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Original Article

Criteria for judging the improvement in subclinical rheumatic valvitis

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Abstract Recent technical improvements in cross-sectional echocardiography have made it possible to detect even mild organic regurgitation of the mitral and aortic valves in patients with acute rheumatic fever. To determine the prevalence and prognosis of subclinical valvitis, we have analyzed 104 patients with acute rheumatic fever referred to our institution. Of 53 patients who had no murmur, 22 of them with polyarthritis, 29 with chorea, and 2 with polyarthritis and chorea, 23 (43.4%) had subclinical valvitis. Isolated mitral regurgitation was the most common valvar lesion, seen in 82.6% of the patients. Isolated aortic regurgitation was detected in 4.4% of the cases, and combined mitral and aortic regurgitation in the remaining 13%. During follow-up, the degree of mitral regurgitation improved in 59.1%, decreased in 18.2%, and increased or remained unchanged in 22.7% according to the length of colour jet. According to criterions of velocity, mitral regurgitation improved in 86.4% of the patients, and increased or unchanged in the remaining 13.6%. Mitral regurgitation disappeared completely in 6 of the patients (27.3%) as judged according to both the length of colour jet and the velocity of regurgitation. Aortic regurgitation improved in all the patients with this problem, disappearing completely in two of the four.

Based on this experience, we suggest that not only the disappearance of regurgitation, but also improvements in the echocardiographic diagnostic criterions of regurgitation, such as the length of the colour jet less than 1 cm, or velocity less than 2.5 m/s, or indicative of regurgitation that is either intermittent or of short duration, should also be considered as criterions indicating improvement in valvar regurgitation in patients with subclinical rheumatic valvitis.

Keywords: Rheumatic fever; rheumatic carditis; cross-sectional echocardiography

Colour flow Doppler echocardiography has been shown to be a more sensitive method than auscultation in detecting minor pathological regurgitation in patients with valvar lesions in the setting of rheumatic fever.[1] An increasing number of such patients have been observed with isolated arthritis and or chorea who have echocardiographic findings suggesting the existence of minor pathologic regurgitation.[2–8] It is important to identify such findings, since minor pathologic regurgitation is accepted as a sign of carditis, a major diagnostic criterion for acute rheumatic fever.[1,4,8–10] The purpose of our study, therefore, was to determine the prevalence and prognosis of mitral and aortic regurgitation as detected echocardiographically among patients with acute rheumatic fever but in the absence of any pathological murmurs of mitral and aortic regurgitation.

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Materials and methods

Between October 1999 and January 2002, 5750 patients were admitted to the Pediatric Cardiology Unit of Meram Medical School Hospital, of whom 104 were diagnosed as having acute rheumatic fever according to the update of the Jones criterions made in 1992.[11] During the period of study, we found 53 patients with no murmur of mitral and aortic regurgitation, but with isolated arthritis and or chorea. These patients constituted our study group. All the patients were examined by two experienced pediatric

cardiologists, who were blind to the clinical diagnosis of each other. Both cardiologists were in agreement about the cardiac findings. All patients had blood analyses, including routine blood count, erythrocytic sedimentation rate measured with the Becton-Dickinson sedi-15 instrument, C-reactive protein level assessed using the Dade-Behring high sensitivity technique, and antistreptolysin O titers, determined using the Dade Behring Nephelometre Latex Anti-Streptolysin O tests. This titer was considered elevated if it was equal or greater than 333 Todd units/ml. All patients also had throat swabs cultured, chest roentgenograms, electrocardiograms, and cross-sectional and colour Doppler echocardiographic investigations. The echocardiographic analyses were performed by one of the cardiologists who was blind to the results of the previous procedures. Cross-sectional echocardiography, Doppler ultrasound, and colour flow mapping were performed in the left lateral decubitus position using Hewlett-Packard Sonos 77020A and Sonos 1000 phased-array sector scanners with 2.5 to 3.5 MHz transducers. In this study, we used parasternal long-axis, apical long-axis, and four and two-chamber views for assessement of the mitral valve, and parasternal long-axis, apical long-axis, and apical five-chamber views for the window for Doppler interrogation of the aortic valve.

Pathologic valvar regurgitation was defined according to previously described criterions.[1,3,4,8] Three consecutive beats were measured and averaged for each measurement.

The criterions for mitral regurgitation were:

- Colour jet identifed in at least two planes.
- Demonstration of a mosaic colour jet.
- Length of the colour jet greater than 1 cm.
- Persistence of the pulsed or continuous wave Doppler signal throughout systole.
- Doppler velocity greater than 2.5 m/s.
- Regurgitation jets directed toward the posterolateral aspect of the left atrium.

The criterions for aortic regurgitation were:

- Persistence of the pulsed or continuous wave Doppler signal throughout diastole.
- Doppler velocity greater than 2.5 m/s.

Those patients without any murmur of mitral or aortic insufficiency, and with normal cross-sectional and M-mode echocardiographic findings in terms of chamber dimensions and ventricular function, but with pathologic mitral and or aortic regurgitation, were considered as having subclinical rheumatic valvitis. The mean period of follow-up was 9.91 $\pm$ 8.14 months, with a range from 2 to 24 months. The patients were evaluated by echocardiographic examination at their initial presentation, and again at 1, 2, 3, 6, 12, 18 and 24 months after the initial presentation. During the period of follow-up, if aortic or mitral regurgitation completely disappeared, or the findings no longer fulfilled our criterions, with the colour jet length being less than one centimetre, the velocity falling to less than 2.5 m/s, or the colour jet being of short duration or becoming intermittent, the patients were deemed to have improved. If the regurgitation continued to be pathologic, and decreased, remained unchanged, or increased, the subclinical valvitis was similarly considered to have decreased, remained unchanged, or inreased in its severity. Our protocol of study was approved by the local ethical committee, and all parents of the patients enrolled in the study gave written informed consent for their inclusion.

Results

We found 104 patients who fulfilled the update of 1992 for the Jones criterions. Of these, 64 (61.5%) had polyarthritis, 51 (49%) had carditis, and 35 (33.6%) had Sydenham's chorea. Other major manifestations, such as erythema marginatum and subcutaneous nodules, had not been detected. Of these patients, 53 did not have an audible murmur, with 22 having polyarthritis, 29 Sydenham's chorea, and two having combined polyarthritis and chorea. Amongst these, 23 (43.4%) had echocardiographic evidence of subclinical rheumatic valvitis, with 16 being female (69.6%), giving a ratio of females to males of 2.28 : 1. Their ages ranged from 5 to 16 years, with a mean of 11.8 years, and a standard deviation of $\pm$ 2.7 years. Amongst these patients with subclinical valvitis, 14 (60.9%) had Sydenham's chorea, and 9 (39.1%) had polyarthritis. Subclinical valvitis was identifed in 14 (48.3%) of the 29 patients with isolated chorea, and 9 (40.9%) of the 22 patients with isolated polyarthritis. In terms of the valvar lesions identified amongst the 23 patients, 19 (82.6%) had isolated mitral regurgitation, only one had isolated aortic regurgitation (4.4%), and combined mitral and aortic regurgitation were found in the remaining 3 (13%).

During the period of follow-up, we judged the progress of the patients to have improved in some cases, for the situation to have improved in that the regurgitation was decreased but the colour jet remained longer than one centimetre, or for the regurgitation either to have worsened or remained unchanged. On this basis, the degree of mitral regurgitation was found to improve in 13 (59.1%) patients, disappearing completely in 6 (27.3%), and the length of colour jet decreasing to less than 1 cm in 4 (18.2%) (Table 1). In the remainder three patients, our 10th, 15th, and 19th cases, the regurgitation became intermittent or

Table 1. Patients with improved mitral regurgitation according to length of the colour jet.

No. of cases	Follow-up time (months)	Length of jet (cm)		Time of improvement (months)
		First	Last	
2	3	1.5	0	3
5	2	2.0	0	2
6*	2	2.3	0	2
7	2	1.9	0	2
8	3	2.0	0	3
9	3	2.3	0	3
10**	24	1.8	1.1	24
14*	12	2.5	0.6	3
15**	18	2.7	1.0	12
16	24	1.5	0.8	24
19**	12	1.5	1.5	12
22	3	2.2	0.9	2
23	3	1.4	0.5	3

*These patients had also aortic regurgitation; **intermittent or not pansystolic

Table 2. Patients with mitral regurgitation jets longer than 1 cm during their last examinations.

No. of cases	Follow-up time (months)	Length of jet (cm)	
		First	Last
3*	24	1.5	1.9
4**	3	1.5	2.2
11	18	1.1	1.5
12	18	2.5	1.5
13	12	2.5	1.5
17	3	2.0	1.2
18	12	1.7	1.4
20	18	1.2	1.5
21	3	1.5	1.5

*This patient had also aortic regurgitation; **patient who developed organic murmur

no longer pansystolic, although the length of colour jet remained 1 cm or longer. The improvement was delayed until between the 12th and 24th months in four patients, although it usually occurred between the second and third months after the diagnosis. The final length of the colour jet, although longer than 1 cm, had decreased in four patients (18.2%), specifically the 12th, 13th, 17th, and 18th cases. It had increased in the 3rd, 4th, 11th, and 20th patients, but remained unchanged in the 21st case (Table 2). One patient, our fourth case, was discharged from the study since an organic murmur due to mitral regurgitation became audible during the assessment at the second month.

According to the velocity of mitral regurgitation, improvement was noted in 19 patients (86.4%), in whom the final velocity was less than 2.5 m/s. In three patients (13.6%), the velocity of regurgitation either remained unchanged, in the 3rd and 21st cases, or increased, in the 4th case (Table 3). Comparing the results obtained by the two methods, we found that, in one of the two patients whose velocity of mitral regurgitation did not change, the length of colour jet also did not change. This was the 21st case. In the other, our third case, the length of the jet had increased. Those patients whose regurgitation had improved according to the length of colour jet (13 cases – 59.1%) also demonstrated improvement according to the velocity of mitral regurgitation. Although the length of colour jet decreased, it still remained longer than one centimetre in four cases (12th, 13th, 17th and 18th cases) who had been judged to be improved according to the velocity of regurgitation. Two patients, the 11th and 20th cases, with an increased length of the colour jet, had improved according to the velocity of mitral regurgitation.

Aortic regurgitation has been detected in four cases, of whom three also had mitral regurgitation (Table 4). The aortic regurgitation disappeared completely in two cases, and improved in the other two cases as judged by the velocity of aortic regurgitation, which was now less than 2.5 m/s. The improvement occurred at around two months. The co-existing mitral regurgitation had also improved in the 6th and 14th cases.

Table 3. Patients with improved, increased, or unchanged mitral regurgitation according to velocity criterions.

No. of cases	Velocity of mitral regurgitation (m/s)	
	First	Last
2	2.5	0
3	3.0	3.0
4	2.7	5.1
5	2.5	0
6	2.5	0
7	2.5	0
8	2.5	0
9	2.5	0
10	3.3	1.5
11	2.5	1.5
12	3.0	2.0
13	3.5	1.5
14	3.0	1.5
15	2.5	1.5
16	5.0	1.1
17	3.4	1.5
18	2.5	1.5
19	2.5	1.5
20	2.5	2.0
22	2.5	1.5
23	2.5	1.5
21	4.0	4.0

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Table 4. Results of follow-up of the patients with aortic regurgitation according to velocity criterions.

No. of cases	Follow-up time (months)	Regurgitation of the valves	Velocity of aortic regurgitation (m/s)	
			First	Last
1	6	Aortic regurgitation	2.5	1.0
3	24	Aortic and mitral regurgitation	2.5	1.5
6	2	Aortic and mitral regurgitation	2.5	0
14	12	Aortic and mitral regurgitation	2.5	0

Although the length of colour jet increased, the velocity of mitral regurgitation did not change in the third case.

Discussion

There is still no single symptom, sign, or laboratory test that is pathognomonic or diagnostic for acute rheumatic fever. Thus, the diagnosis of carditis in rheumatic fever is still usually based on the presence of significant murmurs.[11,12] The Jones criterions, in their 1992 update, owing to insufficient information, do not yet permit the use of echocardiography to document valvar regurgitation without accompanying auscultatory findings as the sole criterion for valvitis in acute rheumatic fever.[11] Congeni and Chun et al.[13,14] reported that up to one-third of their patients had carditis. Most publications from developing countries, however, point to carditis as being the most common manifestation of acute rheumatic fever, being found in over nine-tenths of patients.[15,16] In our study, carditis was seen in just under half of the patients: an incidence comparable to that reported by Al-Eissa et al.[17] Sydenham's chorea, in contrast, was more common than previously reported,[14,17] being seen in one-third of our patients. Nearly all patients with Sydenham's chorea were referred for cardiac investigation to our centre, which is the sole referral institution for children in the city of Konya, which has a population of 1.3 million. This increase probably reflected our referral practice.

There are many reports of patients with rheumatic arthritis and chorea who developed chronic rheumatic heart disease.[18,19] These reports conclude that such patients may have had subclinical carditis. Similarly, other authors have concluded that pathological but subclinical valvitis demonstrated by echocardiography should be accepted as adequate evidence for the diagnosis of carditis.[8,10]

The purpose of our study, therefore, was prospectively to investigate the prevalence of subclinical rheumatic valvitis, to evaluate its prognosis, and to establish echocardiographic criterions to assess the progress of valvar regurgitation as identified among patients with rheumatic fever subsequent to a normal auscultatory examination. In our patients, just over two-fifths of the 53 patients with no murmur were found to have echocardiographic evidence of subclinical rheumatic valvitis. In a similar study also conducted in Turkey, subclinical valvitis was diagnosed in just over half of the patients with acute rheumatic fever but without any murmur.[10] These findings from Turkey have confirmed previous reports that Doppler echocardiography can demonstrate significant valvar incompetence in the absence of auscultatory findings, both during the acute and the quiescent phases of the disease.[3–4]

Isolated mitral regurgitation is well recognised as the most common valvar lesion manifesting as carditis,[14,17] and was present in over four-fifths of our cases with subclinical valvitis. In a study conducted by Figueroa et al.,[4] no individual with subclinical carditis developed a clinically detectable or auscultatory lesion during follow up. Amongst our cohort, however, our fourth patient developed an organic murmur in the presence of an increased colour jet and increased velocity of regurgitation. This patient may represent a later clinical presentation of the cardiac involvement of subclinical valvitis.

To our knowledge, there are a few clinical investigations which have followed-up patients with subclinical valvitis.[2,4,10] These reports, however, did not analyze the echocardiographic findings so as to establish criterions to judge the improvement in valvar regurgitation. During the period of follow-up, we found that mitral regurgitation improved in three-fifths of patients according to the length of colour jet, and in almost seven-eighths according to velocity criterions. These proportions are higher than previously reported in our country.[10] If, however, we take complete disappearance of regurgitation as the sole criterion for improvement, only one-quarter of our patients would be demed to have improved: a ratio comparable to that reported by Özkutlu et al.[10]

According to the velocity criterions, there was an even greater improvement in the degree of mitral regurgitation, this being noted in 86.4% of our cohort. Regurgitation would have been considered

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improved in 59.1% of the patients according to the length of colour jet as well as the velocity criterions. Of the remaining 6 patients in whom mitral regurgitation had improved according to velocity criterions, four had a colour jet longer than one centimetre, and two had an increment in the length of the colour jet. We cannot explain why the velocity of mitral regurgitation decreased whilst the length of colour jet increased. Perhaps the velocities of regurgitation had been misinterpreted in these patients owing to the direction of the regurgitant jet extending toward the posterolateral aspect of the left atrium?

As is well known, secondary prophylaxis is the most benefical and cost-effective part of any programme for the prevention and control of rheumatic heart disease in developing countries.[20] In this setting, accuracy of diagnosis is paramount, since it determines the need for long term follow-up and antibiotic prophylaxis.[4] There has been concern that physiologic regurgitation may be misinterpreted as abnormal or pathologic, resulting in the over-diagnosis of rheumatic fever, since colour Doppler echocardiography is a highly sensitive method which can also detect clinically insignificant physiologic valvar regurgitation.[21–26] It is generally accepted, nonetheless, that if the guidelines for diagnosis of mitral and aortic regurgitation were strictly followed, over-diagnosis of organic regurgitation is highly unlikely.[8] In the study conducted by Minich et al.,[3] the specificity of Doppler for detecting pathologic regurgitation was 94%, with a positive predictive value of 93%. By adding the posterolateral direction of the jet to the diagnostic criterions, the specificity and positive predictive value of Doppler echocardiography for identifying subclinical mitral regurgitation of rheumatic etiology rose to 100%. We used these same echocardiographic criterions both during the initial diagnosis of subclinical valvitis and over the period of follow-up in order to evaluate the prevalence and evolution of subclinical valvar regurgitation. We have found that mitral and aortic regurgitation disappeared completely in one-quarter and one-half of the initially involved patients, respectively. We also found that mitral and aortic regurgitation decreased but did not disappear completely in some patients. When we analyzed the echocardiographic findings of these patients, we observed that the echocardiographic findings had not fulfilled the diagnostic criterions of organic regurgitation. If subtle echocardiographic findings, such as the velocity of regurgitation less than 2.5 m/s, and a colour jet shorter than one centimetre, may be interpreted as physiologic valvar regurgitation, then similar findings should also be taken as indicative of an improvement in subclinical valvitis.

In conclusion, we found that almost half of our patients with acute rheumatic fever but without a significant murmur had echocardiographic evidence of subclinical valvitis. The evidence of valvar regurgitation disappeared completely in one-quarter of the patients with mitral regurgitation, and in half of those with evidence initially of aortic regurgitation. Evidence of an improvement in valvar regurgitation, however, was more common, being found in three-fifths of the patients with subclinical mitral regurgitation, and all the patients with subclinical aortic regurgitation. Although the diagnostic echocardiographic criterions for recognition of subclinical valvitis are well known, the criterions for improvement are not well established. We suggest that, if during follow-up, those patients with insignificant valvar regurgitation who no longer fulfill the diagnostic criterions for regurgitation, in that the velocity is now less than 2.5 m/s, or the colour jet measures less than 1 cm, their subclinical valvitis should be considered to have improved.

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