International Journal of Cardiology 168 (2013) 331–337

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Diverse left ventricular morphology and predictors of short-term outcome in patients with stress-induced cardiomyopathy

Sung Woo Kwon [a,1], Byung Ok Kim [b,1], Myung-Hyun Kim [c], Sung-Joo Lee [d], Ji Hyun Yoon [c], Hyemoon Chung [c], Chi-Young Shim [e], Duk Kyu Cho [f], Sung Kee Ryu [g], Se-Jung Yoon [h], Young Won Yoon [c], Hyuk-Jae Chang [e], Se-Joong Rim [c], Hyuck Moon Kwon [c], Yangsoo Jang [e], Bum-Kee Hong [c,*]

[a] Division of Cardiology, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Republic of Korea
[b] Division of Cardiology, Sanggye-Paik Hospital, Inje University College of Medicine, Seoul, Republic of Korea
[c] Division of Cardiology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea
[d] Division of Cardiology, Department of Internal Medicine, Chungju Medical Center, Chungju, Republic of Korea
[e] Division of Cardiology, Yonsei Cardiovascular Center, Yonsei University College of Medicine, Seoul, Republic of Korea
[f] Division of Cardiology, Myeongji Hospital, Kwandong University College of Medicine, Goyang, Republic of Korea
[g] Division of Cardiology, Seoul Eulji Hospital, Eulji University College of Medicine, Seoul, Republic of Korea
[h] Division of Cardiology, Cardiovascular Center of National Health Insurance Corporation Ilsan Hospital, Goyang, Republic of Korea

ARTICLE INFO

Article history:
Received 22 May 2012
Received in revised form 19 June 2012
Accepted 15 September 2012
Available online 4 October 2012

Keywords:
Takotsubo cardiomyopathy
Echocardiography
Hospital mortality
Prognosis

ABSTRACT

Background: There is paucity of data with regard to the clinical spectrum according to left ventricle (LV) morphological variation in stress-induced cardiomyopathy (SCMP) patients, and still there is controversy in terms of prognosis since some people believe that the published in-hospital mortality data of patients with SCMP are underestimated. Therefore, we sought to investigate the morphological features of LV and in-hospital outcome of patients with SCMP and explored predictors of short-term prognosis.
Methods: This was a multicenter, observational study of 208 SCMP patients. Morphological features of LV were determined by echocardiography and were divided into typical (apical) and atypical ballooning types, which were subcategorized into mid-LV ballooning and basal 'inverted' ballooning type. All-cause mortality of patients with SCMP during hospitalization was recorded.
Results: The apical ballooning type was most common (67.3%) in SCMP followed by the mid-LV ballooning type (28.3%), and the basal 'inverted' ballooning type (4.3%). There were no differences in stressor types and in-hospital mortality between patients with typical and atypical SCMP. Notably, all the in-hospital mortality of SCMP patients occurred in patients with physical stressors, where age, shock, and LV ejection fraction were the independent risk factors for predicting in-hospital mortality.
Conclusions: SCMP patients showed diverse patterns of LV morphology, but there were no definite differences on clinical spectrum among SCMP patients presenting various LV morphological patterns. In terms of short-term prognosis, underlying physical conditions combined with old age, hemodynamic compromise, and low LV systolic function might be the most important factors in SCMP patients.

1. Introduction

Stress-induced cardiomyopathy (SCMP) is regarded as an acute reversible cardiomyopathy that mimics acute coronary syndrome. Traditionally, it is characterized by transient regional wall motion abnormalities of the left ventricular mid and apical segment demonstrating apical ballooning feature. Therefore, it is also termed 'apical ballooning syndrome' or 'Takotsubo cardiomyopathy'. While considerable evidence supports emotional stress as a precipitating cause of SCMP and suggests exaggerated sympathetic stimulation as a probable mechanism of SCMP development [1–3], many other causes have been reported as precipitating factors for development of SCMP, such as physical stress and pharmacological agents. Nowadays, SCMP is increasingly being observed during routine daily practice, including diagnostic or therapeutic procedures [4–7], surgery [8,9], and intensive care [10]. Besides various precipitating causes, a diverse morphological spectrum also has been reported for SCMP. Several case reports suggested that SCMP is associated with various morphological features of the left ventricle (LV), which differ from those in previous reports [5,11]. Moreover, a recent study demonstrated and categorized diverse LV morphological features [12]. Despite the

* Corresponding author at: Division of Cardiology, Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, 612 Eonju-ro, Gangnam-gu, Seoul, 135-720, Republic of Korea. Tel.: +82 2 2019 3311; fax: +82 2 3463 3463.
E-mail address: bkhong@yuhs.ac (B.-K. Hong).
[1] The first two authors equally contributed to this study.

0167-5273/$ – see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ijcard.2012.09.050

acute severity, complications are rare and the long-term prognosis of patients with SCMP is generally considered favorable [13–15]. However, recent study suggested that the short-term prognosis (i.e., in-hospital outcome) of patients with SCMP is not as favorable as generally considered [16]. In concordance with this report, some people have the notion that the published in-hospital mortality data are underestimated [17]. Therefore, we sought to investigate LV morphological features and in-hospital outcome in patients with SCMP and to assess predictors of short-term prognosis.

2. Materials and methods

2.1. Study design and patient selection

Institutional review committee approval and informed consent were obtained. This was a multicenter, observational study conducted at 6 referral centers in South Korea. We enrolled 208 patients admitted to these centers from January 1998 to December 2010, who were diagnosed with SCMP. All patients underwent a diagnostic work-up including electrocardiography (ECG), transthoracic echocardiography, blood chemistry, and coronary angiography. Clinical data including all-cause mortality of patients with SCMP during hospitalization (i.e., in-hospital mortality) of the study population as well as electrocardiographic, echocardiographic, and angiographic data were reviewed from medical records and telephone interviews.

2.2. Diagnosis of SCMP

The diagnosis of SCMP in our study was defined through clinical consensus based on fulfilling the following criteria: (1) an acute cardiac event typically presenting with chest pain and/or dyspnea; (2) transient systolic dysfunction with marked LV contraction abnormality (akinesia or dyskinesia of the LV apical, mid-ventricular or basal segments) extending beyond a single coronary perfusion bed; (3) absence of significant (≥75% luminal narrowing) obstructive coronary artery disease or angiographic evidence of acute plaque rupture [18]; (4) new ECG abnormalities (either ST-segment elevation or T-wave inversion) or modest elevation in cardiac troponin level. These criteria are part of the 'Proposed Mayo Clinic criteria' for diagnosis of SCMP [13].

2.3. Definition of variables

Traditional risk factors were recorded as categorical variables in all patients. Hypertension was defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg, or treatment with antihypertensive agents. Diabetes was defined as treatment with hypoglycemic agents or insulin, fasting glucose ≥126 mg/dL or known but untreated hyperglycemia. History of smoking was considered present if patients currently smoked or smoked until 1 month before the study. Dyslipidemia was defined as total cholesterol ≥240 mg/dL, low density lipoprotein ≥130 mg/dL, high density lipoprotein <40 mg/dL, triglyceride ≥200 mg/dL and/or treatment with lipid lowering agents. Obstructive coronary artery disease (CAD) was defined as ≥50%, but <75% luminal narrowing, whereas non-obstructive CAD was defined as <50% luminal narrowing. The extent of obstructive CAD was categorized into 0-, 1-, 2-, and 3-vessel involvement. Pulmonary hypertension was defined as right ventricular (RV) systolic pressure >35 mm Hg. Shock was defined as sustained hypotension (systolic blood pressure <90 mm Hg for at least 30 min) despite adequate inotropic support and intravenous volume administration [19]. RV involvement was defined as regional wall motion abnormalities (akinesia, dyskinesia, or hypokinesia) of RV [20].

2.4. SCMP subsets according to LV morphological features

LV morphological features were determined by echocardiography. Apical ballooning type was considered as the typical type, whereas the rest were considered as atypical types. Consequently, the atypical type was differentiated into 2 subgroups according to the previous classification by Eitel et al.: 1) mid-LV ballooning type, and 2) basal 'inverted' ballooning type (Fig. 1) [12].

2.5. Statistical analysis

Categorical variables are expressed as numbers and percentages of patients. Continuous data are estimated as mean ± standard deviation. Differences between groups were assessed using the chi-square test for categorical variables and using the Student's t-test for continuous data. Univariate binary logistic regression analysis was used to determine the predictors associated with in-hospital mortality. To clarify the predictors of in-hospital mortality, variables with $p<0.1$ on univariate analysis were then used for multivariate binary logistic regression analysis. Odds ratios (OR) were calculated as an estimate of the risk associated with a particular variable with 95% confidence intervals (CI) based on binomial distributions. All statistical tests were performed with SPSS software, version 15.0 (SPSS Inc., Chicago, Illinois). A 2-tailed $p<0.05$ was considered statistically significant.

3. Results

3.1. Demographic, clinical, and electrocardiographic characteristics of the study population

208 patients with SCMP events were 11 to 92 years of age (mean age 65.8 ± 14.0 years), with 72.6% (151/208) female preponderance (Table 1). Overall, 25.5% were diabetic, 51.0% were hypertensive, 15.9% were dyslipidemic, and 18.8% were smokers. Peak levels of cardiac biomarkers such as creatine kinase, creatine kinase-MB, and troponin T were 836.3 ± 2689.1 mg/dL, 21.5 ± 42.9 mg/dL, and 1.24 ± 2.51 ng/mL, respectively. Chest pain (77/208, 37.0%) and dyspnea (88/208, 42.3%) were the most common presenting cardiovascular symptoms. In 186 patients (89.4%), a significant stressful event less than 48 h before presentation could be identified. Most common triggering conditions for SCMP development were physical stress (156/208, 75.0%) (such as pneumonia, subarachnoid hemorrhage, and post-operative bleeding) followed by emotional stress (19/208, 9.1%) and iatrogenic catecholamine excess (11/208, 5.3%). In the remaining 22 cases (10.6%), the stressors could not be elucidated even with careful history taking and telephone interview (Table 1). At presentation, ECGs showed abnormalities in 201 patients (96.6%), and the details of specific findings are listed in Table 1. Initial corrected QT interval (QTc) was 483.6 ± 60.4 ms, and maximal QTc was 515.8 ± 74.0 ms.

3.2. Acute management and clinical presentations

All patients at initial presentation of SCMP underwent standard treatment for acute coronary syndrome and congestive heart failure using aspirin, clopidogrel, heparin, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, vasodilators, diuretics, and/or aldosterone antagonists. At initial presentation, 11.1% (23/208) of patients had severe hemodynamic compromise (shock), and 25.5% (53/208) had pulmonary edema, with 19.2% (40/208) of patients requiring ventilator care, 3 patients were treated with intra-aortic balloon pump, and 1 patient had treatment with percutaneous cardiopulmonary support. Median hospital stay length was 10.0 days (interquartile range 6.0, 22.0). In-hospital mortality rate was as high as 8.7% (18/208) (Table 1).

3.3. Coronary angiographic characteristics of the study population

All 208 patients underwent coronary angiography. While coronary angiography showed healthy coronary arteries or non-obstructive CAD (<50% luminal diameter stenosis) in 171 patients (82.2%), obstructive CAD with luminal narrowing from 50 to 75% was observed in 37 patients (17.8%) that did not correspond to the area of LV wall motion abnormality. No coronary lesions had angiographic features of acute plaque rupture. None of the patients had spontaneous coronary artery spasm. The presence and extent of obstructive CAD are listed in Table 2.

3.4. Transthoracic echocardiography and morphological features of the left ventricle

Initial left ventricular ejection fraction (LVEF) and LV end-diastolic diameter were 40.9 ± 12.4% and 50.7 ± 6.5 mm, respectively. 2 patients had LV outflow tract obstruction, and 4 patients had mitral regurgitation grade ≥3. Mean RV systolic pressure was 30.4 ± 17.0 mm Hg, and 25.5% (53/208) of patients had pulmonary hypertension (RV systolic pressure >35 mm Hg). RV involvement (biventricular ballooning pattern) was observed in 10 patients (10/208, 4.8%) (Table 2).

Echocardiography revealed diverse morphological features of LV: typical apical ballooning type occurred in the majority of cases (67.3%, 140/208), followed by mid-ventricular ballooning type (28.4%, 59/208), and basal 'inverted' ballooning type (4.3%, 9/208).