Spontaneous coronary artery dissection: an Italian single centre experience

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Abstract

Aims: Spontaneous coronary artery dissection (SCAD) is an emerging cause of acute myocardial infarction (AMI) in young women without typical cardiovascular risk profile. Knowledge on SCAD is based on observational studies and is still scarce. The aim of this monocentric observational study was to evaluate the predisposing factors, clinical features and prognosis of SCAD patients.

Methods: Between 2013 and 2020, 58 patients with angiographic diagnosis of SCAD were identified in our Centre with an overall prevalence of 0.9% among patients admitted for AMI (58 of 6414 patients).

Results: the mean age was 54 ± 11 years and the majority were female (n=50, 86%) with ≤ 1 cardiovascular risk factors (n =35, 60%). The prevalence of Fibromuscolar Dysplasia (FMD) was 39% (7 of 18 screened patients). The rate of major adverse cardiovascular and cerebrovascular events (MACCEs) was used to assess the prognosis. Out-of-hospital cardiac arrest due to ventricular fibrillation was observed in 4 (7%) patients. The majority of patients (n =51, 88%) were treated conservatively without revascularization. The in-hospital and 30-days clinical course was uneventful in most patients (n=54, 93%) with two cardiac death. During a median follow-up of 12 months there were no further deaths. The global rate of SCAD recurrence was significant (n=8, 14%) but predictors have not been identified.

Conclusions: Although overall survival seems good, SCAD is a potentially malignant, not rare disease, which can present with sudden cardiac death and not uncommon recurrence. Prognostic stratification and optimal management of SCAD patients remain to be defined.

Introduction

Spontaneous coronary artery dissection (SCAD) is an underdiagnosed nonatherosclerotic etiology of acute myocardial infarction (AMI) and sudden cardiac death (SCD), which predominantly affects young and middle-aged women without traditional cardiovascular risk factors [1-2]. Although long believed to be a rare type of coronary disease (reported prevalence 0.07-1.1%) [3-7], recent data from large observational cohorts of these patients have shown that SCAD is more common than previously thought (1.0-4.0% of acute coronary syndrome and 24-35% of MI in women aged < 50 years) [8-12]; therefore, the true prevalence is still unknown. The pathophysiology of SCAD is due to non-traumatic and non-iatrogenic separation of the coronary arterial walls by intramural hemorrhage, which can occur with or without an intimal tear. The creation of a false lumen with intramural hematoma and/or intimal disruption may cause luminal stenosis and occlusion, limiting the main coronary flow and leading to myocardial ischemia [1,13,14, 34]. The etiology of SCAD is not yet completely understood. Several SCAD predisposing factors (e.g. extracoronary vascular abnormalities, pregnancy, connective tissue disorders) and precipitating stress events (e.g. intense exercise or emotional stressors) have been identified [14-15]. Fibromuscolar dysplasia (FMD) is the most common SCAD-associated vascular abnormality, with a reported prevalence ranging from 41% to 86% from studies where at least 50% of patients were screened [15-19]. Conversely, pregnancy-associated SCAD (P-SCAD) accounts for a minority of cases (<10%) and identified hereditary connective tissue disorders are rare [10-11]. Coronary angiography is the gold standard for the diagnosis of SCAD and four different angiographic subtypes of SCAD (type 1-4) have been identified. Intravascular imaging - Optical coherence tomography (OCT) and Intravascular ultrasound (IVUS) - can clarify the ambiguous angiographic appearance of SCAD [14-15,20-21]. The optimal management and treatment strategy are not yet well defined. Conservative treatment with medical therapy is preferred for stable patients without ongoing chest pain and/or impaired flow.

Revascularization of dissected artery with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) depends on the patient's clinical status and affected coronary anatomy. PCI for SCAD is associated with high rates of technical failure and does not protect against target vessel revascularization or recurrent SCAD [10-11,14,22]. As already observed in the early series, recent studies have confirmed a considerable mortality rate in the acute phase but the long-term outcome of patients who survived their initial SCAD appears good [10-11,14]. However, SCAD recurrence is significant, with a reported prevalence that varies widely in the literature (from 4.7% to 17%, 2.8%/year) [4,8,23].

Despite a growing interest of the Scientific Community, the available data are still based on observational studies, with absence of randomized trials. Therefore, our knowledge on etiology, optimal therapy and long-term prognosis on SCAD is still scarce. The aim of this monocentric Italian observational study was to evaluate the predisposing factors, clinical and angiographic presentations, therapeutic strategies and finally short- and long-term prognosis of SCAD patients in our Center.

Methods

Definition of study population, data collection and outcomes

In this monocentric observational study, patients aged 18 years and older with angiographic diagnosis of SCAD were identified in the Department of Cardiology at Parma University Hospital from January 2013 through September 2020. Patients were identified using retrospective and prospective methods, with start date of the prospective enrollment on December 28, 2017. The diagnosis of SCAD was made by an experienced interventional cardiologist with a description of the type of coronary artery dissection according to the Saw angiographic classification [20] and the exclusion of atherosclerotic and iatrogenic causes of dissection. The Thrombolysis In Myocardial Infarction (TIMI) flow grade

classification [28] was used to better characterize the SCAD lesions. All angiograms were reviewed by another experienced interventional cardiologist.

Comprehensive data on past medical history, pregnancy history, hormonal therapy, emotional and physical stressors, atherosclerotic risk factors were recorded. Clinical presentation, coronary angiography and other imaging techniques (including screening of extracoronary arteriopathy when available), medical therapy, interventional procedures (PCI or CABG) and in-hospital outcomes of patients were also assessed. All data were obtained from patient reviews and medical records of the hospitalization and registered in the database. The short- and long-term outcomes of patients were obtained through clinical visits, telephone interviews or medical record in case of readmission. The rate of major adverse cardiovascular and cerebrovascular events (MACCEs) was used to assess the prognosis of patients with SCAD. MACCEs were defined as the composite of all-cause death, myocardial infarction (MI), including propagation of initial SCAD lesion and recurrent SCAD (defined as the development of *de novo* dissection with new MI unrelated to the extension of original SCAD lesion [29]), cardiogenic shock, congestive heart failure, need for target vessel revascularization (TVR), stent thrombosis (according to the ARC protocol [24]), acute ischemic stroke and transient ischemic attack. Myocardial infarction (ST-segment elevation MI [STEMI] and non ST-segment elevation MI [NSTEMI]) was defined according to the fourth universal definition [26]. Stroke was defined as the presence of a focal neurologic deficit of central origin lasting >72 hours or lasting >24 hours with imaging evidence of cerebral infarction or intracerebral hemorrhage. Transient ischemic attack (TIA) was defined as a transient episode of neurological dysfunction caused by focal brain ischemia [27]. Furthermore, data on bleeding (according to the BARC score [33]) were recorded. The presence of residual angina (according to Canadian Cardiovascular Society Angina Grading Scale, CCS I-IV) and recurrence of SCAD with adopted diagnostic-therapeutic management were also evaluated. The outcomes were assessed during hospitalization, thirty days after discharge and at the end of follow-up. The follow-up time was defined as the time from diagnosis until death or at the end of follow-up (October 2020). This study was approved by the local ethics committee

and conducted in accordance with the Declaration of Helsinki; for all eligible patients, written informed consent for the study was obtained; a waiver of consent was given for patients who had died or could not be contacted.

Statistical analysis

Baseline characteristics of patients including demographics, clinical and angiography data, and short- and long-term outcomes were reported with descriptive statistics. Continuous variables were presented as mean ± standard deviation (SD) or median and interquartile range as appropriate and compared using the Student's *t-test* for normal distribution. Categorical variables were presented as numbers and percentages (%) and compared using Fisher's exact test or the chi-squared test as appropriate. Cox regression analyses were performed to identify univariate and multivariate clinical predictors of recurrent SCAD. Hazard ratios (HR) with corresponding 95% confidence intervals (CI) were reported. All P values < 0.05 were considered statistically significant. Statistical analysis was performed with the SPSS version 24 (SPSS Inc., Chicago, IL, USA).

Results

Demographics and clinical characteristics of SCAD patients

The clinical characteristics of our SCAD patients are shown in Table 1. Between 2013 and 2020, there were 6414 patients discharged with a diagnosis of AMI from our Centre. In this population, we have identified 58 SCAD cases: 30 (52%) patients were retrospectively identified while 28 (48%) patients were prospectively identified. Among SCAD patients, the mean age was 54 ± 11 years (range 21-83 years) and majority were caucasian female (n= 50, 86%). Therefore, the overall prevalence of SCAD was 0.9% (58 of 6414 patients); considering only female patients < 65 years of age with AMI,

the prevalence of SCAD reached 10% (50 of 481). Only two cases (4%) of SCAD occurred during the peripartum period (within 6 weeks of delivery), including a patient with a history of previous peripartum SCAD at the time of enrollment. At baseline, 35 (60%) patients had one or no traditional cardiovascular (CV) risk factors while 9 (16%) patients had ≥ 3 CV risk factors; arterial hypertension (41%) was the prevalent traditional CV risk factor, followed by smoking (35%) and dyslipidemia (32%). Among non-traditional CV risk factors, only two patients had a known connective-tissue disease and four patients had a history of psychiatric disorder (one patient suffered from anxiety and three patients from depression). Emotional and physical stressors as precipitating factors have not been systematically investigated. However, among 9 (15%) patients investigated for precipitating stressors at hospital admission, 4 patients reported emotional stressor and 5 patients physical stressor. Among 18 (31%) patients screened for extracoronary vascular abnormalities by computed tomography angiography (CTA) or magnetic resonance angiography (MRA), the prevalence of Fibromuscolar Dysplasia (FMD) was 39% (7 of 18 patients), involving the cerebral vascular territories in all cases with a neurological evaluation confirming the diagnosis of FDM; clinical and anatomic characteristics of the patients are reported in table 5. Considering clinical presentation, NSTEMI was the most common diagnosis in 76% (n = 44) and STEMI in 24% (n = 14) of cases; out-of-hospital cardiac arrest due to ventricular fibrillation was observed in 4 (7%) patients. As far as left ventricular function assessment, median left ventricular ejection fraction (LVEF) was 55 ± 5% and wall motion abnormality (LWMA) - hypokinesis or akinesis - occurred in 86% (n = 50) of cases.

Angiographic characteristics and management strategies of SCAD patients

The angiographic findings and in-hospital treatment strategy are summarized in Table 1. There were 56 (96%) patients with only one coronary vessel involved while 2 (4%) patients had a multivessel dissection. Thus, there were 60 dissections in 58 patients, including two dissections healed at the time of index angiogram in patients with history of previous SCAD. The most common coronary artery

involved was left anterior descending artery (48%), followed by left circumflex artery (38%). When describing angiographic appearance of SCAD lesion, type 2 was the most common (63%), followed by type 1 (15%), type 4 (13%) and type 3 (8%), respectively.

Most frequent angiographic appearance (type 2 and type 1) was consistent with the findings of other recent single centre studies [35-36].

Initial TIMI flow grade was 3 in 79% of cases. Intravascular ultrasound (IVUS) was performed in 4 (6%) patients to clarify the ambiguous angiographic appearance of SCAD. The majority of patients (n = 51, 88%) were treated conservatively, without PCI or CABG. Only 7 (12%) patients were treated with PCI as first-choice therapy because of impaired flow and/or ongoing chest pain; in 4 patients PCI and stent implantation were performed without complications while in 3 patients it was not possible to advance a wire into the true lumen distally with subsequent conservative strategy. Records of medical therapy were available for 55 patients; 52 (95%) patients received dual antiplatelet therapy (DAPT) with aspirin (100%) in addition to clopidogrel (55%), ticagrelor (40%) or prasugrel (4%). The prescribed duration of dual antiplatelet therapy was 12 months in nearly half of patients (n = 23, 44%). Almost all patients were discharged home on beta-blocker (95%) and statin (95%) therapy. Of note, after Heart Team discussion only one of the four patients with cardiac arrest due to ventricular fibrillation as first clinical presentation underwent Implantable Cardioverter-Defibrillator (ICD) implantation, in particular subcutaneous ICD (sICD) (Figure 1, A-B).

Short- and long-term outcomes of SCAD patients

The in-hospital, 30-days and long-term outcomes of SCAD patients are showed in Table 2. The in-hospital clinical course was uneventful in majority of patients (n = 54, 93%) with two in-hospital cardiac death: one patient died a few days after prolonged cardiac arrest due to SCAD and the other patient died of cardiac arrest during surgery for malignant bowel obstruction, respectively. There were no MACCEs or recurrent SCAD within 30 days after discharge. During a median follow-up of

12 months (range 0.5 to 108 months) after discharge there were no deaths; 5 (9%) patients had non-fatal myocardial reinfarction, 1 due to the extension of initial SCAD and 4 due to SCAD recurrence (*de novo* dissection) that was treated conservatively. In our registry, the global rate of SCAD recurrence was 14% (n = 8), including both patients with a history of previous SCAD (n = 3) at the time of enrollment and patients with de novo SCAD during follow-up (n = 5). Clinical characteristics of patients with SCAD recurrence are shown in table 4.

During follow-up, 10 (17%) patients had recurrence of chest pain (typical or atypical angina) without evidence of myocardial ischemia by stress imaging (single-photon emission computed tomography or stress echocardiography), except for one patient. Moreover, 6 (10%) asymptomatic patients underwent coronary computed tomography angiography (CCTA) at the discretion of physicians to determine the distant healing of dissection, which was observed in almost all of these patients (5 of 6 patients). Medications at last clinical follow-up versus medications at discharge are showed in Table 3. At long-term follow-up, most SCAD patients were still on aspirin (90%) although with a significant reduction ($p < 0.02$) of adherence to the prescribed antiplatelet therapy despite the absence of major bleeding. A good adherence to the hospital discharge therapy was observed for beta-blockers and ACE-I/ARBs while a significant statin withdrawal rate ($p < 0.01$) was observed, mainly related to side effects.

Discussion

Baseline characteristics, management strategies and outcomes of SCAD patients

The main findings of our study can be summarized in four key points.

1) *SCAD occur mainly in young and middle-aged women, without or with few traditional cardiovascular risk factors and represents the leading cause of MI among childbearing women or in peripartum.*

In our study 4% of SCAD occurred in peripartum, being with pregnancy an established risk factor for SCAD.

This percentage is lower than previous reports, but higher than the prevalence of pregnancy among similarly aged women without SCAD.

However, arterial hypertension, dyslipidemia and smoking were not uncommon in our SCAD population. As mentioned above, emotional and physical stressors were not evaluated for all patients. Since precipitating stressors are frequently observed in SCAD patients [8], systematic investigation with questionnaires is desirable and should be implemented together with a complete evaluation of nontraditional risk factors for coronary disease in women [39].

2*) SCAD should no longer be considered as a rare disease.* In recent years, the SCAD cases in our Centre have been increasing (27 of 58 cases in the years 2018-2020); the greater awareness of the physicians in recognizing a possible SCAD patients combined with improved SCAD diagnostic skills on angiography of interventional cardiologist is changing the epidemiology of this disease. In our cohort, all SCAD patients underwent coronary angiography for acute coronary syndrome (ACS) and/or cardiac arrest. In ambiguous cases, intracoronary imaging (IVUS) and/or coronary computed tomography angiography (CCTA) were very useful to confirm the diagnosis of SCAD.

3) *The overall prognosis of SCAD survivors seems good and the natural history of the dissected vessel is probably spontaneous healing*. Almost all SCAD patients in our Centre were treated conservatively with an uneventful clinical course in the short- and long-term, except for two in-hospital cardiac death and five recurrent MI. PCI has been reserved only for patients with ongoing chest pain and/or impaired flow, in view of the vulnerability of the coronary tree and the high rates of technical failure and complication reported in literature [4,15,23,31,37,38]. The prognosis of SCAD patients undergoing PCI was also good without cardiovascular events during follow-up. Overall, recurrent MI mainly due to SCAD recurrence was the most frequent cardiac event in our population. With regard to pharmacologic therapy, the vast majority of patients (95%) received empirical DAPT for 1-12 months at the discretion of treating physicians. However, SCAD patients are in most cases otherwise

healthy young women and adherence to long-term therapy may be suboptimal; therefore, it is important to encourage the adherence to therapy with adequate counseling on clinical benefits.

4) *Despite good long-term survival, SCAD is a potentially malignant disease*. SCAD almost invariably presents as an ACS, either STEMI or NSTEMI, which can lead to dramatic consequences such as malignant arrhythmias and sudden cardiac death. Ventricular tachycardia or ventricular fibrillation at presentation account for 2.8-10% of cases in reported series [7,8,15,23,31,32]. In our cohort, 4 (7%) patients suffered an out-of-hospital cardiac arrest due to ventricular fibrillation at presentation. The choice to implant the ICD in one of these patient was conditioned by the malignant clinical presentation in the absence of potential ischemic reversible causes, in addition to the coexistence of documented FMD as a possible predisposing factor of recurrence, although no clear evidence of benefit from this strategy is reported in the literature.

After the publication of the International consensus document on the management of SCAD [10,11] and FMD [30], all SCAD patients in our Centre underwent imaging-based screening of all vessels from brain to pelvis with CTA or MRA to assess non-coronary arterial abnormalities including FMD. Only 31% of our SCAD patients had complete FMD screening and 39% of the cohort screened positive for FMD. Before these clear indications, FMD screening was at the discretion of treating physicians and were not routinely done. Consequently, the real prevalence of FMD in SCAD patients is probably underestimated. The possible association between SCAD and predisposing arteriopathies (primarily FMD) with potential clinical-therapeutic implications (e.g. identification of patients at high risk of SCAD recurrence) suggest the importance of assessment for extra-coronary arteriopathies.

According to previous series [4,8,23], the global rate of SCAD recurrence was significant (14%) but risk factors as predictors of recurrence have not been clearly identified. Of note, even chest pain recurrence was not uncommon (17%), although only one recurrence SCAD has been demonstrated in these ten symptomatic patients. As suggested by the ESC position paper on SCAD [11], we believe that CTTA can be useful for decision-making in patient with post-SCAD chest pain (especially in atypical angina) to rule out SCAD recurrence.

Limitations

The present study has several limitations. First of all, this is a non-randomized observational study, with a mixed retrospective and prospective data collection, therefore with inherent weakness of analysis due to selection bias in the retrospective cohort, fragmented baseline data and incomplete follow-up.

Based on this methodology, the results should be taken with caution, in particular the prevalence of SCAD and the association with predisposing factors.

Moreover the small size of the population doesn't provide definitive conclusions about the risk profile and prognosis of SCAD patients, but highlights the importance of a change in our diagnostic tools whenever the suspect of a SCAD is evident. In addition, a systematic screening of precipitating stressors and predisposing factors was not performed. Another limit of the study is that, due to the small sample size and the substantial underreporting in the diagnosis of SCAD which probably occurred in the first years of observations, the prevalence reported by our study could be lower than real. Finally, although SCAD healing was observed in almost all patients who underwent CTTA during follow-up, the absence of angiographic follow up imaging (coronary angiography or CTTA) in all patients doesn't allow to demonstrate the effective healing of the coronary dissection.

Conclusion

Spontaneous coronary artery dissection is an emerging cause of myocardial infarction in young and middle-aged women without the typical cardiovascular risk profile. Although overall survival seems good, SCAD is a potentially malignant disease which can present with ventricular arrhythmias and sudden cardiac death. Moreover, the recurrences of dissection and chest pain are relatively common and affect the quality of life of these patients. Despite recent improvements in the knowledge of this

disease, SCAD remains underdiagnosed and undertreated and the possible association with FMD needs to be further investigated. Available data are still based on observational studies, with absence of randomized trials. The diagnosis is challenging and requires a multidisciplinary approach involving the clinical and interventional cardiologists as long as radiology specialists as main actors working in team. Furthermore, prognostic stratification (e.g. identification of high-risk patients), optimal therapeutic management (e.g. DAPT, ICD) and surveillance strategy remain to be defined.

Knowledge gap and future investigation areas

The potential enlargement of sample size is under evaluation, in order to better describe the real prevalence of the disease in the Italian real world population, as well as a more comprehensive evaluation of non-traditional risk factors, the prevalence of mental stressors and the association with FMD in all patients with SCAD diagnosis, critical aspects which all underscore how SCAD is really a different disease from traditional atherosclerotic coronary disease.

Finally the malignant potential presentation of SCAD with cardiac arrest needs further investigation, as well as best treatment strategies, ideally in a randomized setting.

The evidence coming from prospective or randomized trial is still scarce, and the need is compelling.

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Table 1. Baseline characteristics, angiographic findings and management strategies of SCAD patients.

	n = 58
Demographic characteristics	
Age, yrs	54 ± 11
Females	50 (86)
Caucasian	56 (96)
Clinical characteristics[1]	
Hypertension	23 (41)
Diabetes mellitus	2 (4)
Smoking	20 (35)
Hyperlipidemia	18 (32)
Family history of CHD	12 (20)
Chronic kidney disease	0 (0)
≤ 1 cardiac risk factors	35 (60)
≥ 3 cardiac risk factors	9 (16)
Previous MI	5 (8)
Previous SCAD	3 (5)
Previous revascularization	2 (4)
Previous CVA	0 (0)
Previous PE	3 (5)
History of depression	3 (5)
History of anxiety	1 (2)
Predisposing factors	
FMD[2]	7 (39)
Connective tissue diseases	2 (4)
Oral contraceptives	2 (4)
Peripartum period	2 (4)
Clinical presentation	
STEMI	14 (24)
NSTEMI	44 (76)
Out-of-hospital cardiac arrest	4 (7)
Cardiogenic shock	0 (0)
LVEF, %	55 ± 5
LVWMA	
No abnormality	8 (14)

Hypokinesis or akinesis	50 (86)
Angiographic findings	
Artery involved*	
LM	0 (0)
LAD	29 (48)
LCX	23 (38)
RCA	8 (13)
LM with prox LCX or prox LAD	2 (3)
Angiographic SCAD type*	
Type 1	9 (15)
Type 2	38 (63)
Type 3	5 (8)
Type 4	8 (13)
Use of intracoronary imaging[3]	
IVUS	4 (6)
Initial TIMI flow grade	
TIMI 0	7 (12)
TIMI 1	3 (5)
TIMI 2	2 (3)
TIMI 3	46 (79)
Management strategy	
Conservative therapy	51 (88)
Revascularization therapy	7 (12)
PCI	7 (12)
CABG	0 (0)
Details of PCI procedure	
Stent implantation (DES)	4 (6)
POBA	0 (0)
Overall PCI success	
Successful PCI	4 (6)
Unsuccessful PCI	3 (5)
Discharge medications[4]	
Aspirin	55 (100)
Second antiplatelet agent (DAPT)	52 (95)
Clopidogrel[5]	29 (55)
Ticagrelor[5]	21 (40)
Prasugrel[5]	2 (4)
Warfarin	2 (4)
Statin	52 (95)
ACEi/ARB	43 (78)
Beta blocker	52 (95)
Nitrate or CCB	5 (9)
Time indicated from P2Y12 inhibitor withdrawal, months***	
12 months	23 (44)
1-6 months	9 (17)
Not specified	20 (38)

Values are n (%) or mean ± SD.

SCAD: spontaneous coronary artery dissection; CHD: Coronary heart disease; MI: myocardial infarction; CVA: cerebrovascular accident; PE: Pulmonary embolism; FMD: Fibromuscular dysplasia[2] STEMI; ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction. LVEF: left ventricular ejection fraction. LVWMA: left ventricular wall motion abnormalities.

LM: left main artery; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; IVUS: intravascular ultrasound**;** PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; DES: drug-eluting stent; DAPT: dual antiplatelet therapy; POBA: plain old balloon angioplasty. ACEi: angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB: calcium channel blocker.

[1]Percentages are computed among the 56 patients who had all available clinical data.

[2]Percentages are computed among the 18 patients who have been screened for extra-coronary vascular abnormalities by CTA or MRA.

[3]Percentages are computed among 60 SCAD lesions in 58 patients.

[4]Percentages are computed among the 55 patients who had available in-hospital follow-up.

[5]Percentages are computed among the 52 patients on DAPT at discharge.

Table 2. In-hospital, 30-days and long-term outcomes of SCAD patients.

	n = 58
In-hospital MACCEs	4 (7)
All-cause death	2 (3)
Re-infarction	1 (2)
Extension of initial SCAD	1 (2)
Other	0 (0)
Target vessel revascularization	0 (0)
Stent thrombosis	0 (0)
Cardiogenic shock or CHF	0 (0)
Stroke/TIA	1 (2)
In-hospital bleeding	0 (0)
BARC 1-2	0 (0)
BARC 3-5	0 (0)
Post-discharge 30-days MACCEs	0 (0)
Overall follow-up MACCEs	8 (14)
All-cause death	2 (3)
Recurrent MI	5 (9)
Extension of initial SCAD	1 (2)
Recurrent SCAD	4 (7)
Other	0 (0)
Target vessel revascularization	0 (0)
Stent thrombosis	0 (0)
Cardiogenic shock or CHF	0 (0)
Stroke/TIA	1 (2)
Overall follow-up bleeding	2 (3)
BARC 1-2	2 (3)
BARC 3-5	0 (0)
Overall follow-up recurrent chest pain	10 (17)

Values are n (%) or mean ± SD.
SCAD: spontaneous coronary artery dissection; MACCEs: major cardiovascular and cerebrovascular events, defined as the composite of all-cause death, myocardial infarction (MI), need for target vessel revascularization (TVR), stent thrombosis, cardiogenic shock, congestive heart failure (CHF), acute ischemic stroke and transient ischemic attack (TIA); BARC: Bleeding Academic Research Consortium.

Table 3. Discharge and last follow-up medications of SCAD patients.

	Discharge medications* n = 55	Last follow-up medications* n = 43	p-Value
Aspirin	55 (100)	39 (90)	P = 0.02**
Second antiplatelet agent (DAPT)	52 (95)	16 (37)	P < 0.01**
Warfarin	2 (4)	1 (2)	P = 0.7
Statin	52 (95)	33 (77)	P < 0.01**
ACEi/ARB	43 (78)	28 (65)	P = 0.5
Beta blocker	52 (95)	36 (84)	P = 0.08
Nitrate or CCB	5 (9)	3 (7)	P = 0.7

Categorical variables are expressed as an n (%).
SCAD: spontaneous coronary artery dissection; DAPT: dual antiplatelet therapy; ACEi: angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB: calcium channel blocker.
*Percentages are computed among the 55 and 43 patients who had available in-hospital and long-term medications follow-up, respectively.
**Statistical significance.

Table 4. Clinical characteristics of patients with SCAD recurrence.

Type of SCAD	Site of SCAD	Traditional RF	Treatment	Time to recurrence	FMD
2	RCA	HTA+DM	DAPT 12 months	13 months	No
2	LAD	CAD his+HTA	DAPT NA	84 months	No
2	LAD	CHD his+HTA+smoking	DAPT 12 months	48 months	No
2	LAD	none	DAPT 12 months	12 months	Yes
1	LCX	none	DAPT 12 months	6 months	No

SCAD: spontaneous coronary artery dissection; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery
HTA: Hypertension, DM: diabetes mellitus, CHD his: family history of CHD
DAPT: dual antiplatelet therapy

Table 5. Clinical characteristics and vessel anatomy of patients with diagnosis FMD

Gender	Age (yy)	imaging	Vessel	
F	43	MRA	RICA	Saccular aneurysm
			Left subclavian artery	Focal stenosis
			Supra-aortic vessels	Multiple tortuosity
F	52	MRA	RVA	Multiple tortuosity
			LICA	Dissecant pseudoaneurysm
F	55	CTA	RVA and LVA	Multiple tortuosity+
			RVA	Dissecant pseudoaneurysm
F	49	CTA	RICA + LICA	Multiple tortuosity
			RVA	Dissecant aneurysm
M	69	CTA	Right subclavian artery	Dissecant aneurysm
F	53	CTA	RICA	Saccular aneurysm
F	50	MRA	RVA	Multiple tortuosity
				Stenosis

FMD: Fibromuscular dysplasia; MRA: magnetic resonance angiography; CTA: computed tomography angiography; RICA: right internal carotid artery; RVA: right vertebral artery; LICA: left internal carotid artery
LVA: Left vertebral artery

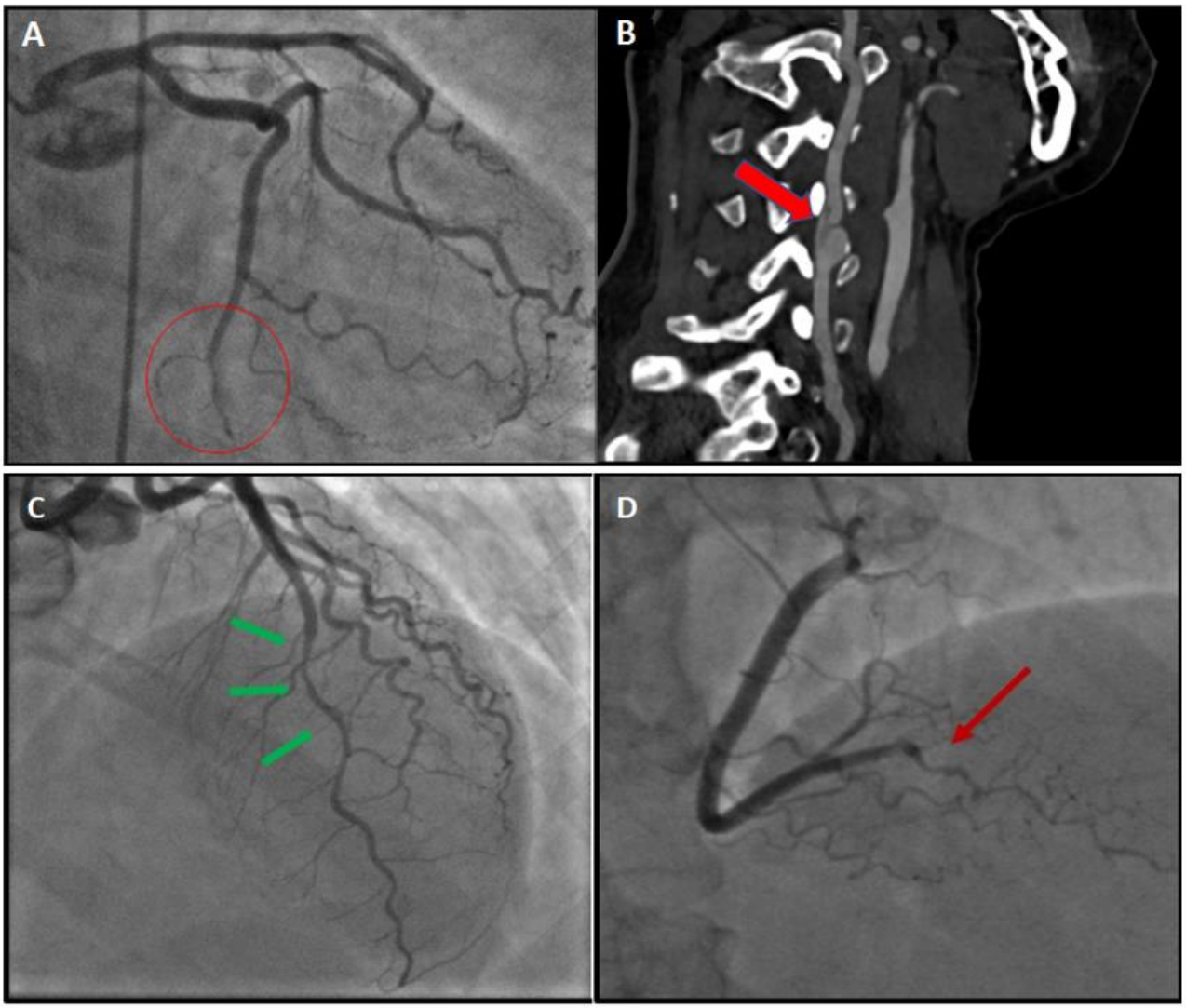

Figure 1. Representative SCAD cases treated with conservative therapy. (A-B): Patient with ventricular fibrillation at presentation. (A): Coronary angiogram of this 48-year-old woman showed a long smooth narrowing in the distal left circumflex coronary artery, suspected for type 2 SCAD (**A**, ***red circle***); **(B)**: Cervical angio-CT showing a dissecting aneurysm of the right vertebral artery in section V2 **(B**, ***red arrow*****)** in the same patient. **(C-D): Patients with NSTEMI at presentation.** In a 41-year-old woman **(C)** and a 46-year-old woman **(D)** who presented with a NSTEMI, type 2 SCAD were found in anterior interventricular artery **(C**, ***green arrow*****)** and posterior interventricular branch of the right coronary artery **(D**, ***red arrow*****)**, respectively; abbreviation in the text.

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