Clinical Utility of Left Atrial Strain in Children in the Acute Phase of Kawasaki Disease

Soo Jung Kang, MD, PhD, Yoo Won Kwon, MD, Seo Jung Hwang, MT, Hyo Jin Kim, MT, Bo Kyeong Jin, MD, and Dong Keon Yon, MD, *Seongnam, Republic of Korea*

Background: We aimed to evaluate the diagnostic utility of peak left atrial longitudinal strain (PALS) during left ventricular (LV) systole to differentiate children in the acute phase of Kawasaki disease (aKD) from controls. We also aimed to compare the diagnostic utility of PALS with those of conventional echocardiographic indices of diastolic function.

Methods: Retrospectively measured PALS, LV longitudinal peak systolic strain, and strain rate obtained via velocity vector imaging were compared in a derivation cohort comprising 95 aKD and 67 controls. The utility of PALS in differentiating aKD from controls was compared with those of E/E′, E/A, and maximum left atrial volume index (LAVImax). Derived cutoffs from receiver operating characteristic curves were validated in a separate validation cohort comprising 37 aKD and 19 controls.

Results: In the derivation cohort, PALS was significantly decreased in aKD as compared with in controls. For differentiating aKD from controls, PALS outperformed E/E′, E/A, and LAVImax. However, cutoffs of PALS (≤40% and ≤39%, before and after adjusting for the presence of significant mitral regurgitation and LV systolic dysfunction, respectively), like those of E/E′, E/A, and LAVImax, showed low sensitivity and poor discriminative ability for differentiating aKD from controls. In the validation cohort, for differentiating aKD from controls, both cutoffs of PALS showed low sensitivity, like those of E/E′, E/A, and LAVImax.

Conclusion: In aKD, impaired left atrial reservoir function could be detected as decreased PALS. For differentiating aKD from controls, PALS outperforms E/E′, E/A, and LAVImax. However, like E/E′, E/A, and LAVImax, PALS as a single parameter is limited in its clinical utility to differentiate aKD from controls because of its low sensitivity and poor discriminative ability. (J Am Soc Echocardiogr 2017;■:■-■.)

Keywords: Kawasaki disease, Atrial, Deformation, Diastolic

Kawasaki disease (KD) is an acute systemic vasculitis occurring in young children.[1] Left ventricular (LV) dysfunction can be detected in children in the acute phase of KD (aKD) and may be related to coronary vasculitis[2] or myocarditis.[3,4] In aKD, both LV systolic dysfunction (LVSD)[5-7] and LV diastolic dysfunction (LVDD)[8,9] have been detected. Since LVDD could precede LVSD and may occur in the absence of LVSD,[8] the early detection of LVDD in aKD could aid in the diagnosis of KD, particularly when clinical criteria are insufficient, as in incomplete KD.[1] Previously, the role of left atrial (LA) function in diastolic heart failure has been investigated in adults.[10,11] However, to date, LA function via myocardial deformation analysis has not been evaluated in aKD.

LA acts as a reservoir of blood during ventricular systole,[12] and peak LA longitudinal strain (PALS) during LV systole, which reflects LA reservoir function, is decreased in patients with heart failure and decreased ejection fraction (EF) due to impaired LA relaxation resulting from elevated LV end-diastolic pressure (LVEDP).[10,13] Thus, LVDD, when present in aKD, may result in abnormalities in LA reservoir function, reflected as a decrease in PALS. We speculated that evaluating PALS in aKD for the detection of LVDD may aid in the diagnosis of KD. However, PALS could be affected by both significant mitral regurgitation (MR) and LVSD. Significant MR, observed in approximately 30% of aKD,[2,7] can cause LA distension.[14] LVSD, by impairing the descent of the mitral annulus to the apex, could impair the LA filling from the pulmonary veins in systole.[15] Therefore, we evaluated the diagnostic utility of PALS in aKD both before and after, adjusting for the effects of significant MR and LVSD.

The aim of this study was to evaluate the clinical utility of PALS in differentiating aKD from controls. We also aimed to compare the utility of PALS in differentiating aKD from controls with that of conventional echocardiographic indices of diastolic function, such as E/A, E/E′, and LAVImax.

From the Department of Pediatrics (S.J.K., Y.W.K., B.K.J., D.K.Y.) and Department of Diagnostic Laboratory Medicine (S.J.H., H.J.K.), CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, Republic of Korea.

Conflict of Interest: None.

Reprint requests: Soo Jung Kang, MD, PhD, Department of Pediatrics, CHA Bundang Medical Center, CHA University School of Medicine, 59 Yatap-ro, Bundang-gu, Seongnam 13496, Korea (E-mail: *kittysooni@chamc.co.kr*).

0894-7317/$36.00

https://doi.org/10.1016/j.echo.2017.11.012

Abbreviations

aKD = Children in the acute phase of Kawasaki disease

CAL = Coronary artery lesion

CI = Confidence interval

EF = Ejection fraction

ε = Strain

ICC = Intraclass correlation coefficient

IVIG = Intravenous immune globulin

KD = Kawasaki disease

LA = Left atrial, atrium

LAVImax = Maximum left atrial volume index

LVEDP = Left ventricular end-diastolic pressure

LV = Left ventricular

LVDD = Left ventricular diastolic dysfunction

LVMI = Left ventricular mass index

LVSD = Left ventricular systolic dysfunction

MR = Mitral regurgitation

MR (–) LVSD (–) aKD = aKD without significant MR or LVSD

NT-proBNP = N-terminal B-type natriuretic peptide

OtheraKD = Remaining aKD excluding MR (–) LVSD (–) aKD

PALS = Peak left atrial longitudinal strain

SR = Strain rate

VCW = Vena contracta width

METHODS

Study Design

We retrospectively studied the clinical and echocardiographic parameters of two separate cohorts, each cohort comprising aKD and controls, for the derivation and validation of cutoffs of PALS, E/A, E/E′, and LAVImax to differentiate aKD from controls. All aKD were further grouped into subgroups on the basis of the presence of significant MR and LVSD.

Derivation and Validation Cohorts

For the aKD in the derivation cohort, children fulfilling the criteria of the American Heart Association for KD[1] and admitted to the CHA Bundang Medical Center for treatment of KD from January 2013 to December 2016 were studied. Only patients with adequate imaging quality for Velocity Vector Imaging (Siemens Medical, Mountain View, CA) analysis were included. Patients with structural congenital heart disease, as well as those with fever and positive blood cultures or evidence of other febrile illnesses resembling KD, such as a history of exudative conjunctivitis, exudative pharyngitis, oral ulcerations, splenomegaly, and vesiculobullous or petechial rashes, were excluded.[16] For controls, children who underwent echocardiography for evaluation of murmur without evidence of cardiac abnormalities were studied. For the validation cohort, a separate group of aKD who fulfilled the previously mentioned criteria for KD[1] and who were treated for KD, as mentioned previously, and a separate group of controls, defined as mentioned previously, were studied.

Echocardiographic Assessment

We reviewed the serial echocardiograms performed in all aKD prior to the initial treatment with intravenous immune globulin (IVIG) and at the convalescent phase (a median of 2 months after initial treatment) and compared them with the echocardiograms performed for the controls. Prior to echocardiography, all aKD received intravenous fluids to help alleviate dehydration and irritability from prolonged fever. Children who were uncooperative were sedated with oral chloral hydrate (25-50 mg/kg) so that they were calm and cooperative during echocardiography examination. After echocardiography was completed, IVIG was administered to all aKD.

Conventional Echocardiography. Transthoracic echocardiograms of all aKD and controls were obtained using commercial ultrasound equipment (Acuson SC 2000; Siemens Medical). Children were classified as having coronary artery lesions (CALs) when the *z*-scores of the internal diameter of the coronary arteries were found to be ≥2.5 in one or more of the right coronary and left anterior descending arteries.[17] The *z*-scores of the coronary arteries were obtained using the measured dimensions of the coronary arteries as well as the nonlinear regression equations based on body surface area.[17] LV EF, LV mass indexed to body surface area, peak early diastolic mitral inflow velocity (E), and peak atrial filling velocity during late diastole (A), E/A, peak early diastolic tissue Doppler velocity at the lateral mitral annulus (E′), and E/E′ were obtained according to the reported guidelines.[18] Conventional LV measurements were recorded at the same time of echocardiography as the images for myocardial deformation analysis and were remeasured at the time of the deformation analysis.

Assessment of Myocardial Deformation. Echocardiographic digital images, which were previously obtained and stored, were analyzed offline. The Velocity Vector Imaging, version 3.0, software (Siemens Medical) was used to obtain PALS, LV longitudinal peak systolic strain (ε), and LV longitudinal peak systolic strain rate (SR). The median frame rate and frame rate ranges used for obtaining images were 54 and 51 to 76 frames per second, respectively. Clinical data and echocardiographic analysis were separately obtained by the different authors of our study. Echocardiographic images were analyzed offline by two independent observers (a pediatric cardiologist and an experienced cardiac sonographer), from whom the allocation of individual children into groups (KD vs controls) was concealed at the time of analysis and who were thus blinded at the time of echocardiographic analysis. After collection of both clinical and echocardiographic data was completed, the two groups of data were matched for statistical analysis. An average of three cardiac cycles was studied. From the apical four-chamber view, the endocardial border of the LA was manually traced at the end of systole, detected at the endpoint of the T wave on an electrocardiogram (Figure 1A).[13] PALS was obtained from the three segments of the LA (septum, lateral wall, and roof) and was averaged (Figure 1B).[19,20] LV longitudinal peak systolic ε and SR were obtained from the six segments of the LV from the apical four-chamber view and were averaged.[21] Contours were evaluated for adequate tracking and adjusted if necessary. LA volume was obtained from the apical four-chamber view automatically by the Velocity Vector Imaging software as follows: After manual tracing at the end of systole, the LA wall was tracked automatically by the software during one cardiac cycle. The time-LA volume curve during one cardiac cycle was obtained automatically by measuring the LA volume from every frame using the single plane disk summation method (modified Simpson's rule)[20,22] (Figure 1C). The LA volume obtained from the time-LA volume curve has been shown to be accurate and in agreement with the LA volume obtained by manual tracking with the disk summation method.[23] Maximum LA volumes were indexed to body surface area.

Assessment of Significant MR and LVSD. All aKD were further grouped into two subgroups, a subgroup of aKD without significant MR or LVSD as MR (–) LVSD (–) aKD and the remaining aKD as OtheraKD. MR was considered significant when it was more than mild MR. MR was graded as significant when the vena contracta width (VCW) was ≥ 0.3 cm and the continuous-wave Doppler jet was dense but partial or parabolic.[24] LVSD was diagnosed as LV longitudinal peak systolic ε < 18%, according to published normal values of LV ε in children.[25]