Using a Low-Risk Population to Estimate the Specificity of the World Heart Federation Criteria for the Diagnosis of Rheumatic Heart Disease

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Background: The 2012 World Heart Federation (WHF) criteria set the minimum standards for echocardiographic diagnosis of rheumatic heart disease (RHD) in a high-risk population without history of acute rheumatic fever. The high sensitivity of the 2012 WHF criteria is well accepted, but the specificity cannot be directly assessed without a confirmatory test. The objective of this study was to estimate the false-positive rate of the WHF criteria through their application in a population at very low risk for RHD.

Methods: The Children's National Health System echocardiography database was searched for patients (6–15 years of age) with an International Classification of Diseases, Ninth Revision, code for "chest pain." Chart review was performed; children with congenital heart disease or systemic disease were excluded. Patients were classified according to WHF criteria as having normal, borderline, or definite RHD on the basis of mitral and aortic valve morphology and the presence of pathologic mitral and/or aortic regurgitation.

Results: A total of 1,251 studies were identified, and 152 were excluded. Fifty studies were randomly chosen from each age, with equal gender distribution, for a total of 500 echocardiograms. No patients met the criteria for definite RHD and four (0.8%) for borderline RHD, both by pathologic mitral regurgitation. No patients met the criteria for borderline RHD on the basis of mitral valve morphology or pathologic aortic regurgitation.

Conclusion: In a US pediatric population, no children had findings of definite RHD, and 0.8% had findings of borderline RHD, most likely representing false-positive results. Although there appears to be some overlap between the findings of borderline RHD and those in the normal pediatric population, our data suggest acceptable specificity for all RHD, with excellent specificity for definite RHD. (J Am Soc Echocardiogr 2015;■:■-■.)

Keywords: Rheumatic heart disease, World Heart Federation criteria, Echocardiogram, Mitral regurgitation, Aortic regurgitation

Rheumatic heart disease (RHD) is the most common acquired cardiovascular disease in children and young adults worldwide.[1] Echocardiographic screening has been shown to have high sensitivity for early disease detection, but its specificity remains in question. In an attempt to standardize echocardiographic diagnosis and improve specificity, in 2012 the World Heart Federation (WHF) set the minimum standard for diagnosis of RHD by echocardiography, which includes criteria for mitral valve (MV) and aortic valve (AV) morphology and function (Tables 1–3).[2] These criteria were meant for use in a high-risk population with no history of acute rheumatic fever (ARF). Application of the WHF criteria in high-risk populations has led to reported prevalence ranges for borderline RHD (1.7%–2.9%) and definite RHD (0.9%–1.2%).[3-5] However, there is no confirmatory test

for RHD and thus no way to confirm that these patients have true pathology. Furthermore, early RHD likely has some overlap with normal findings. A single study comparing RHD prevalence within a high- and low-risk cohort from Australia suggested that up to one third of children diagnosed with borderline RHD may be normal.[5] The application of the WHF criteria in a very low risk population provides a reasonable surrogate for determining the rate of false-positive findings. The objective of this study was to apply the WHF criteria to a population of ethnically diverse, very low risk US children to estimate the false-positive rate of the 2012 WHF criteria.

METHODS

To retrospectively capture a population of children representative of a typical screening population (healthy schoolchildren), the echocardiography database at Children's National Health System was searched for patients aged 6 to 15 years with an International Classification of Diseases, Ninth Revision, code for "chest pain" over a 2-year period (2011–2013). This initial search resulted in an inadequate number of 6-year-old female patients; the search was extended to 2007 for this age group in order to obtain an adequate number of studies. From 2011 to 2013 (extended back to 2007 for 6-year-olds), 1,251 children

underwent echocardiography for a "chest pain" code. The database query was further separated by age and gender, and 25 studies from each age and gender group were randomly selected to obtain 500 total echocardiograms for detailed chart review. The charts of these 500 patients were reviewed to obtain the indications for echocardiography and to assess for the presence of exclusion criteria, including history of congenital heart disease, presence of any systemic disease that could alter cardiac anatomy or physiology, and foreign birth. Additional exclusion criteria at this stage included any technical issue leading to the inability to analyze a study (missing medical record number, no echocardiographic images, etc). When a study was excluded, the corresponding age and gender list was reopened, and another study was chosen at random to replace the excluded study. Chart review resulted in 138 exclusions secondary to underlying cardiac and noncardiac etiologies (Figure 1), with no children identified with medical histories of acute rheumatic fever or RHD; an additional 14 studies were excluded for technical reasons. Parent-reported race/ethnicity was compiled using the hospital's scheduling program. Approval for this study was obtained from the Children's National Health System Institutional Review Board.

Echocardiographic Review

All selected echocardiograms were reviewed retrospectively by a single physician (B.C.C.) according to the 2012 WHF criteria (Tables 1–3).[2] The studies were performed using either a Philips iE33 (Philips Medical Systems, Best, The Netherlands) or a GE Vivid E9 (GE Medical Systems, Wauwatosa, WI) system per our institutional echocardiography protocol. Because this study was retrospective, the choice of probe and frequency and the use of harmonics were at the discretion of the sonographer.

MV leaflet measurements were performed in the parasternal long-axis view. The anterior MV leaflet (AMVL) was measured in mid-diastole, when the valve leaflet was parallel to the ventricular septum with sufficient separation from chordal tissue. Measurement was taken at the thickest portion of the valve leaflet, including any presence of focal thickening and nodularity. The presence of mitral regurgitation (MR) and aortic regurgitation (AR) was assessed in parasternal long-axis and apical four-chamber views; if regurgitation was noted, the grade (trivial, mild, moderate, or severe)[6] and maximal jet length were recorded.[2]

After initial review, any studies found to have abnormal findings according to the 2012 WHF criteria (morphologic or functional) were blindly reviewed by two independent cardiologists with expertise in RHD to determine the final diagnostic category. Any disagreement between the two reviewers was adjudicated by a third cardiologist.

Statistical Methods

Study data were collected and managed using the REDCap electronic data-capture system hosted at the Children's National Health System.[7] Statistical analyses were performed using MedCalc for

Table 1 WHF criteria for the echocardiographic diagnosis of RHD in individuals ≤20 years of age[2]

Definite RHD (A, B, C, or D)
A. Pathologic MR and at least two morphologic features of RHD of the MV
B. MS mean gradient ≥ 4 mm Hg
C. Pathologic AR and at least two morphologic features of RHD of the AV
D. Borderline disease of both the AV and MV
Borderline RHD (A, B, or C)
A. At least two morphological features of RHD of the MV without pathologic MR or MS
B. Pathologic MR
C. Pathologic AR

MS, Mitral stenosis.

Table 2 WHF criteria for pathologic regurgitation[2]

Pathologic MR (all four Doppler criteria must be met)
Seen in two views
In at least one view, jet length ≥ 2 cm
Velocity ≥ 3 m/sec for one complete envelope
Pansystolic jet in at least one envelope
Pathologic AR (all four Doppler criteria must be met)
Seen in two views
In at least one view, jet length ≥ 1 cm
Velocity ≥ 3 m/sec in early diastole
Pandiastolic jet in at least one envelope

Table 3 WHF criteria for morphologic features of the MV and AV[2]

Features in the MV	Features in the AV
AMVL thickening ≥ 3 mm (age specific)	Irregular or focal thickening
Chordal thickening	Coaptation defect
Restricted leaflet motion	Restricted leaflet motion
Excessive leaflet tip motion during systole	Prolapse

Windows version 12.0 (MedCalc Software, Mariakerke, Belgium). Ethnicity and reason for referral are reported as total number and percentage. Prevalence of MR, borderline RHD, and definite RHD are reported as percentages and 95% CIs. Differences between the prevalence of MR and borderline RHD were compared among ethnic groups using a Fisher exact test. In all two-tailed statistical tests, *P* values < .05 were considered to indicate statistical significance.

RESULTS

The breakdown of race/ethnicity and reasons for echocardiography for these 500 children are listed in Table 4. A secondary indication for echocardiography, such as abnormal findings on electrocardiography or a positive family history, was present in <10% of patients.