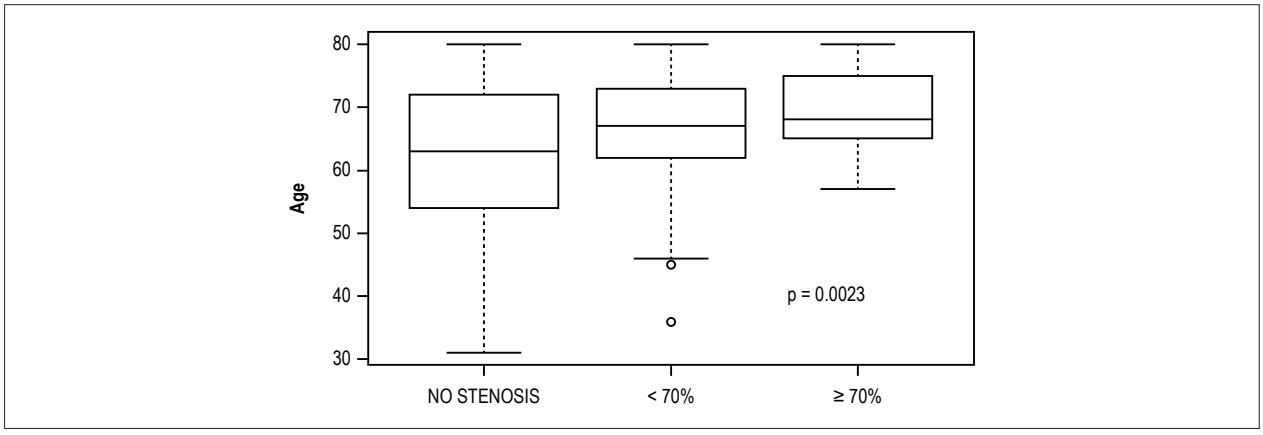

Figure 7 – *Distribution of patients according to age and presence or absence of carotid stenosis.*

Clinically relevant stenosis, which cause stenosis > 70% in one of the carotid arteries, are more prevalent in older patients, but it was not possible to make the same inference regarding left ventricular dysfunction.

Regardless of age, it was found that many patients with very high CVR had carotid atherosclerotic plaques, which is consistent with the results found by Baldassarre et al.[7], Steinvil et al.[8] and Van Der Oord et al.,[9] who correlated carotid atherosclerosis with cardiovascular event (CVE). The latter authors also correlated carotid IMT with CVD, but it was not possible to agree or disagree, since the carotid IMT values were not found in the CVD reports of this study.

The CVD reports of the Hospital de Clínicas de Curitiba only describe the presence of atherosclerotic plaque in the carotid arteries and the degree of stenosis they cause, in addition to their location. Information such as carotid IMT, extension, area and three-dimensional evaluation of plaque volume are not described. This quantitative information is said to be more sensitive in the prediction of CVR according to Naqvi and Lee.[10] Another parameter that is not evaluated is the coefficient of carotid distensibility, considered a significant predictor of CVR.[11]

Regarding the location of the plaques, some findings consistent with other studies were found. The common and external carotid arteries were less affected, as found by

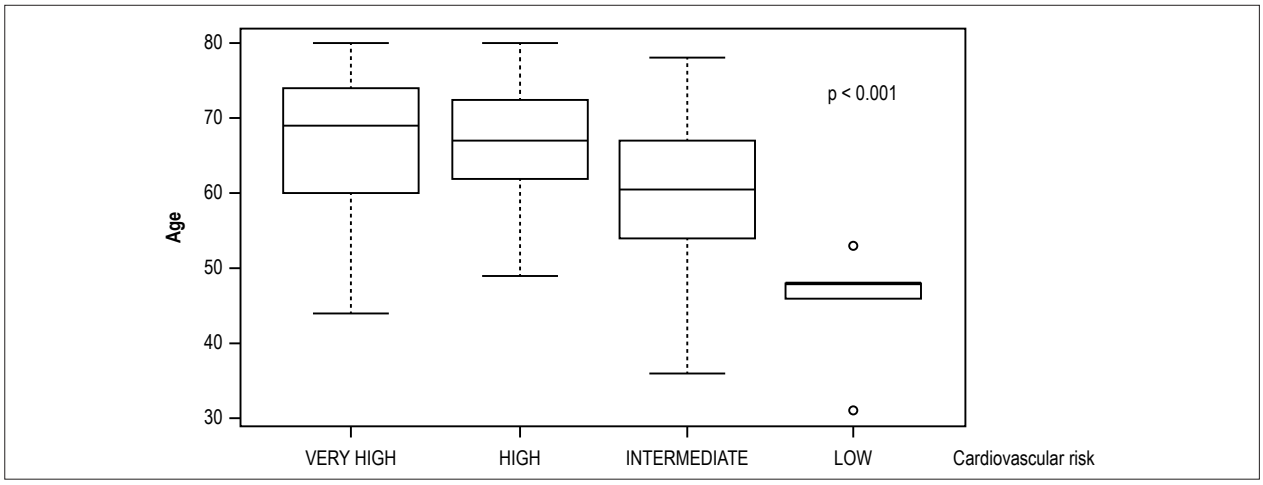

Figure 8 – *Distribution of patients according to age and very high, high, intermediate and low cardiovascular risk.*

Oliveira et al.,[12] who associated CAD with atherosclerotic plaques in bulbs and in internal carotid arteries.

Although atherosclerosis correlates positively with CVR, the presence of the plaque alone may not be of clinical importance. This is explained by the fact that this study has found that most patients with carotid plaques had stenosis of 10 to 30%, which has little or no clinical repercussion.

However, it was possible to obtain a statistically positive correlation between stenosis and carotid artery> 70% and abnormal contractility. This finding was consistent with a study by Sharma et al.,[13] who associated carotid atherosclerosis with left ventricular dyssynchrony. There was also consistency with the findings reported by Engstrom et al.[14] Although they did not correlate with the presence of atherosclerotic plaques per se, they found that patients with diffuse hypokinesia heart failure have high carotid IMT.

Chacal et al.[15] correlated the presence of carotid plaques (more than 5 plaques) with LVEF reduction, but this study did not find the same result, as the number of plaques was not quantified. Although Hedberg et al.[16] found a correlation between moderate to severe carotid stenosis and left ventricular dysfunction, it was not possible to demonstrate a similar statistically significant result.

The difficulties encountered in the preparation of this study include the fact that many medical records do not have notes regarding laboratory tests (important in the stratification of CVR), as these results only appear in the hospital's system and are not printed. Still, many patients who underwent CVD and TTE tests did not have their reports attached to their medical records, making it difficult to perform the research. Many medical records analyzed had to be excluded from the statistical analysis, because many data were missing.

Another obstacle was the illegibility of the notes in the records, which led to the exclusion of some patients from the study, as well as the lack of chronological order of the tests, hospitalizations and appointments in outpatient clinics.

Conclusion

This study demonstrated a relationship between very high cardiovascular risk with carotid artery stenosis, left ventricular dysfunction and myocardial contractile disorders.

Besides, a correlation was found between carotid stenosis and (segmental or diffuse) myocardial contractility disorder, but without correlation with reduced left ventricular ejection fraction.

Authors' contributions

Research creation and design: Wermelinger ACC; Data acquisition: Amorim AGG; Data analysis and interpretation: Wermelinger ACC; Manuscript writing: Amorim AGG; Critical revision of the manuscript as for important intellectual content: Wermelinger ACC.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

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Academic Association

This study is not associated with any graduate programs.

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