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*Review Article*

# The logic for extending the use of echocardiography beyond childhood to detect subclinical rheumatic heart disease*

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**Abstract** Rheumatic heart disease is the only residual morbidity, and the sole cause of mortality, from rheumatic fever. Echocardiography is ideally suited to confirm and follow the course of rheumatic heart disease. Additionally, both minimal valvar pathology in children, and extensive valvar pathology in adults, may not cause a murmur and can be detected only by echocardiography. Whenever possible, echocardiography should be routinely employed for management of patients with rheumatic fever or suspected rheumatic fever.

Keywords: Silent mitral regurgitation; chordae tendineae; Syndenham's chorea; rheumatic polyarthritis; mitral stenosis; mitral annulus

The only residual morbidity, and the sole cause of mortality, associated with rheumatic fever is rheumatic heart disease. During childhood, such disease essentially equates with mitral regurgitation, seen in almost all cases, and aortic regurgitation, encountered in around one-fifth.[1,2] In adults, the dominant lesion is mitral stenosis. Right sided valvar lesions are usually encountered only after the development of significant pulmonary hypertension due to left-sided valvar lesions.[3]

Echocardiography is now an integral part of the practice of specialists involved in both paediatric and adult cardiology. It is ideally suited to confirm the diagnosis of rheumatic heart disease, and to follow its progression or regression.[4,5] It is the only modality to become available in the last 50 years that can aid the clinician in the diagnosis and management of rheumatic fever.

## Background

Employing what was then new technology in the mid and late 1980s some patients with "pure" Sydenham's chorea, and some with isolated polyarthritis who did not have a murmur, had what appeared to be mitral regurgitation on their echocardiograms.[6–8] There were only 3 studies reporting this observation prior to the publication of the update of the Jones criterions produced by the American Heart Association in 1992.[9] Because small amounts of mitral regurgitation can be detected by echocardiography in children with normal hearts,[10] there was justifiable concern that over interpretation of a "physiologic jet" of mitral regurgitation could lead to iatrogenic disease. To avoid an incorrect diagnosis, with all its undesirable baggage, the recommendation made in 1992[9] was that mitral and aortic regurgitation had to be confirmed by auscultation.

We chose not to follow their recommendations because we continued to find echocardiographic evidence of mitral regurgitation in patients with rheumatic fever who did not have a murmur. Employing criterions established by our group,[11] we continued to find silent mitral regurgitation in a surprisingly large proportion of patients with rheumatic fever who had no murmur. For example, of 45 patients with pure chorea, two-thirds had

*Note from the editor:* To retain uniformity with our editorial style, throughout this manuscript the stylistic editor has pluralised "criterion", and some of the bacteriums producing enodcarditis, by adding an "s", or "es", to the singular noun.

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silent mitral regurgitation, as did almost half of a cohort with isolated polyarthritis.[12]

Similar experience reported from around the world where rheumatic fever is endemic[13–29] made us even more secure in our decision. The World Health Organization has now proposed criterions for echocardiographic and Doppler interrogation that more precisely define subclinical mitral regurgitation. These include, first, presence of a colour jet of more than 1 centimetre in length, second that the jet be evident in at least two imaging planes, third that the mosaic jet have a peak velocity greater than 2.5 metres per second, and finally that the Doppler signal should be holosystolic.[30]

## Our current practice

Because auscultation lacks sufficient specificity and sensitivity, we routinely obtain echocardiograms on all patients with confirmed or suspected rheumatic fever. Those with a murmur have the diagnosis of rheumatic heart disease confirmed, thus establishing a baseline. When patients with pure chorea or isolated polyarthritis have no murmur, but are found to have silent mitral and/or aortic regurgitation, we inform the patient and family that rheumatic fever caused damage to the valve that is not enough to be heard, and can only be detected by echocardiography. We manage these patients the same as a patient with a murmur graded at 1, who had an otherwise normal echocardiogram. In addition, these patients are not considered to be free of rheumatic heart disease until a normal echocardiogram is obtained. We also urge the doctors who later assume the care of the patient to obtain follow-up echocardiograms from experienced cardiologists.

## The murmur of mitral regurgitation – anatomic and haemodynamic considerations

The murmur of mitral regurgitation has specific characteristics that permit it to be readily identified by auscultation.[31] It is a high frequency holosystolic regurgitant murmur, which is heard maximally at the cardiac apex. There are good anatomic and haemodynamic explanations for its specific characteristics. The high pressure gradient is responsible for its high frequency. The vibratory activity generated in the left atrium is transmitted by the left ventricular myocardium, enabling the murmur to be heard where the left ventricular apex has its closest approximation to the anterior chest wall. When the murmur of mitral regurgitation is soft, it can be heard more readily if the patient assumes a left lateral decubitus position, when forced expiration brings the apex of the left ventricle closer to the chest wall. The chest wall must transmit the sound of the murmur to the stethoscope, which in turn transmits the sound through the tubing and ear pieces to the tympanic membranes of the examiner. If the left atrium does not transmit enough vibratory energy in terms of sound to the left ventricle and the chest wall, a murmur will not be heard.

Mitral regurgitation is also unique in that the turbulent regurgitant jet goes from an anterior to posterior position into the left atrium, which is the cardiac structure that has the deepest and most posterior position in the chest cavity. Essentially all other heart murmurs, whether systolic or diastolic, are associated with turbulent flow involving structures that are closer to the anterior chest wall.

## Pre-echocardiographic demonstration of silent mitral regurgitation

Very few appreciate that silent mitral regurgitation was described in patients with rheumatic fever before the use of Doppler echocardiography. An elegantly defined study by University of Kansas paediatric cardiologists working at the University of Kansas was reported as long ago as 1966.[32] These investigators used miniature microphones to make phonocardiographic recordings from patients with acute rheumatic fever or known rheumatic heart disease, comparing the findings with those obtained from age-matched controls. All recordings were made through the oesophagus, thus recording from behind the left atrium, with transthoracic recordings made from four different sites, namely at the cardiac apex, the lower left sternal edge, and the pulmonary and aortic areas. The murmur of mitral regurgitation was routinely "louder" on the transoesophageal phonocardiograms than at the cardiac apex, and was not detected over the precordium. Of note was their discovery that one-third of their patients with rheumatic polyarthritis had a typical pansystolic murmur on the transoesophageal recording that was absent on the recording from the apical position and other transthoracic sites. None of the normal controls had a pansystolic murmur detected transoesophageally, or at any of the transthoracic sites.

## Is there a possible relationship between silent mitral regurgitation and mitral stenosis?

Our referral practice is limited to children, which prohibits us from having any meaningful experience with mitral stenosis. We know, however, that some of the children who had mitral regurgitation subsequently developed mitral stenosis as adults, and that some individuals with mitral stenosis cannot recall having an episode of rheumatic fever.[1] We are also

aware of the classic study of Bland and Jones, who were able to follow a cohort of 1000 patients with rheumatic fever for 20 years.[33] Of the third of this cohort who initially had no murmur, almost half had developed mitral stenosis, most without a recognized recurrence of rheumatic fever. It is tempting to speculate that these patients may have had silent mitral regurgitation. There is no way, or course, that this can be proved one way or the other. It is quite likely that this study will or can be repeated.

The recent report of Marijon and colleagues,[34] while conducted on school children, strongly suggests that the demonstration of silent mitral regurgitation in adults may be important in predicting the onset of mitral stenosis before the classical presystolic murmur of advanced stenosis appears. In this landmark study, a cohort of over 5,000 school children in Cambodia and Mozambique underwent screening examinations for the presence of rheumatic heart disease by auscultation and by echocardiography. The physicians who performed the auscultatory examinations had extensive experience with rheumatic fever and rheumatic heart disease, and the echocardiograms were reviewed in Paris by a group who likewise had extensive experience with childhood rheumatic heart disease. The echocardiographic criterions included detection of a jet of mitral regurgitation in two planes, and specific changes of valvar pathology, such as fusion and thickening of the leaflets along with cordal fusion, thickening, and contraction. In Cambodia, the prevalence of rheumatic heart disease as detected by auscultation was 2.2 cases per 1000, whereas the rate increased to 21.5 per 1000 when employing echocardiography. In Mozambique, the difference was even more striking. Using auscultation, the reported rate was 2.03 cases per 1000, a figure which increased to 30.4 cases per 1000 when employing echocardiography. The mitral valve was involved in over nine-tenths of the total number of cases, matching past clinical experience.

The students identified by the screening are survivors of their episodes of rheumatic fever, and represent the "natural" course of the disease. All other studies of rheumatic fever and rheumatic heart disease understandably have had some degree of medical intervention, if nothing more than beneficial bed rest. The pathologic changes noted in the intrinsic mitral valvar apparatus are more typical of rheumatic heart disease that is encountered in adults, and suggest that these students are well on their way to developing mitral stenosis.

The pathologic changes that convert an incompetent to a stenotic valve occur insidiously over several years, most usually without a clear-cut episode of acute rheumatic fever.[33] It is not known whether these changes are the result of continued low grade rheumatic inflammatory activity, the inherent attempt of the valve to "correct" the damage done during childhood, or perhaps both these activities. The fact that white blood cells recovered from stenotic mitral valves react with streptococcuses,[35] and that continuous prophylaxis with penicillin has reduced the incidence of mitral stenosis,[36] would suggest that low grade rheumatic inflammation is responsible. On the other hand, it is well established that fusion of the leaflets begins at the peripheral attachments of the zone of apposition of the leaflets at the fibrous annulus. The fusion then proceeds centrally, resulting in progressive narrowing of the mitral valvar orifice.[5] One could postulate that this fusion is an attempt to reduce the annular dilation. This area is where the leaflets have the closest approximation during diastole, but appears to be the area least affected during the acute episode, showing no vegetations or little evidence of infiltrate. Pathologists and cardiac surgeons appreciated this phenomenon over a half century ago. During the 1950s and early 1960s, cardiac surgeons performed a so-called commissuroplasty by placing bridging sutures across the ends of the zone of apposition between the leaflets to reduce annular size and improve coaptation.[37,38] Commissuroplasty is currently used to narrow the annulus when performing mitral valvoplasty in children with severe mitral regurgitation whose annulus will not accommodate a Carpentier ring.[39]

Fusion of the leaflets, and decreasing cordal length, reduce the amount of mitral regurgitation. The disappearance of the murmur of mitral regurgitation may also partially be explained by normal growth of the individual. While we are not aware of any discussion, and know of no measurements that have been taken, the distance between the left ventricular apex and the chest wall of a 25-year-old adult is perceptively more than in a 10-year-old child.

Whether or not the changes in the mitral valve are the result of continued low grade inflammation or an inherent healing process is more or less academic. What we now know is that these changes can be detected by echocardiography long before the presystolic murmur of mitral stenosis can be heard.

The autoimmune response to an antecedent streptococcal infection that results in rheumatic heart disease has yet to be precisely defined. Because of echocardiography, we now have a logical, but as yet unconfirmed, explanation of how a child could develop mitral regurgitation that later appeared to resolve, and how children with pure chorea or isolated polyarthritis develop mitral stenosis insidiously as adults.

## Conclusion

Whenever possible, echocardiography should be employed in the routine management of patients with confirmed or suspected rheumatic fever. A patient

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should not be considered free of rheumatic heart disease unless a normal echocardiogram has been confirmed by an experienced and knowledgeable cardiologist.

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