Clinical and echocardiographic correlations in rheumatic fever: evaluation of the diagnostic role of auscultation

Romatizmal ateşte klinik ve ekokardiyografik korelasyon:
Oskültasyonun tanısal rolünün değerlendirilmesi

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Objectives: The diagnosis of rheumatic carditis with auscultation can be difficult especially in subclinical cases. We investigated the effectiveness of auscultation in detecting valvular regurgitation in rheumatic fever (RF).

Study design: The study included 112 patients (51 males, 61 females; mean age 11.0±2.4 years; range 6 to 16 years) with RF (n=75) and rheumatic heart disease (n=37). The presence of murmurs of mitral (MR) and aortic (AR) regurgitation on precordial auscultation were noted. Two-dimensional and color Doppler echocardiographic examinations were performed in all the patients to determine pericardial effusions, prolapse and thickening of the mitral valve, and pathologic valvular regurgitations. The sensitivity, specificity, and predictive values of auscultation were calculated for MR and AR.

Results: Seventy-seven patients had cardiac involvement (68.8%; 47 mild, 13 moderate, 17 severe), which was demonstrated by auscultation in 60 patients (77.9%). There were 17 patients with silent carditis. Auscultation enabled detection of MR and AR in 60 (60/72; 83.3%) and 21 (21/37; 56.8%) patients, respectively. Echocardiography revealed silent MR in 12 patients and silent AR in 16 patients. The degree of valvular insufficiency was significantly lower in silent cases than those with evident MR (p=0.003) and AR (p=0.005). Of 12 patients with silent MR, only one patient had mitral valve prolapse and another had thickening of the mitral valve. The sensitivity, specificity, positive and negative predictive values of auscultation were found as 83.3%, 85.0%, 90.9% and 73.9% for MR, and 56.8%, 98.7%, 95.5% and 82.2% for AR, respectively.

Conclusion: Auscultation was found to be more sensitive for MR and more specific for AR. Given considerably low negative predictive value of auscultation for MR and AR, the role of echocardiographic examination to detect cardiac involvement is indispensable in patients with RF.

Key words: Child; echocardiography, Doppler; heart auscultation; heart valve diseases; mitral valve insufficiency/ultrasonography; myocarditis; rheumatic fever/diagnosis; rheumatic heart disease.

Amaç: Romatizmal karditin oskültasyonla tanısı, özellikle subklinik olgularda zor olabilir. Bu çalışmada, romatizmal ateşte kapak yetersizliğinin saptanmasında oskültasyonun etkinliği araştırıldı.

Çalışma planı: Çalışmada, romatizmal ateş (n=75) ve romatizmal kalp hastalığı (n=37) olan 112 hasta (51 erkek, 61 kız; ort. yaş 11.0±2.4; dağılım 6-16) incelendi. Prekordiyal oskültasyonla mitral yetersizlik (MY) ve/veya aort yetersizliği (AY) üfürümleri kaydedildi. Tüm hastalar ikiboyutlu ve renkli Doppler ekokardiyografiyle perikardiyal efüzyon, prolaps, mitral kapak kalınlaşması ve patolojik kapak yetersizliği açısından değerlendirildi. Mitral ve aort yetersizliği için oskültasyonun özgüllük, duyarlılık ve öngördürücü değerleri hesaplandı.

Bulgular: Yetmiş yedi hastada (%68.8) kalp tutulumu (47 hafif, 13 orta, 17 ciddi) saptandı. Bunların 60'ında (%77.9) tanı oskültasyon ile kondu, 17 hastada ise sessiz kardit vardı. Oskültasyon ile 60 hastada (60/72; %83.3) MY, 21 hastada (21/37; %56.8) AY belirlendi. Ekokardiyografide 12 hastada sessiz MY, 16 hastada sessiz AY saptandı. Kapak yetersizliğinin derecesi, hem MY (p=0.003) hem de AY (p=0.005) için sessiz olgularda, yetersizliği belirgin olan olgulara göre daha düşüktü. Sessiz MY'li 12 hastanın birinde mitral kapak prolapsı, birinde de mitral kapak kalınlaşması saptandı. Oskültasyonun duyarlılık, özgüllük, pozitif ve negatif öngördürücü değerleri sırasıyla MY için %83.3, %85.0, %90.9, %73.9; AY için %56.8, %98.7, %95.5, %82.2 olarak bulundu.

Sonuç: Oskültasyon MY için daha duyarlı, AY için daha özgül bulundu. Oskültasyonun negatif öngördürücü değerinin hem MY hem de AY için düşük olması nedeniyle, ekokardiyografik incelemenin romatizmal ateşli hastalarda kardiyak tutulumu saptamada çok önemli olduğu sonucuna varıldı.

Anahtar sözcükler: Çocuk; ekokardiyografi, Doppler; kalp oskültasyonu; kalp kapağı hastalıkları; mitral kapak yetersizliği/ultrasonografi; miyokardit; romatizmal ateş/tanı; romatizmal kalp hastalığı.

Rheumatic fever (RF) is a nonsuppurative inflammatory disease mainly affecting the heart, blood vessels, joints, and subcutaneous tissues. It remains to be the most common cause of acquired heart disease in children and young adults, and continues to be a major public health problem worldwide, especially in developing countries. Because of wide variations in its symptoms and clinical presentation, the diagnosis of the disease may be difficult and a definite diagnosis may not be possible in some children.[1-3] The diagnosis of RF is based on the Jones criteria, which incorporate specific clinical manifestations known as major criteria with supporting clinical and laboratory findings known as minor criteria.[4]

Carditis seen nearly in half of the patients tends to appear early in the acute process and is the most serious clinical manifestation, since it is the only one that can cause death during acute attacks or produce residual disability and late mortality. The diagnosis of rheumatic carditis may be difficult since it may initially be subclinical. Precordial auscultation is the main step to determine cardiac involvement in patients with RF. Echocardiographic examination is very helpful especially in patients with silent valve regurgitations.[1]

This study was designed to determine the effectiveness of auscultation in detecting valvular regurgitation in RF.

PATIENTS AND METHODS

Among patients who were admitted to the Department of Pediatric Cardiology of Medical School of Ankara University from December 1991 to February 2003, we retrospectively included 75 consecutive patients with a diagnosis of RF according to the updated Jones criteria[4] and 37 patients with a diagnosis of rheumatic heart disease (RHD). The patients were evaluated by physical examination, chest X-ray, electrocardiography, complete blood count, acute phase reactants (C-reactive protein and erythrocyte sedimentation rate), anti-streptolysin O (ASO) titer, and echocardiography.

The presence of murmurs of mitral or aortic regurgitation on precordial auscultation and cardiomegaly on chest X-rays were noted. Cardiac involvement was graded as mild in the absence of cardiomegaly on the chest X-ray, as moderate if the cardiothoracic index (CTI) was between 0.5 and 0.6 without any findings of congestive heart failure (CHF), and as severe either if the CTI was greater than 0.6 or was greater than 0.5 in the presence of CHF findings.

Two-dimensional (2-D) and color Doppler echocardiographic evaluations were performed in all the patients with the use of a Toshiba Sonolayer SSH-140A/C machine equipped with 3.75 and 5.0 MHz transducers and, after the year 2000, with the use of a Hewlett Packard Model Sonos 5500 cardiac imager (Andover Massachusetts, USA) equipped with 2-4 and 4-8 band width transducers. Pericardial effusions, prolapse and thickening of the mitral valve were evaluated with 2-D echocardiography, while pathological valvular regurgitation was evaluated with Doppler (color continuous wave, and pulsed wave) echocardiography.

The diagnosis of mitral valve prolapse (MVP) was based on echocardiographic finding of systolic displacement of the mitral leaflets posterior to the mitral annular plane in the parasternal long-axis view and a similar displacement in the apical four-chamber view on 2-D echocardiograms. The apical four-chamber view was not used alone for the diagnosis of MVP.[5]

The diagnosis of pathological mitral and aortic regurgitations were based on the following criteria:[3,6] *(i)* the length of the color Doppler jet of more than 1 cm, *(ii)* demonstration of the mosaic color Doppler jet characteristic of turbulent flow in at least two planes, *(iii)* demonstration of a holosystolic jet for mitral regurgitation (MR) and a holodiastolic jet for aortic regurgitation (AR) with pulsed or continuous wave Doppler, *(iv)* posterior orientation of the jet for MR. Mitral regurgitation was graded on echocardiographic examination by using the ratio of the maximum regurgitation jet area to the area of the left atrium in the plane in which the largest area of the jet was seen in parasternal long-and-short axis and apical four-chamber views; hence, grades 1 to 4 denoted ratios below 20%, from 20% to 40%, greater than 40%, and the extension of the regurgitation jet into the pulmonary veins, respectively.[7] Aortic insufficiency was graded from 1 to 4 according to the ratio of the width of the jet at its origin relative to the width of the left ventricular outflow tract in parasternal long-axis views, that is, less than 20%, from 20% to 30%, from 31% to 56%, and greater than 56%, respectively.[8]

When typical murmurs of MR and/or AR were not heard on auscultation despite the presence of valvular insufficiency by echocardiographic evaluation, cardiac involvement was called as "silent carditis."

Statistical analyses were performed using the SPSS 11.0 package. Student's t-test and chi-square tests were used for comparisons. A *p* value of less than 0.05 was considered significant. Standard defin-

Table 1. Classification of the patients with rheumatic fever according to major clinical findings based on the updated Jones criteria

	Before echocardiographic examination		After echocardiographic examination	
	No. of patients	%	No. of patients	%
Single major finding	52	69.3	46	61.3
- Carditis	11	14.7	11	14.7
- Arthritis	33*	44.0	30	40.0
- Chorea	8*	10.7	5	6.7
≥ 2 major findings	23	30.7	29	38.7
- Arthritis + Carditis	19*	25.3	22	29.3
- Carditis + Chorea	3*	4.0	6	8.0
- Arthritis + Carditis + Chorea	1	1.3	1	1.4

*3 patients with isolated arthritis and 3 patients with pure chorea diagnosed before echocardiographic examination were classified as having ≥ 2 major clinical findings after echocardiographic examination.

itions were used to calculate specificity, sensitivity, and predictive values of auscultation in the diagnosis of rhematic cardiac involvement.[9]

RESULTS

Of 112 patients, 51 patients were males, and 61 were females, with a mean age of 11.0±2.4 years (range 6 to 16 years). Based on the updated Jones criteria, major clinical manifestations of patients with RF before and after echocardiographic examination are shown in Table 1. Forty-one patients had isolated arthritis or pure chorea on admission.

Mitral and aortic regurgitations were detected in 72 and 37 patients, respectively. Auscultatory and echocardiographic findings of patients with MR and AR are shown in Table 2.

Among 72 patients with MR, 10 patients had MVP and 16 patients had a thickened mitral valve.

Twelve patients had silent MR, one of whom had MVP and another had mitral valve thickening.

Of 112 patients, a total of 77 patients had cardiac involvement (40 had active carditis, 37 had RHD; 47 mild, 13 moderate, 17 severe). Cardiac involvement was demonstrated by auscultation in 60 patients (77.9%). There were 17 patients with silent carditis. Six of these were diagnosed as RF and presented with a single major clinical finding (3 with isolated arthritis, 3 with pure chorea). The remaining patients were diagnosed as RHD.

Silent MR was found in 12 patients, and silent AR was present in 16 patients. The majority of patients with silent valvular regurgitation had mild carditis (10/12 for silent MR, 12/16 for silent AR).

Valvular insufficiency was detected by auscultation in 60 patients (83.3%) with MR and in 21

Table 2. Auscultatory and echocardiographic findings of patients with mitral and aortic regurgitation

	Mitral regurgitation (n=72)	Aortic regurgitation (n=37)
Auscultatory findings		
Positive auscultatory findings	66	22
False (+)	6	1
False (-) (silent cases)	12	16
Evident (audible cases)	60	21
Echocardiographic findings		
Positive echocardiographic findings	72	37
Regurgitation		
Grade 1	24	18
Grade 2	28	16
Grade 3	20	2
Grade 4	–	1
Pericardial effusion	10	9
Mitral valve prolapse	10	4
Mitral thickening	16	7

Table 3. The degree of valvular insufficiency associated with mitral and aortic regurgitation

		Degree of valvular insufficiency (mean ± SD)	*p*
Mitral regurgitation	Silent (n=12)	1.3±0.5	
	Evident (n=60)	2.1±0.8	0.003
Aortic regurgitation	Silent (n=16)	1.3±0.5	
	Evident (n=21)	1.9±0.8	0.005

patients (56.8%) with AR. The degree of valvular insufficiency was significantly lower in silent cases than those with evident MR (p=0.003) and AR (p=0.005) (Table 3).

The sensitivity, specificity, and predictive values of auscultation to detect valvular regurgitation are shown in Table 4.

DISCUSSION

Rheumatic fever is a major health problem in many countries, and RHD, a sequela of RF, is a very common cause of cardiovascular mortality and morbidity.[10-12] It is the predominant indication for cardiac surgery in developing countries.[10,13] Although the Jones criteria were updated in 1992,[4] there are still many similarities to a number of diseases, making the diagnosis of RF a difficult task for a physician.[1,2] Our knowledge about the incidence of acute RF and the prevalence of RHD in Turkey is limited and acute RF is still an important problem in our country. Turkey is one of the countries in which the incidence of acute RF is still high.[14-19]

The frequencies of polyarthritis (70.7%) and chorea (16.1%) found in this study are compatible with the previous reports.[16,18,20-22] Clinical cardiac involvement has been reported in nearly one-third of patients with RF in various series and in up to 50% of patients in prospective studies.[3,14,16-19,23] In some studies, the rate of carditis was found as high as 70-75%.[24,25] We observed clinical cardiac involvement in 53.4% of patients with RF (40/75). Erythema mar-

ginatum, which is almost specific for the diagnosis, and subcutaneous nodules are very rare major clinical manifestations of RF;[26] none of these findings were detected in our study group.

Detection of active rheumatic carditis has a great prognostic and therapeutic importance and is based on the updated Jones criteria.[4] The diagnosis of carditis using these criteria may become difficult, especially when carditis is isolated and/or subclinical, or when supportive noncardiac features of RF are not observed despite the presence of apparent carditis, or when previous cardiac findings of patients are not known.[2,27]

Precordial auscultation has been the usual modality for the diagnosis of MR and AR, and the diagnosis of carditis is based on the presence of significant apical systolic and/or basal diastolic murmur(s), the presence of clinical findings of pericarditis, or unexplained CHF findings.[23] Previous studies showed that valvular regurgitation may not always be detected by routine clinical auscultation,[28,29] and according to some studies, auscultation may be a dying art.[30,31] However, our results were in favor of auscultation, with high specificity for detecting AR and high sensitivity for MR.

Since demonstration of valvulitis is the rule for the diagnosis of rheumatic carditis and the diagnosis traditionally depends on characteristic auscultatory findings, documentation of valvular regurgitant lesions by 2-D, pulsed and color Doppler echocar-

Table 4. Sensitivity, specificity, and predictive values of auscultation in patients with mitral and with aortic regurgitation

	Mitral regurgitation (n=72)	Aortic regurgitation (n=37)
False (-) (n)	12	16
False (+) (n)	6	1
Sensitivity (%) (n)	83.3 (60/72)	56.8 (21/37)
Specificity (%) (n)	85.0 (34/40)	98.7 (74/75)
Positive predictive value (%) (n)	90.9 (60/66)	95.5 (21/22)
Negative predictive value (%) (n)	73.9 (34/46)	82.2 (74/90)

diography should theoretically be of significant help, allowing a much more accurate assessment of valve morphology and function.[32] With the widespread use of echo-Doppler examination, valvular involvement which may not be detectable by auscultation and sub-clinical or silent valvular regurgitation can be identi-fied.[3,6,24,33,34]

Since overdiagnosis of RF in patients with only a single major finding of arthritis is a known prob-lem, the detection of silent valvular regurgitation by echocardiography would be of great importance to diagnose RF. However, caution should be increased when interpreting echocardiographic findings because clinically silent, very mild degrees of left heart valve regurgitation may also occur in normal population, reducing the diagnostic yield of echocardiography.[35-37] Trivial degrees of MR may also be related to the process of aging; moreover, the prevalence of MR was found to be 38%-45% in normal adults[35,36] and 2%-4% in children with structurally normal hearts.[37] Minich et al.[38] report-ed that pathologic silent MR of RF could be distin-guished from physiologic MR using the Doppler criteria, particularly when the jet was directed pos-teriorly. On the other hand, aortic regurgitation is very rare in healthy children and adolescents and, if present, it is not holodiastolic;[39] thus, regurgitation of the aortic valve should be considered a patholog-ic condition until proved otherwise.[35,37] We feel that overdiagnosis of MR and AR should be relatively low in our study because of strict echocardiograph-ic criteria used to define pathological valvular regurgitation.

Echocardiographic examination also allows visu-alization of valve structure and detection of other causes of valve dysfunction such as MVP. Prolapse and thickening of the mitral valve are among features of rheumatic MR as postinflammatory sequelae.[40,41] It is also known that the severity of MR is correlated with the presence of MVP.[24,42,43] We noted that the degree of valvular regurgitation was significantly low for both MR and AR and that MVP and thicken-ing of the mitral valve were less frequent in patients with silent valvular regurgitation.

In a study by Veasy et al.,[24] carditis was shown by auscultation in 53 of 74 patients (72%). In our study, carditis was found by auscultation in 60 of 77 patients (77.9%). Ozer et al.[14] found silent carditis in 14% of patients with acute RF. In our study, of 41 patients with RF, presenting with isolated arthritis or pure chorea as major clinical manifestations, subclin-ical carditis was detected by echocardiography in six patients (14.6%).

Veasy et al.[24] found Doppler evidence of MR in 19% of patients who had isolated arthritis or pure chorea as major clinical manifestations. In our study, echocardiographic examination enabled to demon-strate silent MR and AR in 12 (16.7%) and 16 (43.2%) patients, respectively.

Valvular insufficiency was detected by ausculta-tion in 60 patients (83.3%) with MR and in 21 patients (56.8 %) with AR. Although our results indi-cate that auscultation is sensitive for MR and specif-ic for AR, echocardiography remains to be the most important diagnostic tool in rheumatic carditis.

In conclusion, the major clinical manifestations of RF in our country are similar to those of western countries. We believe that precordial auscultation is still the first and main step in the diagnosis of valvulitis. While auscultation is sensitive for MR, it is a specific diagnostic tool for AR. In addition to its value in evaluating valvular structures, including prolapse and thickening of the mitral valve and the presence of pericarditis, echocardiographic examina-tion is very helpful in detecting pathological valvular regurgitation, especially for mild carditis and low-degree valvular insufficiency, which cannot other-wise be detected by auscultation. Given considerably low negative predictive values of auscultation for MR and AR, the importance of echocardiographic examination to determine valvular involvement becomes evident.

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