Title: RELIABILITY AND AGREEMENT OF ECHOCARDIOGRAPHIC MEASURES OF ANTERIOR MITRAL LEAFLET THICKNESS IN PATIENTS WITH RHEUMATIC MITRAL VALVE DISEASE

Authors: Manjit Mahendran, Shyamashree Biswas, Praveen Murugesan, Niveditha Devasenapathy, SUDHEER ARAVA, Palleti Rajashekar, Devagourou Velayoudam, Ganesan Karthikeyan, Saurabh Kumar Gupta

Background & Aims: Rheumatic Heart Disease (RHD) is one of the major causes of premature deaths and morbidity in low and middle-income countries (LMICs). Assessing hard outcomes such as heart failure, mortality or valve replacement are critical for evaluating disease progression. However, this requires prolonged follow-up of large number of patients and may be challenging in LMICs. Echocardiographic measures such as leaflet thickness, may potentially be valuable surrogates for assessing disease progression. In this study we assessed the reliability and agreement in assessing anterior mitral leaflet (AML) thickness by transthoracic echocardiography (TTE).

Methods: In this cross-sectional study, adult patients with Rheumatic mitral valve disease underwent TTE. Sampling was purposive to enrol patients with a range of mitral valve stenosis severity. Still frames of standardized views were recorded to allow measurement of AML thickness and length. Two cardiologists (observers A and B) independently reviewed the recordings. Each observer made two sets of repeated measurements. Among the patients who underwent surgical mitral valve replacement, AML thickness and length were measured from the excised valve using digital calipers. The primary outcome was the intra-observer and inter-observer reliability and agreement in assessing AML thickness by TTE. The secondary outcomes were i) agreement between echocardiographic and surgical/pathologic measures of AML thickness ii) intra-observer and inter-observer reliability and agreement in assessing AML thickness by 3D TTE. We reported reliability using Intra/Inter-Class Correlation coefficient (ICC) and agreement using Bland-Altman Limits of agreement. The smallest detectable change was estimated from ICC.

Results: We enrolled 120 patients with RHD and mitral valve disease. The mean age was 40.2 years and 83 (69 %) were females. Mean (SD) AML maximum thickness measured by Observer A (ObsA) and Observer B (ObsB) were 5.74 (1.44)mm and 6.25 (1.66)mm respectively. The Inter-observer reliability in assessing AML maximum thickness was excellent with Interclass Correlation Coefficient of 0.91 (95 % CI 0.75, 0.95). The smallest detectable change for the same was 0.67mm. The intra-observer reliability was excellent for AML thickness with the Intra-class Correlation Coefficient being 0.998 for both observers. The inter-observer mean-difference (measurement bias) in AML maximum thickness between ObsA and ObsB (5D diffA-B) was -0.51 (0.79)mm [95 % CI -0.66, 0.37]. The inter-observer limits of agreement were -2.08 to 1.06mm. Similar results were seen with 3D echocardiography. Among the 22 patients who underwent surgery, the mean difference in maximal AML thickness between ObsA and Histopathology (HP) was 2.29mm (95 % CI 1.62 to 2.97), while between ObsB and HP it was 2.97mm (95 % CI 2.16 to 3.79). The limits of agreement of AMVL maximum thickness between ObsA and HP were -0.73 to 5.32, while between ObsB and HP, they were -0.69 to 6.63.

Conclusions: This study demonstrates an excellent inter-observer and intra-observer reliability in assessing maximal AML thickness using TTE. The smallest detectable change was 0.67mm. These findings suggest that maximal AML thickness by TTE may serve as a useful surrogate marker for assessing disease progression in clinical studies of RHD. However, there was poor agreement between histopathology and echocardiographic measurements of AML thickness.