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Role of LA Shape in Predicting Embolic Cerebrovascular Events in Mitral Stenosis

Mechanistic Insights From 3D Echocardiography

Maria Carmo P. Nunes, MD, PhD,*† Mark D. Handschumacher, BS,† Robert A. Levine, MD,† Marcia M. Barbosa, MD, PhD,* Vinicius T. Carvalho, MD,* William A. Esteves, MD,* Xin Zeng, MD, PhD,† J. Luis Guerrero, BS,‡ Hui Zheng, PhD,§ Timothy C. Tan, MD, PhD,† Judy Hung, MD†

Belo Horizonte, Brazil; and Boston, Massachusetts

OBJECTIVES This study was designed to assess the role of left atrial (LA) shape in predicting embolic cerebrovascular events (ECE) in patients with mitral stenosis (MS).

BACKGROUND Patients with rheumatic MS are at increased risk for ECE. LA remodeling in response to MS involves not only chamber dilation but also changes in the shape. We hypothesized that a more spherical LA shape may be associated with increased embolic events due to predisposition to thrombus formation or to atrial arrhythmias compared with an elliptical-shaped LA of comparable volume.

METHODS A total of 212 patients with MS and 20 control subjects were enrolled. LA volume, LA emptying fraction, and cross-sectional area were measured by 3-dimensional (3D) transthoracic echocardiography. LA shape was expressed as the ratio of measured LA end-systolic volume to hypothetical sphere volume ([4/3π r^3] where r was obtained from 3D cross-sectional area). The lower the LA shape index, the more spherical the shape.

RESULTS A total of 41 patients presented with ECE at the time of enrollment or during follow-up. On multivariate analysis, LA 3D emptying fraction (adjusted odds ratio [OR]: 0.96; 95% confidence interval [CI]: 0.92 to 0.99; $p = 0.028$) and LA shape index (OR: 0.73; 95% CI: 0.61 to 0.87; $p < 0.001$) emerged as important factors associated with ECE, after adjustment for age and anticoagulation therapy. In patients in sinus rhythm, LA shape index remained associated with ECE (OR: 0.79; 95% CI: 0.67 to 0.94; $p = 0.007$), independent of age and LA function. An in vitro phantom atrial model demonstrated more stagnant flow profiles in spherical compared with ellipsoidal chamber.

CONCLUSIONS In rheumatic MS patients, differential LA remodeling affects ECE risk. A more spherical LA shape was independently associated with an increased risk for ECE, adding incremental value in predicting events beyond that provided by age and LA function. (J Am Coll Cardiol Img 2014;7:453–61)

From the *School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil; †Cardiac Ultrasound Laboratory, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; ‡Cardiovascular Research Laboratory, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; and the §Biostatistics Center, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. This study was partly supported by grants from CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brasília, Brazil) and by the National Institutes of Health/National Heart, Lung, and Blood Institute grant no. R01 HL092101 (Dr. Hung). All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Patients with rheumatic mitral stenosis (MS) are at increased risk for embolic events. Systemic embolization occurs in 10% to 20% of MS patients, with 75% of cases manifesting as cerebral embolism (1–3). Various factors are related to an increased risk for embolization, including age, atrial fibrillation (AF), and left atrial enlargement (4–8). Embolic events do not appear to be related to the severity of MS, and they can be the first clinical manifestations of the disease (1,2). Additionally, systemic embolism is also known to occur in patients in sinus rhythm (5–9).

Rheumatic MS causes chronic pressure overload on the left atrium (LA), which leads to a range of adaptive processes, including LA structural remodeling (10). LA remodeling involves changes not only in atrial size and function but also in the shape of the chamber. Although LA enlargement by itself contributes to an increased risk for thrombus formation (4,7,8,11), the influence of the LA anatomic shape on blood flow pattern and consequently risk for embolic events has not been well defined.

ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional
3D = 3-dimensional
AF = atrial fibrillation
CSA = cross-sectional area
ECE = embolic cerebrovascular event(s)
LA = left atrium/atrial
LAEF = left atrial emptying fraction
LV = left ventricular
MS = mitral stenosis

Three-dimensional (3D) echocardiography allows for the assessment of global LA shape (12) and standardized direct volume and area measurements of the LA without geometric assumptions (13), with superior accuracy compared with conventional echocardiography, especially for an enlarged LA (14). The assessment of LA shape by 3D echocardiography may provide insights into the mechanism that determines blood stasis, which predisposes to embolic events in the setting of MS.

We hypothesized that differential LA remodeling in response to chronic pressure overload contributes to the risk for embolic events. Specifically, a spherical-shaped LA is predisposed to thrombus due to greater stagnant blood flow or to atrial arrhythmias compared with an elliptical-shaped LA of comparable volume. The aim of this study was to assess the role of LA anatomic shape in predicting embolic cerebrovascular events (ECE) in patients with rheumatic MS.

METHODS

Study population. The study prospectively enrolled 212 consecutive patients with mild to severe rheumatic MS referred to a tertiary care center (Hospital das Clinicas, Federal University of Minas Gerais, Belo Horizonte, Brazil) from 2009 to 2012. Patients with moderate or greater mitral regurgitation; significant aortic valve disease; and/or associated systemic diseases that are predictors of ischemic cerebrovascular events, including hypertension and diabetes, were excluded. Transesophageal echocardiography was performed in all patients with AF or with previous embolic events to exclude LA and LA appendage thrombus (n = 73). The presence of LA or LA appendage thrombus was also an exclusion criteria.

Written informed consent was obtained from all patients, and the study was approved by the institutional clinical research and ethics committee.

Outcome assessment. The outcome of this study was defined as the first ECE, including stroke or transient ischemic attack, suspected to be of thromboembolic origin from cardiac source before enrollment into the study or during the follow-up. Transient ischemic attack was defined as an acute neurological deficit of presumed vascular origin lasting <24 h. Stroke was defined as an acute neurological deficit of presumed vascular origin lasting >24 h, or the presence of brain infarction on neuroimaging (15).

Patients were clinically managed on the basis of the American College of Cardiology/American Heart Association 2008 guidelines (16). According to these guidelines, anticoagulation was indicated in patients with MS and AF, or with a prior embolic event.

Twenty healthy subjects with similar sex and age distribution as the cases, and normal standard echocardiograms with good-quality images, were selected as controls.

Echocardiographic evaluation. Transthoracic 2-dimensional (2D) echocardiography was performed according to the recommendations of the American Society of Echocardiography (17). All measurements were performed by a single investigator, blinded to clinical data.

Left atrial volume (LAV) by 2D echocardiography was determined using the modified Simpson rule at end-systole (17). LA linear dimensions were measured in 3 planes: anteroposterior, lateral, and superoinferior at end-systole. A 2D sphericity index was calculated as the ratio between the superoinferior and mediolateral diameters.

Assessment of LAVs by 3D echocardiography. Real-time 3D echocardiography was collected in full-volume mode from 4 heartbeats of breath-holding in expiration.

LAV was measured using customized software (Omni4D, Inc., Beverly Hills, California) (18). LA endocardial borders of the LA on 3D images were traced on 4 equiangular image planes (0°, 45°, 90°,