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Prognostic impact of spontaneous coronary artery dissection in young female patients with acute myocardial infarction: A report from the Angina Pectoris–Myocardial Infarction Multicenter Investigators in Japan

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ABSTRACT

Background: We sought to compare the prognosis of patients with spontaneous coronary artery dissection (SCAD) and atherosclerosis as the cause of acute myocardial infarction (AMI), especially in young females.
Methods and results: A total of 20,195 patients with AMI at 20 institutions between 2000 and 2013 were retrospectively studied. Major adverse cardiac event (MACE: cardiac death, AMI or urgent revascularization) was the endpoint. The overall prevalence of SCAD was 0.31% (n = 63; female, 94%). SCAD developed following emotional stress in 29% of patients. Revascularization was performed in 56% (35 of 63 patients), and SCAD recurrence developed in the originally involved vessel in 6 of 35 patients with revascularization, compared to none among 28 patients after conservative therapy ($p = 0.002$). We compared the clinical characteristics of young female AMI patients aged ≤50 years in the SCAD (n = 45) and no-SCAD groups (atherosclerotic AMI, n = 55). During a median follow-up of 50 months, SCAD recurred in 27% of patients, of which 42% was in the first 30 days. Kaplan–Meier analysis showed a significantly higher incidence of MACE in the SCAD group compared to the no-SCAD group (hazard ratio, 6.91; 95% confidence interval, 2.5 to 24.3; $p < 0.001$), although the rate of successful percutaneous coronary intervention for SCAD was as high as 92%.
Conclusions: Young female patients with SCAD represent a high-risk subgroup of patients with AMI and require close follow-up.

1. Introduction

Spontaneous coronary artery dissection (SCAD) remains a rare but challenging clinical entity, with an estimated prevalence ranging from 0.07% to 1.1% [1,2]. Recent large single center cohort studies of SCAD reported that it could occur in both younger and older females [3,4].

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Moreover, the rate of SCAD recurrence in these cohorts were 17% and 13%, respectively, which was unexpectedly higher than those reported in previous studies [2,5,6]. On the other hand, SCAD has been traditionally considered to occur in young females with minimal atherosclerotic risk factors and not as part of a broader clinical spectrum that includes older patients with coronary artery disease (CAD) [7]. However, there were no systematic study focusing on young female and their prognosis remains unclear, as reported in the recent two large cohort studies [3,4]. Hence, in this study, we focused on the short- and long-term prognosis of young female patients aged less than 50 years with SCAD.

The present study involves a large series of patients who underwent coronary angiography (CAG) due to acute myocardial infarction (AMI) that were enrolled by investigators at multiple centers by the Angina Pectoris–Myocardial Infarction (AP–MI) Study Group [8] that uses conservative and interventional strategies for SCAD in actual clinical practice. We sought to 1) evaluate the prevalence and the short- and long-term outcomes of SCAD, 2) determine the recurrence rate of SCAD, and 3) compare the prognosis of young female patients with non-atherosclerotic AMI due to SCAD and those with atherosclerotic AMI.

2. Methods

2.1. Study population of the multicenter cohort and the definition of SCAD

From January 2000 to December 2013, a total of 20,195 patients with AMI were admitted to 20 cardiovascular institutions in Japan by AP-MI investigators (Appendix A) [8]. SCAD was defined as medial dissection or intramural hematoma without atherosclerotic changes detected by CAG, intravascular ultrasonography (IVUS), or optical coherence tomography (OCT) before any catheter-based intervention [9–11]. We defined SCAD according to the report from Saw et al. [4]. Briefly, their classification system grades coronary dissection on the basis of angiographic appearance into three types: type 1, pathognomonic contrast dye staining in the arterial wall with multiple radiolucent lumens; type 2, diffuse smooth narrowing with mild stenosis; and type 3, mimicking atherosclerosis with focal or tubular stenosis. In all cases in whom type 2 or 3 SCAD was suspected based on angiography, we confirmed the presence of intramural hematoma or a double lumen by intracoronary imaging with IVUS or OCT. The presence of an intimal flap was not necessary for diagnosis. In the present study, the angiographic data of all patients diagnosed with SCAD at each center were collected at the core laboratory of the National Cerebral Cardiovascular Center in Japan and confirmed independently by at least 2 interventional cardiologists. Percutaneous coronary intervention (PCI)-related dissection, post-traumatic coronary artery dissection, and atherosclerotic-related dissection were excluded [12]. Clinical, angiographic, laboratory, and treatment data were collected to clarify the characteristics of and precipitating factors in patients with SCAD.

Since SCAD outside of the setting of atherosclerosis has a relatively younger and more female predominance, our analysis focused on younger female AMI patients with SCAD. Among 20,195 patients with AMI, there were a total of 130 female AMI patients aged 50 years or younger. After exclusion of patients with vasospastic angina pectoris (n = 13), coronary artery embolism (n = 10), systemic lupus erythematosus (n = 3), Kawasaki disease (n = 1), Vasculo-Behcet's disease (n = 1), and other (n = 2), the remaining 100 patients were ultimately included in additional analyses. This retrospective study was conducted in accordance with the 1975 declaration of Helsinki and approved by the institutional review board of each site and informed consent was obtained from each patient.

2.2. Data collection and definitions

Demographic and clinical data such as potential etiologic factors, coronary risk factors, clinical presentation, involved vessel distribution, and initial management strategy were collected. Emotional stress and extreme physical activity were reviewed from medical records. In-hospital and long-term outcomes were determined through medical record and angiographic review. When necessary, a mailed questionnaire and telephone follow-up were also used. Endpoints included major adverse cardiac events (MACE), which consist of cardiac death, non-fatal AMI or urgent revascularization. Recurrent SCAD was defined as the development of de novo dissection, which is distinct from potential propagation of primary SCAD associated with acute coronary syndrome in the initial SCAD lesion within one week of the index event.

AMI was defined according to the following inclusion criteria: (1) continuous chest pain lasting >30 min, (2) new left bundle branch block or ST-segment changes in 2 or more contiguous leads on the 12-lead electrocardiogram (ECG), and (3) subsequent increase in serum creatine kinase (CK) to more than twice the upper limit of normal [13,14]. ST-elevation myocardial infarction (STEMI) was defined as an AMI with new ST elevation at the J-point in 2 contiguous leads with the following cut-off points: ≥0.2 mV in men or ≥0.15 mV in women in leads V_2–V_3, or ≥0.1 mV in other leads [14].

PCI was performed when a patient presented with evidence of ongoing ischemia such as prolonged chest pain, ischemic ST changes, or hemodynamic instability. PCI was considered successful when improvement from Thrombolysis in Myocardial Infarction (TIMI) grade 0 or 1 flow at baseline to TIMI grade 3 flow was achieved. A procedure was considered technically complicated when there was an unexpected need for additional stenting for dissection propagation or expansion of an intramural hematoma during PCI [15].

2.3. Statistical analysis

Normally distributed continuous variables are presented as means ± standard deviation (SD); they were compared using the *t*-test. Non-normally distributed variables are presented as medians (interquartile range, IQR). They were compared using the Mann–Whitney *U* test. Categorical baseline variables were compared using Fisher's exact test or the chi-squared test as appropriate. Cumulative event-free survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. All p values < 0.05 were considered statistically significant. Statistical analysis was performed with JMP version 10 (SAS Institute Cary, NC).

3. Results

3.1. Prevalence, clinical characteristics, and precipitating factors for SCAD

In the study population occurred AMI, the overall prevalence of SCAD was 0.31% (63 per 20,195 subjects) (Fig. 1, Study 1). Table 1 shows the clinical characteristics of patients with SCAD. Among 63 patients with SCAD, the mean age was 46 ± 10 years and 59 (94%) were female. STEMI was the presenting diagnosis in 87% and non-STEMI in 13%. Cardiogenic shock or cardiac arrest was observed in 10 (16%) patients. Potential precipitating factors, including hormonal, vascular, or shear stress-related factors, were identified in 39 (62%) patients. The most common precipitating factor for SCAD was emotional stress in 18 (29%) patients (illness of a family member, n = 1; argument, n = 3; interrogation at a police station, n = 1; excessive work, n = 8; stress associated with raising children, n = 2; panic attack, n = 1; postoperative stress, n = 1; post-earthquake stress, n = 1). Five (8.1%) patients presented with SCAD during the peripartum period. Among 25 subjects that were screened for fibromuscular dysplasia (FMD) by a combination of computed tomography angiography (CTA), magnetic resonance angiography (MRA), and ultrasonography (n = 23) or ultrasonography alone (n = 2), the prevalence of FMD was 20% (5 of 25 patients), which was the second most frequent precipitating factor. One patient was diagnosed with FMD due to concomitant carotid dissection.