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Tei Index in a Sample of Patients with Ankylosing Spondylitis

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Abstract

Background and objectives: Ankylosing spondylitis (AS) is an inflammatory disease of immunological origin which has been correlated with higher cardiovascular risk. Although the risk factors are not clear, many cardiac alterations have been described, such as conduction disturbances, coronary heart disease, aortic root dilation, cardiac valve alterations, and ventricular diastolic dysfunction.

The objective of this study was to evaluate echocardiographic findings in AS patients who were asymptomatic for cardiac disorders, and to compare them with findings from healthy subjects.

Materials and methods: This study compared echocardiographic findings for 22 patients diagnosed with AS who had no previous cardiac abnormalities and 22 healthy subjects. We evaluated the cardiac cavities, left ventricular mass index, indices of systolic and diastolic ventricular function, the function and anatomy of the heart valves, and the myocardial performance index. Some of these measurements were correlated with disease duration and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index).

Results: There was no statistical difference between groups with regards to the size of cardiac chambers, ventricular mass index, and relative thickness of the ventricular wall. As for the ejection fraction, individuals in the AS group had lower levels for this parameter (p=0.02). The myocardial performance index (Tei index), considering TEI ≥ 0.44 as abnormal, was altered in 31.82% of the patient group, while no patient in the control group had an altered Tei index (p=0.009), reflecting poorer ventricular performance in patients with AS.

Conclusion: Individuals with AS have worse indices of myocardial performance, especially those who have had the disease for 20 years or more.

Keywords

Ankylosing spondylitis, Echocardiography, Autoimmunity

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease which tends to affect the spinal column and the sacroiliac joint and which may cause stiffness and limited axial function. It also affects ligaments and articular capsules where they connect to the bones (entheses). Generally the disease affects young, Caucasian men.

Besides the diagnostic criteria for the disease, multiple clinical instruments have been developed to estimate the active extent of the disease, such as the BASFI *(Bath Ankylosing Spondylitis Functional Index)* and the BASDAI [1] (*Bath Ankylosing Spondylitis Disease Activity Index)*. The BASDAI is applied in clinical monitoring of AS, as it evaluates situations which can be modified with treatment, such as fatigue, inflammatory axial pain, peripheral involvement, and morning stiffness. A score of ≥ 4 indicates active disease. The BASFI evaluates the degree of functional incapacity, and shows little variability in patients who have had the disease for a long time, due to irreversible changes.

The cardiovascular system can be affected by AS in various ways, such as changes in electrical conduction, a greater incidence of coronary artery disease, aortic root dilation, cardiac valve alterations, and a higher incidence of diastolic ventricular dysfunction [2], keeping in mind that the epidemiological values for these abnormalities vary significantly in the literature [3-5]. Many studies demonstrate the utility of echocardiography in detecting these anomalies, which are often subclinical. The Tei index is known as an independent predictor of morbidity and mortality and presents an excellent correlation between the detection of cardiac insufficiency [6] and post-infarction prognosis [7]. It is important to stress that this index is simple to calculate, much more easily obtained than the ejection fraction as it does not depend on endocardial border delineation. It also is not significantly influenced by cardiac frequency and arterial pressure [8].

Against the backdrop of cardiovascular diseases, the echocardiograph has been established as one of the main tools in investigating cardiac alterations, having only been overtaken in frequency of use by the electrocardiogram. The echocardiogram is based on the emission of ultrasound waves from the transducer; these waves are reflected and captured back by the apparatus, making it possible to view the heart in real time. This allows several important parameters to be determined, such as the size of the cardiac chambers,

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determination of ventricular function, and valvular anatomy and function. By using Doppler echocardiography, it is possible to determine the velocities of blood flow, and estimate pressure gradients, cardiac deficit, and valvular area. From this richness of details and parameters, various functional indices have been created in an attempt to identify and quantify functional alteration; the Tei index is one of these. Developed by Tei et al. [9] in the 1990s, this index has been proven as an independent predictor of long-term morbidity and mortality [10], the best parameter in assessing mortality after an acute myocardial infarct [11] and an excellent detector of cardiac insufficiency when it is greater than or equal to 0.47 [12]. Furthermore, this index is directly related with myocardial dysfunction: the greater the Tei Index, the greater the dysfunction, and consequently it is of great prognostic value. Individuals without any morpho-functional alteration exhibit values of less than 0.39 +- 5 [10,13].

Ambulatory patients with AS are not routinely sent for echocardiographic evaluation, only when cardiovascular symptoms appear. The objective of this study was to evaluate echocardiographic measurements for patients with in AS who were asymptomatic for cardiac disorders, and to compare them with findings from healthy subjects of the same age. In order to define the prevalence of asymptomatic cardiological alterations in ambulatory patients, we also aimed to correlate the obtained TEI index with disease duration and disease activity indexes.

Materials and Methods

Sample

The study was conducted in the Spondyloarthritis Clinic and the Echocardiography Department at the Hospital de Clinicas at the Universidade Federal do Paraná. Two groups of individuals were organized for the comparison: the spondylitis group and the control group.

In order to create the spondylitis group, 30 patients receiving care from the ambulatory Spondyloarthritis Clinic at the Universidade Federal do Paraná were selected at random. For inclusion, a confirmed diagnosis of AS according to the modified New York criteria was necessary, as well as an age above 18 years [14]. The following patients were excluded: patients with a history of myocardial infarction or angina, patients with a diagnosis of diabetes, hyperthyroidism, or hypertension, patients with a history of previous cardiac procedures (angioplasty, myocardial revascularization, valve replacement) and patients with a history of congenital cardiopathy. Of the 30 which were randomly selected, 08 were excluded (04 for arterial hypertension, 02 for previous myocardial infarction, and 02 for diabetes), leaving 22 patients in the spondylitis group.

In order to create the control group, 22 individuals were invited at random. In order to be included in the study, they needed to be older than 18 years of age and conform to the same exclusion criteria adopted for the spondylitis group.

All the individuals that participated in the study signed the "Terms of Free and Clarified Consent" approved by the Research Ethics Committee at the UFPR Center for the Sciences.

Methods

The echocardiographic examinations for the spondylitis group were performed using a Hewlett-Packard Sonos 5500 model with a 2-4MHz transducer and a Philips Envisor model equipped with a multifrequency 2-5MHz transducer from the echocardiography department at UFPR's Hospital das Clínicas. The echocardiographs for the control group were conducted using a Philips Envisor model equipped with a multifrequency 2-5MHz transducer. A single observer conducted the transthoracic echocardiograms.

Measurements of the left ventricle, right ventricle, and diameter of the aorta and left atrium were made according to the recommendations of the American Society of Echocardiography (ASE) using one-dimensional mode.

The mass of the left ventricle (LVM) was calculated using Devereux et al. [15]'s corrected ASE formula: Mass = 0.8 {1.04 [(LVIDD + PWTD + IVSTD)^3 – LVDD^3]} + 0.6 g [15]; where LVDD represents the internal diameter of the left ventricle in diastole, PWTD represents the posterior wall thickness in diastole, and the IVSTD represents the thickness of the interventricular septum in diastole. Left ventricular mass was indexed to body surface area by dividing the left ventricular mass by body surface area; normal values were considered to be less than 95g/m^2 for women and less than 115g/m^2 for men (*Recommendations for Chamber Quantification*, JASE, December 2005) [16]. We also presented the value for relative wall thickness (RWT), with normal values being <0.42 [16]. Depending on the distribution of the values for this index of left ventricular mass (ILVM) with relation to the relative width of the left ventricle, ventricular geometry was classified into 4 categories [16].

1 – Normal geometry: individuals with an index of left ventricular mass and width relative to normal ventricular walls (ILVM ≤ 115g/m^2 for men and ≤ 95 for women. Both sexes should have RWT >0.42).

2 – Concentric remodeling: characterized by increased relative wall thickness with normal left ventricular mass (ILVM ≤ 115 g/m^2 for men and ≤ 95g/m^2 for women. Both sexes should have RWT >0.42).

3 – Eccentric hypertrophy: corresponds to an increase in the index of ventricular mass with normal relative wall thickness. (ILVM>115g/m^2 for men and >95g/m^2 for women. Both sexes should have RWT ≤ 0.42).

4 – Concentric hypertrophy: characterized by increases in the index of ventricular mass and the relative wall thickness. (ILVM>115g/m^2 for men and >95g/m^2 for women. Both sexes should have RWT >0.42).

Ventricular diastolic function was evaluated via diastolic mitral flow analysis using tissue Doppler imaging at a distance of 1 cm from the lateral mitral annulus. By using mitral diastolic flow, we analyzed the way the left ventricular cavity filled. Mitral flow was measured at the two diastolic peaks, the E and A waves, which indicated the maximum velocity achieved by the blood at the beginning and the end of diastole, respectively (phases of quick filling of the LV and atrial contraction). We took into account the fact that the decrease in ventricular relaxation reflects an altered relation between the E peak and the A peak (the E/A ratio), with values less than 1 [17].

The tissue Doppler allows for measurements of systolic velocity (S), early diastole (E') and late diastole (A´) of the mitral annulus. Based on these parameters, diastolic function was classified into:

1. Normal diastolic function: E/A Ratio>0.8; E'>A'; E/E'<8;

2. Level I diastolic dysfunction: E/A Ratio<0.8; E'<A'; E/E'<8;

3. Level II diastolic dysfunction (pseudo-normal): E/A Ratio 0.8 – 1.5 with a drop of more than 50% in this ratio during the Valsalva maneuver, E/E'=9-12;

4. Level III diastolic dysfunction: Restrictive filling pattern (E/A Ratio>2, deceleration time <160ms, E/E'>12).

Analysis of the systolic function of the left ventricle was made by verifying the ejection fraction using the Teichholz method and fractional shortening of the left ventricle.

In order to calculate the Tei index, or myocardial performance index, according to Tei et al. [10], analysis of blood flow with interpolation was done using pulsed Doppler between the left ventricular exit and the anterior mitral valve leaflet, registering the Doppler spectrum shown in the Figure 1.

Interval a was the result of the measurement of the flow velocity through the mitral valve, from the interruption of the flow in a cardiac cycle until the beginning of the next, and involved the sum of the isovolumetric contraction time (ICT), the ejection time (ET), and the isovolumetric relaxation time (IRT). Interval b, measured

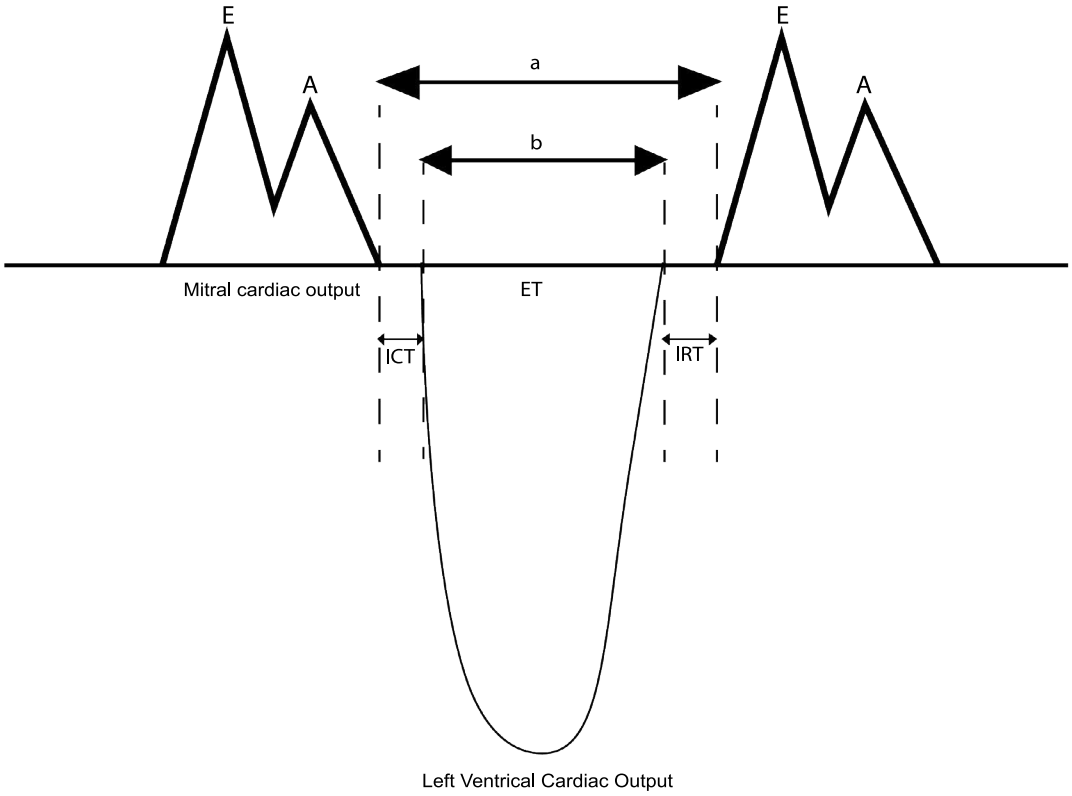


Figure 1: Schematic representation of Doppler time intervals to calculate the index of myocardial performance or Tei index.

by registering the flow velocity through the left ventricular exit, was equal to the ejection time. The Tei index was calculated as (a – b)/b, which corresponds to (ICT + IRT)/ET.

The cutoff points for assessing the aortic root and the Tei index were established according to the literature, and were 37mm and 0.39 +/- 0.5, respectively [18].

Statistical analysis

Using the echocardiogram, morphological and functional cardiac characteristics were analyzed for both groups. For the spondylitis group, the echocardiogram findings were related to the duration of the illness and the index of disease activity (BASDAI).

The continuous variables were tested for distribution type and their results were expressed as a mean and standard variation (parametric distribution) or as a median (non-parametric distribution). The categorical variables were expressed as percentages. The comparison of the groups in with relation to the continuous variables was conducted using analysis of covariance (ANCOVA), considering age and sex as control variables. To evaluate the association between dichotomous variables, Fisher's exact test was used. Values of $p<0.05$ indicated statistical significance. The data were organized into an Excel spreadsheet and were analyzed using the computation program Statistica v.8.0.

Results

There was no statistically significant difference between the groups with regards to age and body surface area. The mean ages and body area were 38.95 years and 1.78m^2 for the spondylitis group and 35.85 years and 1.84m^2 for the control group, respectively.

The male sex was more prevalent in the spondylitis group. Men are more commonly affected by AS by a proportion of 3:1 [19-22]. Male individuals accounted for 81.82% of the spondylitis group and 63.64% of the control group.

The average duration of disease in the AS patients was 16.45 years (3 – 32) and the average BASDAI index was 4.99 (0.14 – 9.87). The BASDAI was not calculated for the control population.

Table 1: Continuous echocardiographic variables for the study population.

	AS Group	Control Group	P
	{n=22}	{n=22}	
Left atrium (mm)	34.5 (23-39)	36.59 (28-40)	0.14
Aortic root	30.91 (21-39)	28.86 (21-36)	0.647
Right ventricle	17.82 (11-25)	19 (10-25)	0.489
Left ventricular mass (g/m^2)	86.43 (65-110)	86.49 (51-115)	0.938
Relative wall thickness	0.36 (0.28-0.53)	0.34 (0.25-0.43)	0.743
Ejection fraction (%)	67.55 (60-77.2)	72.66 (63-87)	0.02

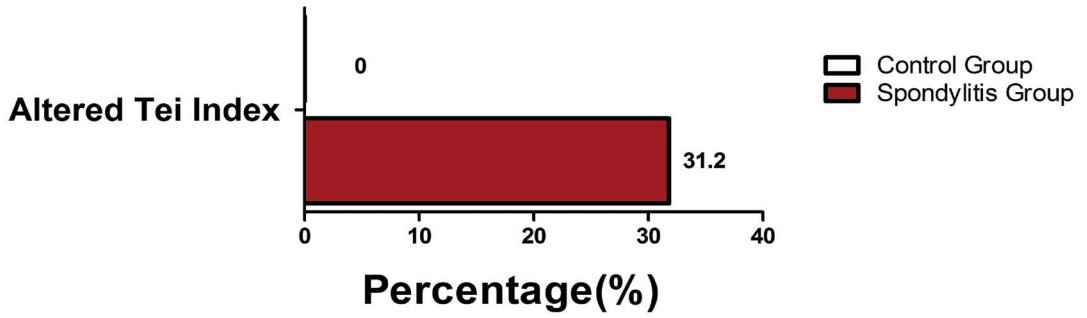
Table 2: Comparison between aortic root measurements between spondylitis group and control group.

	Spondylitis Group	Control Group	P
	{n=22}	{n=22}	
Aortic root <37mm	20 (90.91%)	22 (100%)	
Aortic root =37mm	2 (9.09%)	0 (0%)	
			0.488

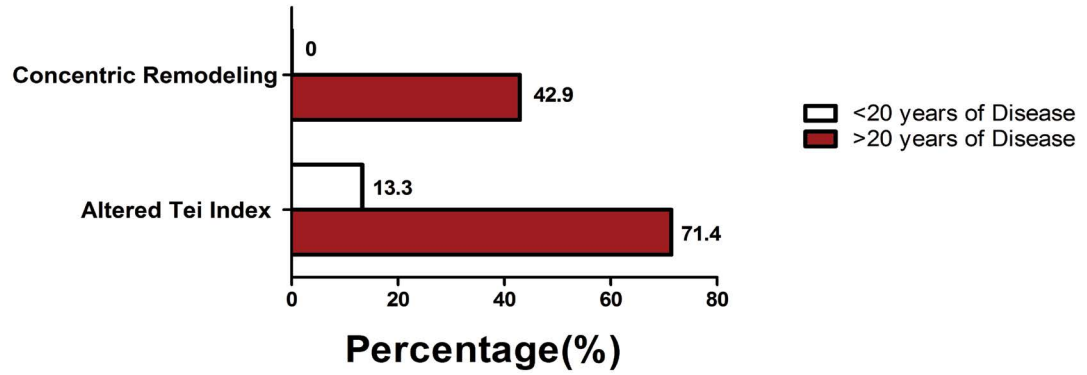
There was no statistical difference between the groups with relation to size of the cardiac cavities, index of ventricular mass, and relative ventricular wall thickness. Individuals in the control group demonstrated more elevated levels of ventricular ejection fraction (p=0.02). The data related to these variables are shown in Table 1.

On average, there was no statistical difference between the groups with relation to the diameter of the aortic root. However, using 37mm as a cutoff point, no patient in the control group presented dilation of the aortic root, and in the spondylitis group, 2 patients had an increase for this parameter (9.09% of patients). Consequently, a tendency towards dilation of the aortic root was seen in patients with AS, albeit a tendency without statistical significance (p=0.488) (Table 2).

As for alterations in ventricular geometry and diastolic function, there was no statistical significance between the groups. Of the 22 patients in each sample, only 1 patient in the spondylitis group



Graph 1: Comparative analysis of alterations in left ventricle Tei Index between AS and control. TEI index among AS and controls



Graph 2: Relationship between disease duration and echocardiographic alterations.

Table 3: Comparison between Tei index for AS and control.

	AS Group	Control Group	P
	{n=22}	{n=22}	
Tei Index < 0.44	15 (68.18%)	22 (100%)	
Tei Index = 0.44	7 (31.82%)	0 (0%)	
			0.009

Table 4: TEI index correlated with Disease duration.

Variable	Duration of Disease =20 years	Duration of Disease >20 years	P
	{n=15}	{n=7}	
Concentric remodeling of the left ventricle	0 (0%)	3 (42.9%)	0.023
Left ventricular hypertrophy	0 (0%)	1 (14.3%)	0.318
Aortic root dilation	1 (6.7%)	1 (14.3%)	1
Diastolic dysfunction of the left ventricle	3 (20.0%)	0 (0%)	0.523
Altered myocardial performance index	2 (13.3%)	5 (71.4%)	0.014
Mild aortic reflux	0 (0%)	1 (14.3%)	0.318
Mild mitral reflux	0 (0%)	1 (14.3%)	0.318

presented diastolic dysfunction, and 0 patients in the control group did (p=1). Only 4 patients with AS displayed abnormal geometry of the left ventricle, compared with 1 from the control group (p=0.345).

With regards to the index of myocardial performance (Tei index) and considering the cutoff of Tei ≥ 0.44 as abnormal, 31.82% of the spondylitis group showed alterations, compared with 0 individuals from the control group (p=0.009), reflecting worse ventricular performance in patients with spondylitis (Graphic 1,Table 3).

The echocardiographic findings for the patients with AS were correlated with the duration of disease and the activity of the disease. As for duration of disease, the patients were subdivided into two groups: more than 20 years' duration and less than 20 years' duration.

Table 5: Correlation between Myocardial performance and BASDAI.

Variable	BASDAI <4	BASDAI >4	P
	{n=8}	{n=14}	
Concentric remodeling of the left ventricle	0 (0%)	3 (21.4%)	0.273
Left ventricular hypertrophy	1 (12.5%)	0 (0%)	0.364
Aortic root dilation	0 (0%)	2 (14.3%)	0.515
Diastolic dysfunction of the left ventricle	1 (12.5%)	1 (7.1%)	1
Altered myocardial performance index	2 (25.0%)	5 (35.7%)	1
Mild aortic reflux	0 (0%)	1 (7.1%)	1
Mild mitral reflux	0 (0%)	1 (7.1%)	1

With regard to the activity of the disease, the patients were separated according to the results obtained by the BASDAI index. Index ratings of <4 were considered to be low disease activity, while ≥ 4 was considered to be high activity. The results of these associations are shown in Tables 4,5 and in Graph 2.

Discussion

Ankylosing spondylitis is an immunological disease of inflammatory character which can cause functional and structural cardiac alterations that are often asymptomatic. Recent studies demonstrate greater cardiovascular morbidity and mortality [23,24] in patients with AS in comparison with the general population. In inflammatory diseases such as systemic lupus erythematosus and rheumatoid arthritis, the correlation between atherosclerosis caused by systemic inflammation [25-27] and the increase in cardiac complications is well-established. In AS, there is still discussion of evidence correlating risk factors with the increase in cardiovascular morbidity and mortality. Some studies have found a mutual relation between the presence of HLA-B27 and morpho-functional alterations such as dilation of the aortic root and 3rd degree atrioventricular block [28,29].

Keeping in mind the ease and the importance of echocardiography, various studies have utilized this resource in order to investigate cardiovascular alterations in patients with AS. In 1996, Ergunay et al. [30] analyzed the cardiac function of 14 patients with AS and compared it with that of 10 healthy volunteers. Systolic function did not differ between the two groups; however, morphological changes and diastolic dysfunction were more common in patients with AS. Furthermore, in an Australian study in 1982, Thomas et al. [31] examined 23 patients with ankylosing spondylitis using M-mode echocardiography. Compared with 22 control individuals, the spondylitis groups had a greater incidence of aortic root dilation, without a correlation between dilation and the degree of inflammatory activity. Roldan et al. [12] published a study conducted on 44 AS patients and 30 control individuals, paired by age and sex. Through a transesophageal echocardiogram, aortic root disease was found in 82% of patients with AS, compared with 27% of the control group. In 41% of the patients, thickening of the aortic valve was seen, and in 34%, thickening of the mitral valve. Almost half of the patients had valvular reflux, and 40% of these had moderate reflux. The findings did not show a correlation with the activity, severity, or therapy for AS, but were correlated with the duration of the disease.

In our case, there was no statistical difference between the spondylitis group and the control group with relation to the size of cardiac cavities, anatomy and functionality of the cardiac valves, ventricular geometry and diastolic function, in contrast with the study by Ergunay et al. [30]. As for the evaluation of the aortic root, 2 patients (9.09%) in the AS group showed dilation of the aortic root compared to 0 volunteers from the control group; nevertheless, this difference we encountered was not statistically relevant (p=0.488).

Although descriptions of various morphological cardiac alterations in AS patients are found in the literature, in our sample these findings were not significant. Nevertheless, due to the small number of participants in our study, we cannot discard these possible abnormalities as determining factors for cardiovascular morbidity and mortality.

In analyzing functional cardiac parameters, the alterations we found were more evident. Individuals in the spondylitis group exhibited lower ejection fractions than those in the control group (p=0.02). The AS group showed worse indices of left-ventricle myocardial performance (Tei index) in comparison with the control group. We observed that 31.82% of the population of the spondylitis group exhibited alterations in the Tei index, while 0 individuals in the control group had alterations in this index (p=0.009).

Cardiac alterations were correlated with disease activity (as measured by the BASDAI) and the duration of the disease (measured in years). Of the individuals whose disease was more than 20 years in duration, 42.9% (03 patients) had concentric ventricular remodeling, and 0 individuals with disease duration of less than 20 years had this alteration (p=0.02). We observed that 71.4% of patients with more than 20 years' disease duration exhibited alterations in the Tei index, and only 13.3% of individuals with less than 20 years' disease duration exhibited this alteration (p=0.014). No correlation between disease activity and echocardiographic alterations was observed.

Conclusions

According to the data in our study, individuals with AS, even those who are asymptomatic from a cardiovascular point of view, exhibit worse indices of myocardial performance. A greater incidence of concentric remodeling and alterations in myocardial performance were demonstrated in those individuals whose disease was more than 20 years in duration.

We conclude that in AS, the major determinant for demonstration of echocardiographic alterations is the disease's duration, not the degree of its activity. In this context, in our opinion, the echocardiogram could be an excellent tool for evaluating patients with AS, as it is low in cost, widely available, and innocuous; it should be routinely ordered for patients with longer disease duration (>20 years).

We believe that, due to the small number of patients included in our sample, there is still a need to conduct studies with larger number of patients in order to confirm these findings with a better stratification of patients by disease duration.

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