VALVULAR INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

Ana Paula Beckhauser,* Liz Vallin,* Claudine J Burkievcz,*
Sonia Perreto,** Marilia Barreto Silva,* Thelma L Skare*

Abstract

Background: Although pericarditis is the most commonly recognized cardiac lesion in Rheumatoid Arthritis (RA), this disease affects all the three cardiac layers.

Objective: To study valvular lesions in RA, trying to correlate them with other clinical variables, auto antibodies and functional class.

Methods: One hundred twenty two controls and 184 patients with RA without cardiac symptoms were studied using bidimensional echocardiography. We also studied smoking habits, age and disease duration, rheumatoid factor, antinuclear antibody, anticardiolipin antibodies, rheumatoid nodules and functional class in RA patients.

Results: We found that 28 RA patients (15.2%) had valvular lesions and that the aortic valve was the most affected. Valvular lesions were more common in patients with disease duration longer than 15 years (p=0.013). No association was found between valvular lesions and sex, age, tobacco exposure, rheumatoid factor positivity, presence of antinuclear antibodies, rheumatoid nodules, anticardiolipin antibodies or functional class.

Conclusion: A small part of RA patients had asymptomatic valvular lesions which occurred more frequently in patients with long disease duration.

Keywords: Rheumatoid Arthritis; Endocardium; Abnormalities.

Resumo

Introdução: Embora a pericardite seja a manifestação cardíaca mais facilmente reconhecida da artrite reumatóide (AR), essa doença afeta os três folhetos do coração.

Objetivo: Estudar o comprometimento valvular na AR tentando correlacioná-lo com variáveis clínicas, auto-anticorpos e índice funcional.

Metodologia: Foram estudados 122 controles e 184 pacientes com AR, assintomáticos do ponto de vista cardiovascular, através de eco-cardiografia bidimensional. Pesquisou-se nesses mesmos pacientes: hábito de fumar, idade, tempo de doença, fator reumatóide, fator antinuclear, anticardiolipinas, presença de nódulos reumatóides e classe funcional.

Resultados: Encontraram-se lesões valvulares em 28 (15,2%) dos pacientes, sendo a válvula aórtica a mais afetada. O aparecimento das lesões valvulares foi mais comum nos pacientes com duração de doença maior do que 15 anos (p=0,013). Não se encontrou associação entre tais lesões e sexo, idade do paciente, exposição ao fumo, fator reumatóide, anticorpos antinucleares, nódulos reumatóides, classe funcional ou presença de anticardiolipinas.

Conclusões: Uma pequena porcentagem de pacientes com AR tem envolvimento valvular assintomático, que é mais comum em pacientes com AR de longa duração.

Palavras-chave: Artrite reumatóide; Endocárdio; Anormalidades.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects joints causing deformities.[1] In this disease the synovial membrane is the main target,[1] although extra-articular manifestations can be found including cardiac ones.

In RA, the heart can be affected in its three

*Serviço de Reumatologia do Hospital Universitário Evangélico de Curitiba – PR – Brasil
**Serviço de Ecocardiografia do Hospital Universitário Evangélico de Curitiba – PR – Brasil

layers.[2] Pericarditis is the cardiac manifestation most readily recognized, but myocardial disease, coronary vasculitis, diastolic dysfunction, accelerated atherosclerotic disease and valvular lesions can also be found.[2] The prevalence of RA valvular heart disease is variable in the literature varying from 3% to 70%.[3,4] This high variability may be due to different genetic backgrounds of the studied population and to different methods used in the detection of valvular disease. In some studies the occurrence of valvular heart disease is associated with male gender and presence of rheumatoid nodules,[5] age, disease duration[2] and degree of inflammatory activity.[6] However, in others such associations could not be found.[7,8]

This study tries to verify the frequency of valvular heart involvement in an RA population as well as its association with rheumatoid nodules, auto--antibodies (rheumatoid factor, antinuclear and anticardiolipin antibodies), disease duration and patients functional class.

Methods

This study was approved by the local Ethic Committee and the enrolled patients gave a written consent. All RA patients that attended the Rheumatology Unit of Hospital Evangélico de Curitiba during 2007 with at least four RA Classification Criteria of the American College of Rheumatology[9] were invited to participate. Patients with arterial hypertension, ischemic myocardial disease, diabetes mellitus, renal failure and chronic obstructive pulmonary diseases, previous rheumatic fever, congenital cardiac lesions and other causes of valvular lesions were excluded. All included patients were asymptomatic from the respiratory and cardiac point of view.

A total of 184 patients were examined through a bidimensional echocardiograph with color Doppler using an Apogee 800 plus ATL apparatus. All tests were done by the same physician according to a standardized protocol. The valves were examined for thickening and a hyperechoic appearance; transvalvular gradients were measured and any regurgitation was quantified using color flow Doppler.

Data such as age, sex, disease duration, smoking habits, rheumatoid nodules at physical examination, rheumatoid factor (RF), antinuclear antibodies (ANA), anticardiolipin antibodies (aCl) and

functional class according to the Criteria of American College of Rheumatology for global functional classification in RA[10] were obtained. Rheumatoid factor was studied by immunoturbidimetry and we considered positive titers those above 15 UI/ml. ANA was studied by immunofluorescence technique using HEp-2 cells and anticardiolipin antibodies were studied by ELISA, and considered as positive values over 10 GPL for aCl IgG and 10 MPL for aCl IgM.

As controls we included 122 declared healthy persons that were going through echocardiography as part of a check up program. None of them had arterial hypertension, ischemic myocardial disease, diabetes mellitus, renal failure, chronic obstructive pulmonary diseases or previous history of valvular lesion.

Data was analyzed through contingency and frequency tables. Associations were calculated using Qui-squared and Fisher and t tests using Graph Pad Prism 4.0® software. Significance adopted was of 5%.

Results

Of 184 studied RA patients, 17 were male and 167 were females with ages between 20 and 85 years (mean 48.2±13.9 years) and disease duration between one and 39 years (mean 8.4± 7.4 years). In the control population 104 were females and 18 were males with ages between 19 and 82 years (mean 51.48±14.41 years). The control population was pared for sex (p=0.13, chi-squared) and age (p=0.99; Mann Whitney).

Thirty-four valvular lesions in 28 patients (15.2% of the studied population) were detected at echocardiography. It was possible to identify 11 cases of aortic regurgitation, six of aortic stenosis, two of aortic valvar thickening, seven cases of mitral regurgitation, six cases of mitral stenosis and two of tricuspide regurgitation (Figure 1). Six patients had mitral and aortic lesions, one had mitral and tricuspid lesion, one had combined aortic and another combined mitral lesions.

In the control population we found seven (5.73%) patients with nine valvular lesions: five aortic insufficiencies, three mitral insufficiencies and one mitral stenosis. Patients with rheumatoid arthritis had more valvular lesions than control population (p=0.017, chi-square).
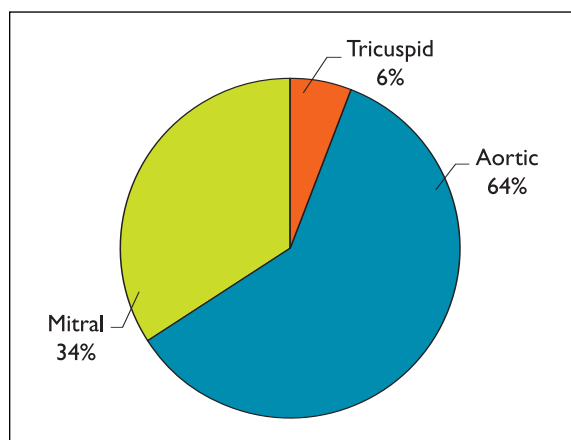
Studying the RA population according to valvu-

Figure 1. Valvular involvement in 184 rheumatoid arthritis patients.

Figure 2. Functional class distribution (in %) in RA patients with and without valvular lesions (p=0.31)

lar lesions and smoking habits we found that 50% (n=14) of patients with valvular lesion were previous or present smokers against 67.9% (n=106) of RA patients without valvular lesions (p=0.37; chi--squared). The study of association between valvular lesions and rheumatoid nodules and rheumatoid factor is summarized in Table I.

ANA were obtained in 26 patients with valvular lesions and were positive in eight (30.7%) and in 151 patients without valvular lesions and were positive in 29 (19.2%) of them (p=0.18; chi-square).

Anticardiolipin antibodies (IgG and IgM) were obtained in 164 patients being weakly positive in 10 (6.09%). In the group with valvular lesions, only one patient was positive for IgM aCl (3.57%). In the group without valvular lesions, nine patients (6.6%) were positive for aCl (three aCl IgM, four aCl IgG and two for both) with p=1.0 (Fisher).

The study of relationship between valvular lesions and age of diagnosis showed that patients with valvular lesion had mean age of 51.3± 18.2 years at diagnosis and patients without valvular le-
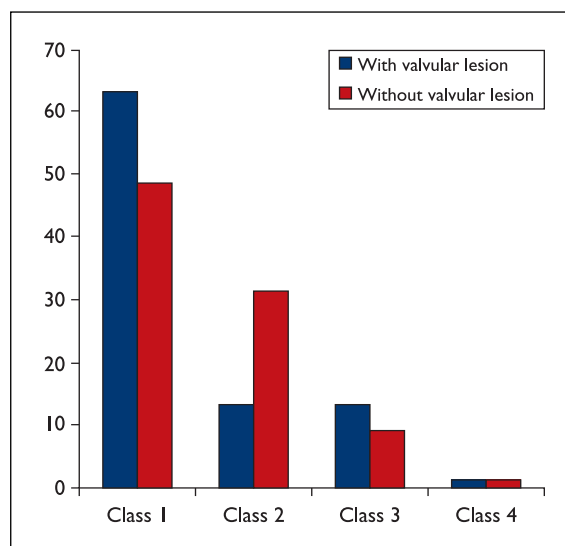
sion had mean age of 47.1± 13.7 years at diagnosis, with p=0.12 (Mann -Whitney).

Functional status was obtained in 168 patients and the results are summarized in Figure 2.

In the study of valvular lesions according to disease duration we found that patients with more than 15 years of disease duration had more valvular lesions than those with less than that (p=0.017, chi-square).

Discussion

The present analysis showed a low frequency of valvular lesion in RA patients detected by bidimensional transthoracic echocardiography. In most of them the lesions were monovalvar and aortic valve was the most affected.

Valvular lesions in RA result from non specific inflammatory process in the valvular base followed by fibrosis and, sometimes, calcification.[4] Rheumatoid granulomata are more specific findings that can be found within cusps causing insufficiency.[4]

Most patients are asymptomatic from the clinical point of view. According to Guedes et al[6], less than 10% develop hemodynamic abnormalities.

Table 1. Study of association between valvular lesions and RF and rheumatoid nodules in 184 RA patients

	With valvular lesion (n=28)	Without valvular lesion (n=156)	p
Positive RF	N=21 (75%)	N=106 (67.9%)	0.45 – Chi-squared
Rheumatoid nodules	N=3 (10.7%)	N=12 (7.7%)	0.70 – Fisher

RF= rheumatoid factor

However, at least 3 reasons are relevant for searching for them:

1. These patients are prone to bacterial endocarditis;[3]
2. Some of the valvular lesion may cause rapid hemodynamic abnormalities requiring surgical treatment.[6] Several authors observed that RA endocardial lesions can cause more functional distress than those from rheumatic fever;[6, 13,14]
3. Valvular lesions may act as source of thromboembolic material causing ischemic vascular lesions.[11,12]

In our research all studied patients were clinically asymptomatic but one must remember that a polyarticular disease such as RA induces low physical activity that decreases cardiac load, which might explain the lack of symptoms.

We could not find any association between valve lesions and tobacco exposure, patients' age, nodules, functional index, presence of rheumatoid factor and antinuclear antibodies. Roldan et al[15] studying valvular heart disease through transesophageal echocardiography also could not find any association with extra articular manifestations. The association with disease duration was positive, as already noted by Coșkun et al.[2]

The aCls prevalence in RA was found to be of 16% by Merkel et al;[16] 7% for Vittecoqet et al[17] and 18% for Brunet et al.[18] None of these authors found any association between aCls and clinical findings or pregnancy loss. Gabrielli et al[19] studied the association of aCl and cardiac valvular lesions and, like us, did not find any relationship.

The use of transthoracic echocardiography can be considered a limitation for this study because it is less accurate than the transesophageal route. The transesophageal route is invasive and would be unacceptable to use in patients without cardiac complaints and in healthy controls

Conclusions

The prevalence of valvular lesion in RA patients, asymptomatic from the cardiac point of view, was 15.2% and the aortic valve the most commonly affected.

We could not find any relationship between cardiac valvular lesions and patients' age, smoking habits, RF, ANA, aCl antibodies, rheumatoid nodules or functional class.

Patients with longer disease duration had higher frequency of valvular lesions.

Correspondence to
Thelma L Skare
Rua João Alencar Guimarães, 796
80310-420 Curitiba PR
E-mail: tskare@onda.com.br

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