Cardiology in the Young (2014), **24**, 359–365
doi:10.1017/S1047951108002126
© Cambridge University Press, 2008

Original Article

Tissue Doppler imaging in rheumatic carditis

Tugcin Bora Polat, Yalim Yalcin, Abdullah Erdem, Cenap Zeybek, Celal Akdeniz, Ahmet Celebi

Department of Pediatric Cardiology, Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Hospital, Istanbul, Turkey

Abstract *Objective:* Our study was undertaken to assess cardiac functions by tissue Doppler echocardiography in patient with primary episode of rheumatic carditis. *Methods:* We divided 82 patients with rheumatic carditis were divided in two groups; 50 patients with mild and 32 patients with mitral regurgitation of grade two or more. A control group consisted of 30 healthy children free of any disease. All children underwent conventional and tissue Doppler echocardiography initially and at the time of the follow-up examination. *Results:* Myocardial systolic wave velocity of the mitral annulus was significantly higher in patients with mitral regurgitation of grade two or more when compared to the control group, but was not different between patients with mild mitral regurgitation and healthy subjects at the time of the initial attack. Myocardial precontraction time, myocardial contraction time, and the ratio of myocardial precontraction and contraction times were significantly prolonged, and the systolic myocardial velocity of the mitral annulus was significantly decreased in patients with mitral regurgitation of grade two or more at the time of the follow-up examination. The myocardial systolic wave velocity was significantly lower, and myocardial precontraction time, myocardial contraction time, and the ratio of the precontraction and contraction times, were significantly longer or greater between patients with grade two or more mitral regurgitation and the control group at follow-up examination. *Conclusion:* We detected subclinical systolic dysfunction of the left ventricle in children with a primary episode of rheumatic carditis due to ongoing ventricular volume overload. Tissue Doppler imaging provides a quantifiable indicator useful for cardiac monitoring of disease during the period of follow up.

Keywords: Rheumatic heart disease; myocardial velocity of the mitral annulus; subclinical systolic dysfunction

First published online: 14 March 2008

Rheumatic heart disease, with progressive left ventricular dilation and dysfunction, is the most common form of acquired cardiac disease in young adults in the developing world.[1] A number of factors may contribute to myocardial damage and detrimentally affect left ventricular myocardial contractility during rheumatic fever.[2,3] The dimensions of the left ventricular cavity, and the ejection fraction, however, are indirect measurements of intrinsic myocardial function, and remain within normal limits, or are higher than normal, during the compensated phase of rheumatic heart disease.[4,5]

Correspondence to: Tugcin Bora Polat, 5. Gazeteciler sitesi A1 Blok 3 nolu villa, Akatlar-Istanbul/ Turkey. Tel: +90 (212) 324 10 19; Fax: +90 (212) 311 32 45; E-mail: tugcin75@mynet.com

Accepted for publication 26 October 2007

Tissue Doppler imaging is able to measure the peak velocity of myocytic shortening in the longitudinal direction, and is believed to give an estimation of global left ventricular systolic function with high feasibility and reproducibility. The velocities derived from the annulus or the base of the left ventricle primarily reflect longitudinal motion, due to the longitudinally directed myocytes which are found in the subendocardium. This may explain why these measurements are particularly sensitive for the assessment of myocardial dysfunction in patients with volume overload.[6,7] As the subendocardial myocytes are aligned longitudinally, we hypothesised that left ventricular long axis function may be altered in patients with rheumatic carditis. This has yet to be elucidated. We prospectively evaluated, therefore, the ventricular performance of

https://doi.org/10.1017/S1047951108002126 Published online by Cambridge University Press

patients after a primary episode of rheumatic carditis, using indexes of tissue Doppler imaging as potential echocardiographic indicators of sub-normal myocardial dysfunction.

Materials and methods

Patients

We studied 82 patients presenting with primary episodes of rheumatic carditis to our hospital over a period of 24 months, basing the diagnosis of acute rheumatic fever on the modified Jones criterions.[8–11] All had evidence of continuing rheumatic activity, including elevated acute phase reactants. Mean age at the time of acute rheumatic fever was 10.3 ± 2.6 years, with a range from 4.6 to 15.8 years, and 32 (39%) were male. We also recruited 30 healthy subjects from children ssen with an innocent murmur over the same period. The protocol was approved by the Local Research Ethics Committee, and all subjects gave informed consent.

All children underwent conventional and tissue Doppler imaging initially and at the time of the follow-up examinaton.

Conventional echocardiographic study

All ultrasound examinations were performed with a commercially available echocardiographic machine (Vivid 3 System, Vingmed–General Electric) equipped with 2.5–5 and 4–8 MHz phased-array transducers. All patients underwent echocardiographic examination within 24 to 48 hours of establishment of the diagnosis of acute rheumatic fever and before starting anti-inflammatory treatment. Valvar regurgitation was diagnosed when color Doppler flow mapping demonstrated reversed flow through the valve in the closed position. To differentiate abnormal from physiological mitral regurgitation,[12] we required the high-velocity turbulent jet to extend beyond the paravalvar region by more than 15 millimetres, confirmed this by colour-guided pulsed Doppler spectral analysis.[13]

On-line computerized planimetry of the maximal regurgitant jet areas was performed, and the mean of three cardiac cycles was taken. The severity of mitral and aortic regurgitation was graded on the basis of the maximal distance of the regurgitant jet from the valvar orifice using the criterions of Helmcke et al.,[14] and Perry et al.,[15] respectively. The dimensions of the left atrium and ventricle were measured from M-mode traces, and by using the recommendations of the American Society of Echocardiography.[16] Left ventricular ejection fraction and fractional shortening were estimated from M-mode tracings using the Teichholz formula[17] and the cubed formula,[18] respectively. Measurements were obtained during four end-expiratory cardiac cycles, taking the average for each parameter.

Tissue Doppler imaging

Tissue Doppler imaging was performed in apical four-chamber planes with the pulsed-wave Doppler sample volume of 4 millmetre length placed successively at the lateral mitral annulus. The incident angle between the interrogating Doppler beam and longitudinal motion of the ventricle was kept as small possible. We measured the myocardial systolic wave velocity, the myocardial precontraction time from the onset of the QRS complex to the beginning of the myocardial systolic wave, and the myocardial contraction time, from the beginning to the end of the myocardial systolic wave, permitting calculation of the ratio between these times. At least 10 cardiac cycles were recorded from each site on a strip-chart recorder at a speed of 100 mm/s.

Follow-up

Patients with rheumatic carditis and congestive heart failure were treated with steroids, along with dietary salt restriction, digoxin, diuretics, and inhibitors of angiotension converting enzyme, whereas patients with carditis but without congestive heart failure were treated with aspirin. Injectable benzathine penicillin G for secondary prophylaxis was initiated or regulated at the time of the index attack in all patients.[19] Follow-up examinations were routinely scheduled in all patients at 3 months after the index attack to study the evolution of valvar lesions. At the time of the follow-up examination, none had clinical or laboratory evidence of ongoing or recurrent rheumatic fever. Repeat echocardiographic examinations were performed by the same operator with the same ultrasound machine and with similar gain settings.

Statistical analysis

Results are expressed as mean, and range. The data were analyzed with SPSS version 10.0 software (SPSS, Chicago, IL). The differences between the groups were explored with the Student's t test. Incidences in the groups were tested for significance with the χ^2 test. For comparison of tissue Doppler imaging, variables obtained in the same individual initially and at the time of the follow-up examinaton, the paired, two-sided Student's t-test was used. A probability value of $p < 0.05$ was considered significant.

Results

Of the 82 patients, 50 (61%) had mild mitral regurgitation, while 20 (24%) had moderate, and

https://doi.org/10.1017/S1047951108002126 Published online by Cambridge University Press

12 (15%) had severe mitral regurgitation. According to the valvar involvement at the time of index attack, we identified 32 patients with mitral regurgitation of grade 2 or more, and 50 patients with mild mitral regurgitation in the index attack. Improper coaptation of the aortic valvar leaflets without prolapse or annular dilation was seen in 7, and all were associated with mild degrees of valvar regurgitation. Of these, 3 also had mild mitral regurgitation, while the remaining 4 were associated with moderate degree of mitral regurgitation.

Conventional echocardiographic findings

At the initial period, patients showed significantly larger left atrial and ventricle dimensions (Table 1). Furthermore, baseline left atrial and ventricle dimensions were significantly larger in patients with mitral regurgitation of grade 2 or more than control group, but no significant differences were noted between patients with mild mitral regurgitation and healthy subjects in the conventional echocardiographic parameters (Table 2). At follow-up

Table 1. Conventional and tissue Doppler indexes of the patients and their controls.

	Patients (n = 82)	Control group (n = 30)	p
At the time of index attack			
LV end-diastolic dimension index, cm/m^2	3.97 (0.34)	3.76 (0.29)	0.004
LV end-systolic dimension index, cm/m^2	2.81 (0.29)	2.61 (0.26)	0.002
Left atrial dimension index, cm/m^2	2.43 (0.31)	2.21 (0.26)	0.001
Fractional shortening, %	32.4 (2.1)	31.3 (1.6)	0.097
Ejection fraction, %	66.3 (3.8)	64.2 (2.7)	0.079
Myocardial systolic wave velocity (cm/s)	11.8 (1.4)	11.2 (1.1)	0.038
Myocardial precontraction time (ms)	86.1 (11.7)	83.5 (10.7)	0.30
Myocardial contraction time (ms)	218 (6.1)	219 (5.9)	0.87
Myocardial precontraction : contraction time ratio	0.39 (0.05)	0.38 (0.04)	0.29
At the time of the follow-up examination			
LV end-diastolic dimension index, cm/m^2	3.85 (0.35)	3.76 (0.29)	0.20
LV end-systolic dimension index, cm/m^2	2.67 (0.29)	2.61 (0.26)	0.34
Left atrial dimension index, cm/m^2	2.33 (0.31)	2.21 (0.26)	0.07
Fractional shortening, %	30.9 (2.1)	31.3 (1.6)	0.35
Ejection fraction (%)	64.1 (2.9)	64.2 (2.7)	0.75
Myocardial systolic wave velocity (cm/s)	10.7 (1.3)	11.2 (1.1)	0.08
Myocardial precontraction time (ms)	86.1 (11.8)	83.5 (10.7)	0.81
Myocardial contraction time (ms)	218 (6.1)	219 (5.9)	0.91
Myocardial precontraction : contraction time ratio	0.39 (0.05)	0.38 (0.04)	0.95

Values are expressed as means with standard deviation shown in parentheses.

Table 2. Demographic and baseline echocardiographic features of the groups.

	Patient with mitral regurgitation of grade two or more (n = 32)	Patient with mitral regurgitation of less than grade two (n = 50)	Control group (n = 30)
Age (years)	10.4 (3.1)§	10.1 (2.3)§	9.9 (2.1)
Sex (male/female)	12/20§	20/30§	12/18
Body surface area (m^2)	1.06 (0.2)§	1.05 (0.19)§	1.04 (0.15)
Mean pulse rate	92 (11)§	86 (8)§	78 (9)
LV end-diastolic dimension index, cm/m^2	4.23 (0.39)‡	3.81 (0.19)§	3.76 (0.29)
LV end-systolic dimension index, cm/m^2	2.95 (0.34)‡	2.72 (0.23)§	2.61 (0.26)
Left atrial dimension index, cm/m^2	2.63 (0.34)‡	2.31 (0.21)§	2.21 (0.26)
Fractional shortening, %	33.4 (1.8)§	29.5 (4.8)§	31.3 (1.6)
Ejection fraction (%)	67.5 (2.8)§	65.5 (4.2)§	64.2 (2.7)
Myocardial systolic wave velocity (cm/s)	12.1 (1.4)$^{\epsilon}$	11.6 (1.4)§	11.2 (1.1)
Myocardial precontraction time (ms)	88.6 (12.5)§	84.4 (10.9)§	83.5 (10.7)
Myocardial contraction time (ms)	219 (6.1)§	218 (6.2)§	219 (5.9)
Myocardial precontraction : contraction time ratio	0.41 (0.05)§	0.38 (0.04)§	0.38 (0.04)

Values are expressed as means with standard deviation shown in parentheses.
Patients' groups compared to control group, $^{\S}p > 0.05$, $^{\epsilon}p = 0.007$, $^{\ddagger}p < 0.001$

https://doi.org/10.1017/S1047951108002126 Published online by Cambridge University Press

Table 3. Comparison of conventional and tissue Doppler indexes of patients obtained initially and at the time of the follow-up examinaton (paired *t* test with confidence intervals).

			Analysis of difference between groups		
	At the time of index attack	At follow-up	Mean alteration in parameters	95% CI	p value
Patients with mitral regurgitation of grade two or more at follow-up examination (n = 23)					
Myocardial systolic wave velocity (cm/s)	12.1 (1.3)	9.6 (1.2)	2.4 (1.4)	1.7 to 3.1	<0.001
Myocardial precontraction time (ms)	90.4 (13.8)	100.5 (8.6)	−10.1 (12.8)	−15.6 to −4.5	0.001
Myocardial contraction time (ms)	218 (6.4)	217 (6.3)	1.1 (7.3)	2.1 to 4.2	0.478
Myocardial precontraction : contraction time ratio	0.41 (0.06)	0.46 (0.03)	−0.048 (0.05)	−0.07 to −0.02	0.001
LV end-systolic dimension index, cm/m^2	3.17 (0.22)	2.81 (0.41)	0.36 (0.28)	0.23 to 0.48	<0.001
Ejection fraction (%)	68.2 (2.8)	64.1 (1.4)	4.04 (3.1)	2.7 to 5.3	<0.001
Patients with mitral regurgitation of less than grade two at follow-up examination (n = 59)					
Myocardial systolic wave velocity (cm/s)	11.1 (1.1)	11.7 (1.4)	−0.56 (1.2)	−0.88 to −0.23	0.001
Myocardial precontraction time (ms)	84.3 (10.4)	80.4 (7.1)	3.9 (9.7)	1.4 to 6.4	0.003
Myocardial contraction time (ms)	219.1 (5.9)	219.3 (6.1)	−0.2 (4.8)	−1.36 to 1.15	0.865
Myocardial precontraction : contraction time ratio	0.38 (0.04)	0.37 (0.03)	0.018 (0.04)	0.006 to 0.03	0.002
LV end-systolic dimension index, cm/m^2	2.75 (0.23)	2.68 (0.19)	0.09 (0.27)	0.01 to 0.15	0.067
Ejection fraction (%)	65.6 (3.9)	64.1 (3.3)	1.56 (3.44)	0.66 to 2.4	=0.001

Values are expressed as means with standard deviation shown in parentheses.

examination, left atrial and ventricular dimensions significantly decreased (Table 1), albeit that ventricular dimensions were not significantly changed in patients with mild mitral regurtation without volume load (Table 3). Ejection fractions and fractional shortening values did not differ significantly between patients and their controls, neither at the initial nor the follow-up examinations (Tables 1, 2 and 3).

Tissue Doppler parameters

The myocardial systolic wave velocity of the mitral annulus was significantly higher than in control group ($p = 0.038$) at the time of index attack, but myocardial time intervals were not different between the patients and healthy subjects either at the time of index attack or during follow-up (Table 1). The myocardial systolic wave velocity of the mitral annulus was significantly higher in patients with mitral regurgitation of grade 2 or more when compared to control group ($p = 0.007$) but was not different between patients with mild mitral regurgitation and healthy subjects at the time of index attack. Myocardial time intervals of the mitral annulus were not significantly different between the two study groups and control group at the time of the index attack (Table 2).

According to the valvar involvement at the time of the follow-up examination, we identified 23 (28%) patients with mitral regurgitation of grade 2 or more, and 59 (72%) patients with mitral regurgitation of less than grade 2. Myocardial precontraction time, and the ratio between precontraction and contraction times, were significantly prolonged ($p = 0.001$), and the myocardial systolic wave velocity of the mitral annulus was significantly decreased ($p < 0.001$) in patients with mitral regurgitation of grade 2 or more at the time of the follow-up examination (Table 3). The myocardial systolic wave velocity of the mitral annulus was significantly lower ($p < 0.001$), and the myocardial precontraction awas longer, and the ration of contractions significantly greater ($p < 0.001$, $p = 0.038$, respectively) between patients with mitral regurgitation of grade 2 or more and the control group, but myocardial systolic wave velocity and all myocardial time intervals of the mitral annulus were not significantly different between patients with mitral regurgitation of less than grade 2 and those making up the control group at follow-up examination (Table 4).

Discussion

Mitral regurgitation is the most common Doppler echocardiographic feature of both a first episode and recurrences of rheumatic carditis. Associated aortic valvar involvement is a less common feature.[19,20] Many efforts have been made to obtain an accurate estimation of the contractile performance of the ventricle in mitral regurgitation. Unfortunately, most indexes of ventricular function used in clinical practice, such as ejection fraction and stroke volume, do not solely reflect the contractile state of the ventricle. Ejection fraction, and left ventricular internal dimensions, are not reliable predictors of left ventricular systolic function after surgical

https://doi.org/10.1017/S1047951108002126 Published online by Cambridge University Press

Table 4. Tissue Doppler indexes of patients according to the valvar involvement at follow-up examination.

	Patients with mitral regurgitation of grade two or more (n = 23)	Patients with mitral regurgitation of less than grade two (n = 59)	Control group (n = 30)
Myocardial systolic wave velocity (cm/s)	9.6 (1.2)‡	11.7 (1.4)§	11.2 (1.1)
Myocardial precontraction time (ms)	100.5 (8.6)‡	80.4 (7.1)§	83.5 (10.7)
Myocardial contraction time (ms)	217 (6.3)§	219 (6.1)§	219 (5.9)
Myocardial precontraction : contraction time ratio	0.41 (0.06)¥	0.36 (0.03)§	0.38 (0.04)

Values are expressed as means with standard deviation shown in parentheses.
Patients' groups compared to control group, §$p > 0.05$; ¥$p = 0.038$; ‡$p < 0.001$

correction of mitral regurgitation. The ejection fraction decreases significantly because of the increased afterload after surgical correction.[21,22]

The explanation for the uncertainty about left ventricular function is the considerable alteration in the loading conditions of the left ventricle in mitral regurgitation. The increased diastolic inflow volume in the left ventricle induces an increased preload. During systole, the left ventricle generally ejects the normal stroke volume through the aortic valve, but also produces a regurgitant flow to the left atrium, suggestive of a decreased impedance to ejection, producing doubt concerning the true contractile state of the myocardium.[21,23]

The assessment of the systolic indexes of the mitral annulus with tissue Doppler imaging allows for an estimation of global left ventricular systolic function, providing information on the velocity of the descent of the base as an estimate of global systolic ventricular function.[24] The onset of subendocardial shortening coincides hemodynamically with an early rapid build-up of intraventricular pressure during the isovolumic contraction period. Shortening of circumferential fibres occurs later, temporally coinciding with the onset of systolic ejection. The temporal lag between the onsets of subendocardial and subepicardial contraction activities correlate with the duration of isovolumic contraction. The differential placement of the longitudinal myocytes in the subendocardium, therefore, may render longitudinal velocity uniquely sensitive to mild or early impairments prior to changes being detectable in the short axis. Thus, tissue Doppler imaging may provide evidence of subclinical myocardial dysfunction in the early period before other conventional Doppler parameters.[25]

Furthermore, tissue Doppler imaging not only defines and measures mitral annular movement but, because of its high temporal resolution, also provides a useful estimate of myocardial time intervals, both systolic and diastolic.[26–28] Myocardial precontraction time is the myocardial systolic time corresponding to the isometric period before the onset of myocardial contraction, whereas myocardial contraction time corresponds to the period of contraction. The ratio between these times, corresponding to the ratio of the left ventricular pre-ejection period to the left ventricular ejection time obtained by standard Doppler assessment of the left ventricular outflow tract, may be considered to be an index inversely correlated with myocardial contractility.[27] In a previous study,[23] the ratio, along with and myocardial systolic wave velocity of the mitral annulus velocity, were the best discriminant cut off values for a postoperative reduction in ejection fraction of less than 10% obtained by receiver operating characteristic curves in patients with asymptomatic severe mitral regurgitation and normal ejection fraction. Moreover, a postoperative ejection fraction of less than 50% was observed in 8% of patients, and all the preoperative systolic tissue Doppler imaging parameters had a significant correlation with changes in ejection fraction.

In our study, tissue Doppler imaging indexes of patients appeared normal in those with little valvar involvement, while we found that for an increase of preload and decrease of afterload in those with significant valvar lesions, there was a concomitant significant increase of myocardial systolic wave velocity of the mitral annulus. This phenomenon can be simply justified by the length-dependent activation seen in the Frank-Starling mechanism, which endows the ventricle with performance characteristics such that the heart ejects whatever volume it receives during diastole. Thus, an increase of the length of the myocytes caused by an increase of end-diastolic volume and decrease of ventricular tension caused by decrease of afterload will lead to an increase of stroke volume, the velocity of shortening, and and also an increase of myocardial systolic wave velocity of the mitral annulus. The sudden increase of preload, and decrease of afterload, has a complex impact on the haemodynamic behavior of the ventricle that is presently still not fully comprehended. As such, this parameter cannot be recommended as an index of ventricular contractility, where significant changes in ventricular filling occur at the time of index attack.

https://doi.org/10.1017/S1047951108002126 Published online by Cambridge University Press

In patients with persistent significant valvar lesions, the systolic myocardial velocity and systolic myocardial time intervals of the mitral annulus deteriorated during follow-up.

Abnormal values of tissue Doppler imaging systolic indexes observed in patients with persistent valvar involvement may be explained by persistent left ventricular volume overload that increases wall stress, causing subendocardial ischaemia and fibrosis.[29] In support of these prognostications, the tissue Doppler imaging indexes were observed to be normal in patients with little valvar involvement during follow-up. These observations concur with recent reports[6,23,24] that the preservation of cardiac functions was paralleled by the disappearance of volume overload.

Some limitations of our study should be noted. Delay of surgery for mitral insufficiency often results in irreversible left ventricular dysfunction in adults. This has prompted a trend toward earlier surgery in adult patients with chronic mitral regurgitation based on echocardiographic assessment.[30] In this respect, our findings may have important clinical implications. In contrast, as do many paediatric centres, we usually continue to delay surgery for children until severe symptoms are present. This approach is a result of the limitations of the size of the patients for valvar replacement, the need for anticoagulation management, and the expectation for early reoperation with ongoing growth.[31–34] Thus, all our current patients were asymptomatic, and had only subclinic impairment of left ventricular systolic functions assessed by tissue Doppler imaging, so we did not recommend surgery. In this respect, it is questionable whether the abnormal indexes may predict a significant reduction in postoperative ejection fraction in asymptomatic children with severe mitral regurgitation and normal ejection fraction, which need to be tested in further studies.

We conclude that, in patients with rheumatic carditis, assessment using tissue Doppler imaging may be useful in providing evidence of subclinical myocardial dysfunction, suggesting contractile disturbance due to ongoing left ventricular volume overload before conventional Doppler parameters. These findings may offer new diagnostic and therapeutic opportunities in the screening and management of these patients, and should be considered in these settings.

References

1. Eisenberg MJ. Rheumatic heart disease in the developing world: prevalence, prevention and control. Eur Heart J 1993; 14: 122–128.
2. Narula J, Chopra P, Talwar KK, et al. Does endomyocardial biopsy aid in the diagnosis of active rheumatic carditis? Circulation 1993; 88: 2198–2205.
3. Taranta A, Markowitz M. Rheumatic Fever, 2nd ed. Kluwer Academic PublishersDordrecht; 1989, p 19.
4. Vasan RS, Shrivastava S, Vijayakumar M, Narang J, Lister BC, Narula J. Echocardiographic evaluation of patients with acute rheumatic fever and rheumatic carditis. Circulation 1996; 94: 73–84.
5. Essop MR, Wisenbaugh T, Sareli P. Evidence against a myocardial factor as the cause of left ventricular dilation in active rheumatic fever. J Am Coll Cardiol 1993; 22: 826–829.
6. Vinereanu D, Ionescu AA, Fraser AG. Assessment of left ventricular long axis contraction can detect early myocardial dysfunction in asymptomatic patients with severe aortic regurgitation. Heart 2001; 85: 30–36.
7. Nagueh SF, Middleton KJ, Kopelen HA, Zoghbi WA, Quinones MA. Doppler tissue imaging: a technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am Coll Cardiol 1997; 30: 1527–1533.
8. Committee on Rheumatic Fever and Bacterial Endocarditis of the American Heart Association. Jones' criteria (revised) for guidance in the diagnosis of rheumatic fever. Circulation 1984; 69: 203–208.
9. World Health Organization. Rheumatic fever and rheumatic heart disease: report of a WHO study group. Geneva, SwitzerlandWorld Health Organization; 1988, 5–58. WHO Technical Report Series 764.
10. Special Writing Group of the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease of the Council of Cardiovascular Disease in the Young of the American Heart Association. Guidelines for the diagnosis of rheumatic fever: Jones' criteria, 1992 update. JAMA 1992; 268: 2069–2073.
11. Feinstein AR, Spagnuolo M. Mimetic features of rheumatic fever recurrences. N Engl J Med 1960; 262: 533–535.
12. Brand A, Dollberg S, Keren A. The prevalence of valvular regurgitation in children with structurally normal hearts: a color Doppler echocardiographic study. Am Heart J 1992; 123: 177–180.
13. Sahn DJ, Maciel BC. Physiological valvular regurgitation: Doppler echocardiography and the potential for iatrogenic heart disease. Circulation 1988; 78: 1075–1077.
14. Helmcke F, Nanda NC, Hsiung MC, et al. Color Doppler assessment of mitral regurgitation with orthogonal planes. Circulation 1987; 75: 175–183.
15. Perry GJ, Helmcke F, Nanda NC, Byard C, Soto B. Evaluation of aortic insufficiency by Doppler color flow mapping. J Am Coll Cardiol 1987; 9: 952–959.
16. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072–1083.
17. Teichholz LE, Cohen MV, Sonnenblick EH, Gorlin R. Study of left ventricular geometry and function by B-scan ultrasonography in patients with and without asynergy. N Engl J Med 1964; 291: 120–128.
18. Feigenbaum H, Popp RL, Wolfe SB. Ultrasound measurements of the left ventricle: correlations with angiocardiography. Arch Intern Med 1972; 1129: 461–475.
19. Massel BF, Fyler DC, Roy SB. The clinical picture of rheumatic fever: the diagnosis, immediate prognosis, course, and therapeutic implications. Am J Cardiol 1958; 1: 436–449.
20. Sanyal SK, Thapar MK, Ahmed SH, Hooja V, Tewari P. The initial attack of acute rheumatic fever during childhood in North India: a prospective study of the clinical profile. Circulation 1974; 49: 7–12.

https://doi.org/10.1017/S1047951108002126 Published online by Cambridge University Press

21. Enriquez-Sarano M, Tajik A, Schaff H, Orszulak T, Bailey K, Frye R. Echocardiographic prediction of left ventricular function after correction of mitral regurgitation: results and clinical implications. J Am Coll Cardiol 1994; 24: 1536–1543.
22. Enriquez-Sarano M. Timing of mitral valve surgery. Heart 2002; 87: 79–85.
23. Agricola E, Galderisi M, Oppizzi M, et al. Pulsed tissue Doppler imaging detects early myocardial dysfunction in asymptomatic patients with severe mitral regurgitation. Heart 2004; 90: 406–410.
24. Pai RG, Bodenheimer MM, Pai SM, Koss JH, Adamick RD. Usefulness of systolic excursion of the mitral anulus as an index of left ventricular systolic function. Am J Cardiol 1991; 67: 222–224.
25. Skoularigis J, Sinovich V, Joubert G, Sareli P. Evaluation of the long-term results of mitral valve repair in 254 young patients with rheumatic mitral regurgitation. Circulation 1994; 90: 67–74.
26. Henry WL, Bonow RO, Rosing DR, Epstein SE. Observation on the optimum time for operative intervention for aortic regurgitation. II. Serial echocardiographic evaluation of asymptomatic patients. Circulation 1980; 61: 484–492.
27. Starling MR, Kirsh MM, Montgomery DG, Gross MD. Mechanisms for left ventricular systolic dysfunction in aortic regurgitation: imporimportance for predicting the functional response to aortic valve replacement. J Am Coll Cardiol 1991; 17: 887–897.
28. Wisenbaugh T. Does normal pump function belie muscle dysfunction in patients with chronic severe mitral regurgitation. Circulation 1988; 77: 515–525.
29. Villari B, Campbell ES, Hess OM, et al. Influence of collagen network on left ventricular systolic and diastolic function in aortic valve disease. J Am Coll Cardiol 1993; 22: 1477–1484.
30. Ross J Jr. The timing of surgery for severe mitral regurgitation. N Engl J Med 1996; 335: 1456–1458.
31. Sanyal SK. Long term sequelae of the first attack of acute rheumatic fever in childhood. In: Emmanouilides GC, Riemenschneider TA, Allen HD, Gutgesell HP (eds). Heart Disease in Infants, Children and Adolescents. Williams & Wilkins, Baltimore, Md, 1995, pp 1416–1440.
32. Kadoba K, Jonas RA, Mayer JE, Castaneda AR. Mitral valve replacement in the first year of life. J Thorac Cardiovasc Surg 1990; 100: 762–768.
33. Borkon AM, Soule L, Reitz BA, Gott VL, Gardner TJ. Five-year follow-up after valve replacement with the St. Jude medical valve in infants and children. Circulation 1986; 74 suppl I: I-110–I-115.
34. Schaffer MS, Clarke DR, Campbell DN, Madigan CK, Wiggins JW, Wolfe RR. The St. Jude Medical cardiac valve in infants and children: role of anticoagulant therapy. J Am Coll Cardiol 1987; 9: 235–239.

https://doi.org/10.1017/S1047951108002126 Published online by Cambridge University Press