Echocardiography in acute rheumatic fever

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INTRODUCTION

“It has become appallingly obvious that our technology has exceeded our humanity” – Albert Einstein.

Rheumatic heart disease (RHD) continues to remain a major health concern across the globe. It is estimated that a minimum of 15.6 million people have RHD in the world, with 2,82,000 new cases being added each year, and is estimated to cause 2,33,000 deaths each year.[1-3] RHD results in enormous disease burden translating into huge economic and social losses in India. Classical rheumatic fever (RF) is still encountered across the country. The diagnosis of RF remains clinical. Valvulitis is sine qua non of acute carditis in RF and no investigation is better than echocardiography in its assessment. Echocardiography along with Doppler assessment gives excellent details of the structural and functional abnormalities in acute RF. Yet, echocardiography is not included as a criterion in the diagnosis of RF. No other indication for echocardiography has undergone such a rigorous scrutiny. In this review, a critical appraisal of the role of echocardiography in the diagnosis of RF is presented.

ECHOCARDIOGRAPHIC FEATURES OF RHEUMATIC CARDITIS

The echocardiographic features of acute rheumatic carditis are summarized in Table 1. Assessment of valvular regurgitation has to be accurate as there is a continuum between physiological and pathological regurgitation.[3,4] The characteristics of a physiological regurgitation include localized jet at the region immediately below or above the plane of valve leaflets (or within 1.0 cm), short signals and a smaller maximum regurgitant area.[3,4] The reported prevalence of physiological valvular regurgitation in normal people is mitral regurgitation in 2.4-45%,[5,6] aortic regurgitation in 0-33%,[5,6] tricuspid regurgitation in 6.3-95%[6,7] and pulmonary regurgitation in 21.9-92%.[6,8] Hence, definite criteria for pathological regurgitation have been proposed [Table 1] and are widely used.[3] Rheumatic nodules (beaded appearance of leaflets) are found in nearly 40-50% of the patients with acute carditis and are shown to disappear following treatment of carditis.[9,10]

Nodules may be more useful for diagnosing recurrence of RF among patients with established RHD, but the sensitivity and specificity of these nodules is not known. The utility of any other structural abnormality for the echocardiographic diagnosis of acute rheumatic carditis in the absence of pathological valvular regurgitation is not well established. A recent study had used a composite score of 8 echocardiographic parameters and concluded that a score of 6 out of 16 identifies echocardiographic carditis precisely.[11] However, the majority of the patients with carditis in that study had pathological mitral or aortic regurgitation.

SUBCLINICAL CARDITIS

A significant number of patients with suspected acute rheumatic carditis have no clinical murmurs but have documented regurgitation on echocardiography. Thus, a new category of “subclinical carditis,” “echocarditis” or “asymptomatic carditis” has emerged. Subclinical carditis is relatively common in RF.[12] The reported prevalence of subclinical carditis in RF ranges from 0 to 53% [Table 2]. The probable causes for widely varying estimates include population studied, expertise of physician, echocardiographic criteria used and referral bias (secondary/tertiary setting). A metaanalysis of

Table 1: Echocardiographic features of rheumatic carditis

| Valvular regurgitation (WHO suggested) |   |
|--------------------------------------|---|
| A regurgitant jet > 1 cm in length   |   |
| A regurgitant jet in at least two planes |   |
| A mosaic color jet with a peak velocity > 2.5 m/s |   |
| Jet persists throughout systole (mitral valve) and diastole (aortic valve) |   |
| Leaflet                             |   |
| Prolapose                           |   |
| Coaptation failure                  |   |
| Thickening (> 4 mm)                 |   |
| Reduced mobility                    |   |
| Nodules                             |   |
| Annular dilatation                  |   |
| Chordal elongation/rupture           |   |
| Increased echogenicity of subvalvular apparatus |   |
| Pericardial effusion                |   |
| Ventricular dilatation and dysfunction (almost always with significant regurgitation) |   |
various studies on subclinical carditis reported a weighted pooled prevalence of 16.8% (95% confidence interval [CI] 11.9-21.6). With the application of the World Health Organization echocardiographic criteria, the prevalence of subclinical carditis increased slightly to 18.1% (95% CI 11.1-25.2). These estimates are based on nearly 20 studies that included more than 1700 RF cases from areas of the globe with high prevalence of RHD, except sub-Saharan Africa.

The outcome of patients with subclinical carditis is less well established. The metaanalysis reported a weighted pooled prevalence of persistence or deterioration of subclinical carditis at 3-23 months after diagnosis in 44.7% (95% CI 19.3-70.2). These studies confirm that subclinical carditis is a major Jones criterion influences the outcome. Even though subclinical carditis is shown to be relatively frequent, the outcome is not well established.

### INCLUSION OF ECHOCARDIOGRAPHY AS A “JONES CRITERION” – THE PROS

For echocardiography to be included as a diagnostic criterion, three things need to be established. Firstly, the incidence of subclinical carditis should be significant. Secondly, the outcome of subclinical carditis should not be benign and thirdly, treatment or prophylaxis should alter the outcome. Even though subclinical carditis is shown to be relatively frequent, the outcome is not well established. It is not known whether subclinical carditis follows the same evolution as audible valvular lesions. Studies of long-term follow-up have most likely included most of the patients with subclinical carditis in the no-carditis group, which is shown to have uniformly good prognosis. Additional diagnosis of carditis by echocardiography does not alter the acute treatment as only symptomatic treatment is needed in patients with mild valvular lesions. However, such patients may need additional secondary prophylaxis because the duration of prophylaxis is determined by the presence or absence of carditis. Hence, it may be argued that it is wiser to perform an echocardiography before stopping prophylaxis in countries with limited resources.

Fever alone may produce pathological regurgitation that disappears with the offset of fever. Such patients may be wrongly labeled as RF. Overdiagnosis leads to undesirable stigma and exposure of patients to the rigors of an unnecessary prophylaxis. The availability of echocardiography is also limited in areas where RF is highly prevalent. The theme of arguments against the inclusion of echocardiography as a criterion is that it may pose another barrier in the diagnosis of RF. For all these reasons, it is still argued that echocardiography should not be included as a criterion for the diagnosis of RF.

### INCLUSION OF ECHOCARDIOGRAPHY AS A “JONES CRITERION” – THE CONS

Even in the golden era of clinical auscultation, a number of patients with no audible murmurs in the first attack of RF developed RHD on follow-up, suggesting that carditis was missed by clinical examination. Clinical skills are declining in the West and probably also in India. Murmurs may be missed even by experienced clinicians because of associated tachycardia. More importantly, it is realized that the mild valvular regurgitation is not only subclinical but, in the acute phase, even moderate mitral or aortic regurgitation may not be clinically audible. Echocardiography is more sensitive and more accurate in diagnosing valvular involvement in acute RF. Pre-existing valvular lesions can worsen due to recurrences; hence, accuracy in the diagnosis is very essential. Echocardiography not only confirms and quantifies valvular regurgitation but is also useful in establishing an alternative cause of murmur. Furthermore, echocardiography is of immense value in ruling out infective endocarditis in patients of established RHD presenting with recent onset worsening of symptoms. In areas with a high prevalence of RF, the consequences of underdiagnosis are likely to be greater than overdiagnosis. Recent analyses have suggested that subclinical carditis as a major Jones criterion influences the diagnosis of acute RF in 11-16% of patients only. In the majority of patients, the major criterion of acute RF still remains polyarthritis, clinically overt carditis or chorea. A negative echocardiographic assessment may be useful to reassure the family and a positive finding will help to reinforce penicillin prophylaxis.

The suggested relative utility of echocardiography in

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**Table 2: Studies of subclinical carditis using WHO criteria in rheumatic fever**

| Country | Year | Number of cases | Clinical carditis (%) | Subclinical carditis (%) | No carditis (%) |
|---------|------|----------------|-----------------------|-------------------------|----------------|
| Brazil* | 2008 | 56             | 27 (48.2)             | 11 (19.6)               | 18 (32.1)      |
| Nepal   | 2007 | 51             | 40 (78.4)             | 5 (9.8)                 | 6 (11.8)       |
| Thailand| 2004 | 44             | 17 (39)               | 3 (7)                   | 24 (55)        |
| Turkey  | 2003 | 104            | 51 (49)               | 23 (22)                 | 30 (29)        |
| Brazil  | 2003 | 40             | 28 (70)               | 2 (5)                   | 10 (25)        |
| Chile   | 2001 | 35             | 15 (43)               | 11 (31)                 | 9 (25)         |
| New Zealand* | 2000 | 59             | 35 (59)               | 8 (14)                  | 16 (27)        |
| India   | 2000 | 163            | 110 (67)              | 11 (7)                  | 42 (26)        |
| Turkey  | 1999 | 22             | 5 (23)                | 9 (41)                  | 8 (36)         |
| USA     | 1997 | 27             | 21 (78)               | 2 (7)                   | 4 (15)         |
| Qatar   | 1992 | 19             | 8 (42)                | 10 (53)                 | 1 (5)          |
| Qatar*  | 1989 | 22             | 12 (55)               | 8 (36)                  | 2 (9)          |
| Brazil  | 1991 | 22             | 8 (36)                | 5 (23)                  | 9 (41)         |
| France  | 1995 | 100            | 50 (50)               | 30 (30)                 | 20 (20)        |
| India*  | 1995 | 63             | 35 (56)               | 0 (0)                   | 28 (44)        |
| New Zealand* | 1994 | 34             | 15 (44)               | 5 (15)                  | 14 (41)        |

* Incomplete use of WHO criteria, Modified from Tubridy–Clark M and Carapetis JR 2007 [32]
various syndromes of RHD is presented in Table 3. The major confusion for the clinician in ordering an echocardiography is in patients with polyarthritis and chorea with no clinical evidence of carditis. Patients with chorea are shown to have a high incidence of clinical/subclinical carditis and the utility is not questioned.\textsuperscript{[15,21,34]} The putative new syndromes of pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection and post-streptococcal reactive arthritis should be diagnosed with extreme caution in Indian patients as many patients on follow-up may develop valvular lesions.

The utility of screening all asymptomatic school children with echocardiography is not known. Recent studies have reported an unexpectedly high prevalence of RHD in Africa with the routine use of echocardiography (21.5-30.4/1000 school children).\textsuperscript{[35,36]} A recent echocardiographic screening survey from India has also suggested a very high prevalence rate.\textsuperscript{[37]} The authors have attributed this to subclinical carditis. The term subclinical carditis should be reserved for patients with echo-identified cardiac lesions in the clinical setting of acute RF. “Subclinical RHD” may be a preferable term for asymptomatic school children with echo-identified cardiac lesions. Because the “echo criteria for subclinical carditis” have been studied in patients with other clinical features of acute RF, it should be strictly applied to this group only. The long-term clinical outcome and the effectiveness of prophylaxis in patients with subclinical RHD should be known before this strategy is adopted in clinical practice.

**RECENT GUIDELINES**

The recent Australian\textsuperscript{[38]} and New Zealand\textsuperscript{[39]} guidelines on RF have accepted echocardiographic subclinical carditis as a major criterion. All patients with suspected or definite RF should undergo echocardiography to identify evidence of carditis. The guidelines have also categorized severity of carditis and have recommended prophylaxis accordingly. With miniaturization of technology, echocardiography in hand-held and mobile forms may be made available in remote areas of the world. The underprivileged populations need guidelines that increase the sensitivity for acute RF to help avoid underdiagnosis. Hence, in India also we need to incorporate subclinical carditis as a major criterion as any other region with high prevalence of RF/RHD.

To conclude, the utility of echocardiography in the diagnosis of subclinical carditis is well established. However, long-term outcome of patients with subclinical carditis is less well established. It is suggested that all patients with suspected or definite RF should undergo echocardiography to identify carditis and to assess the severity of carditis. Such an approach is likely to avoid wrong diagnosis and minimize underdiagnosis.

| Table 3: Utility of echocardiography in different forms of RF/RHD |
|---------------------------------------------------------------|
| **Chronic RHD** | **Utility not questioned** |
| Insidious onset rheumatic carditis | Useful |
| Rheumatic chorea | Useful |
| Recurrent attacks of RF in patients without RHD | Should be useful |
| Recurrent attacks of RF in patients with RHD | Useful if prior echo available |
| Primary episode of RF | May be useful |

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