Late Detection of Left Ventricular Dysfunction Using Two-Dimensional and Three-Dimensional Speckle-Tracking Echocardiography in Patients with History of Nonsevere Acute Myocarditis

Thibault Caspar, MD, MSc, Marie Fichot, MD, Mickaël Ohana, MD, PhD, Soraya El Ghannudi, MD, PhD, Olivier Morel, MD, PhD, and Patrick Ohlmann, MD, PhD, *Strasbourg, France*

Background: Acute myocarditis (AM) often involves the left ventricular (LV) subepicardium that might be displayed by cardiac magnetic resonance even late after the acute phase. In the absence of global or regional LV dysfunction, conventional transthoracic echocardiography (TTE) does not accurately identify tissue sequelae of AM. We sought to evaluate the diagnostic value of two-dimensional (2D) and three-dimensional (3D) speckle-tracking echocardiography to identify patients with a history of AM with preserved LV ejection fraction (LVEF).

Methods: Fifty patients (group 1: age, 31.4 ± 10.5 years; 76% males) with a history of cardiac magnetic resonance–confirmed diagnosis of AM (according to the Lake Louise criteria) were retrospectively identified and then (21.7 ± 23.4 months later) evaluated by complete echocardiography including 2D and 3D speckle-tracking analysis, as well as 50 age- and gender-matched healthy controls (group 2: age, 31.2 ± 9.5 years: 76% males). Patients with a history of severe clinical presentation of AM (sudden death, ventricular arrhythmia, heart failure, alteration of LVEF) were excluded.

Results: At diagnosis, peak troponin and C-reactive protein were 11.97 (interquartile range, 4.52-25.92) μg/L and 32.3 (interquartile range, 14.85-70.45) mg/L, respectively. Mean delay between acute phase and follow-up study TTE was 21.7 ± 23.4 months. LVEF was not statistically different between groups (62.1% vs 63.5%, $P = .099$). Two-dimensional global longitudinal strain (GLS) was lower in magnitude in group 1 (−17.8% vs −22.1%, $P < .0001$) as were 2D layer-specific subepicardial GLS (−15.4% vs −19.7%, $P < .0001$) and subendocardial GLS (−20.71% vs −25.08%, $P < .0001$). Three-dimensional global longitudinal, circumferential, area, and radial strains were lower in magnitude in group 1 (−11.80% vs −14.98%, $P < .0001$; −12.57% vs −15.12%, $P < .0001$; −22.28% vs −25.87%, $P < .0001$; 31.47% vs 38.06%, $P < .0001$, respectively). Receiver operating characteristic curve analysis showed that subepicardial GLS displayed a better diagnostic performance to detect sequelae of AM as compared with GLS (area under the curve = 0.97 vs 0.93, $P = .045$).

Conclusions: In patients with a history of AM, a subtle LV dysfunction can be detected by 2D and 3D speckle-tracking echocardiography, even though LVEF is conserved, adding incremental information over conventional TTE. (J Am Soc Echocardiogr 2017;■:■-■.)

Keywords: Acute myocarditis, Two-dimensional speckle-tracking, Three-dimensional speckle-tracking, Layer-specific strain, Echocardiography

The diagnosis of acute myocarditis (AM) can be challenging due to the lack of specific diagnostic features.[1] Clinical presentation of AM is heterogeneous and includes asymptomatic, pseudo acute coronary syndrome, severe acute heart failure, ventricular arrhythmia, and sudden death.[2] The disease remains sometimes unrecognized, therefore the real incidence of nonfatal myocarditis is likely greater than actually diagnosed.[3] Prognosis in myocarditis patients also varies.[4] AM has been reported in up to 12% of cases of sudden cardiac death,[5] and long-term follow-up studies have documented the development of secondary dilated cardiomyopathy in up to 30% of patients.[3] Little is known about the outcome of patients with mild cases of AM with preserved left ventricular (LV) function, but scarce data support a benign prognosis of this condition.[6] Historically, the diagnostic gold standard of AM relies on endomyocardial biopsy.[7] However, endomyocardial biopsy is employed only in severe AM including heart failure or LV dysfunction since serious complications may occur after such invasive strategy.[8] The current reference standard for noninvasive diagnosis of myocarditis is cardiac magnetic resonance (CMR) imaging according to the Lake Louise consensus criteria.[3] This modality enables the disclosure of myocardial damage, which typically involves the subepicardium. Late gadolinium enhancement (LGE) reflects irreversible myocardial injury (i.e., necrosis

From the Departments of Cardiology (T.C., M.F., O.M., P.O.) and Radiology (M.O., S.E.G.), University Hospital of Strasbourg, Strasbourg, France.

Reprint requests: Thibault Caspar, MD, MSc, Service de Cardiologie, Nouvel Hôpital Civil, 1 Place de l'Hôpital, 67091 Strasbourg Cedex, France (E-mail: *thibault.caspar@chru-strasbourg.fr*).

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Abbreviations

2D = Two-dimensional

2DSTE = Two-dimensional speckle-tracking echocardiography

3D = Three-dimensional

3DSTE = Three-dimensional speckle-tracking echocardiography

AM = Acute myocarditis

AUC = Area under the curve

CMR = Cardiac magnetic resonance

GAS = Global area strain

GCS = Global circumferential strain

GLS = Global longitudinal strain

GRS = Global radial strain

IQR = Interquartile range

LGE = Late gadolinium enhancement

LV = Left ventricular

LVEF = Left ventricular ejection fraction

PSS = Postsystolic shortening

ROC = Receiver operating characteristic

RV = Right ventricular

STE = Speckle-tracking echocardiography

TTE = Transthoracic echocardiography

and fibrosis).[7] Conventional two-dimensional (2D) echocardiography has traditionally played a limited role in the diagnostic workup of AM.[9] The advent of novel imaging modalities such as 2D and three-dimensional (3D) speckle-tracking has expanded the scope of echocardiography,[10,11] providing accurate assessment of LV global and regional functions with a possibility to detect subtle LV global and regional dysfunctions.[12] Recent software allows a layer-specific analysis of myocardial deformation with separation of endocardial and epicardial strains. Whether or not these new imaging techniques have incremental value over conventional echocardiography in the workup of myocarditis remains unclear.

We hypothesize that layer-specific 2D and 3D speckle-tracking echocardiography (2DSTE, 3DSTE) would help to discriminate patients with normal LV ejection fraction (LVEF) and a history of AM from healthy controls.

MATERIAL AND METHODS

Study Population

We retrospectively identified patients admitted between 2008 and 2015 in our institution for AM, confirmed by the Lake Louise CMR criteria. Patients with history of severe clinical presentation (sudden death, ventricular arrhythmia, heart failure, alteration of LVEF, dilated cardiomyopathy) were excluded as well as patients with age <18 years or poor visual analysis of LV wall motion by TTE (two or more uninterpretable LV segments). Patients underwent CMR at the acute phase and were reevaluated remotely by complete echocardiography. Age- and sex-matched subjects (normal volunteers, with no history of prior cardiac disease) were recruited to compose a control group. All the patients, including control patients, gave written informed of consent at the time of echocardiography to participate in the study, which was approved by our Institutional Review Board.

Cardiac Magnetic Resonance

CMR was performed in the first few days following the acute episode of AM on a 1.5 Tesla (Aera XQ MRI, Siemens, Erlangen, Germany) or a 3 Tesla (Achieva 3.0 T X-series, Phillips Medical Systems, Best, The Netherlands) imaging system equipped with a dedicated six-channel cardiac coil. The CMR imaging protocol included was standardized and included T2-weighted sequences in the search for myocardial edema, and postcontrast (Gadovist at a dose of 0.1 mmol/kg, Bayer Healthcare, Leverkusen, Germany) early-gadolinium enhancement T1-weighted fast spin echo sequences and 3D LGE inversion recovery gradient echo sequences (spatial resolution, 1-2 mm) in the search for myocardial hyperemia and necrosis/fibrosis, respectively. The interpretation of LGE was based on magnitude LGE images and confirmed with a phase-sensitive reconstruction. Hyperenhancement (with a nonischemic pattern) was considered positive if present in two orthogonal views. The diagnosis of AM was made according to Lake Louise consensus criteria.[3] The localization of LGE was defined by using a 17-segment tomographic standard model.[13]

Echocardiography

Unlike the CMR study, which was performed in the acute phase of AM, echocardiography was performed at the time of study inclusion, at a mean period of time of 22 ± 23 months after initial diagnosis of AM, using a Vivid S9 Ultrasound Machine and a M5Sc transducer (GE Vingmed Ultrasound AS, Horten, Norway). Routine 2D grayscale cine loops were obtained in end-expiratory apnea from the parasternal views and three apical (four-chamber, two-chamber, and three-chamber) views and stored digitally. Frame rates were higher than 60 Hz. Echocardiographic recordings were analyzed offline by two experienced observers (T.C., M.F.) blinded to patient data, using commercially available software (EchoPAC version 113, GE Vingmed Ultrasound AS). Each observer independently studied one batch including 25 patients from each group (25 AM and 25 controls), and each batch of 50 patients was analyzed in a random order. LV volumes and ejection fractions were assessed by the apical biplane Simpson method.

Two-Dimensional STE

The myocardial strain was evaluated on a frame-by-frame basis by automatic tracking of acoustic markers (speckles) throughout the cardiac cycle. The myocardial borders were traced from the three apical views in the end-systolic frame of the 2D images for analysis of the longitudinal strain. Region of interest width was manually adapted if necessary so as to exclude pericardium from analysis.

The peak systolic strain was defined as the maximum value of the peak negative strain (myocardial shortening) or peak positive strain (myocardial lengthening) during systole. The peak systolic longitudinal strain was assessed in all 17 longitudinal LV segments, and the segmental values were averaged to give the global longitudinal strain (GLS). Right ventricular (RV) longitudinal strain was assessed in apical four-chamber view and obtained by averaging all six segments of RV free wall and septum (RV GLS) or only the three free wall RV segments (RV free wall GLS). Postsystolic shortening (PSS) was defined as the segmental shortening in diastole beyond minimum systolic segment length (peak negative strain in diastole minus peak negative strain in systole). If minimum segment length was within systole, PSS was zero by definition. Therefore, PSS could only take negative values. Early systolic lengthening was defined as peak positive early strain (representing maximum segmental systolic lengthening). Two-dimensional strain parameters were assessed both in the subendocardial (internal) layer of the myocardium and in the subepicardial (external) layer of the myocardium.