

What Clinicians Should Know About Spontaneous Coronary Artery Dissection

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CME Activity

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Learning Objectives: On completion of this article, you should be able to (1) identify the clinical features, presentation and diagnosis strategies of myocardial infarctions (MIs) caused by spontaneous coronary artery dissection (SCAD), (2) differentiate short-term and long-term management strategies for MI caused by SCAD compared with atherosclerotic MI, and (3) recognize conditions associated with SCAD, especially fibromuscular dysplasia.

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Abstract

Spontaneous coronary artery dissection (SCAD) is an important cause of acute coronary syndrome and sudden death in young persons, particularly women. Associated conditions include fibromuscular dysplasia, peripartum status, and episodes of extreme emotion or exercise. Because of heightened awareness and improved diagnostic accuracy, it is increasingly important for clinicians to understand SCAD. Moreover, short-term and long-term management strategies diverge from typical strategies for atherosclerotic disease. In this Concise Review, we aim to highlight the key points about SCAD, including presentation, diagnosis, associated conditions, and short-term and long-term management.

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Spontaneous coronary artery dissection (SCAD) is an important cause of acute coronary syndrome (ACS), which can occur in young persons, predominantly women, without atherosclerotic coronary artery disease or atherosclerotic risk factors.¹ SCAD causes myocardial ischemia and myocardial infarction (MI) due to obstruction of coronary blood flow from intimal dissection and/or intramural hematoma formation (Figure). Although

originally believed to be rare, with reported prevalence ranging from 0.07% to 1.1%,¹⁻⁴ SCAD is likely more common than previously thought. SCAD due to intramural hematoma without intimal tear may be misdiagnosed on invasive angiography; however, recent heightened awareness and advanced intravascular imaging have improved recognition of SCAD.^{5,6} SCAD is reported as the cause of MI in 10% to 30% women younger than



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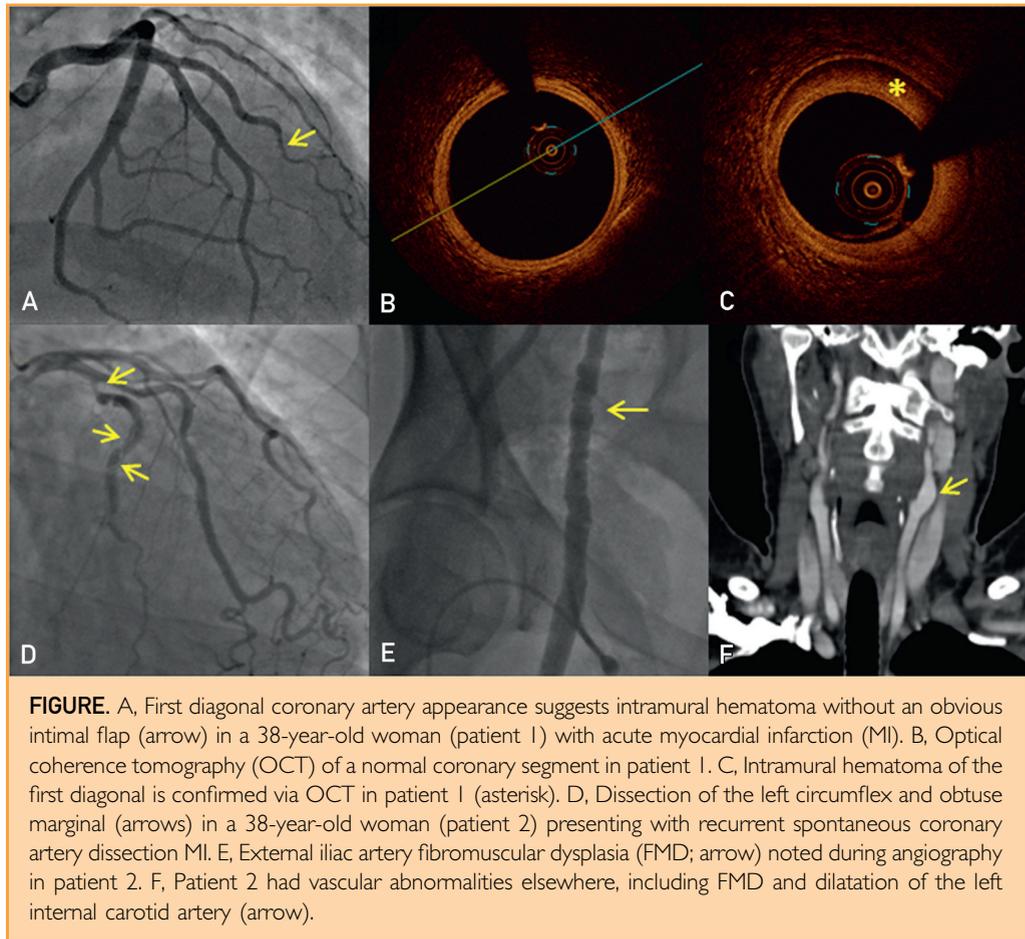


FIGURE. A, First diagonal coronary artery appearance suggests intramural hematoma without an obvious intimal flap (arrow) in a 38-year-old woman (patient 1) with acute myocardial infarction (MI). B, Optical coherence tomography (OCT) of a normal coronary segment in patient 1. C, Intramural hematoma of the first diagonal is confirmed via OCT in patient 1 (asterisk). D, Dissection of the left circumflex and obtuse marginal (arrows) in a 38-year-old woman (patient 2) presenting with recurrent spontaneous coronary artery dissection MI. E, External iliac artery fibromuscular dysplasia (FMD; arrow) noted during angiography in patient 2. F, Patient 2 had vascular abnormalities elsewhere, including FMD and dilatation of the left internal carotid artery (arrow).

50 years^{2,7,8} and is the most common cause of pregnancy-associated MI.⁹

Although SCAD can be a fatal event, most series suggest that early and long-term survival is good.^{1,10} However, the burden of subsequent complications is notable,^{1,10} with 10-year Kaplan-Meier estimated rates of major adverse cardiovascular events, including recurrence, congestive heart failure, MI, and death as high as 47% and SCAD recurrence rates as high as 29%.¹ The natural history of SCAD has been observed as markedly different from atherosclerotic coronary disease, and patients typically have little or no atherosclerotic plaque.¹ Although the precipitants of coronary dissection are uncertain, pathologic evaluations, the absence of typical risk factors, and vessel appearance on intravascular imaging all suggest different pathophysiologic mechanisms than atherothrombotic ischemic MI.^{1,11-13} Accordingly, short-term and long-term management strategies also differ substantially.^{14,15}

SCAD PRESENTATION AND DIAGNOSIS

SCAD presents primarily as non-ST-elevation MI and ST-elevation MI. SCAD can also present as unstable angina or sudden cardiac death.^{1,10} Patients are usually women (74%-92% in published series^{1-3,10}) with a mean age of 42 to 52 years (Table).^{1,10} Typical presenting symptoms are consistent with ACS, including chest pain, dyspnea, diaphoresis, and/or nausea. Diagnostic findings include abnormal electrocardiographic findings, elevated cardiac biomarkers, and regional wall motion abnormalities on echocardiography. Because these patients are often young, fit, and otherwise healthy, SCAD may not be considered in the initial differential diagnosis. This absence of suspicion of evolving ACS in patients with SCAD may preclude or delay proper diagnosis if serial electrocardiograms and troponin levels are not included in the evaluation. Patients instead may be misdiagnosed as having pericarditis, Takotsubo cardiomyopathy, or gastrointestinal reflux without

appropriate workup for ACS. Therefore, an index of suspicion and appropriate exclusion of acute ischemia are indicated.

When ACS is recognized, coronary angiography should be immediately performed. On coronary angiography, SCAD may appear as a double lumen due to contrast filling into an intimal dissection plane (false lumen). However, SCAD commonly presents with intramural hematoma with no visible intimal flap. This can mimic the appearance of vasospasm, atherosclerosis, or normal coronaries. Therefore, in this group, intravascular ultrasonography or optical coherence tomography should be considered at the time of angiography to diagnose intramural hematoma due to SCAD.

SHORT-TERM MANAGEMENT

Correctly diagnosing SCAD is critical because the recommended short-term management differs from guidelines for ACS due to atherosclerotic disease.^{1,14} In particular, patients with SCAD have notably elevated rates of complications from percutaneous coronary interventions (PCIs), even in those who present with preserved coronary blood flow.^{1,10,14} In a series that retrospectively reviewed short-term management strategies of 189 patients, 50% of patients with SCAD presenting with normal or near-normal coronary blood flow had an unsuccessful PCI procedure, and 13% subsequently required emergency coronary artery bypass graft surgery (CABG).¹⁴ A PCI procedure was considered unsuccessful if the interventionalist could not cross the coronary artery with a wire or if there was final loss of coronary blood flow or stenosis greater than 30% after intervention.

In those with occluded coronary blood flow or hemodynamic instability, PCI or CABG can salvage viable myocardium, although the rate of PCI procedure failure may be as high as 53%.¹⁴ However, in patients who are otherwise stable with preserved coronary blood flow, conservative management is associated with favorable outcomes.^{1,10,14,16} Therefore, conservative management with cardiac medications only and close observation are recommended in this subgroup.¹⁴ Conservative medications are empiric and include single-antiplatelet therapy, β -blocker, and statin therapy only for patients with dyslipidemia. A few conservatively managed patients experience clinically significant

TABLE. Features and Management of Spontaneous Coronary Artery Dissection

Typical demographic characteristics
Female
Mean age of 42-52 years (range, teens to ≥ 70 years)
No or minimal atherosclerotic risk factors
Associated conditions
Noncoronary vasculopathy, especially fibromuscular dysplasia
Pregnancy or postpartum state
Extreme stressors
Extreme emotion
Extreme exercise
Connective tissue disorders
Systemic inflammatory states
Presentation
Non-ST-elevation myocardial infarction
ST-elevation myocardial infarction
Ventricular fibrillation arrest
Unstable angina
Diagnosis
Coronary angiography
Intravascular imaging
Intravascular ultrasonography
Optical coherence tomography
Treatment
Preserved coronary blood flow (TIMI 2-3) and hemodynamically stable: conservative therapy with inpatient monitoring (approximately 5 days)
Poor coronary blood flow (TIMI 0-1) and/or hemodynamically unstable: revascularization with percutaneous coronary intervention or coronary artery bypass grafting
Outpatient management
Cardiac rehabilitation
Medical genetics evaluation
Imaging for vascular abnormalities, including fibromuscular dysplasia
Mental health assessment and care
Avoidance of pregnancy
Limitation of exogenous hormones
Long-term cardiology follow-up
TIMI = Thrombolysis in Myocardial Infarction.

progression of dissection in the early period after SCAD presentation, so inpatient monitoring for 5 days is recommended.¹⁴ If a patient experiences progression that leads to vessel occlusion, hemodynamic instability, notable symptoms, or ischemia, emergency revascularization with PCI or CABG should be reconsidered.

ASSOCIATED CONDITIONS

The underlying pathogenesis of SCAD remains unclear. Traditional atherosclerotic risk factors are not common among patients with SCAD. Rather, associated clinical conditions include peripartum status, discrete episodes of extreme exercise or emotion, and connective tissue diseases, such as Marfan syndrome, Ehlers-Danlos syndrome type IV, and Loeys-Dietz syndrome.¹

Some of these patients are fit athletes who regularly exercise without any other clear predisposing factors.¹⁷ Increased coronary vessel eosinophils have been suggested as part of the underlying pathogenesis on early pathology studies, but this theory has been refuted.¹¹⁻¹³ The high prevalence of young women and association with peripartum status indicates a potential hormonal contribution.¹

Recent observations suggest that SCAD may be the manifestation of a systemic vasculopathy distinct from the heritable connective tissue diseases. The presence of extracoronary vascular abnormalities (EVAs) in patients with SCAD, especially fibromuscular dysplasia (FMD), is significant with prevalence rates of 25% to 86%.^{1,18-20} In a series of 115 Mayo Clinic SCAD Clinic outpatients who underwent comprehensive imaging, 66% had detectable EVAs (FMD, aneurysms, dissection, and aortic tortuosity) with wide anatomical distribution, including the abdomen (36%), pelvis (28%), and neck (27%). The most common EVA was FMD (45%).²¹

Coronary artery tortuosity has been found to be markedly more prevalent in patients with SCAD compared with controls matched for age, sex, and hypertension (78% vs 17%; $P < .001$). More so, angiographic features of tortuosity are associated with higher rates of recurrent SCAD and the presence of EVA, including FMD.²²

LONG-TERM MANAGEMENT

Much remains to be learned about long-term management of patients with SCAD. Because patients are at risk for future events, including recurrent SCAD, MI, congestive heart failure, or target vessel revascularization,¹⁴ regular follow-up is pertinent. Follow-up after the initial hospitalization and cardiac rehabilitation (CR) period usually consists of annual visits with an electrocardiogram and comprehensive history and physical examination. Earlier or more frequent visits are indicated, depending on recent course of events (eg, insertion of a stent), symptoms (eg, recurrent chest pain), or changes in health status, such as consideration of elective surgery or pregnancy.

Despite the clear benefits of CR after MI,²³ overall CR participation rates, especially among women, remain low.²⁴ Patients with SCAD are often young women frequently perceived as

otherwise fit. However, CR is encouraged for both emotional and physical health advantages¹⁵ and considered both beneficial and safe among patients with SCAD.²⁵

In a cross-sectional study of 158 SCAD survivors, depression and anxiety symptoms were common, especially among young and peripartum women.²⁶ As such, in addition to encouraging CR participation, monitoring short- and long-term mental health in patients with SCAD is recommended. Recognition of depression and anxiety can help tailor treatment, including therapy to develop adequate coping strategies, family or marriage counseling, or use of antidepressants.

Data-driven recommendations regarding cardiac medications specific to patients with SCAD are lacking. All patients are treated with low-dose aspirin because the marked benefit of aspirin observed in large ACS populations likely outweighs the risk. Those with percutaneous intervention are given dual antiplatelet therapy if indicated by the procedure performed. Statins are not routinely prescribed but recommended for those with hyperlipidemia who meet criteria for treatment on the basis of primary prevention guidelines. β -Blockers or angiotensin-converting enzyme inhibitors are considered in those with left ventricular dysfunction. In the Mayo Clinic SCAD Clinic experience, nitrate-responsive chest pain in the absence of stress-induced ischemia is common and may represent coronary vasospasm. Symptomatic improvement may be achieved with long-acting nitrates or calcium channel blockers. The potential role of TGF- β signaling inhibition for patients with vasculopathy is intriguing but remains undefined. Therefore, routine losartan therapy is not recommended and often poorly tolerated due to hypotension.

Because the pregnant and postpartum states are associated with SCAD, patients are discouraged from pursuing future pregnancy.²⁷ Likewise, hormonal contraceptives or exogenous hormonal therapies are avoided. Instead, alternative options, such as condoms, intrauterine devices, or tubal ligation, are recommended. Low-dose transdermal hormonal therapy may be considered in those with severe menopausal symptoms unresponsive to nonhormonal approaches.

Because of the notable prevalence of EVAs, including FMD among patients with SCAD,

comprehensive imaging of the vasculature is recommended.^{15,18,21} Patients evaluated in the Mayo Clinic SCAD Clinic undergo a one-time, single-acquisition computed tomography angiography of the vasculature spanning the neck to pelvis according to a protocol with radiation reduction strategies designed specifically for patients with SCAD.^{18,21} Imaging of the cerebral vessels can be considered and is recommended for those who are diagnosed as having FMD.^{28,29} Although we typically use computed tomography angiography to image the vasculature because of its higher resolution, magnetic resonance imaging or ultrasonography can be used as alternative imaging modalities. Additional evaluation, imaging, or longitudinal follow-up is pursued as indicated by the abnormalities found on imaging.

Finally, medical genetics counseling is advised for patients with SCAD primarily to elucidate the presence of a relevant family history of SCAD, vasculopathy, or a monogenetic connective tissue disorder. This is particularly relevant because SCAD occurring within families has been observed.³⁰

Many questions remain unanswered regarding the pathogenesis, natural history, and ideal short-term and long-term management decisions for patients with SCAD. The current Mayo Clinic SCAD Registry, initiated by the interest of 2 patients with SCAD and accelerated via the use of social media,³¹ has enrolled more than 450 patients in the "Virtual" Multicenter Spontaneous Coronary Artery Dissection (SCAD), which includes a SCAD DNA biorepository of blood samples from patients and first-degree relatives. The retrospective review and prospective follow-up of these patients are aimed to further understand SCAD and provide evidence-based recommendations.

CONCLUSION

SCAD is an important cause of sudden cardiac death and ACS, particularly in young women. Increased awareness and accurate diagnosis of SCAD are important because the short-term and long-term management strategies differ from those for typical atherosclerotic disease. SCAD has been associated with extreme exercise, emotion, and the peripartum state. Extracoronary vascular abnormalities, including fibromuscular dysplasia, are common and may represent an underlying systemic vasculopathy. Imaging

for extracoronary vascular abnormalities, referral for CR, consideration of mental health, and discussion regarding reproduction are important components of care for patients with SCAD. Because SCAD can initially be misdiagnosed, it is key for clinicians to consider SCAD in patients who have ACS without typical risk factors or coronary atherosclerosis.

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