

Prognostic value of clinical and Doppler echocardiographic findings in children and adolescents with significant rheumatic valvular disease

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ABSTRACT

- Introduction** : The diagnosis of acute rheumatic fever (RF) is based on clinical findings. However, during the chronic phase of the disease, the clinical approach is not sufficient for the follow-up of the patients and the Doppler echocardiography is a tool for the diagnosis of cardiac involvement. Prognostic variables that influence long-term outcomes are not well known.
- Methods** : 462 patients with RF according to Jones criteria were studied, and followed-up from the initial attack to 13.6 ± 4.6 years. All patients underwent clinical assessment and Doppler echocardiography for the detection of heart valve involvement in the acute and chronic phases. Multivariate logistic regression analysis was used to identify the factors influencing long-term heart valve disease.
- Results** : Carditis occurred in 55.8% and subclinical valvulitis in 35.3% patients. In the chronic phase, 33% of the patients had significant valvular heart disease. No normal Doppler echocardiography exam was observed on patients who had severe valvulitis, although heart auscultation had become normal in 13% of these. In the multivariate analysis, only the severity of carditis and the mitral and/or aortic valvulitis were associated with significant valvular heart disease. Chorea or arthritis were protective factors for significant valvular heart disease, odds ratio 0.41 (95% C.I. 0.22 – 0.77) and 0.43 (95% C.I. 0.23 – 0.82), respectively.
- Conclusions** : Our study suggests that the use of Doppler echocardiography during RF helps to identify prognostic factors regarding the development of significant valvular heart disease. Initial severe carditis is an important factor in the long-term prognosis of chronic RHD, whereas arthritis and chore during the initial episode of RF appears to be protective. Strict secondary prophylaxis should be mandatory in high risk patients.
- Keywords** : Doppler echocardiography, prognosis, rheumatic fever, rheumatic valvular disease

INTRODUCTION

Even in the 21st century, acute rheumatic fever (RF) and chronic rheumatic heart disease (RHD) remain the major cause of cardiovascular disability in school children and

young adults from developing countries, and represent a high burden for public health.^[1] Cardiac involvement in the first attack and/or in recurrent episodes is determinant as it causes cumulative injury and permanent heart valve damage.^[2] The initial attack affects mostly the young population, but the cardiac damage remains throughout adulthood. The long-term follow up data of RF patients using Doppler echocardiography are not widely available. The objective of the present study is to characterize the clinical and Doppler echocardiographic profile of individuals diagnosed with RF both in the acute and in the chronic phases of the disease, and to define prognostic factors of significant valvular heart disease. Determination of these factors may help stratify the risk

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early in the acute phase of the disease and be a useful tool to stress the need for keeping secondary prophylaxis.

MATERIALS AND METHODS

The study was conducted at a tertiary care hospital of a federal university. The hospital is part of the public health system and assists mainly low-income patients from the metropolitan region of a big city and from the interior of the state, who were treated at a basic health care unit with a suspicion or a diagnosis of RF. The population of that metropolitan region is about three million inhabitants. The infant mortality rate in this region is about 19.1 deaths/1000 live born, and mortality from RF (including children, adolescents, and adults) is about 6% (data of 2011, from the Ministry of Health). The prevalence of RF in the region is 3.6/1000.^[3]

In the period from 1987 to 2009, 630 patients were followed-up at the outpatient clinic specific to RF of a tertiary care hospital. From these patients, 462 were selected after they had met all the following inclusion criteria: (a) diagnosis of RF in accordance with the criteria of Jones (1992, 2004),^[4] (b) age of less than 18 years at initial attack, (c) one color Doppler echocardiographic assessment was made before the end of the 12th week from the beginning of the acute phase and (d) another color Doppler echocardiographic assessment was made at least 24 months after the diagnosis. From the 168 patients excluded, 56 did not fully comply with the Jones criteria, four patients had congenital heart disease or other clinical conditions that could cause a valvular dysfunction and 108 patients did not have color Doppler echocardiographic assessments as required.

The clinical and Doppler echocardiographic follow-up schedule was the one already adopted as a standard in the RF Outpatient Clinic, and is summarized in Figure 1. Patients were seen by at least one of the team researchers in several visits during the follow-up period, which ranged from 2 to 23 years (mean 13.6 ± 4.6 years).

The scheme adopted for secondary prophylaxis was the standard use of penicillin G benzathine every 21 days. Sulfadiazine was only used in four patients. The 28-day interval regimen was adopted in 32 patients who had mild valvular lesions, in prophylaxis for more than 10 years and with difficulty to adhere to the 21-day interval regimen. At the first consultation, the patient received a booklet, signed by a caregiver, in which there was the prescription of the medication and a timetable with the dates of the shots. The clinical consultation was scheduled for one of the dates when the injection of penicillin G benzathine was to be given. The medication was freely available at the clinic, where the injections were given by nursing professionals. The prophylaxis was considered as irregular when the injection was given with a delay of more than 1 week.

Patients were assessed for cardiac involvement in the acute and chronic phases of the disease by means of clinical examination, chest radiography, electrocardiography and Doppler echocardiography. The acute phase was considered as the interval from the onset of clinical signs and symptoms to the 12th week, and the chronic phase as the period of disease after 2 years of the diagnosis. Carditis was diagnosed according to the clinical findings in the acute phase, and was classified as mild, moderate or severe, according to the Service protocol, following recommendations described by Decourt^[5] and Markowitz and Gordis.^[6] Subclinical carditis was defined as that in which the patients with RF showed normal cardiovascular clinical examination, chest radiography and electrocardiography, and Doppler echocardiography showed non-physiological mitral and/or aortic regurgitation usually associated with valvular thickening.

The presence of cardiac involvement in the chronic phase was called RHD, and was assessed by means of clinical parameters similar to those used in the acute phase; it was stratified as absent, mild, moderate or severe. Valvular heart disease was the term used for mitral and/or aortic valve involvement as identified by Doppler echocardiography in the chronic phase of RF.^[7]

In the Doppler echocardiographic assessment of cardiac involvement in the acute and chronic phases, mitral and/or aortic valve lesions were analyzed and classified as absent (normal morphology with or without physiological regurgitation), mild, moderate or severe. The parameters used to quantify the severity of valvular dysfunction were those classically described.^[8] The term significant valvular heart disease was defined when mitral and/or aortic regurgitation or mitral stenosis was moderate or severe. The criteria used to differentiate physiological from non-physiological regurgitation were those classically described by several authors^[9-11] and recommended in the latest WHO review.^[12]

The data were analyzed using the Epi Info version 6.04. Categorical variables were compared using the chi square test (χ^2) or Fisher test. A *P*-value of <0.05 was taken to be statistically significant. Agreement analyses were assessed according to the Kappa index. The response variable was significant valvular heart disease in the chronic phase, which was tested in univariate and multivariate analyses. A logistic regression model was developed, which initially included all variables with a *P*-value <0.25 obtained in the univariate analysis. The variables were then eliminated using a stepwise procedure until the final model included only those with statistical significance, considered for *P*-values ≤0.05. Multivariate analysis was carried out using the MULTLR software program. The research protocol was approved by the Research Ethics Committee of the UFMG.

RESULTS

Of the 462 patients included in the study, 261 (56.5%) were female. Their ages in the first attack ranged from 3 to 17 years (mean of 9.4 ± 2.4 years). According to the clinical presentation in the first attack, as defined by the Jones major criteria, carditis occurred in 258 patients (55.8%), chorea in 232 (50%), arthritis in 195 (42.2%), subcutaneous nodules in nine (1.9%) and erythema marginatum in six (1.3%). Carditis was mild in 135 patients (52.3%), moderate in 44 (17%) and severe in 79 (30.7%). The irregular prophylaxis was observed

with 94 patients (20.3%). Therefore, for 368 patients, or 79.7% of the total, the prophylaxis was considered to be regular.

Table 1 shows that there was a good correlation between the clinical assessment and Doppler echocardiography as regards the severity of valvular involvement in RF (Kappa index = 0.48). The best association was observed when carditis was moderate or severe (Kappa index = 0.87). Of the 204 patients with normal clinical examination, electrocardiography and chest radiography, 72 (35.3%) showed non-physiological valvular alterations, 12 of whom (16.7%) had moderate valvulitis. Of the patients

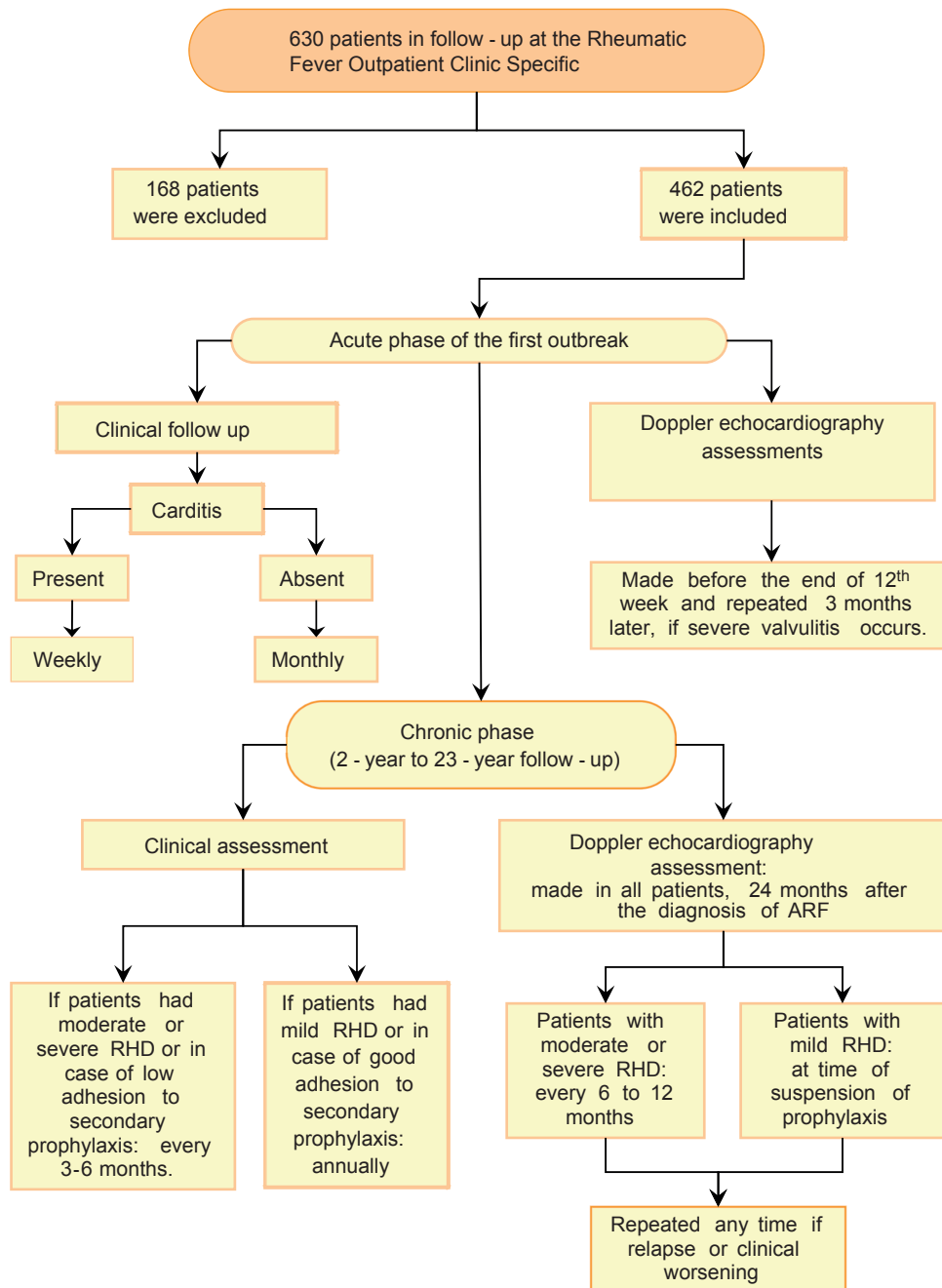


Figure 1: The clinical and Doppler echocardiographic follow-up schedule

without carditis, 122 presented with chorea and 62 with polyarthritis as the only manifestation of RF; 20 patients presented with both. There was a significant statistical association between the presence of chorea and subclinical carditis ($P < 0.0001$).

Of the 462 patients, 75 (16%) had recurrence at some point of the follow-up. Of those with recurrence, 42 (56%) had had carditis in the first attack and 33 (44%) chorea and/or arthritis. When the presence of overall recurrence was considered, the recurrence rate was the same (16.2%) in these two groups. However, when occurrence of carditis in the recurrence was considered, there was a statistically significant association between recurrence with carditis and the presence of carditis in the first attack ($P = 0.0002$). Of the 22 patients who had recurrence with carditis, 20 (91%) had presented with carditis in the initial attack, whereas in the 33 patients without carditis in the first attack, only two (6%) had recurrence with carditis.

The age of the patients by the end of the study ranged from 12 to 35 years (mean of 21 ± 5.1 years). A total of 183 (39%) patients had normal cardiovascular examination in chronic phase; 279 (61%) showed signs of valvular heart disease on clinical examination, of whom 86% had a heart murmur consistent with mitral regurgitation (MR) and 34% with aortic regurgitation (AoR).

In this chronic phase, 164 (35.5%) Doppler echocardiographic studies were normal. Of the 298 (64.5%) patients with abnormal Doppler echocardiographic study, 148 (49.6%) had significant valvular heart disease. In comparison with the acute phase [Table 2], there was a reduction in the severity of significant lesions in 10% of the patients. Regression of mild valvulitis was observed in 33 cases (24%) and of moderate valvulitis in four (3.4%). However, no regression of valvular lesions was observed in any of the patients with severe valvulitis on Doppler echocardiography, although the clinical examination of 11 (13%) of these patients had become normal during the follow-up. There was a decrease in the severity of moderate valvulitis in 47 (40.5%) patients and in 21 (27.6%) of those with severe lesions. Lesions remained unchanged in 68% of mild, 53% of moderate and 72% of severe cases. Worsening was observed in 11 (7.8%) cases of mild valvulitis and in seven (6%) of moderate valvulitis. All cases with worsened valvular lesion were related to recurrence with carditis following an irregular secondary prophylaxis.

Of the 72 patients with subclinical valvulitis, 52 (72%) remained with valvular alteration on Doppler echocardiography; four of them (5.5%) remained with moderate lesions and none developed worsening of the degree of valvular lesion. Only two patients with subclinical valvulitis developed heart murmur during the follow-up, after recurrence with carditis.

The univariate analysis [Table 3] shows statistical

Table 1: Agreement between clinical assessment (carditis) and Doppler echocardiographic findings (valvulitis) in the first attack in patients with acute rheumatic fever (n = 462)

Clinical assessment (carditis)	Doppler echocardiographic findings (valvulitis)			
	Absent (n = 132)	Mild (n = 138)	Moderate (n = 116)	Severe (n = 76)
Absent (n = 204)	132	60	12	0
Mild (n = 135)	0	70	65	0
Moderate (n = 44)	0	8	22	14
Severe (n = 79)	0	0	17	62

Kappa index = 0.48

Table 2: Progression to chronic rheumatic heart disease according to the severity of carditis or valvulitis in the initial attack of rheumatic fever (n = 462)

Clinical (carditis) and Doppler echocardiographic assessment (valvulitis) in the acute phase of rheumatic fever	Doppler echocardiographic assessment (valvular disease)			
	Absent (n = 164)	Mild (n = 150)	Moderate (n = 86)	Severe (n = 62)
Carditis				
Absent (n = 204)	152	48	4	0
Mild (n = 135)	10	80	36	9
Moderate (n = 44)	2	12	22	8
Severe (n = 79)	0	10	24	45
Valvulitis				
Absent (n = 132)	127	5	0	0
Mild (n = 138)	33	94	11	0
Moderate (n = 116)	4	43	62	7
Severe (n = 76)	0	8	13	55

significance between the following clinical data of the initial attack and significant chronic valvular heart disease: presence of carditis, severity of carditis, absence of chorea, recurrence of carditis, severity of MR, severity of AoR and MR associated with AoR. The following other variables analyzed did not show statistically significant associations: gender, positive family history for RF, recurrence of chorea, recurrence of arthritis, number of recurrences, length of disease duration ≥ 10 years, presence of arthritis and age of patients at the initial attack ≤ 10 years.

Among the variables included in the multivariate analysis [Table 4], only significant carditis and severity of valvulitis showed statistical significance. The presence of chorea or arthritis in the initial attack, unaccompanied by carditis, was not associated with significant valvular heart disease, odds ratio 0.41 (95% C.I. 0.22-0.77) and 0.43 (95% C.I. 0.23-0.82), respectively, thus indicating that these were protective factors.

DISCUSSION

Demographics of the study population are in agreement

Table 3: Clinical and Doppler echocardiographic variables present in acute rheumatic fever (n = 462) and associated with significant chronic valvular heart disease (moderate or severe mitral and/or aortic regurgitation or mitral stenosis)

Clinical and Doppler echocardiographic variables	Significant chronic valvular heart disease		Chi square	P value
	Present	Absent		
Carditis present	144	114	130.61	<0.0001
Severity of carditis absent	10	194		
Mild	45	90	201.95	<0.0001
Moderate	30	14		
Severe	69	10		
Chorea present	43	189	44.6	<0.0001
Arthritis present	57	138	2.25	0.14
Recurrence with carditis	14	6	5.09	0.02
Mitral regurgitation: absent	3	134		
Mild	16	118		
Moderate	60	47		
Severe	75	9		
Aortic regurgitation: absent	71	256	237.67	<0.0001
Mild	4	24		
Moderate	29	21		
Severe	50	7		
Associated MR and AoR	83	49	70.74	<0.0001
No associated MR and AoR	71	259		

MR: Mitral regurgitation, AoR: Aortic regurgitation

Table 4: The multivariate analysis: The association between clinical and Doppler echocardiographic variables and significant chronic valvular heart disease

Explanatory variables	OR	OR 95% C.I.	P-value
Severity of carditis	4.75	2.46–9.17	<0.0001
Presence of arthritis	0.41	0.22–0.77	0.0058
Presence of chorea	0.43	0.23–0.82	0.0101
Severity of valvulitis	15.99	8.45–30.27	<0.0001

with those found in the literature, showing a higher frequency of RF in the age range between 5 and 15 years (95.7%), and predominance among females (56.5%), probably due to the high prevalence of chorea.^[13,14] The most common manifestation was carditis (55.8%). However, the most common isolated manifestation was chorea (26%) and the least frequent association was between chorea and arthritis (4.3%), similar to Meira *et al.*'s findings.^[15] Seckeler and Hoke^[16] found a 64.4%, 15.3% and 59.5% prevalence of carditis, chorea and arthritis in the Americas, respectively. Data from the present study corroborate with Seckeler and Hoke's findings only as regards carditis (55.8%), with a higher rate of chorea (50%) and lower rate of arthritis (42.2%). In a recent study, Tunks *et al.*^[17] point out the difficulty in diagnosing chorea, as an isolated manifestation, as well as atypical joint abnormalities in countries with a high prevalence. The hospital has an Abnormal Movements Outpatient Clinic of the Department of Neurology to which patients with a suspected diagnosis of Sydenham chorea are referred for a proper differential diagnosis. If the diagnosis is confirmed, the patients are referred to the RF Outpatient Clinic of UFMG. This may explain the higher frequency of chorea found in the present

study. As regards arthritis as an isolated manifestation, cases of atypical arthritis were excluded, unlike in other studies,^[18,19] and this may have reduced the frequency of this manifestation.

Doppler echocardiography, which has a higher sensitivity than cardiac auscultation, is important in the assessment of heart valves in the acute and chronic phases of RF, as has already been reported by several authors.^[10-12] The frequency of subclinical carditis was 35.3% and there was statistical significance with the occurrence of chorea in RF. These valvular abnormalities showed Doppler echocardiographic resolution in only 28% of the patients; however, none of them developed worsening in relation to the initial examination.

Prognostic factors for RF associated with progression to valvular heart disease have also been studied by several authors, even before the introduction of Doppler echocardiography. Although not all findings agree, the prognosis of RF is known to be directly related to the severity of the cardiac involvement in the initial attack.^[20-22] By means of clinical findings, Décourt^[5] observed that in patients with mild carditis, the clinical manifestations disappeared in the chronic phase in approximately 80% of them. He also reported that in patients with moderate or severe carditis, residual heart disease would be the most probable outcome. In a clinical study of 1000 patients with RF, Bland *et al.*^[23] observed that the signs of heart disease disappeared in 16% of the patients after 20 years. Vasan and Selvaraj^[22] also reported that valvular lesions and murmurs resolve in approximately one-third of the patients with acute carditis within 5–10 years. We observed a similar outcome, with improved cardiac auscultation in 33% of the patients however without a

corresponding Doppler echocardiographic improvement. Although a 10% reduction in the severity of significant valvulitis had been observed after 2 years of disease, Doppler echocardiography became normal in only four (3.4%) patients who had had moderate valvulitis in the first episode of RF, and in 33 (24%) of those with mild lesions. No severe valvular lesion resolved completely, although the cardiac auscultation had become normal in 13% of the patients with severe valvulitis in the initial assessment (subclinical chronic heart disease).

In a study including 258 patients with RF, Meira *et al.*^[7] verified that the main prognostic factors for severity of valvular heart disease were moderate or severe carditis, recurrences of RF and low maternal education. In a follow-up of 139 patients with chronic RHD for 5.0 ± 3.7 years, Yavuz *et al.*^[24] used uni- and multivariate analyses to study the correlation between AoR and MR alone and associated in the initial attack of RF, as well as the effects of the presence of MR and of AoR with valvular involvement in the final assessment. They concluded that the best predictors of severity of rheumatic valvular heart disease were the severity of the initial valvulitis and the presence of MR associated with AoR. In a recent study, Yilmazer *et al.*^[25] investigated predictive factors of valvular heart disease in 88 patients with rheumatic carditis followed-up for a period of 2.95 ± 1.4 years and, according to a logistic regression multivariate analysis, they observed that ventricular dilatation was an independent risk factor associated with persistence of mitral valve disease. They did not find a correlation with severity of valvular involvement in the initial assessment, and concluded that their findings could have resulted from myocardial involvement and not from severity of valvulitis. In the present study, all patients with severe valvulitis showed increased left ventricular chambers, and none had left ventricular systolic or diastolic dysfunction on Doppler echocardiography. Improvement in the severity of valvular regurgitation was accompanied by clinical improvement and reduction of the size of cardiac chambers, and was not correlated with myocardial involvement.

The variables associated with significant valvular heart disease were the severity of carditis in the initial attack (moderate or severe) and the severity of valvulitis (moderate or severe MR or AoR). The presence of arthritis as well as the presence of chorea in the initial attack were related to a better prognosis in relation to significant valvular heart disease. Despite being associated with subclinical carditis, chorea was an independent variable considered as a protective factor for significant valvular heart disease. Patients with chorea in the initial attack had a greater chance of presenting with subclinical carditis, but developed significant valvular heart disease less frequently. Although subclinical valvulitis had not worsened significantly, Doppler echocardiographic resolution occurred in only 28% of the patients. Other

authors^[26,27] also observed an association between chorea and subclinical valvulitis, and persistence of the lesions throughout time; however, the role of subclinical carditis, especially in the cases of chorea, is not well established. By means of Doppler echocardiography, Pastore *et al.*^[28] observed an association between chorea and mild valvular heart disease. However, Bland,^[29] in a follow-up of patients with isolated chorea for 20 years, showed that 23% developed mitral stenosis. Likewise, Carapetis and Currie^[30] also reported that 68% of the patients with chorea who developed chronic RHD had no evidence of carditis in RF.

It is reasonable to expect some variation in the interpretation of the tests as the result of the great period of follow-up, the change of the equipment used (two types) and the change of cardiology investigators, although all of them had extensive experience in the field of RHD. Furthermore, the study is not immune to the limitations inherent to all retrospective studies, especially those related to data records.

In conclusion, our study suggests that the use of Doppler echocardiography in RF, in conjunction with clinical data, is able to identify prognostic factors regarding the development of significant valvular heart disease and defines the group of patients at a higher risk of persistence of the valvular heart disease. In these patients, a stricter and closely monitored secondary prophylaxis is recommended to prevent recurrence of RF and, consequently, the worsening of already present cardiac damage. Initial severe carditis is an important factor in the long-term prognosis of chronic RHD.

REFERENCES

1. Carapetis JR, Zühlke LJ. Global research priorities in rheumatic fever and rheumatic heart disease. *Ann Pediatr Cardiol* 2011;4:4-12.
2. Stollerman GH. Rheumatic fever. *Lancet* 1997;349:935-42.
3. Alves Meira ZM, de Castilho SR, Lins Barros MV, Maria Vitarelli A, Diniz Capanema F, Moreira NS, *et al.* Prevalence of rheumatic fever in children from a public high school in Belo Horizonte. *Arq Bras Cardiol* 1995;65:331-4.
4. Dajani AS. Guidelines for the diagnosis of rheumatic fever: Jones Criteria, 1992 update. Special writing group of the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease on the Council of Cardiovascular Disease in the Young of the American Heart Association. *JAMA* 1992;268:2069-73.
5. Décourt LV. Doença Reumática. 2nd ed. Brasil/ São Paulo: Savier; 1972.
6. Markowitz M, Gordis L. Rheumatic Fever. 2nd ed. Philadelphia: WB Saunders Co; 1972.
7. Meira ZM, Goulart EM, Colosimo EA, Mota CC. Long term follow up of rheumatic fever and predictors of

- severe rheumatic valvar disease in Brazilian children and adolescents. *Heart* 2005;91:1019-22.
8. Bonow RO, Carabello BA, Chatterjee K, Leonn AC, Faxon DP, Freed MD, *et al.* ACC/AHA 2006 guidelines for Management of Patients with valvular heart disease. *Circulation* 2006;114:84-231.
 9. Minich LL, Tani LY, Pagotto LT, Shaddy RE, Veasy LG. Doppler echocardiography distinguishes between physiologic and pathologic “silent” mitral regurgitation in patients with rheumatic fever. *Clin Cardiol* 1997;20:924-6.
 10. Veasy LG. Rheumatic fever – T. Duckett Jones and the rest of the story. *Cardiol Young* 1995;5:293-301.
 11. Ramakrishnan S. Echocardiography in acute rheumatic fever. *Ann Pediatr Cardiol* 2009;2:61-4.
 12. Rheumatic fever and rheumatic heart disease: Report of a WHO expert consultation on rheumatic fever and rheumatic heart disease. World Health Organization. Geneva, 2001 Oct 29 - Nov 1. Geneva: WHO; 2004
 13. Borges F, Barbosa ML, Borges RB, Pinheiro OC, Cardoso C, Bastos C, *et al.* Características Clínicas Demográficas em 99 Episódios de Febre Reumática no Acre, Amazônia Brasileira. *Arq Bras Cardiol* 2005;84:111-4.
 14. Pereira BA, da Silva NA, Andrade LE, Lima FS, Gurian FC, de Almeida Netto JC. Jones criteria and underdiagnosis of rheumatic fever. *Indian J Pediatr* 2007;74:117-21.
 15. Meira ZM, Goulart EM, Mota Cde C. Comparative study of clinical and Doppler echocardiographic evaluations of the progression of valve diseases in children and adolescents with rheumatic fever. *Arq Bras Cardiol* 2006;86:32-8.
 16. Seckeler MD, Hoke TR. The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. *Clin Epidemiol* 2011;3:67-84.
 17. Tunks RD, Rojas MA, Edwards KM, Liske MR. Do rates of arthritis and chorea predict the incidence of acute rheumatic fever? *Pediatr Int* 2011;53:742-6.
 18. Smith MT, Lester-Smith D, Zurzynski Y, Noonan S, Carapetis JR, Elliott EJ. Persistence of acute rheumatic fever in a tertiary children’s hospital. *J Paediatrics Child Health* 2011;47:198-203.
 19. Pileggil GCS, Ferriani VP. Atypical arthritis in children with rheumatic fever. *J Pediatr (Rio J)* 2000;76:49-54.
 20. Taranta A, Markowitz M. Rheumatic Fever. Boston: Kluwer Academic Publishers; 1989. p. 103.
 21. Meira ZM, Goulart EM, Araújo FD, Capuruço CA, Mota CC. Influência dos surtos de recidiva da febre reumática no desenvolvimento de valvopatia crônica em crianças e adolescentes. *Rev Méd Minas Gerais* 2008;18:236-42.
 22. Vasan RS, Selvaraj N. Natural History of Acute rheumatic Fever. In: Narula J, Virmani R, Reddy KS, Tandon R, editors. *Rheumatic Fever*. Washington, DC: American Registry of Pathology; 1999. p. 347-58.
 23. Bland EF, Duckett Jones T. Rheumatic fever and rheumatic heart disease. A twenty year report of 1000 patients followed since childhood. *Circulation* 1951;4:836-43.
 24. Yavuz T, Nisli K, Oner N, Dindar A, Aydogan U, Omeroglu RE, *et al.* Long term follow-up results of 139 Turkish children and adolescents with rheumatic heart disease. *Eur J Pediatr* 2008;167:1321-6.
 25. Yilmazer MM, Oner T, Tavlı V, Cilengiroğlu OV, Güven B, Meşe T, *et al.* Predictors of chronic valvular disease in patients with rheumatic carditis. *Pediatr Cardiol* 2012;33:239-44.
 26. Figueiroa FE, Fernandez MS, Valdes P, Wilson C, Lanás F, Carrion F, *et al.* Prospective comparison of clinical and echocardiographic diagnosis of rheumatic carditis: long term follow up of patients with subclinical disease. *Heart* 2001;85:407-10.
 27. Lanna CC, Tonelli E, Barros MV, Goulart EM, Mota CC. Subclinical rheumatic valvitis: a long-term follow-up. *Cardiol Young* 2003;13:431-8.
 28. Pastore S, De Cunto A, Benettoni A, Berton E, Taddio A, Lepore L. The resurgence of rheumatic fever in a developed country area: the role of echocardiography. *Rheumatology (Oxford)* 2011;50:396-400.
 29. Bland EF. Chorea as a manifestation of rheumatic fever: a long-term perspective. *Trans Am Clin Climatol Assoc* 1961;73:209-13.
 30. Carapetis JR, Currie BJ. Rheumatic chorea in northern Australia: a clinical and epidemiological study. *Arch Dis Child* 1999;80:353-8.

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