Differential Impact of Net Atrioventricular Compliance on Clinical Outcomes in Patients with Mitral Stenosis According to Cardiac Rhythm

In-Jeong Cho, MD, Hyuk-Jae Chang, MD, PhD, Soo Yeon Lee, MD, Chi Young Shim, MD, PhD, Geu-Ru Hong, MD, PhD, and Namsik Chung, MD, PhD, *Seoul, Republic of Korea*

Background: Net atrioventricular compliance (Cn), a parameter for the net compliance of the left atrium and left ventricle, is known to be a useful predictor of outcomes in patients with mitral stenosis (MS). The present study aimed to evaluate whether the impact of Cn on symptom status and clinical outcomes, as well as its contribution toward systolic pulmonary artery pressure (SPAP), differed according to cardiac rhythm.

Methods: We retrospectively reviewed patients ($N = 308$) with rheumatic pure MS. Doppler-derived Cn was calculated using planimetered mitral valve area and E-wave downslope of transmitral flow. The primary endpoint was defined as a composite of all-cause death, percutaneous mitral valvotomy, surgical mitral valve replacement, admission for heart failure, and stroke.

Results: Overall, there were 178 patients (58%) with sinus rhythm (SR) and 130 patients (42%) with atrial fibrillation (AF). In multivariable linear regression analysis, there was a significant independent association between Cn and SPAP in patients with SR ($P = .014$), but not in those with AF ($P = .112$). During a median follow-up of 38 months, 130 patients (27%) experienced the study endpoint. In multivariable Cox regression, high Cn was associated with a more favorable prognosis in patients with SR (hazard ratio = 0.83; 95% CI, 0.69-0.99; $P = .038$). Conversely, high Cn was not found to offset the burden of adverse clinical outcomes in those with AF (hazard ratio = 1.18; 95% CI, 0.99-1.40; $P = .071$).

Conclusions: Cn appears to be associated with SPAP and clinical outcomes in MS patients with SR. The predictive role of Cn in patients with AF requires further clarification. (J Am Soc Echocardiogr 2017;■:■-■.)

Keywords: Compliance, Mitral valve stenosis, Outcome assessment, Cardiac rhythm

INTRODUCTION

In mitral stenosis (MS), increased transmitral gradient frequently results in an elevation of left atrial (LA) pressure, and its subsequent backward transmission predisposes patients to pulmonary venous hypertension, which is known to be an underlying mechanism for exercise intolerance and the development of dyspnea among patients.[1] Apart from valvular stenosis, LA compliance is considered to be a key component in the development of pulmonary hypertension (PHT), particularly as LA compliance influences backward transmission of the transvalvular gradient of the mitral valve.[2,3]

From the Division of Cardiology, Severance Cardiovascular Hospital (I.-J.C., H.-J.C., S.Y.L., C.Y.S., G.-R.H., N.C.), and Severance Biomedical Science Institute (H.-J.C.),Yonsei University College of Medicine, Seoul, Republic of Korea.

This research was supported by Leading Foreign Research Institute Recruitment Program through the National Research Foundation of Korea funded by the Ministry of Science, ICT and Future Planning (grant no. 2012027176).

Reprint requests: Hyuk-Jae Chang, MD, PhD, Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul, 03722, Republic of Korea (E-mail: hjchang@yuhs.ac).

0894-7317/$36.00

http://dx.doi.org/10.1016/j.echo.2017.01.014

When LA compliance is reduced, the left atrium becomes stiffer and the same volume of blood entering the left atrium will produce a much larger increase in LA pressure as well as symptom development.[2]

Net atrioventricular compliance (Cn) derived from Doppler echocardiography is known to be an important physiologic determinant of PHT in patients with MS.[1,4] In clinically relevant MS, pulmonary artery pressure is chiefly governed by LA compliance.[1] Notably, patients with low Cn, indicative of low LA compliance, often present with an increase in systolic pulmonary artery pressure (SPAP).[1] Further still, Nunes and colleagues[5] documented that Cn not only contributed toward PHT but also appeared to be a powerful predictor of adverse outcomes in patients with MS.

Moving forward, the highest frequency of atrial fibrillation (AF) in rheumatic heart disease typically manifests in those with MS, and the prevalence of AF in valvular heart disease has been reported to be up to 75%.[6,7] Yet prior studies utilizing Doppler-estimated Cn for prediction of clinical outcomes were performed predominantly in patients with sinus rhythm (SR)[5] or in small samples of patients with MS.[3] Although the presence of AF tends to significantly influence LA compliance, and Cn appears to be higher in MS patients with AF as compared with those with SR,[3] it remains to be clarified whether a high Cn might represent a favorable clinical predictor in patients with MS and AF. Therefore, this study set forth to evaluate the clinical impact of Cn on symptom status and clinical outcomes and whether

Abbreviations

AF = Atrial fibrillation

Cn = Net atrioventricular compliance

HR = Hazard ratio

ICC = Intraclass correlation coefficient

LA = Left atrial

LV = Left ventricular

MS = Mitral stenosis

MVA = Mitral valve area

NYHA = New York Heart Association

PHT = Pulmonary hypertension

SPAP = Systolic pulmonary artery pressure

SR = Sinus rhythm

its contribution toward SPAP differed on the background of cardiac rhythm (e.g., SR vs AF) in a large sample of patients with MS.

METHODS

Patients

We retrospectively reviewed all patients diagnosed with rheumatic MS from the echocardiography laboratory of a tertiary referral center for valvular heart disease from January 2010 through December 2014. Exclusion criteria included patients with >1+ mitral valve regurgitation, patients with >1+ aortic valve regurgitation and/or more than mild aortic stenosis, patients with congenital or myopathic lesions that could affect pulmonary artery pressure, and patients who planned to undergo surgery or percutaneous procedures at the time of performing echocardiography. Hence the analytic samples included herein were 308 patients with rheumatic pure MS. This study was approved by the Institutional Review Board of Yonsei University, Severance Hospital, Seoul, Korea.

Echocardiographic Examination

Left ventricular (LV) internal diameter, septal thickness, and LV posterior wall thickness were measured at end diastole from the parasternal short-axis view. The LV mass was calculated using the formula set forth by the American Society of Echocardiography,[8] and LV mass was indexed for the body surface area. The LA volume was calculated from the parasternal long-axis view and apical four-chamber view using the prolate ellipse method[9] and was indexed for the body surface area. Mitral valve area (MVA) was additionally assessed by two-dimensional planimetry.

The calculated SPAP was defined as 4 × (maximum velocity of tricuspid regurgitant jet)^2 + right atrial pressure. Right atrial pressure was estimated by measuring the inferior vena cava diameter and its response to inspiration.[10] PHT was defined as a SPAP ≥ 35 mmHg on echocardiography. The mean transmitral pressure gradient was measured from a continuous wave Doppler signal across the mitral valve by tracing its envelope. MVA by pressure half time was calculated using the formula 220/pressure half time.[11] Cn was determined using the following equation: Cn (mL/mmHg) = 1270 × (planimetric MVA/E-wave downslope).[5,12] Figure 1 shows a representative image of the measurement of Cn. Cn was measured and calculated by an experienced echocardiographer who was masked to the patient's medical records, and the attending physician was blinded to the Cn value. Echocardiographic measurements were averaged for three beats in patients with SR and for five beats in those with AF.

Intra- and interobserver variability levels for measurements of Cn were determined. Measurements were performed by one observer based on the analysis of each 10 random images in SR and AF. Then the observer performed repeated analysis in at least a one-month interval, while remaining blind to results from the first analysis. Additional image analysis was performed by a second observer who was unaware of the other observer's measurements. The measurements were performed on the same cardiac cycle, and the values were averaged five times for each image.

Study Endpoint

Patients were studied after initial echocardiographic evaluation across a median of 38 months (interquartile range, 12-55 months) for a composite endpoint that included all-cause death, percutaneous mitral valvotomy, mitral valve replacement, inpatient admission for heart failure, and incidence of stroke. The occurrence of any of the aforementioned clinical events that made up the composite study endpoint was ascertained by review of hospital records and by telephone interview, as necessary.

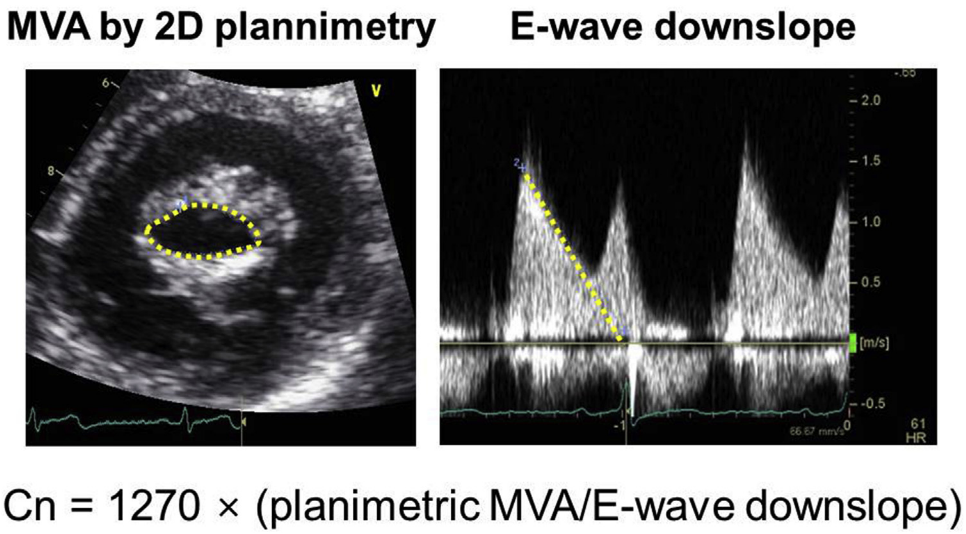

Figure 1 Representative image of the measurement of Cn. *2D*, Two-dimensional.