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Post-discharge prognosis of stress cardiomyopathy in women: a retrospective cohort study ☆

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ABSTRACT

Background/objectives: There is limited information on the prognosis of stress cardiomyopathy (SCM) after hospital discharge. The aim of this retrospective cohort study was to determine the post-discharge prognosis of women with SCM compared to female controls with ST-segment elevation myocardial infarction (STEMI).
Methods: SCM cases were identified through chart reviews of women hospitalized at a single tertiary care medical center between 2002 and 2012. Controls were randomly selected (2:1 ratio) among women admitted with a validated diagnosis of STEMI during the same period. The primary outcome was a composite of cardiovascular readmissions and death from any cause. Risk of the composite outcome was estimated from multivariate Cox proportional hazard regression models.
Results: Over an average follow-up of 24 months, incidence rates of the composite outcome were 140/1000 person-years among cases (n = 50) and 347/1000 person-years among controls (n = 100; $P < 0.001$). SCM women had a lower unadjusted risk of cardiovascular readmissions and death vs. STEMI women (HR: 0.47; 95% CI: 0.27, 0.82). This difference in risk was reduced after adjustment for demographic and clinical confounders (HR: 0.64; 95% CI: 0.30, 1.33). The lower risk of developing the composite outcome among SCM women was driven by a lower risk of death, while the risk of cardiovascular readmissions was similar between groups.
Conclusion: Risk of death and cardiovascular readmissions post-discharge was lower among women with SCM than among women with STEMI. Incidence rates of cardiovascular readmissions, however, were similar, indicating that SCM may not be a benign condition.

1. Introduction

Stress cardiomyopathy (SCM) [1], also known as Takotsubo cardiomyopathy, transient apical ballooning syndrome, or broken heart syndrome, was first described in the early 90s in Japan [2]. SCM, however, is prevalent worldwide [3] and accounts for up to 3% of hospital admissions for acute coronary syndromes, reaching almost 10% of all admissions among female patients [4–7]. Up to 90% of cases are diagnosed in post-menopausal women [5]. An emotionally stressful trigger such as an accident, the death or illness of a close relative, or a natural disaster [8] is typically identifiable in 40 to 70% of patients, while a physical stressor is present in approximately one third [5,9]. The clinical presentation of SCM is similar to that of an acute coronary syndrome accompanied by signs and symptoms of heart failure. The echocardiogram typically shows transient left ventricular systolic dysfunction and wall motion abnormalities involving the apical and mid-portions of the left ventricle, although atypical forms have been described [9–12].

Although this condition can present serious acute complications such as heart failure, cardiogenic shock, and life threatening arrhythmias, the current evidence suggests that its overall prognosis is good, with a complete recovery in the vast majority of patients and a 1-year recurrence rate around 5% [5,13–16]. More recent studies, however, suggest a somewhat different picture, showing that SCM patients may have high 1-year mortality rates from non-cardiovascular causes [17] as well as high rates of re-hospitalization for atypical chest pain and other cardiovascular causes [18]. The available information on the long-term morbidity and mortality of this condition, however, is limited and mostly based on case series.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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The objective of this retrospective cohort study was to assess the post-discharge prognosis of women diagnosed with SCM compared to female controls with an ST-segment elevation myocardial infarction (STEMI). The outcome was a composite of death from any cause and cardiovascular-related hospital readmissions.

2. Methods

2.1. Study population

2.1.1. Cases

Since the vast majority of SCM patients are female, to eliminate confounding by gender only female patients were included in this analysis. SCM cases were identified through chart reviews of women hospitalized at the UMass Memorial Medical Center in Worcester, MA with an ICD-9 code of 429.83 (takotsubo cardiomyopathy) as well as from catheterization and echocardiography lab lists between January 1, 2002 and December 31, 2012. To be eligible, cases had to have a first episode of SCM and fulfill Mayo Clinic diagnostic criteria (transient wall motion abnormality involving the left ventricular segments with or without apical involvement; absence of obstructive coronary plaque or evidence of plaque rupture or thrombosis at the coronary angiogram; new ST-segment elevation and/or T wave inversion or modest troponin elevation) [19]. Consistent with these criteria, women with a history of head trauma, intracranial bleeding, pheochromocytoma, myocarditis or hypertrophic cardiomyopathy were excluded. Two trained physician abstractors independently reviewed all SCM cases and agreement on the diagnosis was reached in 100% of cases.

2.1.2. Controls

Controls were selected from a cohort of women with STEMI enrolled in the Worcester Heart Attack Community Surveillance Study (WHAS). Details about this study have been described elsewhere [20–22]. Briefly, this was a population-based study examining long-term trends in the incidence and in-hospital and post-discharge case-fatality rates of acute myocardial infarction among residents of central Massachusetts. Individuals with a principal or secondary discharge diagnosis of acute myocardial infarction (ICD-9 code 410), with the exclusion of patients with peri-operative or trauma-associated myocardial infarction, were recruited from 16 teaching and community hospitals in central Massachusetts between 1975 and 2009 (the number of hospitals became smaller during the course of the study as a result of hospital mergers and consolidations). A diagnosis of STEMI was defined according to standard diagnostic criteria [23]. The duration of follow-up ranged from 2 to 8 years depending on the index period of hospitalization.

For key predictors such as age we did not anticipate substantial confounding with case/control status, as SCM and STEMI both occur more frequently in post-menopausal women. Thus, controls were randomly sampled (rather than selected by individual matching) in a 2:1 ratio of controls to cases among women enrolled in the WHAS between 2002 and 2009. Confounding was addressed by including in multivariable models all baseline characteristics that were associated with the outcomes under study [24–26].

2.2. Study outcome

The main study outcome was a composite of death from any cause and cardiovascular readmissions. The date corresponding to the earliest event was used in time-to-event analyses. Death status was ascertained through a review of the medical record and through a systematic search of the Death Master File from the Social Security Administration. In the WHAS, cardiovascular readmissions were coded as an aggregate diagnosis, and defined as any readmission for myocardial infarction, angina, stroke, transient ischemic attack, coronary revascularization, cardiac arrhythmia, or heart failure. Trained physician abstractors blinded to the study outcome obtained information about cardiovascular readmissions for cases and controls through reviews of each participant's medical record.

2.3. Confounders

The selection of possible confounding variables was based on the published literature and on whether these variables were associated with the study outcomes in univariate analyses. Information regarding potential confounders such as age, race, marital status, coronary risk factors (hypertension, cholesterol levels, diabetes, smoking status, family history of coronary heart disease, body mass index), other co-morbidities (history of angina, heart failure, stroke, cancer (any cancer), liver disease and kidney disease/renal failure), and medications prescribed at the time of hospital discharge (e.g., aspirin, beta-blockers, ACE inhibitors/angiotensin receptor blockers, warfarin, clopidogrel, statins, calcium-channel blockers, nitroglycerin, diuretics) was collected from the medical record by trained nurses and physician abstractors. Since information about Killip class at admission was not collected in a large number of cases and controls, systolic blood pressure at admission was used as a proxy.

This study was approved by the Institutional Review Board at the University of Massachusetts Medical School.

3. Data analysis

t-Test (or non-parametric tests where appropriate for non-normally distributed continuous variables) and chi square were used to compare baseline characteristics of cases and controls. Survival curves were generated by the Kaplan–Meier method and log-rank testing was used to compare survival curves. Participants were censored at the date of last contact or loss to follow-up. Risk of death and cardiovascular readmissions (with the STEMI as the reference group) was estimated from Cox proportional hazard regression models adjusted for covariates that were associated with the study outcomes in univariate analyses. Results are presented as unadjusted and adjusted hazard ratios with 95% confidence intervals; P-values < 0.05 were considered significant. All statistical analyses were performed using SAS/STAT® version 9.3, SAS Institute, Cary, NC.

4. Results

4.1. Baseline characteristics of cases and controls

Among 356 women diagnosed with SCM between January 2002 and December 2012, we identified a cohort of 50 female patients with complete angiographic and echocardiographic data with a first episode of SCM and who met Mayo Clinic diagnostic criteria. Clinical characteristics at admission (showed in Table 1) were fairly similar between SCM cases and STEMI controls ($n = 100$), except for age (mean, 65 years in cases and 71 years in controls) and for a higher prevalence of hyperlipidemia and other coronary risk factor among women with STEMI. The latter also tended to have a higher prevalence of non-cardiovascular co-morbidities and were also more likely to have a history of angina, stroke and heart failure compared with women with SCM. While SCM women apparently had a worse clinical presentation, as indicated by a lower systolic blood pressure at admission and a worse ejection fraction, they less frequently developed complications such as pulmonary edema and hypotension during hospitalization. With the exception of warfarin and diuretics, at discharge SCM women less frequently received pharmacological treatments such as aspirin, beta-blockers, lipid lowering agents and ACE inhibitors compared to women with STEMI.