Spontaneous Coronary Artery Dissection in Relation to Physical and Emotional Stress: A Retrospective Study in 4 Arab Gulf Countries

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Abstract: Spontaneous coronary artery dissection (SCAD) has emerged as an important cause of acute coronary syndrome and sudden cardiac death. The triggers for SCAD often do not include traditional atherosclerotic risk factors. The most commonly reported triggers are extreme physical or emotional stress. The current study compared in-hospital and follow-up events in patients with SCAD with and without reported stress. Data from 83 patients with a confirmed diagnosis of SCAD were collected retrospectively from 30 centers in 4 Arab Gulf countries (KSA, UAE, Kuwait, and Bahrain) from January 2011 to December 2017. In-hospital myocardial infarction (MI), percutaneous coronary intervention (PCI), ventricular tachycardia/ventricular fibrillation, cardiogenic shock, death, ICD placement, dissection extension) and follow-up (MI, de novo SCAD, death, spontaneous superior mesenteric artery dissection) events were compared between those with and without reported stress. Emotional and physical stress was defined as new or unusually intense stress, within 1 week of their initial hospitalization. The median age of patients in the study was 44 (37-55) years. Foty-two (51%) were women. Stress (emotional, physical, and combined) was reported in 49 (59%) of all patients. Sixty-two percent of women with SCAD reported stress, and 51 % of men with SCAD reported stress. Men more commonly reported physical and combined stress. Women more commonly reported emotional stress ($P < 0.001$). The presence or absence of reported stress did not impact on overall adverse cardiovascular events ($P = 0.8$). In-hospital and follow-up events were comparable in patients with SCAD in the presence or absence of reported stress as a trigger. (Curr Probl Cardiol 2021;46:100484.)

Introduction

Spontaneous coronary artery dissection (SCAD) is emerging as an important cause of acute coronary syndrome, especially in young females without conventional coronary risk factors.[1-6] Registry data of SCAD has been predominantly of patients from North America or Europe. We seek to share the results of our gulf SCAD registry, with a focus on culturally-distinct risk factors, mechanisms, and potential interventions. SCAD is defined as an epicardial coronary artery dissection that is not iatrogenic and is not associated with atherosclerosis or trauma.[28] The presentation of SCAD is similar to atherosclerotic ACS.[3-5,7-9] The causes of SCAD are hypothesized to be multifactorial with contributions from genetic factors, hormonal influences, inherited or acquired arteriopathies, or systemic inflammatory diseases, often compounded by environmental precipitants or stressors.[10] Spontaneous arterial tear or intramural hematoma may occur from a complex interaction between a vulnerable patient (ie, 1 with underlying arteriopathy) and potential triggers such as intense exercise (isometric or aerobic), lifting heavy objects, intense emotional stress, intense valsalva, retching, vomiting, bowel movement, coughing, labor and delivery, recreational drugs, and corticosteroid injection.[4,6,11-17] However, this connection is not the case for all patients, highlighting the incomplete understanding of the pathophysiology of this disease process. Stress cat-echolamine surge during these events has been postulated to lead to coronary artery shear stress that, at least in part, contributes to the pathophysiology of SCAD. Although this hypothesis has not been specifically tested in patients with SCAD, a similar mechanism was proposed in other stress-induced cardiovascular conditions such as conditions such as takotsubo cardiomyopathy.[18,19]

Extreme physical or emotional stress are the most commonly reported triggers.[4] Emotional stressors have more often been reported in women, whereas physical stressors have more often been reported among men with SCAD.[1,29] Identification of risk markers or risk factors for recurrent SCAD has been and remains an important clinical goal. Small sample size of studies has been a limitation, and to date, only severe coronary tortuosity has been identified as a risk factor for recurrence, with recurrence most likely to occur in a segment of tortuosity.[20] Patients with SCAD are at high risk for adverse cardiovascular events both in hospital and post discharge due to extreme stress at the time of myocardial infarction and reduced physical and mental functioning after discharge.[21-27] A scientific statement from the American Heart Association has classified research priorities into the areas of pathogenesis with key questions including the

roles of physical and emotional stress on SCAD.[10] The aim of the present study was to investigate in-hospital and follow-up events in patients with SCAD, stratified by presence or absence of reported stress as a trigger, in 4 Arab Gulf countries.

Methods

Study Population

The Gulf SCAD study is a multicenter, multinational, retrospective, observational study that enrolled 83 patients with confirmed diagnosis of SCAD between January 2011 and December 2017, from 30 centers including 25 tertiary referral facilities and 5 regional hospitals in 4 Arab Gulf countries as follows: Kingdom of Saudi Arabia (68 patients from 25 centers), United Arab Emirates (8 patients from 2 centers), Kuwait (4 patients from 2 centers), and Bahrain (3 patients from 1 center).

Patients were diagnosed with SCAD based on angiographic and intravascular imaging whenever available, for ambiguous lesions and according to physician discretion (6 IVUS and 5 OCT). Coronary angiograms were reviewed by the primary cardiologist from each center and confirmed by the principal cardiologist from King Faisal Specialist Hospital and Research Center (Jeddah branch). The findings were classified as type I, type II, or type III angiographic SCAD.[17,28]

The following patients were excluded: patients judged to have atherosclerosis as the cause of SCAD (48), patients found to have coronary artery dissection due to blunt trauma, surgical instruments, or those that are catheter-induced (153), and in case of disagreement between the primary and principal cardiologist (15). None of the patients declined to participate in this registry.

Through medical record review and telephone follow-up, baseline characteristics, socioeconomic status, atherosclerotic risk factors, management strategies, and in-hospital and postdischarge events were recorded. The study protocol was approved by the Institutional Review Board of King Faisal Specialist Hospital and Research Center and each of the participating hospitals. The patients were divided into 2 groups: those who reported stress (physical, emotional, combined [physical + emotional]) and those who did not report stress at the time of their hospital presentation.

Our stress questionnaire was simplified due to the retrospective nature of the study and to facilitate gathering information by telephone. Subjects were initially asked if they had experienced a significant emotional or physical stressor which was defined as new or unusually intense, within 1 week of their initial hospitalization. If the subjects recalled that stress occurred at

this time, they then were asked to assign their stressor a number from 1 to 4. "1" would be considered mild, "2" moderate, "3" severe, and "4" extreme. Subjects scoring their stressor "1" or "2" or who did not recall a stress before the event were considered to not have sustained a stress for the purpose of this study. Subjects were asked to recall the circumstance or activity that caused the stress. For physical stress, was the stressor isometric, such as a resistance exercise, for example, weight lifting, or aerobic such as running. For emotional stress, subjects were asked to describe the event, such as a family event, for example, divorce, death or spouse, or work related, such as joblessness. Finally, subjects were asked if they believed the stress, either physical or emotional, triggered their heart attack.

In-hospital events are the events that the patient did not present with, but developed after being hospitalized and included recurrent ventricular tachycardia/ventricular fibrillation, cardiogenic shock, death, implantable cardioverter defibrillator implantation, and dissection extension.

Follow-up events, are the events that occurred postdischarge from the hospital and included myocardial infarction, de novo SCAD, death, and spontaneous superior mesenteric artery dissection.

De novo coronary artery dissection is defined as a new dissection in different epicardial vessels, with resolution of the prior dissection in the originally affected vessels.

Extension of the dissection is defined as a continuation of an already-established dissection, either spontaneously or iatrogenically.

Clinical Assessment

A complete medical history was recorded through medical record review and telephone follow-up for any missing variables. Presence and type of stress were recorded for all patients as well as marital and socioeconomic status, and mental health history. Routine laboratory studies were obtained during hospitalization. Telemetry and 12-lead ECG data were analyzed by cardiologists. Transthoracic echocardiographic and coronary angiography reports were obtained for all patients with a confirmed diagnosis of SCAD. In-hospital events were compared between those with and without reported stress.

Clinical Follow-up

Follow-up data were obtained in all patients from standardized telephone interviews and treating physician reports. Follow-up events were compared between those with and without reported stress.

Statistical Analysis

Categorical data were summarized with absolute numbers and percentages. Numeric data were summarized with median and 25th-75th quartiles. Comparison between different groups was performed using chi-square test or Fisher's exact (if the expected frequency is less than 5) for categorical variables and Mann−Whitney *U*test for continuous variables. Kaplan-Meier analysis was used to plot the cumulative survival and differences between curves were assessed by the log-rank test. All the analyses were performed using (STATA) software, Version (14.2) (Stata-corp; College Station, TX). *P* value of less than 0.05 was considered statistically significant.

Results

Stress Characteristics by Gender

As shown in Table 2, stress (emotional, physical, and combined) was reported in 49 (59%) of all patients. The remaining 34 (41%) of patients with SCAD had no reported stress. In those who reported stress, the majority had emotional stress 33/49 (67.34%), and the rest had either physical 9/49 (18.36%) or combined (physical + emotional) stress 7/49 (14.28%). In the 42 (50.6%) female patients, stress (emotional, physical, and combined) was reported in (66.7%) 28/42. In the 41 (49.4%) male patients, stress (emotional, physical, and combined) was reported in 51.2% (21/41). Men reported significantly more physical stress 19.5% (8/41) than women. Women reported more emotional stress 61.9% (26/42) than men, ($P < 0.001$).

Demographic Characteristics of SCAD Patients According to Presence or Absence of Reported Stress on Hospital Presentation

Eighty-three patients with SCAD were identified retrospectively over a period of 6 years with a median follow-up time of 18.8 months (interquartile range: 9.06-40.1 months). As shown in Table 1, the median age of patients in the study was 44 (37-55) years. When comparing those with stress (emotional, physical, and combined) and without identifiable stress, the age difference was not statistically significant ($P = 0.85$). In the 42 (50.6%) female patients, stress (emotional, physical, and combined) was reported in (66.7%) 28/42. The majority of the study participants were Arab 84.34% (70/83). When comparing those with and without

TABLE 1. Demographic characteristics of SCAD patients according to to presence or absence of reported stress on hospital presentation.

	All patients ($n = 83$)	Stress ($n = 49$) emotional = 33 physical = 9 combined = 7	No stress ($n = 34$)	*P* value
Demographics				
Age, y	44 (37-55)	42 (37-55)	46 (37-55)	0.85
BMI (kg/m^2)	27 (24.8-30)	27 (25-31)	27 (25-30)	0.51
Arabic ethnicity	70 (84.34%)	40 (81.63%)	30 (88.23%)	0.54
Marital status				0.10
Divorced	11 (13.25%)	10 (20.41%)	1 (2.9%)	
Married	63 (75.9%)	34 (69.38%)	29 (85.29%)	
Single	3 (3.61%)	1 (2%)	2 (5.88%)	
Widowed	6 (7.23%)	4 (8.16%)	2 (5.88%)	
Remarried	10 (12.05%)	8 (16.32%)	2 (5.88%)	0.19
Socioeconomic factors				
Unemployed	33 (39.76%)	21 (42.85%)	12 (35.29%)	0.51
Employed	50 (60.24%)	28 (57.14%)	22 (64.7%)	
Secondary education	60 (72.29%)	36 (73.46%)	24 (70.58%)	0.81
Postsecondary education	23 (27.71%)	13 (26.53%)	10 (29.41%)	
Monthly income $\geq$10 SAR/mo	21 (25.30%)	12 (24.48%)	9 (26.47%)	1.00
Monthly income $<$10 SAR/mo	62 (73.70%)	37 (75.51%)	25 (73.52%)	
Smoker	37 (44.58%)	23 (46.93%)	14 (41.17%)	0.66
Comorbidities				
Diabetes mellitus				0.80
Insulin dependent diabetes mellitus	4 (4.82%)	3 (6.12%)	1 (2.94%)	
Noninsulin dependent diabetes mellitus	17 (20.48%)	10 (20.40%)	7 (20.58%)	
Arterial hypertension	26 (31.33%)	16 (32.65%)	10 (29.41%)	0.81
Dyslipidaemia	32 (38.55%)	18 (36.73%)	14 (41.17%)	0.82
Congestive heart failure	2 (2.41%)	1 (2%)	1 (2.94%)	1.00
Cerebral vascular accident	1 (1.20%)	1 (2%)	0 (0.00%)	1.0
Chronic kidney disease	2 (2.41%)	0 (0.00%)	2 (5.88%)	0.16
Anxiety	28 (33.73%)	26 (53.06%)	2 (5.88%)	$<$0.0001
Depression	12 (14.46%)	10 (20.40%)	2 (5.88%)	0.11
Migraine	19 (22.89%)	17 (34.69%)	2 (5.88%)	0.003
Hypothyroid	6 (7.23%)	3 (6.12%)	3 (8.82%)	0.69

identifiable stress, the difference in ethnicity was not statistically significant ($P = 0.54$). In regards to marital status, those without identifiable stress were more likely to be married 85.29% (29/34), and less likely to be single 5.88% (2/34), compared to those with identifiable stress only 69.38 % (34/49) are married and 2% (1/49) are single, ($P = 0.10$). Being remarried was reported in 12% of the cohort, when comparing both groups, the difference was not statically significant ($P = 0.19$).

TABLE 2. Stress characteristics by gender.

	All patients ($n = 83$)	Men ($n = 41$)	Women ($n = 42$)	*P* value
Stress				<0.001
None	34 (40.96%)	20 (48.78%)	14 (33.33%)	
Emotional stress	33 (39.76%)	7 (17.07%)	26 (61.90%)	
Physical stress	9 (10.84%)	8 (19.51%)	1 (2.38%)	
Combined stress (physical and emotional)	7 (8.43%)	6 (14.63%)	1 (2.38%)	

Employment status, monthly income, and the level of education were not significant factors when comparing those with and without reported stress, ($P = 0.51$, $P = 1.00$, and $P = 0.81$, respectively). Coexisting comorbidities and traditional risk factors are shown in Table 1.

Smoking was reported in 45% of the cohort, and cardiac risk factors were reported in 30% of the cohort. When comparing those with and without reported stress, these differences were not statically significant ($P = 0.66$ and $P = 0.80$, respectively). Patients with reported stress (emotional, physical, and combined) were more likely to have history of anxiety and migraine, when compared to those without reported stress ($P < 0.0001$ and $P = 0.003$, respectively). However, the history of depression between the 2 groups was not statically significant ($P = 0.11$).

Clinical Presentation and Angiographic Distribution

As shown in Table 3, at-hospital presentation 10 patients (12%) had ventricular arrhythmia, 6 of which ocurred in those who reported stress (12.24%) and 4 in those without identifiable stress (11.76%), $P = 1.00$.

Acute was present in 49.4% of the patients and 47% presented with non-ST-elevation acute coronary syndrome (NST-ACS). A small number of the patients presented with chest pain (3.6%). Acute ST segment elevation myocardial infarction was more common in those with identifiable stress. However, NST-ACS and chest pain was more in those without identifiable stress ($P = 0.03$). The median LV ejection fraction was 45% (40%-55%). There was no difference between the 2 groups with regards to LV ejection fraction ($P = 0.12$). A reduce LV ejection fraction of less than 35% occurred in 14 patients (17%). Only 29% of the patients presenting and diagnosed with SCAD had normal cardiac wall motion. There was no difference between the 2 groups with regards to elevation of cardiac enzymes or elevation of inflammatory markers (CRP and WBC) ($P > 0.05$).

TABLE 3. Clinical presentation and angiographic distribution.

	All patients (n = 83)	Stress (n = 49) emotional = 33 physical = 9 combined = 7	No stress (n = 34)	P value
Hospital presentation				
Ventricular arrhythmia	10 (12.05%)	6 (12.24%)	4 (11.76%)	1.00
Acute coronary syndrome				0.03
Chest pain	3 (3.6%)	0 (0.00%)	3 (8.82%)	
ST-elevation myocardial infarction	41 (49.4%)	28 (57.14%)	13 (38.23%)	
Non-ST-elevation acute coronary syndrome	39 (46.99%)	21 (42.85%)	18 (52.94%)	
2-D echocardiogram on admission				
Left ventricular ejection fraction (%)	0.45 (0.4-0.55)	0.45 (0.4-0.5)	0.45 (0.5-0.6)	0.12
LV EF <0.35	14 (16.87%)	10 (20.4%)	4 (11.76%)	0.38
Lab test on admission				
WBC (g/L) median (IQR)	10 (6.45-12)	10 (6-12)	9 (7-12)	0.85
CRP (mg/L) median (IQR)	10 (3-15)	10 (3-19)	9 (3-15)	0.62
Troponin (ng/L) median (IQR)	2.69 (0.05-20)	3 (0.1-16.3)	2.4 (0-22.5)	0.87
CK (U/L) median(IQR)	265 (108.5-737)	200 (107-854)	297 (94-492)	0.85
CKMB (ug/L) median (IQR)	33 (5.85-84.5)	24 (4-130)	36 (6-65)	0.69
Angiographic characteristics of the SCAD lesions				
Coronary artery territory involved				0.39
Branch vessel	3 (3.61%)	1 (2%)	2 (5.8%)	
Left anterior descending	36 (43.37%)	20 (40.8%)	16 (47%)	
Left circumflex artery	8 (9.64%)	3 (6.12%)	5 (14.7%)	
Left main	10 (12.05%)	6 (12.24%)	4 (11.76%)	
Multivessel	8 (9.64%)	5 (10.2%)	3 (6.12%)	
Right coronary artery	18 (21.69%)	14 (28.57%)	4 (11.76%)	
Lesion characteristics				0.33
Type 1	43 (51.81%)	23 (46.93%)	20 (85.82%)	
Type 2	35 (42.17%)	23 (46.93%)	12 (35.29%)	
Type 3	3 (3.61%)	1 (2%)	2 (5.8%)	
Multitype	2 (2.41%)	2 (4%)	0 (0.00%)	
TIMI coronary grade flow				0.29
TIMI 0	8 (9.64%)	5 (10.2%)	3 (8.82%)	
TIMI 1	13 (15.68%)	7 (14.28%)	6 (17.64%)	
TIMI 2	21 (25.30%)	16 (32.65%)	5 (14.7%)	
TIMI 3	41 (49.40%)	21 (42.85%)	20 (85.82%)	
Max stenosis severity (%)	80 (50-95)	80 (50-95)	80 (60-96)	0.50
Max dissection length (mm)	25 (18-36)	25 (19-39)	23 (15-36)	0.61

In terms of coronary vessel distribution, 12% of the patients had left main involvement, 43% of the patients had left anterior descending artery involvement, 21.7% patients had right coronary artery involvement, 9.6% of the patients had left circumflex artery involvement, and 9.6% of the patients had multivessel SCAD. Branch vessel involvement was seen in 3.6% of the patients. There was no difference between the 2 groups with regards to coronary vessel distribution ($P > 0.05$). Type I SCAD was present in 52% of patients, 42% had type II, and 3.6% had type III. Two patients (2.4%) were felt to have multiple types of dissections. Most commonly, patients had TIMI-3 coronary grade flow in the affected artery (49%), followed by TIMI-2 flow (25%), with no difference between the 2 groups ($P = 0.33$ and $P = 0.29$, respectively). Maximal stenosis severity of 80% (50-95) and maximal lesion length of 25 mm (18-36) were similar in both groups.

Strategy and Patient Management

As shown in Table 4, management of SCAD was not different between the stress and no stress groups ($P = 0.63$). Forty percent of patients had only medical treatment. Over half of patients underwent coronary revascularization, including percutaneous coronary intervention (53%) and coronary artery bypass grafting (7%). Medications prescribed at discharge and at follow-up are shown in (Table 4). Both groups received similar discharge medications. Statins were more commonly prescribed to patients who reported stress compared to those who reported no stress ($P = 0.03$).

All patients in the study were prescribed aspirin. Most patients (91.5%) were prescribed a P2Y12 inhibitor (17 patients had Ticagrelor, 3 patients had Prasugrel and the remaining patients were placed on Clopidogrel). Beta blockers were prescribed in 90%, and 85% received statin therapy. By the median follow-up time of 18.8 months (interquartile range: 9.06-40.1 months), there was a major decrease in a P2Y12 inhibitor use (62%). This decrease was similar in the stress and no stress groups. ACEI or ARB was used in 66% of cases, and this medication use continued into the follow-up period. Calcium channel blocker and nitroglycerin were used in minority of patients, 11% and 33%, respectively.

In-Hospital Events and Follow-up Events

In-hospital events are the events that the patient did not present with, but developed after being hospitalized, as shown in Table 5. When

TABLE 4. Strategy and patient management.

	All patients ($n = 83$)	Stress ($n = 49$) emotional = 33 physical = 9 combined = 7	No stress ($n = 34$)	*P* value
Intervention				0.63
Medical management only	33 (39.76%)	20 (53%)	13 (38.23%)	
Percutaneous coronary intervention	44 (53.01%)	26 (53%)	18 (52.94%)	
Coronary artery bypass grafting	6 (7.23%)	3 (6.12%)	3 (8.82%)	
Discharge medications	Total No (82)	Total No (48)	Total No (34)	
Aspirin	82 (100%)	48 (100%)	34 (100%)	1.00
P2Y12 inhibitor	75 (91.46%)	43 (89.58%)	32 (94.11%)	0.46
Beta blocker	74 (90.24%)	42 (87.5%)	32 (94.11%)	0.30
Calcium channel blocker	9 (10.97%)	5 (10.41%)	4 (11.76%)	1.00
Statin	70 (85.36%)	45 (93.75%)	25 (73.52%)	0.03
Angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB)	54 (65.85%)	36 (75%)	18 (52.94%)	0.06
Nitroglycerin	27 (32.92%)	17 (35.41%)	10 (29.41%)	0.64
Follow-up medication	Total No 81	Total No (48)	Total No (33)	
Aspirin	79 (97.53%)	47 (97.91%)	32 (96.96%)	0.51
P2Y12 inhibitor	50 (61.72%)	29 (60.41%)	21 (63.63%)	0.82
Beta blockers	76 (93.82%)	44 (91.66%)	32 (96.96%)	0.64
Calcium channel blocker	11 (13.58%)	5 (10.41%)	6 (18.18%)	0.34
Statin	64 (79.01%)	39 (81.25%)	25 (75.75%)	0.59
Angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB)	53 (65.43%)	34 (70.83%)	19 (57.57%)	0.24
Nitroglycerin	13 (16.04%)	6 (12.5%)	7 (21.21%)	0.36

comparing those who reported stress and those who did not report stress, recurrent VA occurred in 8% (4/49 patients) vs 3% (1/34 patients), respectively. Cardiogenic shock was seen only in those who reported stress 8% (4/49 patients).

Death from recurrent VA occurred only in those who reported stress in 2% (1/49 patients). Implantable cardioverter defibrillator placement due to recurrent ventricular arrhythmia and low LVEF occurred in only those who reported no stress. Extension of dissection occurred in 2% (1/49 patients) vs 6% (2/34 patients), respectively. One patient had retrograde extension of the dissection in a diagonal branch during balloon angioplasty of the left anterior descending artery.

TABLE 5. In-hospital events and follow-up events.

	Total ($n = 83$)	Stress ($n = 49$)	No stress ($n = 34$)	*P* value
In-hospital events				
Recurrent ventricular arrhythmia	5 (12.05%)	4 (8%)	1 (3%)	0.85
Cardiogenic shock	4 (4.82%)	4 (8.16%)	0	0.64
Death	1 (1.20%)	1 (2%)	0	1.00
Implantable cardioverter-defibrillator	1 (1.20%)	0	1 (2.94%)	0.41
Extension of dissection	3 (3.61%)	1 (2%)	2 (5.88%)	0.56
Composite	8 (9.6%)	5 (10.2%)	3 (8.8%)	1.00

	Total (n = 82)	Stress ($n = 48$)	No stress ($n = 34$)	*P* value
Follow-up events				
Myocardial infarction	6 (7.32%)	3 (6.25%)	3 (8.82%)	0.69
De novo SCAD	4 (4.88%)	2 (4.16%)	2 (5.88%)	1.00
Death	1 (1.22%)	0	1 (2.94%)	0.41
Spontaneous superior mesenteric artery dissection	1 (1.22%)	1 (2%)	0	1.00
Composite	6 (7.32%)	3 (6.25%)	3 (8.82%)	0.69
Overall composite events	12 (14.45%)	8 (16.3%)	4 (11.76%)	0.8

The second patient had extension of the dissection to an obtuse marginal branch during the stenting of the left circumflex artery. The third patient had a spontaneous extension of the dissection in a posterolateral branch 12 hours post PCI. The composite in-hospital events were not statistically significant between the 2 groups ($P = 1.00$).

Follow-up events are the events that occurred postdischarge from the hospital, as displayed in Table 5. When comparing those who reported stress and those who did not report stress, myocardial infarction occurred in 6% vs 9%, respectively. Within the stress group, 4% had de novo SCAD, and 2% had spontaneous superior mesenteric artery dissection. In those who did not report stress, 6% had de novo SCAD, and 1 patient died from myocardial infarction associated with VA.

The composite follow-up events were comparable between the groups ($P = 0.69$).

As shown in Table 5, the overall composite events (in-hospital and follow-up) were not statistically significant between patients who reported stress and those who reported no stress ($P = 0.8$, Fig 1).

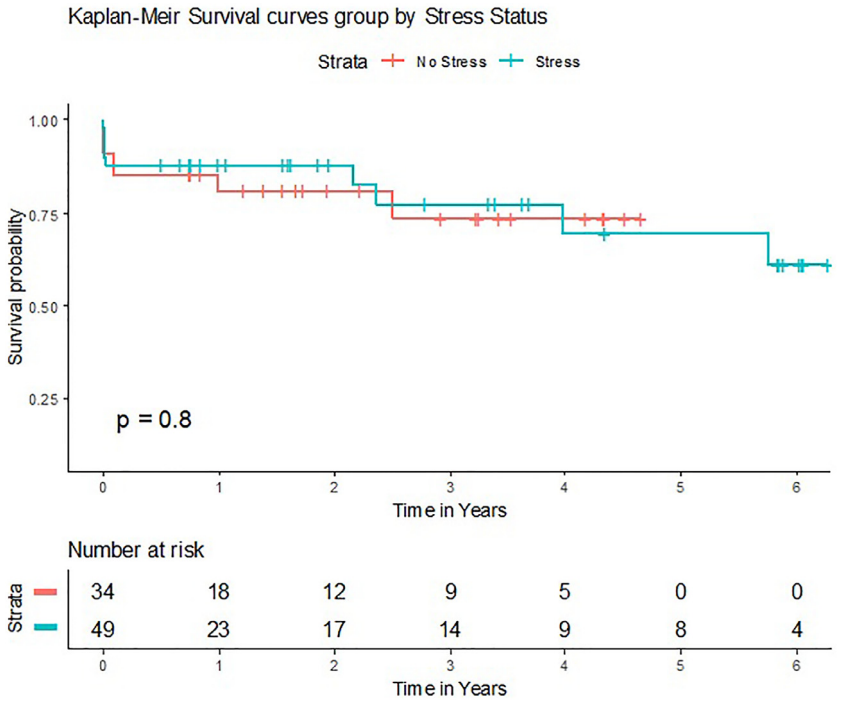

FIG 1. Kaplan-Meier curve for overall composite events of patients with SCAD according to presence or absence of reported stress. Overall, in-hospital and follow-up events were comparable in patients with SCAD in the presence or absence of reported stress as a trigger ($P = 0.8$).

Discussion

Our study provides a unique examination of patients with SCAD in the Arab Gulf countries.

Compared to western registries, as shown in Table 6. We identified 68 patients with SCAD from 25 centers in Kingdom of Saudi Arabia, estimating a prevalence of 0.04% from all cases of NST-ACS and ST-elevation myocardial infarction and we found a lower percentage of SCAD as compared to Western registries.[1,34-36] We also identified a lower percentage of female patients (50.6%) with a similar average age (45.99). In the female group of patients presenting with SCAD, we found a higher percentage of pregnancy-associated SCAD (28.5%) and multiparity (21.4%) of patients. Our male SCAD patients commonly had traditional risk factors for coronary artery disease. We identified no patients with fibromuscular dysplasia, a common condition in western registries of patients with SCAD.[10] With regard to precipitating stressors, intense emotional stress

TABLE 6. Angiographic prevalence, demographics, risk factors, clinical presentation, angiographic distribution, in-hospital and follow-up events of patients with SCAD in the Arab Gulf countries compared to western registries.

	Gulf-SCAD registry	Western-SCAD registry	References
Angiographic prevalence (all cases of ACS, %)	0.04%	1-4	1,34-46
Gender (female, %)	50.6	77-95	5,8,34,37
Age (mean, y)	45.99	45-53	1,4,8,10,34,35
Diabetes mellitus (%)	25.3	2-11	1-6,10,34,38,39
Arterial hypertension (%)	31.3	18-51	1-6,10,34,38,39
Dyslipidaemia (%)	38.5	10-52	1-6,10,34,38,39
Smoker (%)	44.5	8-57	1–6,10,34,38,39
Pregnancy-associated SCAD (%)	28.5	2-12	1,2,8,10,34,37
Multiparity (≥4 births, %)	21.4	9-10	4,10
Exogenous hormones (oral contraceptives, postmenopausal therapy, %)	12	10.7-12.6	1,4
Fibromuscular dysplasia (%)	Not screened	25-86	4,6,10,40
Systemic inflammatory disease (%)	1.2	<1-8.9	2,4
Emotional stress (%)			
All patients	40	40	4
Female	62	55	1
Male	17	24	1
Physical stress (%)		24	
All patients	11	2.8-21	4
Female	2	44-72	1,19
Male	20		1,19
Migraine (%)			
Female	40.5	41.6	41
Male	5	4.7	41
Anxiety (%)	34	37	42
Depression (%)	14	33	42
Hypothyroidism (%)	7	26	43
Hospital presentation (%)			
STEMI	48	26-87	3-5,8-10
NSTE-ACS	47	13-69	
Coronary artery territories involvement (%)			1,3-5,8-10,44
LM	12	4	
LAD	43.4	45-61	
RCA	21.7	10-39	
LCX	9.6	15-45	
Multivessel	9.6	9-23	
Lesion characteristics (%)			
Type 1	51.8	29.1	2,4,5,8
Type 2	42.2	67.5	
Type 3	3.6	3.4	

(*continued*)

TABLE 6. (*continued*)

	Gulf-SCAD registry	Western-SCAD registry	References
Acute management (%)			
Medical	40	49.7-89.7	4,3,9
PCI	53	16.7-47.1	
CABG	7	2.2-7.4	
In-hospital event (%)			
VA	12	3-11	1,3,4,8,9
Sudden cardiac death	1.2	<1	1,3,4,8,9,45
Cardiogenic shock	5	2-5	3,8
Implantable cardioverter-defibrillator	1.2	6.8	45
Extension of dissection	3.6	5-10	1,3,4
PCI for extension of dissection	1.2	14	1,3,4
Follow-up event (%)			
Intermediate-term median follow-up time of 18.8 months (interquartile range: 9.06-40.1 months)			
Myocardial infarction	7.3	15-22	4,8,46
De novo SCAD	5	10-19	1,4,8,9,18,47
Death	1.2	<1.2	8,10,46

was reported in 40% of patients preceding their event which appears to be comparable with data from Western societies. In our data, 11% reported physical stress before their event which is half the percentage reported from Western data.[4] In our male SCAD patients we found a lower percentage (51%) of reported stress (emotional, physical, and combined), as compared to (73.7%) in the western registries.[29]

Our female SCAD patients displayed more emotional stress (62%) compared to the male SCAD patients, who displayed more physical (20%) and combined stress (15%), which is in agreement with western data.[1,29]

The differences between our patient population and those previously described require additional study, as they could be explained by differences in genetic predisposition, lifestyle, culture, or utilization of medical services between the 2 populations.[30]

The aim of the present study was to investigate in-hospital and follow-up events in patients with SCAD, stratified by presence or absence of reported stress as a trigger.

Similar comparative outcome analysis has been performed regarding patients with atherosclerotic myocardial infarction or takotsubo cardiomyopathy, but not regarding SCAD.[31-33] In our study, there was no difference between composite in-hospital and follow-up events regarding those patients who reported stress and those who reported no stress. We postulate that this may be due to the subjective over-reporting of stress or recall bias.

Although it did not reach statistical significance, all cardiogenic shock events occurred in the stress group. This observation may be due to transient catecholamine surge from stress as a trigger. However, all cardiogenic shock patients presented with acute ST-elevation myocardial infarction, making it difficult to surmise that the cardiogenic shock occurred mainly due to stress.

Future larger-scale prospective and epidemiologic studies will help further our understanding of the demographic, pathogenesis, treatment, and anatomical factors associated with recurrence and allow more accurate prediction and ultimate prevention of recurrent SCAD.

Primary Strength

This study provides information about patients with SCAD in a unique population, from the Arab Gulf countries. In addition, the study drew patients from a large number of centers in that region. Finally, this is the first study to examine stress as a trigger for overall adverse cardiovascular events (in-hospital and follow-up) in patients with SCAD.

Limitations

First, the small sample size as well as selection, referral, and attrition biases due to the unavoidable nature of a registry. For instance, the current cohort, by default, did not incorporate patients who did not survive their initial SCAD. Second, the retrospective analysis may have underestimated the prevalence of SCAD in the Gulf region. Third, measurement bias could not be formally excluded. Nevertheless the data collection was standardized based on the computerized database of our hospital, with data entry and analysis performed by physicians blinded to the eventual categorization of patient groups. Patients were acutely managed in the intensive or coronary care units, allowing standardized and close monitoring of heart rhythm and hemodynamics. Finally, our population sample remains small with limited long-term follow-up. Stress evaluation in the present study was not conducted by validated methods; we had to simplify our questionnaire with regard to subjects' stresses because of the retrospective nature of the study and the use of telephone interviews.

Clinical Implications

Patients with SCAD are thought to have primary events and possible recurrent adverse cardiovascular events triggered by physical or emotional stress. This may lead clinicians to advise patients with SCAD to

avoid physical exercise to prevent recurrent events. Our findings indicate that episodes of physical or emotional stress do not have a significant impact in patients with SCAD and that patients with SCAD can be encouraged to engage in regular exercise. Self-identified emotional stress was more common in our female patients. Although not shown to be associated with a significant increase in recurrent adverse cardiovascular events, exploration of reported emotional stress would be expected to provide improved understanding and a potential opportunity for intervention in female patients with SCAD. Such intervention could have a positive impact on cardiovascular and overall health.

In conclusion, in-hospital and follow-up events were comparable in patients with SCAD in the presence or absence of reported stress as a trigger. Female SCAD patients displayed more emotional stress compared to male patients, who themselves displayed more physical and combined stress. In male SCAD patients, we found a lower percentage of reported stress as compared to western data. Recall, cultural, and gender biases may be contributing factors, given SCAD epidemiology and demographics. Further studies on SCAD pathogenesis are needed to confirm our findings.

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