Fall 12-24-2021

Spontaneous Coronary Artery Dissection

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Doctoral Project III

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PA963: Doctoral Project III

Assignment #1

October 21, 2021

Introduction

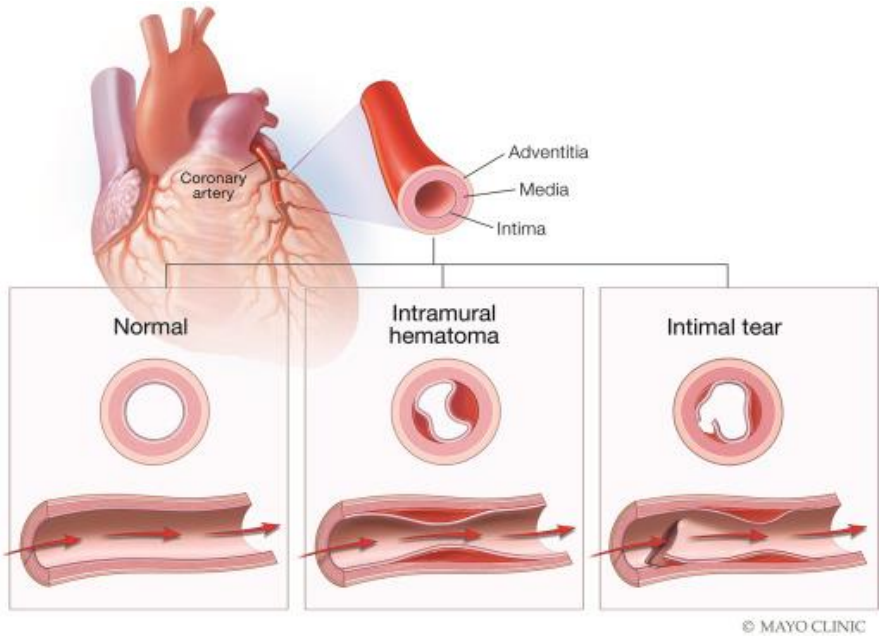
Spontaneous coronary artery dissection (SCAD) is a common cause of myocardial infarction (MI) in women under 50 years old and in peripartum women. To our knowledge, SCAD was first reported in 1931.[1] Until recently, research on SCAD had been lacking and medical providers have overlooked SCAD as a cause of acute coronary syndrome (ACS). In the last 10-15 years, substantial research has contributed to the understanding of SCAD. The presenting symptoms of atherosclerotic ACS and SCAD ACS are indistinguishable, but their pathogenesis differs greatly. Because the pathogenesis of these conditions differ so greatly, so do their risk factors, treatment, after-care management, and recurrence rates. The recent research on SCAD has shown that it is more common than once believed. Because of this, increasing the awareness of SCAD amongst medical professionals is essential to assuring that an index of suspicion for SCAD events in young health women remains high and are appropriately identified, treated, and managed.

Significance

SCAD causes 35% of MIs in women $\leq$ 50 years old, 43% of pregnant women, and 1%-4% of all MIs .[2,3,4,5,6] Spontaneous coronary artery dissection effects young, healthy, peripartum, and pregnant women. MIs caused by atherosclerotic coronary artery disease (CAD) are often precipitated by well-known risk factors such as age, gender, hyperlipidemia, hypertension, heredity, tobacco use, and obesity. As persons with SCAD are typically young and healthy, they do not usually have these risk factors. The lack of typical atherosclerotic CAD risk factors in SCAD patients can lead physician assistants to overlook ACS and MI as the cause of a SCAD patient's chest pain. Increased awareness and understanding of the risk factors precipitating a SCAD event, its diagnosis, treatment, recurrence risks, recurrence

prevention, and identification of concurrent comorbidities is essential to improve overall outcomes for these patients.

Pathophysiology. Unlike the plaque formation vessel obstruction of atherosclerotic CAD, ACS and MIs caused by SCAD occur when an intramural hematoma forms within a cardiac vessel. The dissecting cardiac vessel forms a false lumen that increasingly compresses the vessel's true lumen and obstructs blood flow to the downstream myocardium. The dissection and intramural hematoma is hypothesized to 1) a tear in the intimal layer of the cardiac vessel that leads to the separation of the arterial wall to form a false lumen, or 2) a spontaneous rupture of the vasa vasorum which leads to the formation of a hemorrhage within the vessel wall. In both, an intramural hematoma develops and compresses the artery's true lumen restricting blood flow to the downstream myocardium causing myocardial ischemia, infarction, and the associated complications of this (see Figure 1).[2,7]



Screening. Research has shown that SCAD events typically occur in females between the ages of 30 and 50 years who are otherwise healthy and lack risk factors for atherosclerotic CAD. Common conditions associated with an increased risk for atherosclerotic CAD MIs are age, family history, hypertension, hyperlipidemia, diabetes, obesity, lack of exercise, tobacco use, stress, history of preeclampsia, and some autoimmune disorders.[7] Medical providers use screening tools that target atherosclerotic CAD when assessing patients with chest pain. When CAD screening tools are applied to a SCAD patient with chest pain, the screening is often unremarkable. Assessments that identify little to no risk for CAD in SCAD patients with chest pain can lead medical providers to erroneously overlook ACS and MIs caused by SCAD. Some medical conditions have been linked to an increased risk for a SCAD event. Screening for these may help PAs identify young, healthy females with chest pain as having a SCAD event.

Many of SCAD patients have a history of fibromuscular dysplasia (FMD), pregnancy, multiparity (> 4 births), migraine headaches, inherited arteriopathy or connective tissue disorders, use of exogenous hormones, and/or systemic inflammatory disease (See Table 1).[8] Additionally, SCAD patients have reported similarities in precipitating activities or factors preceding their SCAD event such as consistencies in vigorous exercise, stressful turmoil, and/or menstrual or peripartum states around the time of their SCAD events (see Table 2).[9]

Table 1. Conditions Associated with SCAD and Atherosclerotic MIs

Conditions Associated with SCAD	Conditions Associated with Atherosclerotic MIs
Fibromuscular Dysplasia	Age: Men age 45 or older and Women 55 or older

Pregnancy	Family History
Multiparity (≥4births)	Hypertension
Migraine Headaches	Hyperlipidemia
Exogenous hormones: oral contraceptives, postmenopausal therapy, infertility treatments, testosterone, corticosteroids.	Diabetes
Stress	Stress
Possibly History of Preeclampsia	History of Preeclampsia
	History of Tobacco Use
	Lack of Physical Activity
	Autoimmune Condition: Rheumatoid Arthritis, Lupus
	History of preeclampsia

Table 2. Precipitating Factors to SCAD and Atherosclerotic MIs

Precipitating Factors to SCAD	**Precipitating Factors to Atherosclerotic MIs**
Intense Exercise (isometric or aerobic)	Sudden change in position, typically occurring after awakening from sleep
Sexual Activity	Sexual Activity
Recreational Drugs (cocaine, methamphetamines)	Recreational Drugs (cocaine, methamphetamines)
Intense Emotional Stress	
Labor and Delivery	
Intense Valsalva (retching, vomiting, bowel movement, coughing, lifting heavy objects)	
Exogenous hormones/hormone modulators	
B-hcg Injections, Steroid Injections, Clomiphene	

Diagnosis. Regardless of their cause, both atherosclerotic and SCAD ACS and MIs typically present with chest pain and are often detected by electrocardiogram (ECG) and/or elevations in troponin. SCAD cases present as ST-segment-elevation MIs in up to 87% of patients, non-ST-segment-elevation MI in up to 69% of patients, cardiogenic shock in 5% of patients, and ventricular arrhythmias/sudden cardiac death in up to 11% of patients.[2,7] SCAD events often present suddenly and with intense symptoms. This leads SCAD patients to seek immediate medical evaluation within the first few hours of the onset of their symptoms. Troponin levels measured within the first few hours of an ACS episode may be normal. The 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation ACS (NSTE-ACS) recommends repeating a troponin level in persons with concern for ACS at 3 and 6 hours if the prior have been normal.[10] Serial troponins can be crucial in identifying an ACS event in a patient with new onset NSTE-ACS. Once an ECG indicating cardiac ischemia or an elevated troponin level has been identified, further evaluation with coronary angiography is warranted.

Coronary angiography is the gold standard for the diagnosis of acute SCAD. If the diagnosis of SCAD is uncertain on coronary angiography, intracoronary imaging, such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT), may be used. Because OCT requires the use of forceful contrast injection and wiring of the vessel, it could increase the risk for further dissection.[11]

Management. SCAD is best treated conservatively. Cardiac revascularization with coronary artery bypass grafting, or percutaneous coronary intervention is used less often because they pose risk for further injury to the affected vessel.[7] However, cardiac revascularization is sometimes necessary to stabilize a patient depending on the degree of injury

to the myocardium. The duration of hospitalization and observation following a SCAD event has been under investigation. The cardiac injury caused by SCAD typically occurs over time as the cardiac artery dissection. A retrospective SCAD registry study found that 1:6 SCAD patients treated conservatively experienced recurrent MI within the first 14 days from their initial episode due to the extension of their original dissection.[11] In response to this, patients with a SCAD event are admitted for cardiac observation. During this time, medication interventions are initiated (see Table 3), and patients undergo cardiac monitoring. Cardiac monitoring is important as there is a risk the dissected vessel will dissect further on its own, causing an increased risk for dissection complications from the resulting myocardial ischemia such as ventricular arrhythmias, heart failure, cardiac arrest, and death.[2] In cases where the SCAD event results in left main or proximal 2-vessel dissection, then CABG should be considered and weighed against its risks for further vessel injury. In cases where the SCAD event results in active or ongoing ischemia or hemodynamic instability, percutaneous coronary intervention or CABG should be considered and weighed against their risks of further vessel injury and based on the local surgeons' expertise of these therapies. While most SCAD patients do well with conservative measures and observation, it is estimated that about 14% of hospitalized SCAD patients require revascularization.[2]

Post-SCAD medication recommendations include clopidogrel, aspirin, β-adrenergic blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins for those meeting treatment guidelines for hyperlipidemia.[7,8] Clopidogrel is typically reduced quickly following a SCAD event. However, the long-term outcomes of this treatment warrant further investigation. Aspirin 81mg a day is also initiated following a SCAD event and often continued indefinitely (Table 3).[8] Because of the increased risk for bleeding and menorrhagia,

along with the current uncertainty of its benefits in SCAD survivors, individual consideration and selection of aspirin use is necessary. Many experts recommend β-blocker use in all SCAD patients while others suggest their use should be limited to those with left ventricular dysfunction, arrhythmias, or hypertension.[2,8] Consistent with national guidelines for treatment after an MI, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers should be used for left ventricular systolic dysfunction. Statins should be used in accordance with current hyperlipidemia guidelines and not routinely after a SCAD event. Finally, SCAD patients often experience chest pain following their event and therapies such as nitrates, β-blockers, calcium channel blockers, and ranolazine can offer relief.[2,8]

Table 3. Common Treatments Used for Acute SCAD and Atherosclerotic ACS/MIs

Acute SCAD Management	**Acute Atherosclerotic ACS/MI Management**
Aspirin 325mg, sublingual nitroglycerine, and oxygen at the onset of chest pain	Aspirin 324mg, sublingual nitroglycerine, and oxygen at the onset of chest pain
Cardiac Catheterization: avoid interventional procedures if possible	Cardiac Catheterization: Cardiac Stent or Bypass procedure when possible
Observation/Hospitalization	Thrombolytics
Daily aspirin 81mg, possibly clopidogrel for a year or less	Antiplatelet Therapy
β -blocker	β -blocker
ACE inhibitor if CHF	ACE inhibitor
CMF GDMT as warranted	Statins
Nitrates, Calcium channel blockers and ranolazine as needed.	

Post-SCAD management and counseling also differs from that of atherosclerotic ACS and MIs (See Table 4). Lifestyle, exercise, stress management, and psychological health are

crucial therapeutic topics of counseling for SCAD survivors. Many SCAD survivors report being counselled on lifestyle changes and therapies that target traditional atherosclerotic CAD rather than the non-atherosclerotic causes of SCAD. SCAD survivors are typically young, healthy women who exercise, eat well, and do not have the usual risk factors for atherosclerotic CAD. It is important for physician assistants to be familiar with the precipitating factors for SCAD events and use this information to support their evaluation for SCAD and counseling of SCAD survivors. Precipitating factors include hormone changes, intense exercise (isometric or aerobic), intense valsalva (vomiting, bowel movement, coughing, lifting heavy objects), labor and delivery, intense emotional stress, recreational drugs (cocaine, methamphetamines), exogenous hormones, β-hCG injections, corticosteroid injections, and clomiphene.[8,9,10] Additionally, underlying medical conditions have been associated with an increased risk for SCAD events. Post-SCAD care includes evaluation for the prior associated conditions, counseling on the risk factors associated with SCAD recurrence such as stress, anxiety, pregnancy, exogenous estrogen, and intense exercise (See Table 2).[8,9,10]

Table 4. Aftercare management of SCAD and Atherosclerotic ACS/MIs.

Cardiac Rehab	Cardiac Rehab
Pregnancy prevention counseling	Dietary counseling and modification
Avoid exogenous estrogen	Exercise
Behavioral health counseling	Manage hypertension, hyperlipidemia and other predisposing factors.
Stress management	
Avoid strenuous exercise (aerobic/isometric)	

CT head-pelvis and renal ultrasound to screen for additional vessel abnormality (FMD)	
Genetic evaluation for predisposing conditions	
Management of any identified predisposing conditions (fibromuscular dysplasia, autoimmune and connective tissue disorders)	

SCAD recurrence. A prospective study of 115 patients with a median follow-up of 21 months from their first SCAD event, documented a 4.7%-22% risk of SCAD recurrence (20% 5-year Kaplan–Meier estimates, 2.8%/y).[8,9] As compared to CAD MIs, the risk for CAD MI recurrence is 80 per 1000 person-years in men and 77 per 1000 person-years in women.[8,13]

Screening for vascular and connective tissue abnormalities in post-SCAD patients is also recommended. Greater than 60% of SCAD patients have some form of extracoronary vascular arteriopathies (EVAs) such as dilatation, tortuosity, aneurysm, dissection, or fibromuscular dysplasia (FMD). FMD, a nonatherosclerotic arteriopathy, is the most common vascular abnormality and occurs in multiple anatomical areas, most frequently in the head, abdomen (abdominal aorta and renal arteries), pelvis (iliac arteries), and neck (cervical and internal carotid arteries).[8,10,11,16.] Intracranial abnormalities are not uncommon regardless of whether EVAs or FMD are identified elsewhere, and this has led researchers to recommend intracerebral imaging in most SCAD survivors.[8,9,11] At present, recommendations for follow-up and maintenance screening are not well defined and often deferred to vascular specialists with a knowledge of EVAs and FMD.[8] Further study evaluating larger cohorts and increased follow-up duration is needed to better understand the implications of FMD and EVAs on SCAD patients.

Conclusion

Increasing the awareness and understanding of SCAD is essential as SCAD causes 35% of ACS and MIs in women under the age of 50 years. Both SCAD and atherosclerotic CAD cause acute coronary syndrome and myocardial infarctions, but due to their pathogenesis, they differ significantly. Recognizing the precipitating factors and associated conditions of SCAD will help physician assistants screen, diagnosis, and appropriately treat SCAD patients. Understanding the difference in pathophysiology and risk factors for SCAD will enable PAs to treat and counsel SCAD survivors using the best evidence available.

Key Points

- SCAD causes 35% of myocardial infarction in women under the age of 50 years old
- Physician assistants must maintain a high index of suspicion for SCAD events in young, healthy, and perinatal women presenting with chest pain.
- Risk factors for SCAD differ from coronary artery atherosclerotic myocardial infarction risk factors.
- Observation and pharmacological therapies are the preferred methods of treatment for a SCAD event. Interventional therapies with stent or bypass may be pursued if necessary.
- Post-SCAD care includes CTA evaluation of the head, neck, chest, abdomen, and pelvis to look for extracoronary vascular abnormalities; cardiac rehabilitation; consideration of antiplatelet therapies (clopidogrel and aspirin), pregnancy prevention counseling; screening for underlying vascular and connective tissue disorders; blood pressure management with a goal of 120/80 or less; stress

management; behavioral health counseling with a focus on anxiety and depression; exercise and activity counseling; and avoidance of triptans in migraine headache.

References

1. Saw J, Mancini GBJ, Humphries KH. Contemporary review on spontaneous coronary artery dissection. *J Am Coll Cardiol.* 2016;68:297-312.

2. Hayes SN, Kim ESH, Saw J, et al. Spontaneous coronary artery dissection: current state of the science: a scientific statement from the American Heart Association. *Circulation.* 2018;137:e523-e557.

3. Nishiguchi T, Tanaka A, Ozaki Y, Taruya A, Fukuda S, Taguchi H, et al. Prevalence of spontaneous coronary artery dissection in patients with acute coronary syndrome. *Eur Heart J Acute Cardiovascular Care*. 2016;5:263-270.

4. Rashid HN, Wong DT, Wijesekera H, Gutman SJ, Shanmugam VB, Gulati R, et al. Incidence and characterization of spontaneous coronary artery dissection as a cause of acute coronary syndrome – a single-center australian experience. Int J Cardiol. 2016;202:336-338.

5. Tweet MS, Eleid MF, Best PJ, Lennon RJ, Lerman A, Rihal CS, et al. Spontaneous coronary artery dissection: revascularization versus conservative therapy. *Circ Cardiovascular Interv*. 2014;7:777-786

6. Saw J, Aymong E, Mancini GB, Sedlak T, Starovoytov A, Ricci D. Nonatherosclerotic coronary artery disease in young women. *Can J Cardiol.* 2014;30:814-819.

7. Saw J. Spontaneous coronary artery dissection. *Can J Cardiol* 2013;29:1027-33.

8.Tweet MS, Kok SN, Hayes SN. Spontaneous coronary artery dissection in women: What is known and what is yet to be understood. *Clin Cardiol*. 2018;41(2):203-210. doi:10.1002/clc.22909

9. Clare R, Duan L, Phan D, Moore N, Jorgensen M, Ichiuji A, et al. Characteristics and clinical outcomes of patients with spontaneous coronary artery dissection. *J Am Heart Assoc.* 2019;8:e012570.

10. Tweet MS, Hayes SN, Codsi E, Gulati R, Rose CH, Best PJM. Spontaneous coronary artery dissection associated with pregnancy. *J Am Coll Cardiol*. 2017;70(4):426-435. doi:10.1016/j.jacc.2017.05.055

11. Prasad M, Tweet MS, Hayes SN, Leng S, Liang JJ, Eleid MF, et al. Prevalence of extracoronary vascular abnormalities and fibromuscular dysplasia in patients with spontaneous coronary artery dissection. *Am J Cardiol.* 2015;115:1672-1677.

12. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64(24):e139-e228. doi:10.1016/j.jacc.2014.09.017

13. Waterbury TM, Tweet MS, Hayes SN, Eleid MF, Bell MR, Lerman A, et.al.. Early natural history of spontaneous coronary artery dissection. *Circ Cardiovasc Interv.* 2018 Sep;11(9):e006772. doi: 10.1161/CIRCINTERVENTIONS.118.006772.

14. Lebrun S, Bond RM. Spontaneous coronary artery dissection (SCAD): The underdiagnosed cardiac condition that plaques women. *Trends in Cardiovascular Medicine.* 2018;28:340-345.

15. Peters SAE, Colantonio LD, Dai Y, et al. Trends in recurrent coronary heart disease after myocardial infarction among US women and men between 2008 and 2017. *Circulation*. 2021;143(7):650-660. doi:10.1161/CIRCULATIONAHA.120.047065

16. Saw J, Humphries K, Aymong E, et al. Spontaneous coronary artery dissection: clinical outcomes and risk of recurrence. *J Am Coll Cardiol*. 2017;70(9):1148-1158. doi:10.1016/j.jacc.2017.06.053