Journal of Cardiology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Functional recovery of regional myocardial deformation in patients with takotsubo cardiomyopathy

Sung-Ai Kim (MD)*, Sang-Ho Jo (MD), Kyoung-Ha Park (MD, PhD), Hyun-Sook Kim (MD, PhD), Sang-Jin Han (MD), Woo-Jung Park (MD, PhD)

Division of Cardiology, Hallym Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Republic of Korea

ARTICLE INFO

Article history:
Received 25 May 2016
Received in revised form 24 August 2016
Accepted 20 September 2016
Available online xxx

Keywords:
Takotsubo cardiomyopathy
Recovery
Speckle tracking
Echocardiography

ABSTRACT

Background: Takotsubo cardiomyopathy (TC) is acute, but completely reversible in the absence of significant coronary artery disease. This study aims to assess the functional recovery of regional myocardial deformation in patients with TC using 2-dimensional (2D) speckle tracking echocardiography.

Methods: Thirty-three patients diagnosed with TC (mean age 63 years, 26 female) prospectively underwent serial 2D echocardiography on day 1 (initial presentation), day 4 [the middle, interquartile range (IQR), 2–5 days], and day 21 (recovery, IQR 13–32 days). Twenty-one (64%) patients showed classical type of TC with akinesis of mid-left ventricular (LV) and apical segments and 12 (36%) of patients presented with mid-LV variant with apical sparing. Myocardial deformations were serially assessed using 2D strain analysis. All echocardiographic values on day 21 were compared with the corresponding values from 30 controls of similar age and gender.

Results: LV ejection fraction (EF) gradually improved at follow-up ($32 \pm 8\%$ on day 1 vs. $62 \pm 4\%$ on day 21, $p < 0.001$). Despite no difference in LVEF between the patients with complete recovery (LVEF >60% on day 21) and controls, the patients showed significantly lower global longitudinal strain than controls. On regional analysis of the mid-LV segments, both longitudinal and circumferential strains of patients with TC were similarly diminished on day 1. During recovery, longitudinal strain showed more delayed recovery than circumferential strain compared to the values of controls.

In LV apex of controls, circumferential strain normally presented higher value than longitudinal strain. In LV apex of patients with classical TC, the reduced circumferential strain on day 1 rapidly increased with a wide variation to maintain augmented circumferential shortening.

Conclusions: Quantifying LV myocardial deformation in patients with TC is informative in the detection of persistent subtle LV dysfunction and improves our understanding of regional myocardial mechanics during recovery.

Introduction

Takotsubo cardiomyopathy (TC) is a cardiac condition characterized by acute, but completely reversible, left ventricular (LV) dysfunction in the absence of significant coronary artery disease. Although the exact pathophysiologic mechanism of TC has not been fully elucidated, catecholamine-mediated myocardial stunning is the most favored explanation for the development of TC [1]. Excessive catecholamine leads to microvascular dysfunction and can directly affect the cardiac myocyte, leading to structural alteration of calcium handling protein that may contribute to the LV contractile dysfunction in patients with TC [2–4]. Additionally, the wall motion abnormality of TC characteristically shows rapid recovery, occurring within a few days to weeks. However, more detailed evaluations revealed that subtle LV dysfunction in TC persists for weeks or months even after the normalization of LV ejection fraction (LVEF) [5–7].

Two-dimensional (2D) strain imaging has been proposed as a reliable means to define regional LV systolic function and has facilitated the early detection of subtle changes in LV myocardial

* Corresponding author at: Division of Cardiology, Hallym Sacred Heart Hospital, Hallym University College of Medicine, # 896, Pyeongchon-dong, Dongan-gu, Anyang-Si, Gyeonggi-do, 431-070, Republic of Korea. Fax: +82 31 383 3486.
E-mail address: 237419@hallym.or.kr (S.-A. Kim).

http://dx.doi.org/10.1016/j.jjcc.2016.09.006
0914-5087/

deformation during the earlier stage of hypertension, diabetes, aortic stenosis, and various cardiovascular (CV) risk factors with preserved LVEF [8–12].

Although there are a few longitudinal data on myocardial deformation of the longitudinal and/or radial directions or LV torsion in patients with TC [5,13,14], we prospectively assessed the serial changes of regional myocardial deformations and investigated the characteristics of functional recovery of LV dysfunction in patients with TC.

Methods

Study population

A total of 33 consecutive patients diagnosed with TC were prospectively identified. Patients with significant arrhythmia and valvular heart disease were excluded. Thirty subjects of similar age and gender who had a normal echocardiography were recruited as controls. The diagnosis of TC was based on the modified Mayo clinic criteria [1]: (1) transient akinesia/hypokinesia of mid-left ventricular (LV) segments with or without apical involvement beyond single major coronary artery distribution, (2) absence of obstructive coronary artery disease or acute plaque rupture on the coronary angiogram, (3) new electrocardiographic abnormalities (either ST-segment elevation and/or T wave inversion) or biomarker elevation, and (4) no pheochromocytoma or myocarditis. Patients with TC had at least three serial echocardiographic examinations; after the initial presentation (day 1), follow-up examinations were performed every 2 days to capture the intermediate stage of recovery and final examination to identify whether full recovery was performed before or after discharge. The study protocol was approved by the local ethics committee of the Hallym University College of Medicine and informed consent was obtained from all individual participants of the study.

Echocardiography

Comprehensive echocardiographic images were obtained using commercially available Vivid 7 machine (GE-Vingmed, Horten, Norway) or Vivid I machine (GE-Vingmed) echocardiographic system. Echocardiography was performed according to American Society of Echocardiography recommendations [15]. The LV volumes and LVEF were obtained by the modified biplane Simpson's method from the apical 4- and 2-chamber views.

Two-dimensional speckle tracking

All echocardiographic data were digitally recorded in cine loop format and 2D strain analysis was performed offline using custom 2D strain imaging software (EchoPac, Version 11.0, GE-Vingmed) by one investigator who was blinded to the clinical data. Frame rates of 60–90 Hz were used because they are considered optimal for 2D speckle tracking.

The endocardial borders were traced at the end-systolic frame and an automated tracking algorithm outlined the myocardial motion. The width of the region of interest (ROI) was adjusted to include the entire thickness of the LV myocardium. The software automatically divided the cross-sectional images into six standard segments of inferoseptal, anteroseptal, anterior, anterolateral, posterior, and inferior. The circumferential peak systolic strain of the six segments was determined in the short-axis view of the LV base, mid-LV (papillary muscle level), and apex.

The longitudinal peak systolic strain of the six segments were determined in the apical two-, three- and four-chamber views of the LV base, mid-LV, and apex. LV global performance was measured by assessing the averaged global longitudinal strain and a bull's eye plot of peak systolic strain using the automated functional imaging technique based on 2D longitudinal strain imaging in the apical two-, three- and four-chamber views [16,17]. The software automatically checked the tracking quality within the ROI and the tracking quality was verified for each segment. The ROI was manually adjusted if necessary and the segments with poor tracking despite manual readjustments were excluded from analysis. Echocardiographic data on day 21 obtained from the patients with TC were compared with the corresponding values of the controls.

Statistical analysis

Continuous variables are expressed as mean $\pm$ SD and were compared using Student t test. Categorical data are presented as percentages and were compared using the χ^2 test.

Repeated measures analysis of variance with the Bonferroni post hoc test was used to compare the serial changes in the heart rate, EF, LV volumes, and regional myocardial deformations during recovery. The strain measurements were repeated by the same observer >3 weeks later to verify the intraobserver variability and strain measurements were performed by two independent blinded observers on the same echocardiographic images to verify the interobserver variability. The reproducibility of strain measurements was determined as intraclass correlation coefficient (ICC) with 95% confidence interval (CI) and mean absolute difference with 95% limits of agreement (LOA) using Bland–Altman analysis [18]. An ICC value >0.75 was interpreted as excellent, 0.4–0.75 as fair-to-good, and <0.4 as poor. The significance level was set at $p < 0.05$. Statistical analyses were performed using SPSS version 23.0 (IBM, Armonk, NY, USA).

Results

Twenty-one (64%) patients showed the classic type of TC with akinesis of the mid-LV and apical segments, while 12 (36%) patients presented with mid-LV variant with apical sparing. Follow-up echocardiography after the initial presentation (day 1) was performed on day 4 [intermediate, interquartile range (IQR) 2–5 days] and on day 21 (recovery, IQR 13–32 days). The baseline characteristics of the study population are summarized in Table 1. The mean age of the patients with TC was 63 $\pm$ 15 years (range 35–82 years), and they were predominantly women (79%). The serial echocardiographic measurements during recovery in patients with TC were shown in Table 2.

Fig. 1 indicates an example of bull's eye plot of peak systolic strain in a patient recovering from TC in which the global longitudinal strain value gradually improved over time. In Fig. 2, the serial changes of the circumferential and longitudinal myocardial deformations were presented from LV base to apex in patients recovering from TC. Although the LV base showed normal or hyperkinetic wall motion in 2D echocardiography, 2D strain analysis revealed reduced values on day 1 and only the circumferential strain on day 21 caught up with the value of the controls. In the mid-LV level, both longitudinal and circumferential strain were similarly diminished on day 1 and significantly improved in stages. However, longitudinal strain showed slower improvement than the circumferential strain on day 21 compared to the values of controls. In LV apex of the controls, the absolute value of circumferential strain was significantly higher than that of longitudinal strain in contrast with the similar values of those strains in LV base and mid-LV. In LV apex of patients with classical TC, both strains were significantly diminished on day 1, circumferential strain rapidly increased with a wide variation to catch up the value of controls. On the other hand, LV apex of

Please cite this article in press as: Kim S-A, et al. Functional recovery of regional myocardial deformation in patients with takotsubo cardiomyopathy. J Cardiol (2016), http://dx.doi.org/10.1016/j.jjcc.2016.09.006