JACC: CARDIOVASCULAR IMAGING
VOL. 9, NO. 4, 2016

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2016.01.009

Multimodality Imaging for Spontaneous Coronary Artery Dissection in Women

Marysia S. Tweet, MD,[a] Rajiv Gulati, MD, PhD,[a] Eric E. Williamson, MD,[b] Terri J. Vrtiska, MD,[c] Sharonne N. Hayes, MD[a]

ABSTRACT

Spontaneous coronary artery dissection (SCAD) has gained attention as a key cause of acute coronary syndrome and sudden cardiac death among women. Recent advancements in cardiac imaging have improved identification and accelerated awareness of SCAD. Accurate diagnosis of SCAD through use of imaging is critical, as emerging evidence suggests that the optimal short- and long-term management strategies for women with SCAD differs substantially from that of women with atherosclerotic coronary disease. This review summarizes the application of both invasive and noninvasive imaging for the diagnosis, assessment, surveillance, and treatment of women affected by SCAD.
(J Am Coll Cardiol Img 2016;9:436–50) © 2016 by the American College of Cardiology Foundation.

Spontaneous coronary artery dissection (SCAD) is emerging as a much more common cause of acute coronary syndrome and sudden cardiac death than previously recognized, especially in women. The primary event at the level of the arterial wall may involve hematoma formation in the media, separation of the intimal layer, or both. These processes are distinct from atherosclerosis. Antegrade coronary blood flow may be directly impeded by an intimal dissection plane within the lumen or indirectly compromised by compression from medial hematoma. The consequence of the dissection process may be myocardial ischemia, myocardial infarction (MI), or sudden cardiac death. Unlike atherosclerotic coronary artery disease, SCAD has a propensity for young women without traditional risk factors (1), some of whom are highly fit (2).

SCAD was previously considered a rare event, a belief reinforced by published reports of only isolated cases, small single-center case series, and postmortem descriptions. Due to a combination of heightened awareness of the impact of heart disease in women and SCAD in particular, the availability of sensitive biomarker assays, the advent of adjunctive intravascular imaging during coronary angiography (CA), and prevalent noninvasive vascular imaging (3), SCAD is now more commonly recognized. Subsequently, this has amplified familiarity of the SCAD angiographic patterns in patients who may have previously been misdiagnosed as atherosclerosis, spasm, or vasculitis. Despite recent estimates of higher prevalence than previously reported (1,4), SCAD remains incompletely understood. Ongoing efforts aim to further define SCAD and delineate the environmental, molecular and genetic contributors to incident SCAD. Both invasive and noninvasive cardiovascular imaging techniques are integral to the diagnosis, characterization, and management of patients with SCAD. Moreover, multimodality imaging is critical for ongoing efforts to elucidate the cause and mechanism of SCAD. This report reviews the role of multimodality imaging in the diagnosis, evaluation, surveillance, and treatment of women with this condition (**Central Illustration**).

EPIDEMIOLOGY, ETIOLOGY, AND DEMOGRAPHICS

SCAD prevalence remains uncertain and in retrospective studies has been reported as 0.07% to 1.1% (1,5–7). With the exception of 1 community-based study, these studies determined prevalence via angiographic databases, some of which included forensic databases and/or patients who had dissection associated with

From the [a]Division of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota; [b]Division of Cardiovascular Radiology, Department of Radiology, Mayo Clinic, Rochester, Minnesota; and the [c]Division of Abdominal Radiology, Department of Radiology, Mayo Clinic, Rochester, Minnesota. The Mayo Clinic SCAD and DNA Registries are funded in part by the Mayo Clinic Division of Cardiovascular Diseases and SCAD Research, Inc. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received October 2, 2015; revised manuscript received January 12, 2016, accepted January 28, 2016.

atherosclerosis. In addition, these studies included patient cohorts undergoing diagnostic angiography prior to the use of intravascular imaging such as intravascular ultrasound (IVUS) or optical coherence tomography (OCT), which are pertinent for distinguishing SCAD when obvious features are not apparent on angiography (8). Forensic databases may be limited as SCAD can be missed at autopsy if it is not specifically considered in the differential at the time of postmortem examination, and fatal dissections can occur in the distal coronary arteries not be routinely examined (9). Therefore, these aforementioned studies likely under-appreciate the frequency of SCAD (8,10,11) with SCAD being more prevalent, chiefly in women, than previously reported when intravascular imaging is employed (12).

The first description of coronary dissection is credited to Dr. Pretty (13) in 1931, who described the sudden death of a 42-year-old multiparous and otherwise healthy woman following chest pain, nausea and vomiting. Autopsy revealed dissection and rupture of the right coronary artery. Since then, autopsy series have observed SCAD in young women but have not provided conclusive evidence of its underlying pathogenesis. In 1982, Robinowitz et al. (14) evaluated the coronary arteries in 8 women with SCAD and range of 26 to 47 years of age, 75% of whom presented with sudden cardiac death. In these patients, dissection occurred primarily in the outer third of the media with inflammatory infiltrates, predominantly eosinophilic granulocytes, noted in the adventitia. Out of these observations came a proposed mechanism for dissection whereby localized eosinophilia with hormone-enhanced release of lytic collagenase, peroxidase, acid phosphatase, and major basic protein lead to erosion of the coronary media and adventitia (15,16). However, another series found that eosinophilic infiltrates are not consistently present and may be a reactionary mechanism (17). Inherent abnormalities and neovascularization of the underlying vasa vasorum are thought to increase susceptibility for plaque rupture in typical atherosclerosis (18); one may hypothesize that dysfunctional vasa vasorum could contribute to the underlying pathogenesis of SCAD.

In recent series, patients with SCAD are most often women (74% to 92%) with mean age ranging from 42 to 52 years (1,19). Patients present with acute coronary syndrome including ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, and sudden cardiac death (1,19). Predisposing factors may include female sex; extracoronary vascular abnormalities (EVA) such as fibromuscular dysplasia (FMD), coronary/arterial tortuosity, peripartum state, recent episode of extreme emotion or exertion, and connective tissue disorders (1,19,20). Among women with SCAD, up to 18% of dissections are associated with the peripartum/pregnant state (1). The presence of any EVA in patients with SCAD is high and includes aneurysms, noncoronary dissections and most commonly, FMD. The prevalence of FMD among SCAD patients has been observed as high as 25% to 86% (21–24).

Discriminating SCAD from atherosclerotic disease in the acute setting is particularly important given the markedly elevated risks of percutaneous coronary intervention with SCAD (1,25). In patients presenting with definite MI, SCAD is most often diagnosed by characteristic findings on CA. Selective utilization of adjunctive imaging techniques, specifically intravascular imaging, may increase diagnostic sensitivity (26). In uncertain cases of SCAD, such as those patients with a borderline troponin elevation and nonspecific findings on electrocardiogram, other imaging modalities such as coronary computed tomography angiography (CTA), echocardiography, myocardial perfusion imaging (MPI), or cardiac magnetic resonance (CMR) may suggest myocardial ischemia or infarction, which may then lead to CA and accurate diagnosis. Examples of this include regional wall motion abnormalities on echocardiography, decreased myocardial perfusion on coronary CTA, or regional endocardial or late gadolinium enhancement on CMR.

In light of the fact that SCAD vessels can heal with conservative management alone (1,19,27,28) in contrast to the approach to those with atherosclerotic obstruction, interventionalists are increasingly taking a “less is more” approach. Thus, percutaneous coronary intervention is avoided in stable SCAD patients who have preserved flow, even in the presence of significant obstruction or infarction (27). However, percutaneous coronary intervention or coronary artery bypass graft surgery remains appropriate for those patients who are clinically unstable or demonstrate compromised coronary blood flow, even if pregnant (**Figure 1**) (27). There are insufficient data to favor one revascularization technique over another, so decisions should be made based on individual patient characteristics and availability of surgical and interventional expertise.

The rate and frequency of healing and SCAD extension is not yet known. However, an important subset of patients initially treated conservatively may experience clinically significant SCAD progression

ABBREVIATIONS AND ACRONYMS

CA = coronary angiography

CMR = cardiac magnetic resonance

CTA = computed tomography angiography

EVA = extracoronary vascular abnormalities

FMD = fibromuscular dysplasia

IVUS = intravascular ultrasound

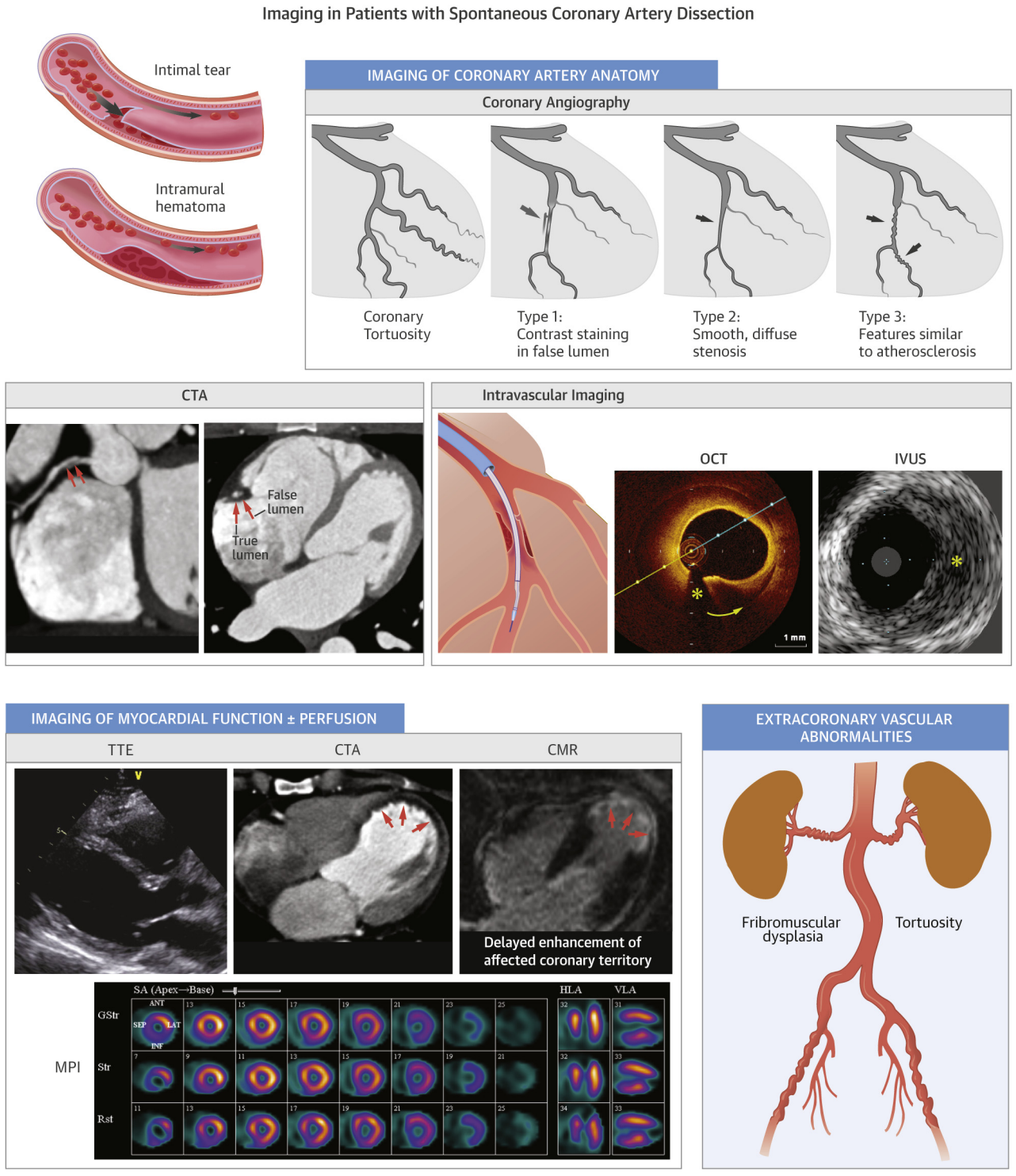
MPI = myocardial perfusion imaging

OCT = optical coherence tomography

PET = positron emission tomography

SCAD = spontaneous coronary artery dissection

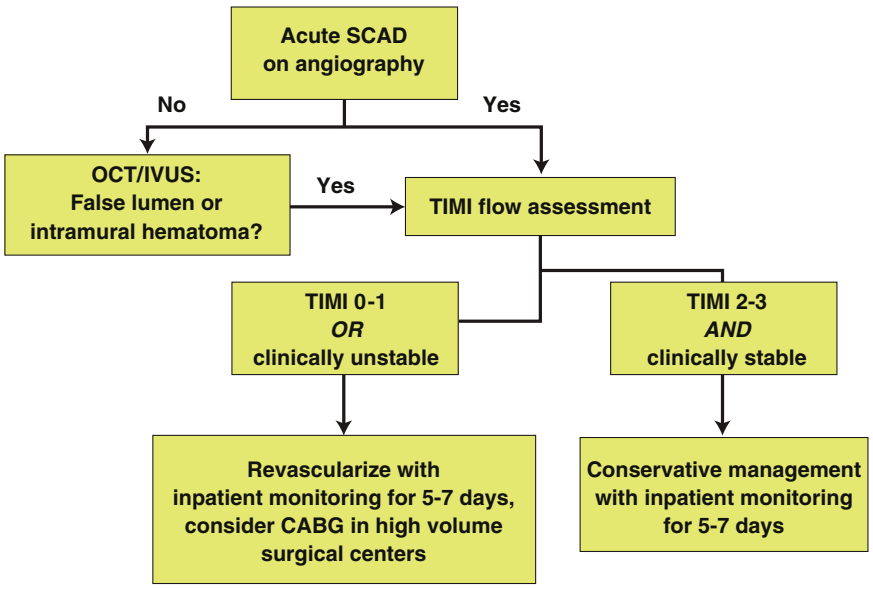
CENTRAL ILLUSTRATION **Imaging in Patients With Spontaneous Coronary Artery Dissection**



Tweet, M.S. et al. J Am Coll Cardiol Img. 2016; 9(4):436-50.

Continued on the next page

FIGURE 1 SCAD Management



Proposed management algorithm based on a study of acute management of 189 spontaneous coronary artery dissection (SCAD) patients. IVUS = intravascular ultrasound; OCT = optical coherence tomography; TIMI = Thrombolysis In Myocardial Infarction. Reprinted with permission from Tweet et al. (4).

and require revascularization, suggesting a role for more prolonged clinical observation during the acute management of these patients (27). EVA including spontaneous dissections in other arterial territories are common in SCAD; therefore, the risks of routine CA to monitor for healing outweigh potential benefits. Future use of coronary CTA may discern the natural history of SCAD coronaries with minimal procedural risk to the patient.

Initial proper diagnosis of MI etiology is critical, as it has important implications for acute and long-term management, subsequent evaluations, prognosis, physical activity guidelines, and reproductive decisions. Even though SCAD series have reported good short- and long-term survival (1,19), patients remain at risk for considerable burden of major adverse cardiac events, many of which are recurrent SCAD MIs usually occurring in a different coronary territory (1). Therefore, SCAD patients require continued cardiovascular follow-up and judicious application of cardiac imaging based upon pertinent clinical events.

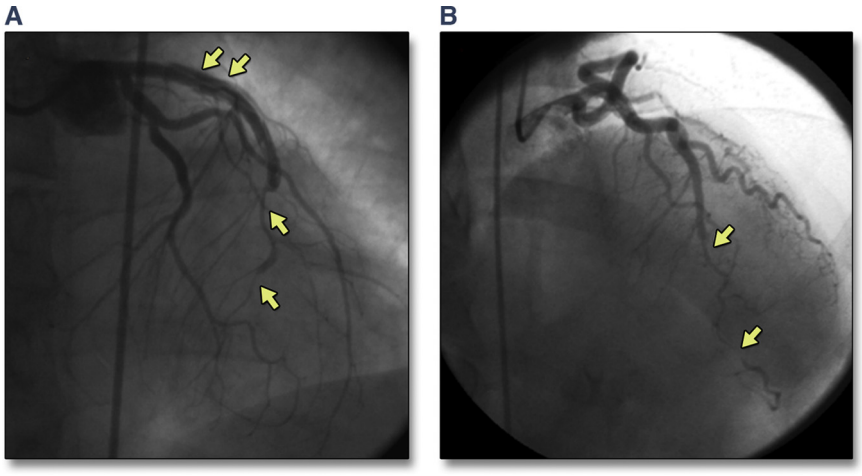
SCAD IMAGING

CA AND INTRAVASCULAR TECHNIQUES. Invasive CA with intravascular imaging is the gold standard for the diagnosis of acute SCAD even among pregnant or young women in whom radiation exposure may be of concern. On CA, SCAD appears as a

CENTRAL ILLUSTRATION Continued

Multimodality imaging is integral to studying both coronary anatomy and myocardial perfusion of patients with SCAD. The **top left panel** demonstrates SCAD coronary intimal disruption and intramural hematoma. The **right upper panel** shows patterns of SCAD as seen on coronary angiography. The **middle left panel** demonstrates an example of SCAD as seen on CTA. The **middle right panel** shows intravascular findings of intramural hematoma on OCT and IVUS as demarcated by the **asterisks**. The **left lower panel** demonstrates the use of TTE for regional wall motion assessment, CTA for myocardial perfusion assessment (**arrows** demonstrate lack of contrast in the LAD territory), and CMR demonstrating late gadolinium enhancement consistent with myocardial infarction, fibrosis or inflammation (**arrows** demonstrate late gadolinium enhancement in the LAD territory). The **left lower panel** also shows an example of MPI in a SCAD patient with lack of perfusion in the LAD territory. The **right lower panel** demonstrates extracoronary vascular abnormalities including fibromuscular dysplasia which are commonly observed in patients with SCAD. CMR = cardiac magnetic resonance; CTA = computed tomography angiography; LAD = left anterior descending; IVUS = intravascular ultrasound; MPI = myocardial perfusion imaging; OCT = optical coherence tomography; SCAD = spontaneous coronary artery dissection; TTE = transthoracic echocardiography.

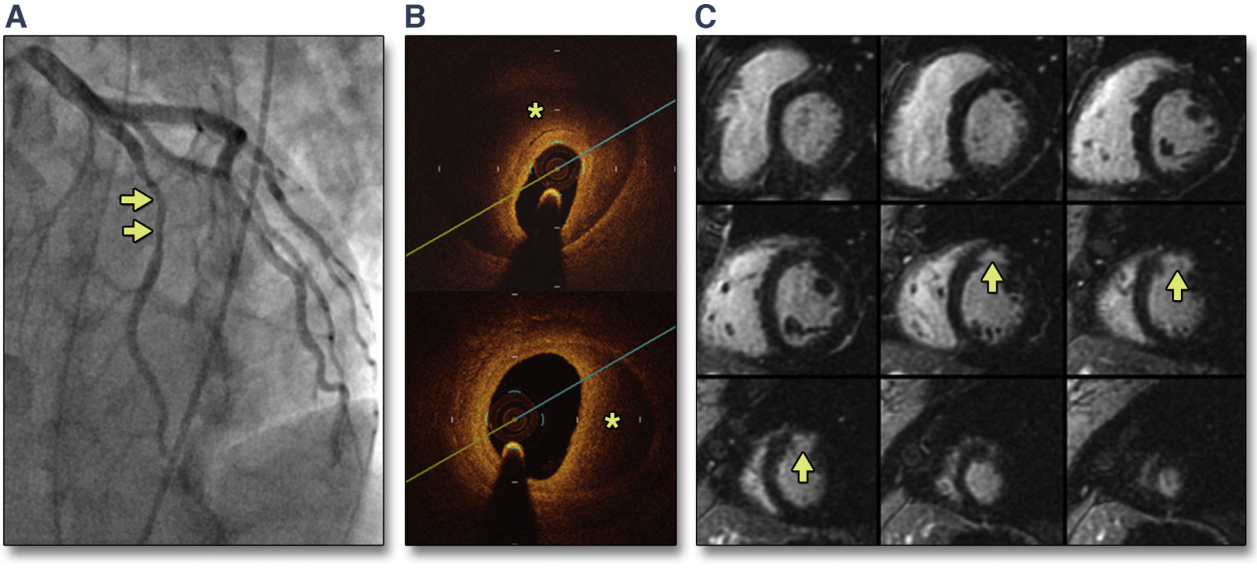
FIGURE 2 SCAD on Coronary Angiography



Two patient examples of SCAD affecting the left anterior descending coronary artery **(arrows)**. The first patient **(A)** is a 37-year-old female who presented with chest pain following exertion and ST-segment elevation myocardial infarction. The second patient **(B)** is a 40-year-old female who presented with chest pain and non-ST-segment elevation myocardial infarction. Abbreviation as in Figure 1.

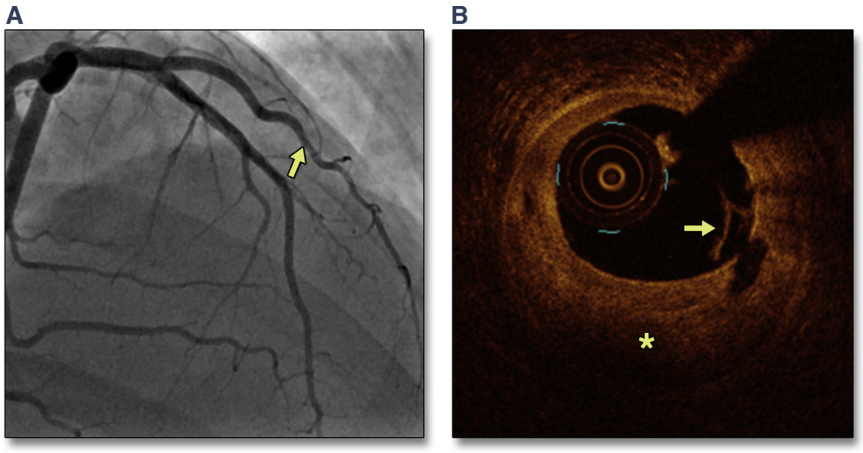
noniatrogenic, nonatherosclerotic dissection plane with contrast filling into the false lumen (Figure 2). Subtle dissection planes or smooth stenoses primarily from intramural hematoma may not be apparent on CA alone, contributing to a misdiagnosis of atherosclerosis, vasospasm or normal coronary arteries (Figures 2 and 3, Online Videos 1 and 2). In a cohort of 168 SCAD patients (92% women),

FIGURE 3 Use of OCT and Cardiac Magnetic Resonance in SCAD



Patient example of a 43-year-old female who presented with ventricular fibrillation and uncertain narrowing in the mid left anterior descending coronary artery **(A, arrows)**. OCT confirmed intramural hematoma **(B, asterisks)**, and cardiac magnetic resonance demonstrated late gadolinium enhancement consistent with transmural infarct in the corresponding myocardial territory **(C, arrows)**. See Online Videos 1 and 2. Abbreviations in Figure 1.

FIGURE 4 Use of OCT in SCAD

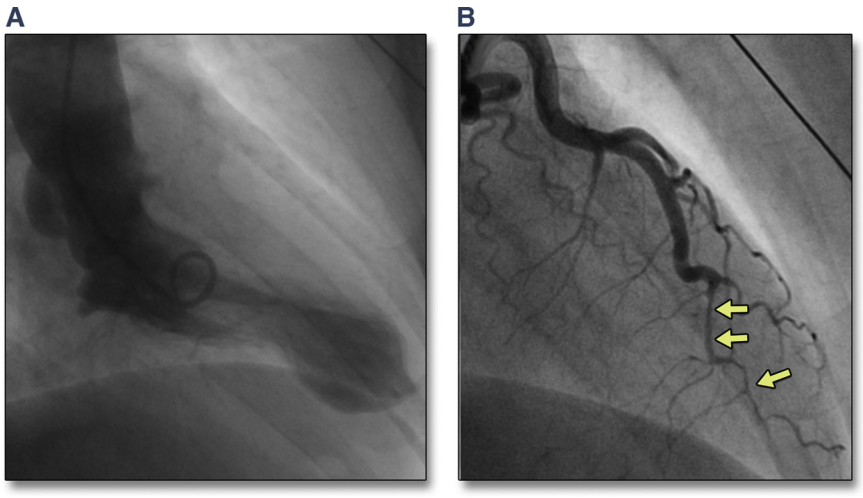


Patient example of a 38-year-old female with history of chest pain, non–ST-segment elevation myocardial infarction, and ambiguous lesion in the diagonal coronary artery **(A, arrow)**. OCT showed separation of the intima **(B, arrow)** and intramural hematoma **(B, asterisk)**. Abbreviations in Figure 1.

the majority (67%) had SCAD, which appeared as diffuse stenosis, whereas only 29% appeared as having multiple lumens due to contrast staining into a false lumen and 4% had an appearance mimicking atherosclerosis (19,29). These patterns have been referred to as Type 2, Type 1, and Type 3, respectively (29).

IVUS and OCT can clarify the ambiguous appearance of SCAD (10,30), and both techniques can visualize the coronary intima, media, and adventitia with identification of intramural hematoma ± intimal disruption (Figure 4). IVUS was introduced in the 1980s and provides grayscale images of the coronary vessel and wall via a catheter with an ultrasound

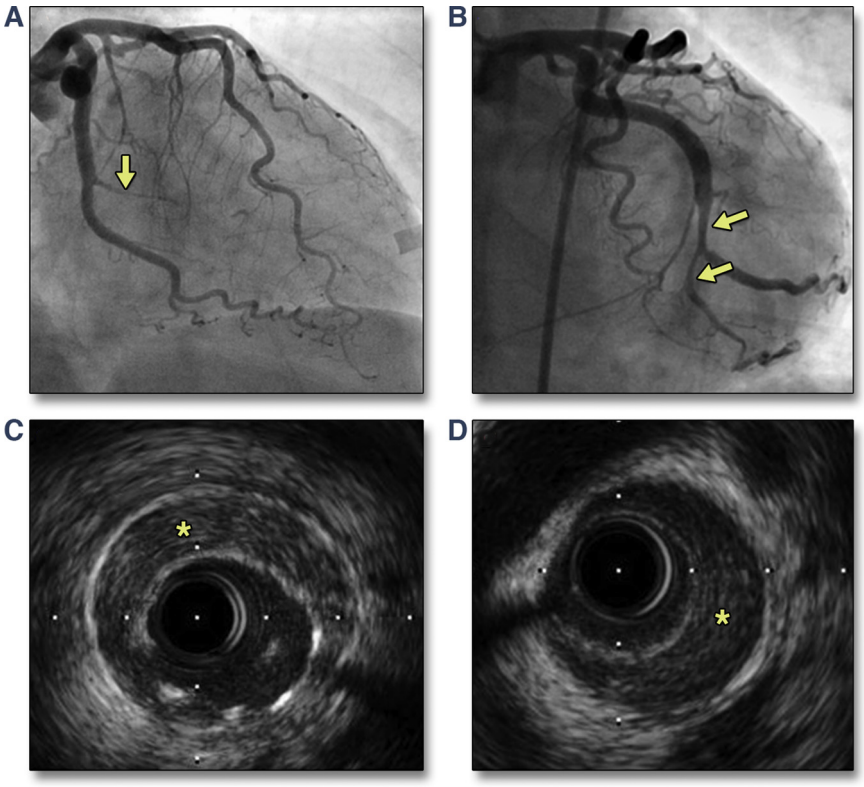
FIGURE 5 SCAD Presenting With Left Ventricular Wall Motion Similar to Takotsubo Cardiomyopathy



Patient example of a 53-year-old female who presented with ST-segment elevation myocardial infarction. The ventriculogram appeared similar to that of Takotsubo cardiomyopathy **(A)**; coronary angiogram revealed SCAD of the left anterior descending coronary artery **(B, arrows)**. See Online Video 3. Abbreviation as in Figure 1.

JACC: CARDIOVASCULAR IMAGING, VOL. 9, NO. 4, 2016
APRIL 2016:436–50

FIGURE 6 Use of IVUS in SCAD



Patient example of a 55-year-old female who presented with chest pain, non–ST-segment elevation myocardial infarction, and SCAD of the obtuse marginal coronary artery **(A, arrow)**. Her SCAD was treated with 2 stents with subsequent propagation of the hematoma **(B, arrows)**. IVUS showed an underexpanded stent in the setting of hematoma **(C, asterisk)** and hematoma in the nonstented region **(D, asterisk)**. Abbreviations as in **Figure 1**.

tip (31). IVUS is a familiar technique that is widely available, provides satisfactory depth of visualization, and does not require contrast. However, it has limited resolution, which can result in diagnostic uncertainty. OCT provides high-resolution (<10 μm) images via detected backscatter of near-infrared light (31) with enhanced diagnostic certainty. OCT also can give insight to the structure of the vasa vasorum (32) and further elucidate SCAD mechanisms (1,27). However, OCT requires a firm contrast injection with the theoretical risk of hydraulic worsening of dissection, and the image detector is proximal to distal tip of catheter, which may limit imaging of the distal segment.

Intravascular imaging can also help differentiate SCAD from Takotsubo cardiomyopathy. SCAD patients may demonstrate septal and apical wall motion abnormalities similar in appearance to Takotsubo cardiomyopathy due to SCAD of the left anterior descending coronary territory (**Figure 5**, Online Video 3). Particularly if there is not an overt dissection plane on angiography, patients may be misdiagnosed, as Takotsubo cardiomyopathy also commonly affects women in the setting of stress although typically an older patient population (1,27,33).

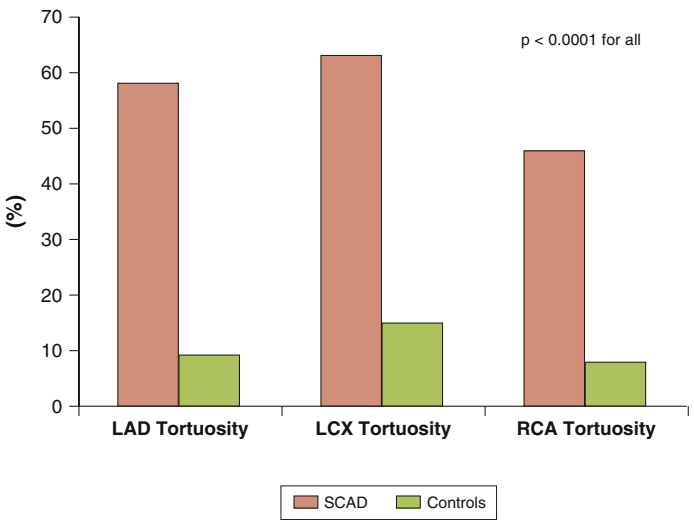
In addition to diagnosis, intravascular imaging can guide therapy. Stent malposition has been observed in SCAD due to hematoma resorption (**Figure 6**) (34), and intravascular imaging may facilitate optimal percutaneous coronary intervention in SCAD when indicated (35). Therefore, cautious interpretation of the angiographic images and a low threshold for intravascular imaging should be incorporated, particularly in younger patients with myocardial infarction, ambiguous vessel appearance or tortuosity on conventional CA, absence of atherosclerotic risk factors, peripartum status, FMD, or those with recent extreme physical or emotional stress.

Importantly, CA may demonstrate the impressive coronary tortuosity, an observation that does not

require intravascular imaging and can be used to identify a phenotype of patients at higher risk for adverse outcomes. In a series of 246 patients with confirmed SCAD on CA, coronary tortuosity was highly prevalent in SCAD patients occurring in 78% as compared to 17% in matched controls (**Figure 7**). Subtypes included symmetric tortuosity within a vessel, symmetric multivessel symmetry, corkscrew, microaneurysm, and coronary FMD. Severe tortuosity correlated with recurrent SCAD events, and recurrent SCAD most frequently recurred in tortuous segments (20).

Following the initial diagnosis of SCAD, further invasive CA in the absence of concerns for progressive myocardial ischemia or infarct is discouraged as the procedural risks often outweigh any potential benefit of documenting anatomy or "healing." These risks include radiation exposure as many of these patients are young women and the risk of iatrogenic dissection(s) of the coronary and extracoronary arteries as vascular fragility and noncoronary abnormalities are common. However, repeat CA and revascularization with percutaneous coronary intervention or coronary artery bypass grafting may be necessary for those with persistent or progressive cardiac symptoms, evidence of ischemia or infarct, in light of risks for SCAD recurrence and in-stent restenosis (1,27).

FIGURE 7 Coronary Tortuosity Is Prevalent in SCAD



In a study of 246 SCAD patients, coronary tortuosity was notably more prevalent when compared to matched controls. LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery; SCAD = spontaneous coronary artery dissection. Reprinted with permission from Eleid et al. (20).

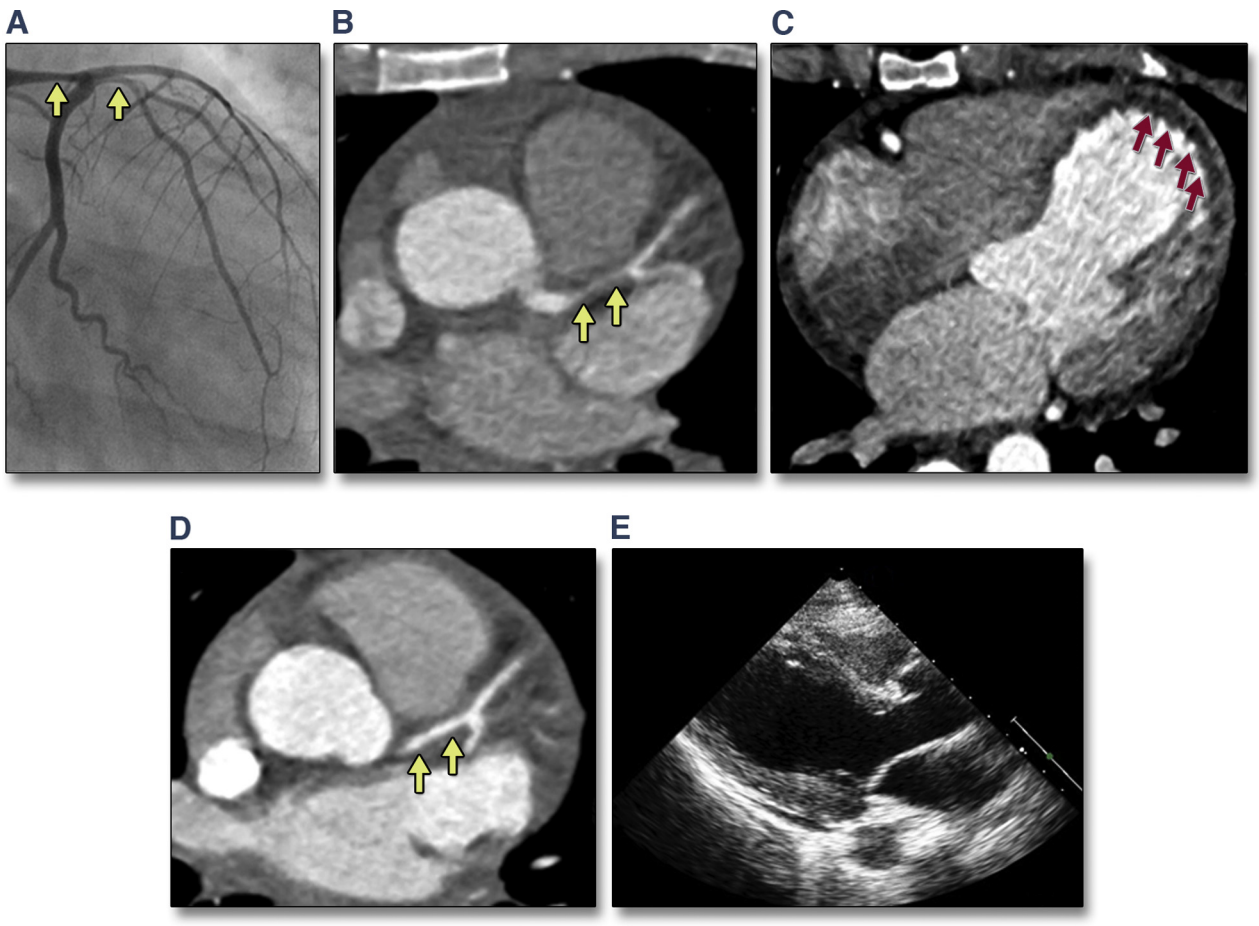
CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY. Coronary CTA is a gated, noninvasive diagnostic imaging technique used to characterize coronary and cardiac anatomy, and lack of myocardial contrast uptake may also allude to perfusion defects. In atherosclerotic disease, coronary CTA demonstrates a sensitivity and specificity as high as 94% and 83%, respectively, for identifying atherosclerotic lesion stenoses of >70% when compared to CA (36,37). While SCAD can be recognized on coronary CTA (38,39), current large coronary CTA studies do not distinguish SCAD from other causes of vessel obstruction, so its reliability in acute SCAD and in long-term follow-up is still evolving. Of specific concern to young women, coronary CTA requires contrast and radiation; however, prospective, electrocardiogram-triggered, dual-source CT systems can minimize this exposure (40).

Potential advantages of coronary CTA for SCAD patients include it being noninvasive, quick, readily accessible, and accuracy similar in women compared to men (41). In addition to direct evaluation of the coronary arteries, coronary CTA can identify first pass myocardial perfusion defects in regions of ischemia/infarction (**Figure 8**). "Triple rule-out" computed tomography studies, commonly performed for uncertain chest pain syndrome in the emergency department, include dedicated imaging of the coronaries and potentially could diagnose early SCAD prior to electrocardiogram or troponin changes. However, coronary calcifications and soft plaque are absent in SCAD. Therefore, the usual recognition patterns used for atherosclerotic coronary disease are not applicable for SCAD patients, and clear diagnostic criteria have not yet been developed.

Intramural hematoma can sometimes be visualized on the coronary CTA in SCAD patients, but this can be challenging since the hematoma can mimic the appearance of artifact due to cardiac motion in the central coronary arteries or of adjacent myocardium in distal branch vessels (**Figure 8**). Additionally, the limited spatial resolution of CT can make accurate evaluation of the lumen and vessel wall of small, distal coronary arteries problematic. Since the pretest probability for coronary disease in SCAD patients is often low in the setting of minimal typical risk factors, female sex and young age, even proximal SCAD can be missed by the interpreter if not considered as part of the differential and specifically evaluated.

Even if SCAD is considered, careful 2-dimensional, double oblique analysis using dedicated software should be performed. However, the pitfalls discussed previously may still impact accuracy of the

FIGURE 8 Coronary CTA in SCAD



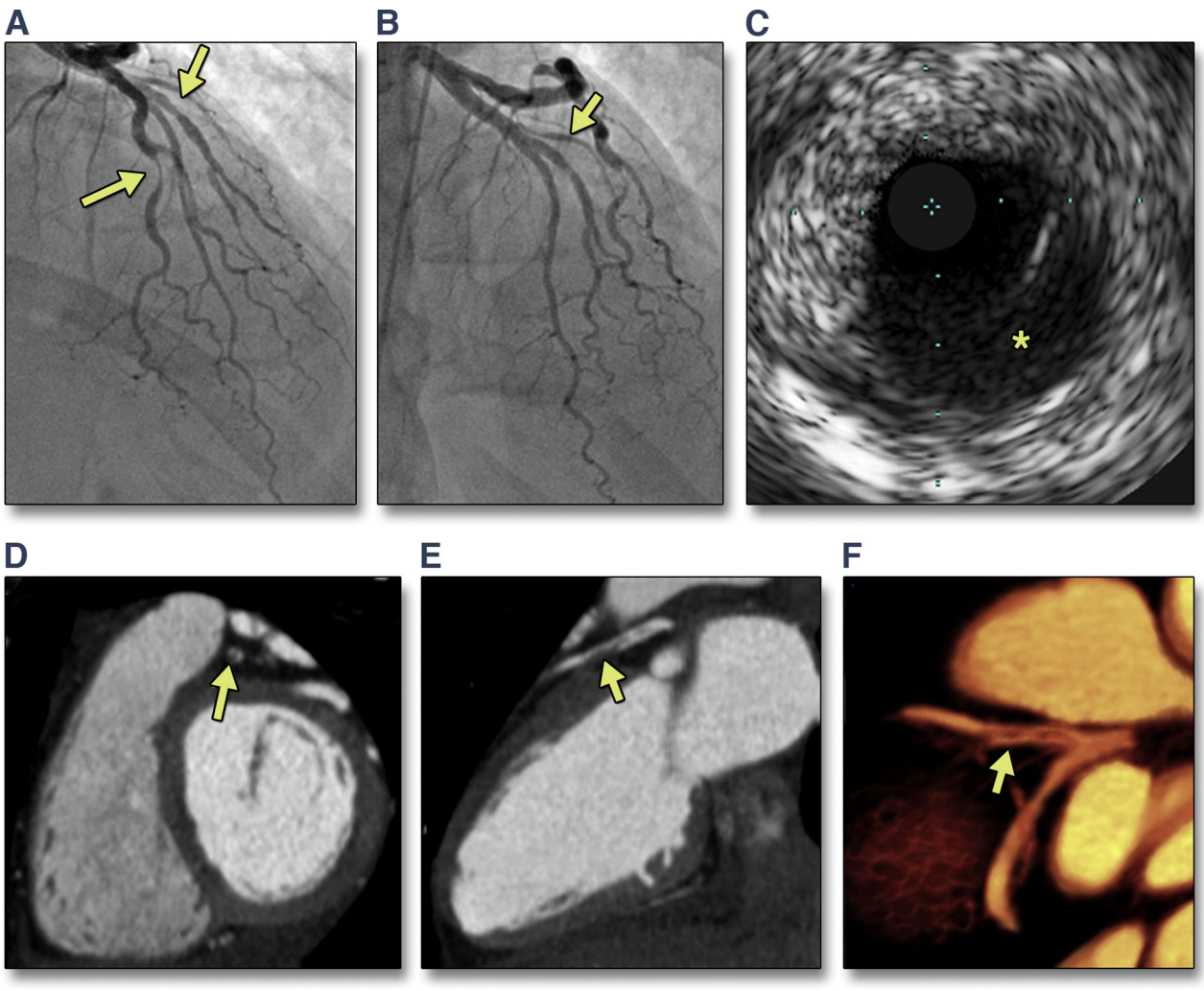
Patient example of a 32-year-old female who presented with postpartum chest pain, ST-segment elevation myocardial infarction, and spontaneous coronary artery dissection (SCAD) of the left main and left anterior descending (LAD) coronary artery **(A, arrows)**. The coronary computed tomography angiography (CTA) showed LAD intramural hematoma **(B, arrows)** and a myocardial perfusion defect in the left ventricular apex **(C, arrows)**. Her presenting echocardiogram appeared similar to Takotsubo cardiomyopathy **(E)**. Follow-up coronary CTA demonstrated interval resolution of the LAD intramural hematoma **(D, arrows)**.

assessment. As a result of these technical and interpretation limitations, coronary arteries may be reported as normal on coronary CTA in SCAD patients, and a negative coronary CTA does not fully exclude SCAD. When cardiac biomarkers are elevated or SCAD is suspected in the acute setting, patients should undergo CA to identify the culprit. After the initial diagnosis of SCAD, coronary CTA may be a worthwhile alternative to invasive CA to assess vessel healing, particularly if a patient continues to report chest pain. Commonly in our experience, patients describe nitrate-responsive chest pain at rest, which is not reproduced with exercise, suggesting a possible vasospastic component. Coronary CTA is a noninvasive approach that can characterize the coronary anatomy but also patency of any implanted grafts.

In the future, there may be a role for coronary CTA in SCAD patients who present with subsequent events. For instance, a 42-year-old female with known history of SCAD presented to our emergency department with chest pain, troponin elevation, and electrocardiography consistent with non-ST-segment elevation myocardial infarction. Her coronary CTA demonstrated persistent SCAD with possible progression but preserved filling of the distal coronaries. She was otherwise stable, successfully medically managed, and dismissed without the need for invasive CA or risk of iatrogenic dissection (Figure 9).

ECHOCARDIOGRAPHY. Echocardiography is an important, portable imaging technique frequently used for the assessment of regional wall motion abnormalities and left ventricular function due to

FIGURE 9 IVUS and Coronary Computed Tomography Angiography in SCAD

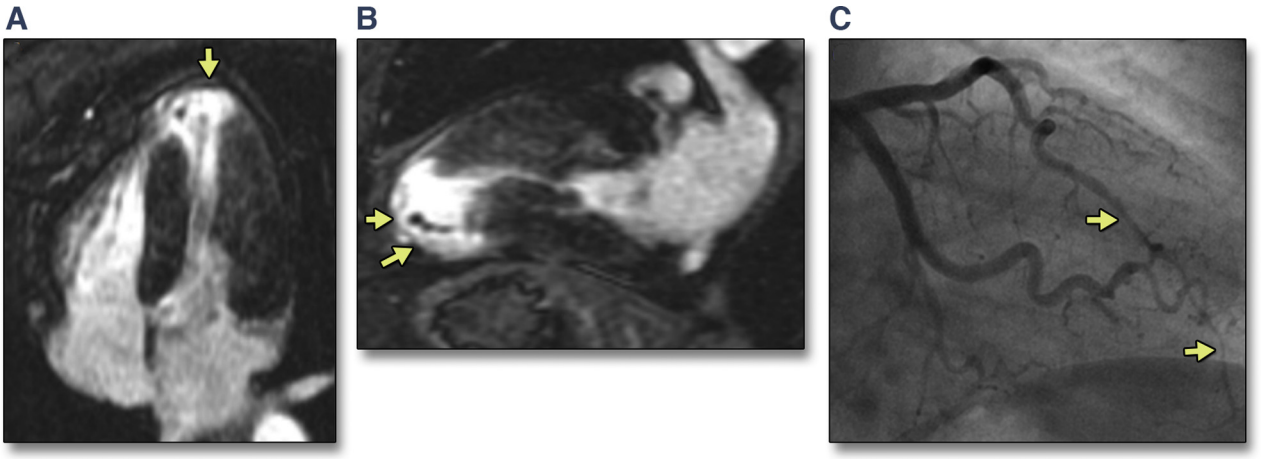


Patient example of a 42-year-old female who presented with chest pain and non–ST-segment elevation myocardial infarction. She had SCAD **(A and B, arrows)** with IVUS showing intramural hematoma in the setting of intimal disruption **(C, asterisk)**. She subsequently returned 3 weeks later with recurrent chest pain and non–ST-segment elevation myocardial infarction. Coronary computed tomography angiography showed persistent SCAD **(D to F, arrows)** with possible progression but preserved filling of the distal coronaries. She was otherwise stable, successfully medically managed and dismissed without undergoing invasive coronary catheterization. Abbreviations as in Figure 1.

ischemia and/or infarction in acute SCAD. The option of serial evaluation combined with avoidance of ionizing radiation exposure is an advantage in this predominantly young female patient population. Similar to other causes of MI, left ventricular function due to SCAD can range from severely impaired and associated with cardiogenic shock to normal, depending on the extent of vessels affected.

Follow-up echocardiography is beneficial for monitoring ventricular recovery that can occur in many, but not all, patients (27). A minority of patients has persistent dysfunction, some of whom require implantation of a cardiac defibrillator or consideration for cardiac transplantation. Stress echocardiography is highly valuable in assessment of SCAD patients with recurrent chest pain. Further echocardiographic evaluation of patients with SCAD may help determine predictors of which patients are most likely to recover myocardial function via parameters such as regional wall motion abnormalities, chamber size, and diastolic function. Moreover, advanced echocardiographic techniques, such as contrast and strain

FIGURE 10 Cardiac Magnetic Resonance in SCAD



Patient example of a 48-year-old female with history of myocardial infarction but "normal coronaries" at an outside facility. She underwent cardiac magnetic resonance which demonstrated transmural late gadolinium enhancement consistent with infarction of the LAD coronary artery distribution **(A, arrow; B arrows)**. Reinterpretation of the coronary angiogram demonstrated findings suggestive of SCAD of the distal LAD **(C, arrows)**. Abbreviations as in Figure 8.

imaging, may be indicative of underlying perfusion and myocardial dysfunction in SCAD and have yet to be studied further.

NUCLEAR MPI. MPI, such as single-photon emission computed tomography and positron emission tomography (PET), assesses perfusion to the myocardium at rest and following exercise by detection of radioactive tracers. While MPI is not typically used in the setting of acute SCAD, it does have high diagnostic accuracy in women particularly with the incorporation of attenuation correction and optimized imaging techniques (41). It may be an alternative modality to assess SCAD patients for ischemia during clinical work-up for symptoms such as chest pain. Myocardial flow reserve can be assessed by PET (42) and may offer an approach to further understanding SCAD.

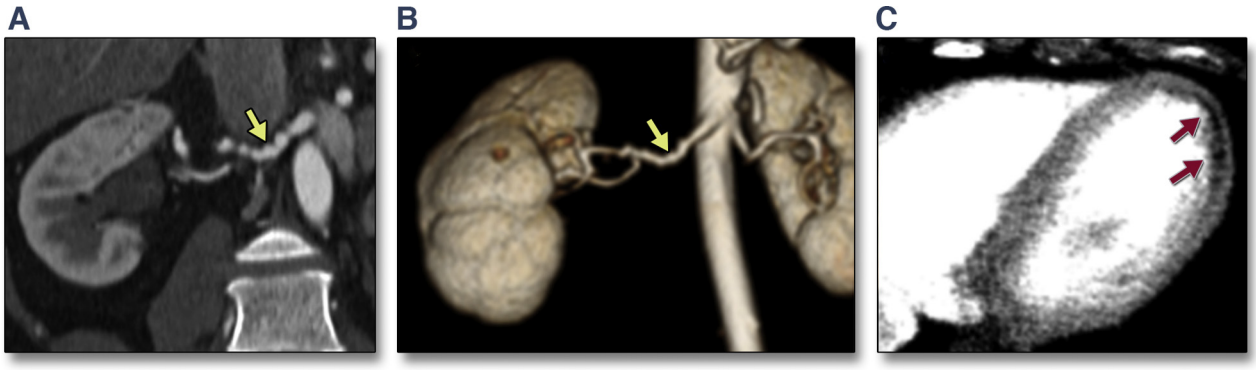
CARDIAC MAGNETIC RESONANCE. CMR is a noninvasive, nonradiating modality that can assess cardiac anatomy, ventricular function, myocardial perfusion, and late gadolinium enhancement for detection of ischemia/infarction, inflammation or fibrosis (43). CMR has been shown to be generally safe and accurate in assessing perfusion abnormalities in women (41). Although not always the first test of choice for acute coronary syndrome, CMR may reveal ischemia/infarct in patients with minimal risk factors who present with chest pain or sudden cardiac arrest but have an equivocal initial troponin or electrocardiogram. For instance, a prospective study of 161 consecutive patients (42% women) with chest pain but nondiagnostic electrocardiogram underwent rest CMR within 12 h of presentation. In these patients, CMR detected myocardial injury with a sensitivity and specificity of 84% and 85%, respectively, with abnormal wall motion being the strongest contributor to diagnosis (44). Another study of 62 patients (32% women) with acute chest

TABLE 1 Applicability of Multimodality Imaging for SCAD

Imaging Techniques
Acute SCAD
• CA with careful review • Intravascular ultrasound or optical coherence tomography for uncertain diagnosis • Peripheral angiography to assess for EVA such as FMD • Echocardiography to assess regional wall motion abnormalities • Coronary CTA with heightened attention to coronaries, extracoronary vessels, and myocardial perfusion • CMR to assess for regional wall motion abnormalities and endocardial and/or transmural delayed enhancement of a coronary territory
Early post-SCAD
• Repeat CA if clinically indicated (e.g., evidence of new ischemia/infarction, persistent symptoms, hemodynamic or rhythm abnormalities) • Echocardiography to assess extent of myocardial injury or recovery • Stress echocardiography to assess extent of myocardial ischemia, injury or recovery • MPI to assess extent of myocardial ischemia, injury or recovery • Coronary CTA to assess anatomy in stable patient with recurrent symptoms • CMR to assess extent of myocardial injury or recovery
Post-SCAD surveillance
• SCAD protocol computed tomography angiography to assess for EVA such as FMD • Stress echocardiography if clinically indicated (e.g., new or persistent symptoms) • Stress MPI if clinically indicated • CA or coronary CTA if clinically indicated

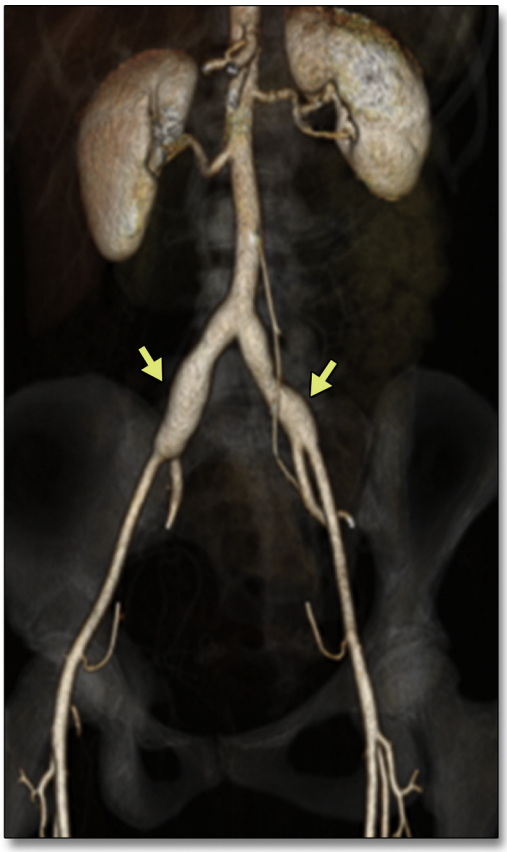
CA = coronary angiography; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; EVA = extracoronary vascular abnormalities; FMD = fibromuscular dysplasia; MPI = myocardial perfusion imaging; SCAD = spontaneous coronary artery dissection.

FIGURE 11 Fibromuscular Dysplasia and Myocardial Perfusion Defect in SCAD



Patient example of fibromuscular dysplasia of the right renal artery in a female with history of SCAD at 44 years of age **(A and B, arrow)**. Although her computed tomography study did not include dedicated cardiac imaging, an incidental myocardial perfusion defect was visualized in a territory consistent with her prior SCAD **(C, arrows)**. Abbreviation as in Figure 1.

FIGURE 12 Extracoronary Vessel Abnormalities in SCAD



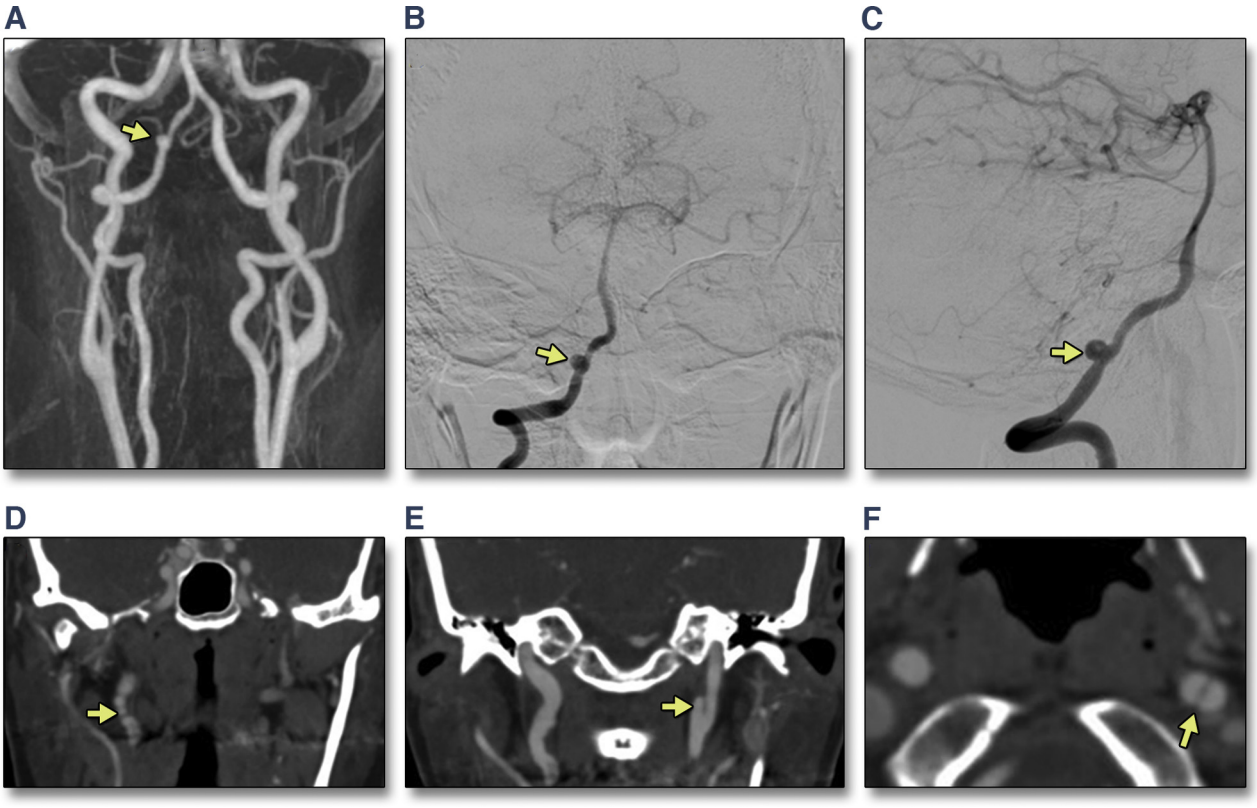
Patient example of bilateral common iliac aneurysms **(arrows)** in a female with history of SCAD at 39 years of age. Abbreviation as in Figure 1.

pain but negative initial biomarkers and changes on electrocardiogram found that the specificity, positive predictive value and accuracy of a protocoled CMR can be as high as 96%, 85%, and 93%, respectively (45).

This strategy may identify a subset of SCAD patients with an ambiguous presentation or retrospectively reveal the diagnosis of infarction. Abnormalities in SCAD patients on CMR may appear similar to patients with infarction from other causes, and as such abnormal wall motion, edema, abnormal perfusion, and late gadolinium enhancement can be present in the affected coronary territory. In a 41-year-old female who presented with ventricular fibrillation arrest and SCAD of the left anterior descending coronary artery, CMR confirmed the region and extent of infarction (**Figure 3**). In another case, CMR identified a region of transmural infarction in the left anterior descending coronary artery distribution in a 48-year-old with history of MI but "normal coronaries" at an outside facility. Reinterpretation of the coronary angiogram demonstrated smooth LAD narrowing consistent intramural hematoma and SCAD of the distal LAD (**Figure 10**). Into the future, further advancements in CMR may even allow for coronary artery assessment using navigator/3D heart approaches that already aid in the review of the proximal coronary arteries (46).

NONCORONARY IMAGING. FMD is the most frequent co-existing condition and has been reported in as many as 25% to 86% of SCAD patients (21–24), FMD is a poorly understood nonatherosclerotic and noninflammatory disease, which can lead to dissection, dilation,

FIGURE 13 Extracoronary Vessel Abnormalities in SCAD



Patient example of a 4 mm aneurysm arising from the distal right vertebral artery at the posterior inferior cerebellar artery origin on magnetic resonance imaging and angiography in a 51-year-old female with SCAD **(A to C, arrows)**. Fibromuscular dysplasia of the right internal carotid artery **(D, arrow)** and dilation with dissection of the left internal carotid artery **(E and F, arrows)** in a 49-year-old female with SCAD. Abbreviation as in Figure 1.

aneurysm, and stenosis in other arterial territories (47). In a series of 115 SCAD patients (95% women) undergoing imaging to detect EVA utilizing a dedicated protocol (**Table 1**) (24), 66% demonstrated vascular abnormalities (**Figures 11 and 12**). FMD was most frequent, affecting 45% of patients (21). In that population, 23% of 40 patients with head imaging had intracerebral vascular abnormalities (**Figure 13**) (21).

Visceral angiography has been used at the time of initial CA to diagnose EVA, but the emergency setting, unstable hemodynamic status, and prior contrast load may impact patient safety and limit feasibility. To reduce the risk of invasive procedures of SCAD patients, outpatient computed tomography or magnetic resonance imaging may be utilized to diagnose and follow-up EVA in SCAD patients. Head-to-head comparison studies in SCAD have not been performed, but the higher resolution of computed tomography across multiple vascular territories may improve detection of more subtle vascular abnormalities often seen in SCAD when compared to magnetic resonance imaging.

SEX-SPECIFIC CONSIDERATIONS

As SCAD primarily affects young women, including those of childbearing age, discretion regarding the timing and choice of imaging modality is pertinent. In the setting of an acute MI of unknown etiology, CA is the gold standard despite substantial exposure to radiation. If the diagnosis remains uncertain after CA alone, intravascular imaging is a critical adjunctive technique for determining underlying etiology. While coronary CTA does expose patients to radiation, advanced techniques such as prospective, electrocardiogram-triggered, dual-source computed tomography systems can minimize radiation to as low as 1 mSv while allowing adequate assessment of

the coronary arteries (40). Similarly, radiation reduction strategies can be used in studies for the identification of EVA (21). Echocardiography to assess myocardial function is a readily accessible, portable technique that does not expose the patient to radiation. Coupled with stress testing, it is a valuable tool for evaluation of ischemia if recurrent symptoms occur. MPI stress imaging is an alternative modality to assess SCAD patients for ischemia. A disadvantage of MPI is radiation exposure to the patient, although PET radiation exposure may be as low as 2mSv (N-13 ammonia) or 3mSv (Rb-82) without limiting accuracy (41,48). CMR does not expose the patient to radiation and is beneficial for evaluation of cardiac function and infarction etiology. Magnetic resonance imaging may also be used for EVA identification. However, these vascular studies can be time consuming, not readily accessible, and resolution is limited. CMR currently cannot reliably assess the coronary artery anatomy, although this may change with future advancements.

GENETIC CONSIDERATIONS

Familial SCAD is a recent novel finding (49), which encourages ongoing DNA studies in the Mayo Clinic SCAD Registry. The Mayo Clinic SCAD Registry was established and accelerated via a patient-driven online community and social media efforts (50). Since its development in 2010, more than 500 patients with confirmed SCAD on CA have been enrolled into the prospective registry, and more than 700 patients and their relatives have provided DNA specimens for the biorepository work. Incorporation of the genetic underpinnings along with imaging findings may elucidate specific SCAD phenotypes/genotypes and help determine risk of future events tailored to specific individuals. This understanding will further guide studies on treatment strategies and recommendations regarding exercise intensity, future pregnancies and so forth, with a focus on tailoring recommendations to the patients' phenotype and genetic predisposition.

CONCLUSIONS

SCAD is increasingly recognized as a significant cause of acute MI in young women. Advanced imaging techniques are crucial for appropriate diagnosis and follow-up of these patients. As most of these patients are young women, consideration of radiation exposure should guide decision making. While there remains a paucity of specific research in the optimal role of imaging in SCAD patients, each modality offers unique capabilities that should be customized to the individual patient. Further evaluation of the multiple available options for imaging is necessary in order to improve our understanding of SCAD and to positively impact clinical decision making.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Sharonne N. Hayes, Division of Cardiovascular Diseases, Mayo Clinic College of Medicine, 200 First Street Southwest, Rochester, Minnesota 55905. E-mail: hayes.sharonne@mayo.edu.

REFERENCES

1. Tweet MS, Hayes SN, Pitta SR, et al. Clinical features, management, and prognosis of spontaneous coronary artery dissection. Circulation 2012;126:579–88.

2. Naderi S, Weinberg I, Lindsay M, Wood M. Spontaneous coronary artery dissection patients significantly more fit than the average patient referred for exercise stress testing. J Am Coll Cardiol 2015;65 Suppl A:A315.

3. Hayes SN, Wood SF, Mieres JH, Campbell SM, Wenger NK. Taking a giant step toward women's heart health: Finding policy solutions to unanswered research questions. Women's Health Issues 2015;25:429–32.

4. Grosseto D, Santarelli A, Carigi S, et al. Incidence of spontaneous coronary artery dissection in all comers patients referred for acute coronary syndrome. Eur Heart J Acute Cardiovasc Care 2012;1:61.

5. Vanzetto G, Berger-Coz E, Barone-Rochette G, et al. Prevalence, therapeutic management and medium-term prognosis of spontaneous coronary artery dissection: results from a database of 11,605 patients. Eur J Cardiothorac Surg 2009;35:250–4.

6. Mortensen KH, Thuesen L, Kristensen IB, Christiansen EH. Spontaneous coronary artery dissection: A Western Denmark Heart Registry Study. Catheter Cardiovasc Interv 2009;74:710–7.

7. Maeder M, Ammann P, Angehrn W, Rickli H. Idiopathic spontaneous coronary artery dissection: incidence, diagnosis and treatment. Int J Cardiol 2005;101:363–9.

8. Nishiguchi T, Tanaka A, Taruya A, et al. Clinical characteristics and angiographic features of optical coherence tomography verified spontaneous coronary artery dissection in patients with acute coronary syndrome (abstr). Eur Heart J 2015;6:300.

9. Desai S, Sheppard M. Sudden cardiac death: Look closely at the coronaries for spontaneous dissection which can be missed. A study of 9 cases. Am J Forensic Med Pathol 2012;33:26–9.

10. Alfonso F, Paulo M, Dutary J. Endovascular imaging of angiographically invisible spontaneous coronary artery dissection. J Am Coll Cardiol Intv 2012;5:452–3.

11. Alfonso F, Paulo M, Gonzalo N, et al. Diagnosis of spontaneous coronary artery dissection by optical coherence tomography. J Am Coll Cardiol 2012;59:1073–9.

12. Nishiguchi T, Tanaka A, Ozaki Y, et al. Prevalence of spontaneous coronary artery dissection in patients with acute coronary syndrome. Eur Heart J Acute Cardiovasc Care 2013 Sep 11 [E-pub ahead of print].

13. Pretty H. Dissecting aneurysm of coronary artery in a woman aged 42: rupture. Br Med J 1931;1:667.

14. Robinowitz M, Virmani R, McAllister HA Jr. Spontaneous coronary artery dissection and eosinophilic inflammation: A cause and effect relationship? Am J Med 1982;72:923–8.

15. Borczuk AC, van Hoeven KH, Factor SM. Review and hypothesis: the eosinophil and peripartum heart disease (myocarditis and coronary

artery dissection)—coincidence or pathogenetic significance? Cardiovasc Res 1997;33:527–32.

16. Tchernitchin A, Barrera J, Arroyo P, Mena M, Vilches K, Grunert G. Degranulatory action of estradiol on blood eosinophil leukocytes in vivo and in vitro. Agents Actions 1985;17:60–6.

17. Dowling G, Buja L. Spontaneous coronary artery dissection occurs with and without periadventitial inflammation. Arch Pathol Lab Med 1987;111:470–2.

18. Gössl M, Versari D, Hildebrandt HA, et al. Segmental heterogeneity of vasa vasorum neovascularization in human coronary atherosclerosis. J Am Coll Cardiol Img 2010;3:32–40.

19. Saw J, Aymong E, Sedlak T, et al. Spontaneous coronary artery dissection: Association with predisposing arteriopathies and precipitating stressors and cardiovascular outcomes. Circ Cardiovasc Interv 2014;7:645–55.

20. Eleid M, Guddeti R, Tweet M, et al. Coronary artery tortuosity in spontaneous coronary artery dissection: Angiographic characteristics and clinical implications. Circ Cardiovasc Interv 2014;7:656–62.

21. Prasad M, Tweet MS, Hayes SN, et al. Prevalence of extracoronary vascular abnormalities and fibromuscular dysplasia in patients with spontaneous coronary artery dissection. Am J Cardiol 2015;115:1672–7.

22. Toggweiler S, Puck M, Thalhammer C, et al. Associated vascular lesions in patients with spontaneous coronary artery dissection. Swiss Med Wkly 2012;142:w13538.

23. Saw J, Ricci D, Starovoytov A, Fox R, Buller CE. Spontaneous coronary artery dissection: prevalence of predisposing conditions including fibromuscular dysplasia in a tertiary center cohort. J Am Coll Cardiol Intv 2013;6:44–52.

24. Liang JJ, Prasad M, Tweet MS, et al. A novel application of CT angiography to detect extracoronary vascular abnormalities in patients with spontaneous coronary artery dissection. J Cardiovasc Comput Tomogr 2014;8:189–97.

25. Tweet MS, Eleid MF, Best PJ, et al. Spontaneous coronary artery dissection: revascularization versus conservative therapy. Circ Cardiovasc Interv 2014;7:777–86.

26. Saw J, Mancini GBJ, Humphries K, et al. Angiographic appearance of spontaneous coronary artery dissection with intramural hematoma proven on intracoronary imaging. Catheter Cardiovasc Interv 2016;87:E54–61.

27. Tweet MS, Eleid MF, Best PJM, et al. Spontaneous coronary artery dissection: Revascularization versus conservative therapy. Circ Cardiovasc Interv 2014;7:777–86.

28. Alfonso F, Paulo M, Lennie V, et al. Spontaneous coronary artery dissection: long-term follow-up of a large series of patients prospectively managed with a "conservative" therapeutic strategy. J Am Coll Cardiol Intv 2012;5:1062–70.

29. Saw J. Coronary angiogram classification of spontaneous coronary artery dissection. Circ Cardiovasc Interv 2014;84:1115–22.

30. Antonsen L, Thayssen P, Jensen LO. Large coronary intramural hematomas: a case series and focused literature review. Cardiovasc Revasc Med 2015;16:116–23.

31. Finn AV, Chandrashekhar Y, Narula J. IVUS and OCT: Either or survivor…. J Am Coll Cardiol Img 2011;4:1047–9.

32. Aoki T, Rodriguez-Porcel M, Matsuo Y, et al. Evaluation of coronary adventitial vasa vasorum using 3D optical coherence tomography – animal and human studies. Atherosclerosis 2015;239:203–8.

33. Chou AY, Sedlak T, Aymong E, et al. Spontaneous coronary artery dissection misdiagnosed as takotsubo cardiomyopathy: a case series. Can J Cardiol 2015;31:1073.e5–8.

34. Lempereur M, Fung A, Saw J. Stent malapposition with resorption of intramural hematoma with spontaneous coronary artery dissection. Cardiovasc Diagn Ther 2015;5:323–9.

35. Satogami K, Ino Y, Kubo T, et al. Successful stenting with optical frequency domain imaging guidance for spontaneous coronary artery dissection. J Am Coll Cardiol Intv 2015;8:e83–5.

36. Leipsic J, Abbara S, Achenbach S, et al. SCCT guidelines for the interpretation and reporting of coronary CT angiography: a report of the Society of Cardiovascular Computed Tomography Guidelines Committee. J Cardiovasc Comput Tomogr 2014;8:342–58.

37. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) Trial. J Am Coll Cardiol 2008;52:1724–32.

38. Russo V, Marrozzini C, Zompatori M. Spontaneous coronary artery dissection: role of coronary CT angiography. Heart 2012;99:672–3.

39. Torres-Ayala SC, Maldonado J, Scott Bolton J, Bhalla S. Coronary computed tomography angiography of spontaneous coronary artery dissection: a case report and review of the literature. Am J Case Rep 2015;16:130–5.

40. Achenbach S, Goroll T, Seltmann M, et al. Detection of coronary artery stenoses by low-dose, prospectively ECG-triggered, high-pitch spiral coronary CT angiography. J Am Coll Cardiol Img 2011;4:328–37.

41. Mieres JH, Gulati M, Bairey Merz N, et al. Role of noninvasive testing in the clinical evaluation of women with suspected ischemic heart disease: a consensus statement from the American Heart Association. Circulation 2014;130:350–79.

42. Cho S-G, Kim JH, Cho JY, Kim HS, Bom H-S. Myocardial blood flow and flow reserve in proximal and mid-to-distal lesions of left anterior descending artery measured by N-13 ammonia PET/CT. Nucl Med Mol Imaging 2013;47:158–65.

43. Wu E, Judd RM, Vargas JD, Klocke FJ, Bonow RO, Kim RJ. Visualisation of presence, location, and transmural extent of healed Q-wave and non-Q-wave myocardial infarction. Lancet 2001;357:21–8.

44. Kwong RY, Schussheim AE, Rekhraj S, et al. Detecting acute coronary syndrome in the emergency department with cardiac magnetic resonance imaging. Circulation 2003;107:531–7.

45. Cury RC, Shash K, Nagurney JT, et al. Cardiac magnetic resonance with T2-weighted imaging improves detection of patients with acute coronary syndrome in the emergency department. Circulation 2008;118:837–44.

46. Moghari MH, Annese D, Geva T, Powell AJ. Three-dimensional heart locator and compressed sensing for whole-heart MR angiography. Magn Reson Med 2015 Jun 10 [E-pub ahead of print].

47. Olin JW, Gornik HL, Bacharach JM, et al. Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association. Circulation 2014;129:1048–78.

48. Nandalur KR, Dwamena BA, Choudhri AF, Nandalur SR, Reddy P, Carlos RC. Diagnostic performance of positron emission tomography in the detection of coronary artery disease: a meta-analysis. Acad Radiol 2008;15:444–51.

49. Goel K, Tweet M, Olson TM, Maleszewski JJ, Gulati R, Hayes SN. Familial spontaneous coronary artery dissection: Evidence for genetic susceptibility. JAMA Intern Med 2015;175:821–6.

50. Tweet MS, Gulati R, Aase LA, Hayes SN. Spontaneous coronary artery dissection: a disease-specific, social networking community-initiated study. Mayo Clin Proc 2011;86:845–50.

KEY WORDS cardiac imaging, coronary angiography, coronary computed tomography angiography, echocardiography, fibromuscular dysplasia, intravascular imaging, myocardial infarction, spontaneous coronary artery dissection, women

APPENDIX For supplemental videos, please see the online version of this article.