JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

VOL. 68, NO. 3, 2016
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2016.05.034

THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Contemporary Review on Spontaneous Coronary Artery Dissection

Jacqueline Saw, MD,[a] G.B. John Mancini, MD,[a] Karin H. Humphries, DSc[b]

ABSTRACT

Spontaneous coronary artery dissection (SCAD) is gaining recognition as an important cause of myocardial infarction, especially in young women. There has been a surge in the diagnosis of SCAD in recent years, presumably due to an increased use of coronary angiography, and the clinical availability and application of high-resolution intracoronary imaging. The improved recognition and diagnosis, together with increased publications and attention through social media, have considerably raised awareness of this condition, which was once believed to be very rare. Recent publications of moderate to large contemporary case series have helped elucidate the early natural history, presenting characteristics (clinical and angiographic), underlying etiology, management, and cardiovascular outcomes with this condition, thus providing observations and important clinical insights of value to clinicians managing this challenging and perplexing patient cohort. The aim of our review is to provide a comprehensive contemporary update of SCAD to aid health care professionals in managing these patients in both the acute and chronic settings. (J Am Coll Cardiol 2016;68:297–312)

Spontaneous coronary artery dissection (SCAD) is gaining recognition as an important cause of myocardial infarction (MI), especially in young women. The first report of SCAD, by Pretty (1) in 1931, was of a 42-year-old woman who died unexpectedly following repetitive retching and vomiting, which elicited coronary artery rupture from dissection of an atheromatous aneurysm. Over the next 8 decades, subsequent SCAD publications consisted mostly of isolated case reports and small case series. However, there has been a surge in the diagnosis of SCAD in recent years, presumably due to the increased use of coronary angiography in patients presenting with acute coronary syndromes (ACS), as well as the clinical availability and application of high-resolution intracoronary imaging (especially optical coherence tomography [OCT]) that enhances diagnosis (2–4). As such, of the ~1,500 reported SCAD cases to date, about one-half were published in the past 5 years (5–15).

The improved recognition and diagnosis, together with the increased number of publications and attention through social media, have considerably raised awareness of this condition (16), once believed to be very rare. The first online community of SCAD patients on Inspire (17), developed by WomenHeart (The National Coalition for Women With Heart Disease) as a social networking site, has improved patient awareness. Simultaneously, publications of larger contemporary case series of SCAD have helped elucidate the early natural history, presenting characteristics (clinical and angiographic), the underlying etiology, the management, and the outcomes of this condition. These studies have provided observations and important clinical insights, reflected in expert opinions on management strategies, which are of

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Division of Cardiology, Vancouver General Hospital, Vancouver, British Columbia, Canada; and the [b]BC Centre for Improved Cardiovascular Health, Vancouver, British Columbia, Canada. Dr. Saw has received research grants and speaker honoraria from AstraZeneca; has received research grants and speaker honoraria and been a consultant, a member of the advisory board, and a proctor for Boston Scientific and St. Jude Medical; has received speaker honoraria from Sunovion; has been a member of the advisory board for Abbott Vascular; and has received research grants from Servier. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received April 10, 2016; revised manuscript received April 26, 2016, accepted May 3, 2016.

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

CABG = coronary artery bypass graft

CTA = computed tomography angiography

DAPT = dual antiplatelet therapy

FMD = fibromuscular dysplasia

IMH = intramural hematoma

IVUS = intravascular ultrasound

MACE = major adverse cardiac events

MI = myocardial infarction

MRA = magnetic resonance angiography

OCT = optical coherence tomography

PCI = percutaneous coronary intervention

SCAD = spontaneous coronary artery dissection

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

value to clinicians managing this challenging and perplexing patient cohort. The aim of our review is to provide a comprehensive contemporary update of SCAD to aid health care professionals managing these patients in both the acute and chronic settings.

DEFINITION OF SCAD

SCAD is defined as a spontaneous separation of the coronary artery wall that is not iatrogenic or related to trauma. As such, dissections due to blunt trauma, surgical instruments, or those that are catheter-induced are not deemed to be SCAD. Furthermore, contemporary usage of the term SCAD is typically reserved for the nonatherosclerotic variant, and most modern series exclude SCAD due to atherosclerotic coronary artery disease. For the purpose of our review, and because this disease is distinct from atherosclerotic disease, the term SCAD refers to "nonatherosclerotic SCAD" and is the focus of this paper.

EPIDEMIOLOGY

SCAD was previously, incorrectly believed to be very rare and to be frequently associated with pregnancy. Unfortunately, the true incidence and prevalence of SCAD in the general population is unknown due to significant underdiagnosis of this condition. For decades, SCAD diagnosis was plagued by a low clinical index of suspicion of seemingly healthy young women presenting with ACS who had not undergone coronary angiography. At the other extreme, SCAD patients who presented with sudden cardiac death may not have been captured in various databases. In addition, the current "gold standard" for a SCAD diagnosis (i.e., coronary angiography) has major limitations because it does not image the arterial wall, and many clinicians are unfamiliar with nonpathognomonic angiographic variants of SCAD. Furthermore, intracoronary imaging was infrequently used to aid diagnosis. Therefore, the previous reports of SCAD prevalence on coronary angiography of 0.2% to 1.1% were underestimates of the true prevalence of SCAD (18–20). In a recent Japanese series of 326 ACS patients who underwent routine OCT imaging, SCAD was diagnosed in 4% of cases (21). However, caution should be exercised in using this incidence estimate because 77% of these patients were men, and thus a proportion of these dissections were likely related to atherosclerosis. We suspect that a more accurate estimate of the SCAD prevalence in patients presenting with ACS is 1.7% to 4% on the basis of modern series (13,21). In the extreme case of sudden cardiac death, SCAD was reported in 0.5% (8 of 1,647) of cases in an autopsy series (22), although this prevalence could be an underestimate.

The incidence of SCAD in young women has been further explored. In the older series by Vanzetto et al. (18) of women younger than 50 years of age who presented with ACS, the prevalence of SCAD was 8.7% (10.8% in patients with ST-segment elevation myocardial infarction [STEMI]). Contemporary series reported a much higher prevalence of SCAD in young women with ACS (22% to 43%). In a single-center Canadian series of women younger than 50 years of age who underwent coronary angiography (n = 177; mean age 45.4 years), SCAD was observed in 9.0%, and was the cause of MI in 24.2% (23). In a recent Japanese series, SCAD was the cause of MI in 35% (45 of 130) of women younger than 50 years of age (15). In a recent Australian series of women younger than 60 years of age (n = 23) who underwent angiography, SCAD accounted for 22.5% of ACSs (13). In the series by Elkayam et al. (24) of much younger women (mean age 34 years) with pregnancy-related MI, SCAD was the most frequent cause of MI, accounting for 43% of MIs (56 of 129), which occurred predominantly in the third trimester or post-partum phase. Therefore, the incidence of SCAD is not rare in young women presenting with ACS, especially those with pregnancy-related MI.

SCAD affects women in >90% of cases. In contemporary series that excluded patients with atherosclerotic causes, women accounted for 92% to 95% of the population with SCAD (6,9,10,12–14). The reported mean age ranged from 44 to 55 years in contemporary series, reflecting a relatively young to middle-age population (6,9,10,12–15). In the Vancouver cohort of 168 patients, 58% were ≥50 years of age, 62% of affected women were post-menopausal, and the oldest patient was 84 years of age (9). In another series, the oldest reported patient was 78 years of age (7). In terms of racial distribution, all races can be affected, although most of those in North America were Caucasians (81% to 83%) (7,9), which was similar to the racial distribution among patients who underwent percutaneous coronary intervention (PCI) in British Columbia.

MECHANISM AND PATHOPHYSIOLOGY

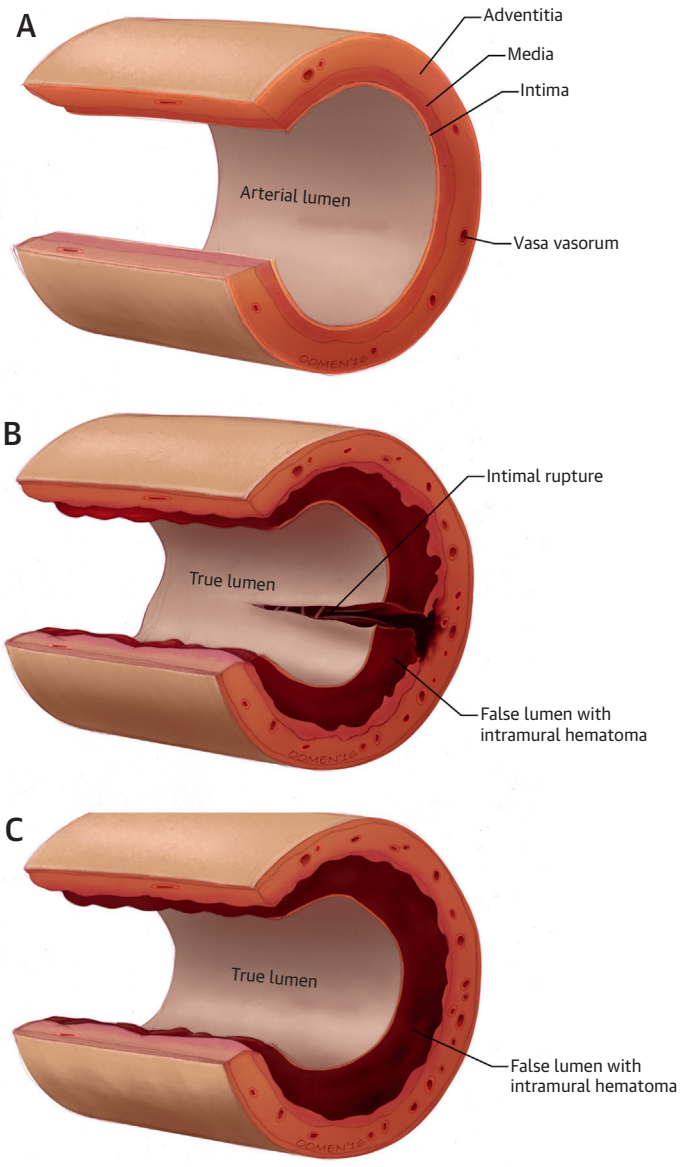
The arterial dissection with SCAD can occur within or between any of the 3 layers (intima, media, or adventitia) of the coronary artery wall. Two potential mechanisms for the initiation of arterial wall

separation have been proposed (25) (**Figure 1**). The first is the intimal tear hypothesis, in which a primary disruption in the intimal–luminal interface creates an entry point for intramural hematoma (IMH) accumulation inside the false lumen, leading to separation of the arterial wall. The second is the medial hemorrhage hypothesis, in which a hemorrhage into the arterial wall is the primary mechanism, perhaps due to spontaneous rupture from the increased density of the vasa vasorum. It is possible for the latter process, with increased pressure from IMH, to cause a rupture into the true lumen, resulting in a "reverse" intimal rupture. Intuitively, the pathognomonic angiographic appearance of multiple lumens would require the presence of visible intimal disruption. However, the presence of intimal disruption does not imply a specific mechanism for genesis of the tear.

SCAD invariably results in accumulation of blood within the false lumen, which can compress the true lumen to varying degrees, depending on the amount of IMH and the arterial wall response to the IMH. It has been hypothesized that in the setting of atherosclerosis, the presence of medial atrophy and scarring limits propagation of the dissection plane (26). Conversely, in the setting of SCAD, where predisposing arteriopathies have weakened the arterial wall architecture, once the dissection plane occurs, anterograde and retrograde propagation can be quite extensive. This has been observed in SCAD found by intracoronary imaging, where the mean length of dissection was >45 mm (27).

The presence of true lumen compression by IMH can result in myocardial ischemia and infarction. Occlusion of the lumen by thrombi in the true or false lumen may also occur, such as at intimal rupture sites. Two large angiographic series and 1 OCT (25 SCAD arteries) series showed lack of thrombus in the arterial lumen (9,10,27). However, 1 small OCT study of 11 patients showed thrombi in the false or true lumen in all cases, but most were insignificant (28). Thus, it appears that thrombi play a secondary pathophysiologic role compared with IMH as the primary cause of ACS with SCAD.

FIGURE 1 Mechanisms of SCAD



(A) Normal coronary artery. **(B)** Intimal rupture initiating tear, with intramural hematoma formation. **(C)** Spontaneous bleeding into the arterial wall, creating a false lumen filled with intramural hematoma. SCAD = spontaneous coronary artery dissection.

PREDISPOSING AND PRECIPITATING ETIOLOGIES

The underlying etiology of SCAD appears to be multifactorial. There is often an associated underlying predisposing arteriopathy, which may be compounded by a precipitating stressor, culminating in the phenotypic expression of SCAD (**Table 1**). Many potential predisposing nonatherosclerotic arteriopathies for SCAD have been reported. The most dominant association reported is fibromuscular dysplasia (FMD).

FMD. We reported the first case series of concomitant SCAD and extracoronary FMD in 2011 (5). Since then, a high prevalence of FMD has been observed in 72% to 86% of SCAD cohorts who were routinely screened (6,9). The Vancouver series (n = 168) included a high proportion of patients who underwent invasive

TABLE 1 Potential Predisposing and Precipitating Factors for SCAD

Predisposing causes
Fibromuscular dysplasia
Pregnancy-related: antepartum, early post-partum, late post-partum, very late post-partum
Recurrent pregnancies: multiparity or multigravida
Connective tissue disorder: Marfan syndrome, Loeys-Dietz syndrome, Ehler-Danlos syndrome type 4, cystic medial necrosis, alpha-1 antitrypsin deficiency, polycystic kidney disease
Systemic inflammatory disease: systemic lupus erythematosus, Crohn's disease, ulcerative colitis, polyarteritis nodosa, sarcoidosis, Churg-Strauss syndrome, Wegener's granulomatosis, rheumatoid arthritis, Kawasaki, giant cell arteritis, celiac disease
Hormonal therapy: oral contraceptive, estrogen, progesterone, beta-HCG, testosterone, corticosteroids
Coronary artery spasm
Idiopathic
Precipitating stressors
Intense exercises (isometric or aerobic activities)
Intense emotional stress
Labor and delivery
Intense Valsava-type activities (e.g., retching, vomiting, bowel movement, coughing)
Recreational drugs (e.g., cocaine, amphetamines, metamphetamines)
Intense hormonal therapy (e.g., beta-HCG injections, corticosteroids injections)

HCG = human chorionic gonadotropin; SCAD = spontaneous coronary artery dissection.

angiographic screening for FMD of the renal and iliac arteries during their coronary angiographies. Therefore, the sensitivity of diagnosing extracoronary FMD was higher than other reported series. In a study from the Mayo Clinic, FMD was diagnosed in 52% of 95 SCAD patients who had comprehensive computed tomography angiography (CTA) screening, which supported the observed strong association between SCAD and FMD. In another series by Toggweiller et al. (29), FMD was diagnosed in 3 of 12 SCAD patients using magnetic resonance angiography (MRA). MRA has lower resolution than CTA, which, in turn, has lower resolution than invasive angiography in diagnosing FMD, which provides an explanation for the different prevalences of FMD in these studies. Pathologically, the presence of FMD can weaken artery architecture, which is characterized by dysplasia and disorganization and/or destruction of smooth muscle cells, fibroblasts, and the connective tissue matrix, affecting any of the 3 arterial layers and elastic laminas. FMD-affected arteries are prone to dissection and aneurysm formation (30). There are 3 published histopathologic case reports of coronary FMD that caused SCAD (31–33), which established the biological proof of causation. Thus, the observed dominant association between SCAD and FMD strongly suggests that many SCAD cases are due to coronary FMD. The ability to diagnose coronary FMD on angiography and intracoronary imaging will be very helpful in establishing the link between FMD and SCAD (34–36). A recent case series of 32 patients described the angiographic appearance and intracoronary imaging of coronary FMD without overlying SCAD among patients with documented extracoronary FMD (36). Angiographic features of coronary tortuosity (100%), dilation and/or ectasia (56%), and irregular (59%) or smooth (19%) stenoses were frequently observed in these patients with suspected coronary FMD. Another study showed that coronary tortuosity was more prevalent in SCAD patients (78% of a 246-patient cohort vs. 17% of 313 control subjects) (37), which raised the suspicion that this may be related to the underlying coronary FMD because of the dominant association with SCAD (36).

PREGNANCY-RELATED SCAD. Although early retrospective series suggested that ~30% of SCAD cases were peri-partum, modern series failed to replicate such high percentages. In contemporary series, pregnancy-related SCAD accounted for <5% of SCAD cases (8,9,12). Pregnancy-related SCAD can occur antepartum, early post-partum (within 6 weeks of delivery), late post-partum (6 weeks to 12 months), and very late post-partum (12 to 24 months) (38). High progesterone levels during pregnancy can weaken arterial media through alteration of the elastic fiber and mucopolysaccharide content, and impairment of collagen synthesis. Estrogen also can create a hypercoagulable state. Together, a weakened arterial wall and a prothrombotic state were believed to increase the risk of SCAD and thrombosis (39,40); although, as alluded to previously, thrombosis is likely less important in the pathophysiology of SCAD. In histopathologic reports of peri-partum SCAD, abnormalities of fragmented and disorganized elastic and collagen fibers, microcystic mucinous pools, cystic medial necrosis, and inflammatory infiltration were observed at arterial dissection planes (41). Periadventitial eosinophilic infiltrates have also been observed, but are of unknown significance. Although these eosinophilic granules may play a role in weakening the arterial wall through breakdown of the medial-adventitial layer via lytic substances, they may simply be due to reactive changes from SCAD (42). Hemodynamic changes during late pregnancy can also predispose to SCAD. The augmented cardiac output and circulatory volume during pregnancy can increase shear stress, causing microstructural changes in the aorta, which can also extend to the coronary arteries (43). The increased

intra-abdominal pressures during labor can also increase arterial shear stress. Together, these hemodynamic stresses can precipitate pregnancy-related SCAD when superimposed upon arterial architectural changes related to pregnancy or other predisposing etiologies (e.g., FMD). There has also been a recent observation of a potential association between breastfeeding with late and very late postpartum pregnancy-related SCAD, suggesting that hormonal changes with lactation may compound the effects of pregnancy (44).

RECURRENT PREGNANCIES. With the hormonal changes that occur with each pregnancy, repeated exposure with multiple recurrent pregnancies can lead to chronic repetitive impairment of arterial wall integrity (38,41). Multiparous (or even multigravida) women are believed to be at higher risk for SCAD. In a 168 patient series, 8.9% were multiparous, with ≥4 births, and 8.3% were grand multigravida, with ≥5 pregnancies (9).

HORMONAL THERAPY. Long-term exposure to exogenous estrogen or progesterone is postulated to cause similar long-term changes in coronary arterial architecture, and it is believed to be an important risk factor for SCAD (7,9). In a presented series of 215 SCAD patients, 12.4% were actively on hormone replacement therapy, and these patients had higher recurrent MI (29.2% vs. 6.5%; $p = 0.03$) on follow-up compared with those not on hormone replacement therapy (45).

SYSTEMIC INFLAMMATORY DISEASE. Several chronic systemic inflammatory conditions were reported to be potentially associated with SCAD (**Table 1**), although most of these were only case reports, and the pathophysiological links were not established. The prevalence of concomitant systemic inflammatory disease was 8.9% in the 168 patient series. In a smaller series by Alfonso et al. (8), 27 patients diagnosed with isolated SCAD underwent laboratory screening for inflammatory and immunologic markers; however, none were diagnosed with systemic inflammation on screening. This is in keeping with the observation that the incidence of acute inflammation associated with SCAD was very low (<1%) (9). The link between systemic inflammation and SCAD is suspected to be due to chronic inflammation from vasculitis (46).

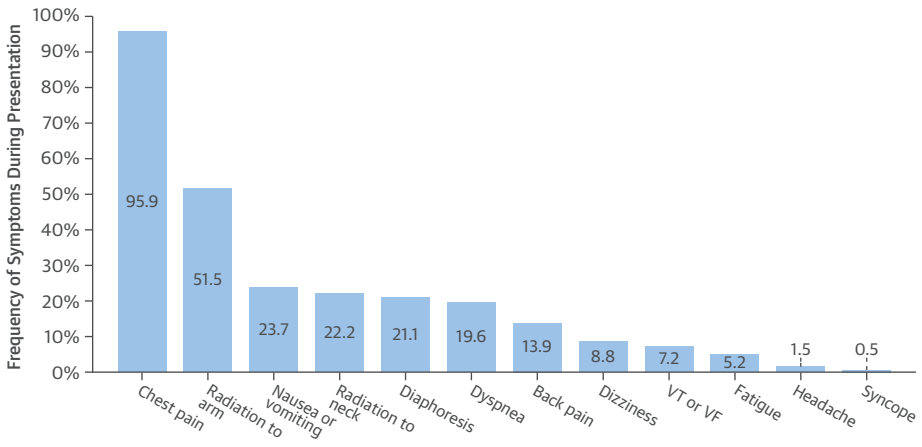
CONNECTIVE TISSUE DISORDER. Several connective tissue disorders have also been associated with SCAD (**Table 1**), most notably Marfan and Ehler-Danlos type 4 syndromes. However, the reported frequency of these associated connective tissue conditions is infrequent (1% to 2%) (9,47). Thus, although many of these disorders can be identified on genetic screening, the yield is low unless patients have clear clinical characteristics suggestive of these disorders.

PRECIPITATING FACTORS. Precipitating stressors that result in a Valsalva-like increase in thoracoabdominal pressure or that raise catecholamines can increase cardiocirculatory shear stress, which can trigger SCAD, especially in patients with underlying predisposing arteriopathies. These stressors include intense emotional stress, physical activities (especially isometric exercises), hormonal therapy, sympathomimetic drugs, and intense Valsalva-like activities (e.g., childbirth, coughing, retching, vomiting, bowel movement) (1,7,9,38,48–50). Physical stressors that have the commonality of intense bearing-down Valsalva-like activities transiently increase intrathoracoabdominal pressures, which can be transmitted to coronary arteries as shear stress. Emotional stress is speculated to have a different pathophysiological trigger, presumably related to stress catecholamines. A catecholamine surge may increase myocardial contractility or vasospasm, which can increase arterial shear stress, leading to intimal rupture or disruption of the vasa vasorum (9). It is unknown if long-term elevated catecholamine exposure can induce structural changes in the arterial wall. Acute exposures to high-dose hormonal therapy (e.g., injections of beta-human chorionic gonadotropin, corticosteroids) have also been implicated as triggers for SCAD, potentially through accelerated arterial architectural disruption or hemodynamic stress (e.g., acute hypertension) (48,50). In a prospective cohort, as many as 57% of patients reported precipitating stressors preceding their SCAD event; ~40% reported having severe emotional stress, and 24% reported significant physical activities (9). Men and women have different prevalences of predisposing and precipitating factors. In a recent paper, men ($n = 25$) were more likely to report isometric exercises (44.0% vs. 15.6%; $p = 0.004$), but were less likely to report emotional stressors (24.0% vs. 54.8%; $p = 0.05$) compared with women ($n = 263$) (51). These findings highlight potential lifestyle changes that may affect recurrent SCAD risk.

CLINICAL PRESENTATION

There is a wide spectrum of clinical presentations and severity of SCAD. Almost all patients with SCAD present with ACS and elevation of cardiac enzymes (9,11,12,15). The proportion who presented with STEMI varied widely in different series, ranging from 24% to 87% (9–15). A small proportion can be complicated with ventricular arrhythmias (3% to 10%)

FIGURE 2 Frequency of Symptom Presentation of SCAD



Chest pain is the most commonly reported symptom with SCAD presentation (51). SCAD = spontaneous coronary artery dissection; VF = ventricular fibrillation; VT = ventricular tachycardia.

(9–11), cardiogenic shock (<3%) (9,11), or sudden cardiac death (<1%), although this presentation may be underestimated (22).

Chest discomfort was the most common presenting symptom, as reported in 96% of patients (n = 196) (52). Less frequent symptoms included radiation to the arms or neck, nausea or vomiting, diaphoresis, dyspnea, and back pain (**Figure 2**). The average time from symptom onset to hospital presentation was 1.10 days, and patients with non-STEMI had longer delays from presentation to coronary angiography compared with those with STEMI (2.0 vs. 0.8 days; p = 0.002). Overall, ~34% of SCAD patients had unstable symptoms (ongoing pain and/or ischemia or stuttering and/or recurrent pain that required medications for pain relief) before arrival at the catheterization laboratory.

There is also a wide variation in elevation of cardiac enzyme levels. In the Vancouver cohort, the median troponin I elevation was 6 μg/l (normal <0.05 μg/l), with a wide interquartile range of 0.7 to 200 μg/l (9). Interestingly, in the Japanese series, the mean peak creatine kinase level (normal levels 25 to 250 IU/l) was lower in young women with SCAD versus non-SCAD patients (1,689 IU/l vs. 2,874 IU/l; p = 0.025) (15). This suggests that the myocardium in jeopardy with SCAD may be smaller than that with atherosclerotic disease. In line with this observation, the in-hospital left ventricular ejection fraction during SCAD presentation was relatively preserved, ranging from 51% to 56% (7,9,11). Ejection fraction has also been observed to improve after the acute presentation. In a series of 131 SCAD patients who had baseline and repeat left ventricular function assessment, the mean ejection fraction improved from 55.7% to 60.4% (p < 0.001), and the proportion of patients with ejection fractions <50% improved from 19.1% to 6.9% (p < 0.001) (53). This improvement in left ventricular function may represent normalization of stunned myocardium following spontaneous arterial healing of SCAD.

DIAGNOSIS OF SCAD

Accurate and early diagnosis of SCAD is important because the management and investigation of SCAD is different from atherosclerotic disease. Coronary angiography is widely available and is the first-line imaging for patients presenting with ACS. However, coronary angiography has significant limitations in diagnosing SCAD because it is a 2-dimensional luminogram that does not image the arterial wall. Dedicated intracoronary imaging (OCT and intravascular ultrasound [IVUS]) that images the arterial wall layers improves SCAD diagnosis, but it is not as widely available and is associated with additional risks and costs (**Table 2**). Thus, coronary angiography remains instrumental in SCAD diagnosis, and angiographers should gain familiarity with the angiographic variants of SCAD.

The conventional angiographic description of SCAD includes the appearance of extraluminal contrast staining, multiple radiolucent lumens, spiral dissection, and intraluminal filling defects (54).

However, such descriptions and the National Heart, Lung, and Blood Institute classification for coronary dissections were devised in the pre-stent era for angioplasty-induced dissections. The predominant angiographic appearance of SCAD consists of smooth narrowing of varying severity and length due to IMH. Thus, a SCAD angiographic classification was described to better characterize the appearance (55).

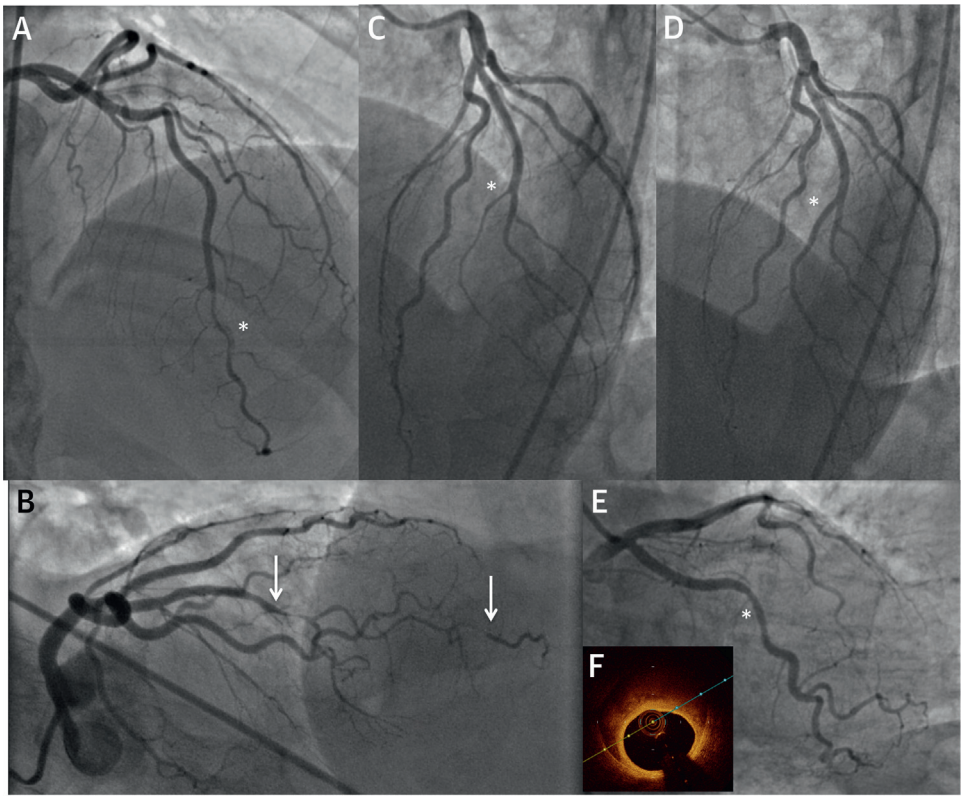
SCAD ANGIOGRAPHIC CLASSIFICATION. Type 1 describes the pathognomonic appearance of arterial wall contrast staining with multiple radiolucent lumens (**Figure 3A**). Type 2 describes diffuse stenosis of varying severity and length (typically >20 mm), and with appreciable, but often subtle, abrupt changes in the arterial caliber from the normal diameter to diffuse smooth narrowing. This diffuse narrowing may be bordered by normal artery segments that are proximal and distal to the IMH (type 2A variant), or it may extend to the apical tip of the artery (type 2B variant) (**Figures 3B and 3C**) (27). Type 3 describes focal or tubular (typically <20 mm) stenosis that mimics atherosclerosis, which requires intracoronary imaging to confirm diagnosis (**Figure 3D**). A simple algorithm to aid the diagnosis of SCAD was proposed together with this classification (**Figure 4**) (55).

TABLE 2 Advantages and Disadvantages of Intracoronary Imaging for SCAD

Advantages	Disadvantages
Definitive diagnosis of SCAD	Invasive, requires anticoagulation
Confirm true lumen entry by coronary wire	Costly
Facilitate stent sizing	Not available in all laboratories
Confirm adequate stent apposition	Possible risks of extending dissection by:
Confirm full coverage of dissected segment	Guide catheter, coronary wire
Facilitate diagnosis of potential arteriopathy	Imaging catheter
	Hydraulic extension (with OCT)
	Vessel occlusion (by catheter, embolization)

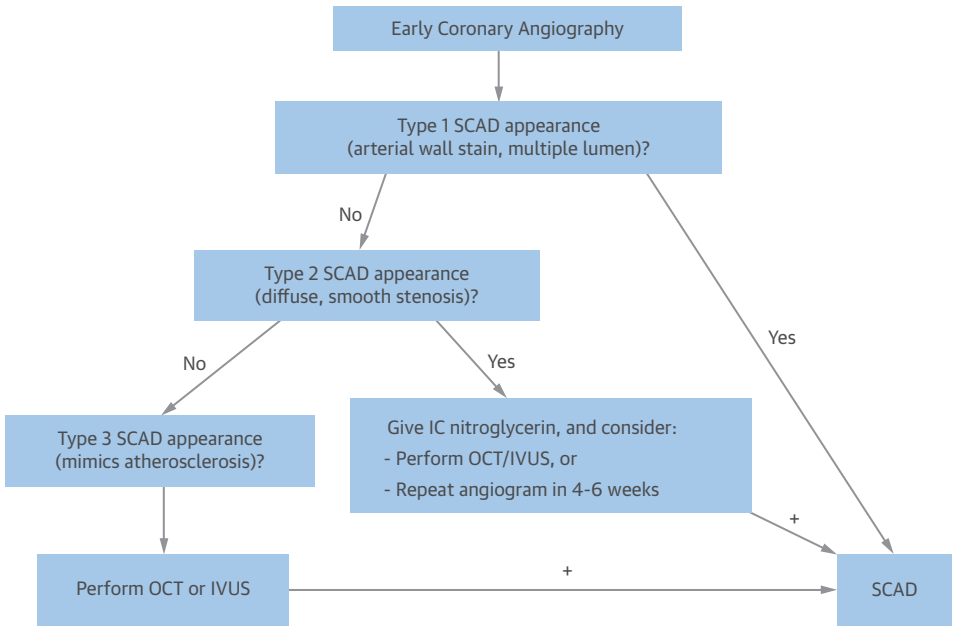
OCT = optical coherence tomography; SCAD = spontaneous coronary artery dissection.

FIGURE 3 Angiographic Classification of SCAD



(A) Type 1 spontaneous coronary artery dissection (SCAD) of distal left anterior descending (LAD) artery with staining of artery wall **(asterisk)**. **(B)** Type 2A SCAD of mid-distal LAD **(between arrows)**. **(C)** Type 2B SCAD of diagonal branch **(asterisk)**, which healed 1 year later **(asterisk in D)**. **(E)** Type 3 SCAD of mid-circumflex artery **(asterisk)**, with corresponding optical coherence tomography showing intramural hematoma in **(F)**.

FIGURE 4 Simple Algorithm for SCAD Diagnosis



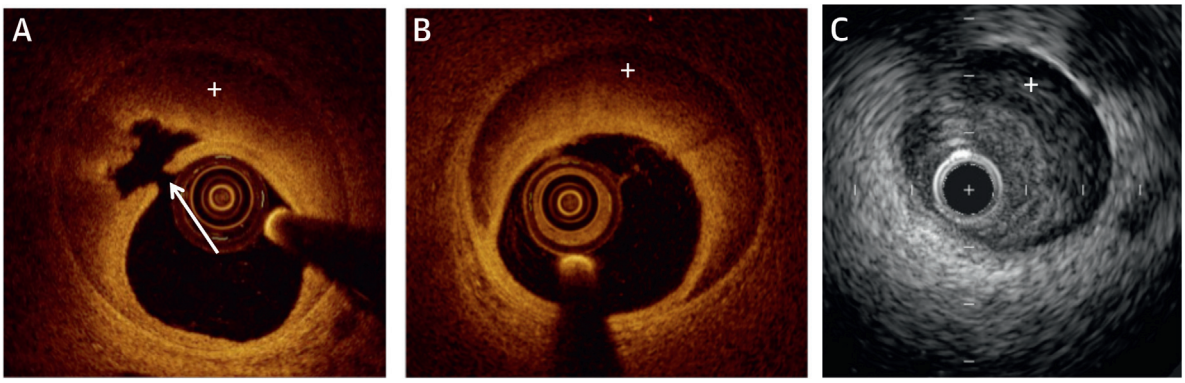
Early performance of coronary angiography is encouraged to assess for presence of type 1 angiographic SCAD appearance. If absent, the type 2 angiographic SCAD appearance should be sought, and optical coherence tomography/intravascular ultrasound (OCT/IVUS) or repeat angiography to confirm SCAD should be considered. If type 3 angiographic SCAD appearance is present, OCT/IVUS should be performed.
IC = intracoronary; SCAD = spontaneous coronary artery dissection. Reprinted with permission from Saw (55).

Using this classification, the most common SCAD angiographic appearance was type 2 in 67.5% of cases (137 of 203), followed by type 1 in 29.1% (59 of 203), and type 3 in 3.4% (7 of 203) (9). Other investigators have also reported diffuse smooth stenosis to be the most common angiographic manifestation (13,15,28). These findings highlight the importance of familiarity with the nonpathognomonic variants of SCAD (types 2 and 3) to improve diagnosis. The type 2 variants are associated with very long lengths of narrowing (mean 58 mm) and can be readily identifiable as SCAD after familiarity with this appearance; however, intracoronary imaging or repeat angiography in 4 to 6 weeks should be considered if the diagnosis is uncertain. The type 2B variant may be mistaken as "normal vessel tapering," but there is usually a discernible demarcation from a normal vessel to stenosis. Furthermore, there is usually a corresponding regional wall motion abnormality on ventriculography. The type 3 variant may be significantly underdiagnosed (mean length 22 mm), and may be mistaken for atherosclerotic disease if intracoronary imaging is not performed (27).

SCAD DISTRIBUTION. Any coronary artery can be affected by SCAD, with the left anterior descending artery being the most commonly involved (34% to 42%) (9,11,12). Overall, the left anterior descending artery and its branches (diagonal or septal) are affected in 45% to 61%, the circumflex and branches (ramus, obtuse marginal) in 15% to 45%, the right coronary artery and branches (acute marginal, posterior descending, posterolateral) in 10% to 39%, and the left main in 0% to 4% of cases (9-13,15). Most dissections affected the mid to distal segments, with <10% affecting the proximal left anterior descending, circumflex, right coronary, or left main arteries (9). Multiple arteries were dissected in 9% to 19% of cases, and noncontiguous >1 artery dissections occurred in 5% to 10% of cases (9-13,15). The mean stenosis severity was 79%, and the mean length of dissection was 46 mm (9). Thrombolysis In Myocardial Infarction (TIMI) flow grade 0 was observed in 24% to 44% of cases, TIMI flow grade 1 in 5% to 13%, TIMI flow grade 2 in 15% to 26%, and TIMI flow grade 3 in 19% to 55% of cases (9,12,15).

INTRACORONARY IMAGING. Both OCT and IVUS provide complementary details to diagnose SCAD, which requires the presence of IMH or a double lumen (**Figure 5**) (28). OCT has a superior spatial resolution of 10 to 20 μm versus IVUS, with lower resolution

FIGURE 5 Intracoronary Imaging of SCAD



(A) OCT image showing false lumen with intramural hematoma (IMH) **(plus sign)** and intimal rupture **(arrow)**. **(B)** OCT image showing false lumen with IMH **(plus sign)**. **(C)** IVUS image showing false lumen with IMH **(plus sign)**. Abbreviations as in Figures 1 and 4.

(~150 μm), but better penetration. For SCAD imaging, OCT is superior for visualizing intimal tears, intraluminal thrombi, false lumens, and IMH, but it is limited by optical penetration and shadowing, and may not depict the entire depth of the IMH. IVUS has adequate resolution to visualize IMH and false lumens, but the lumen–intimal interface is not as clearly delineated as with OCT. IVUS does provide deeper vessel visualization with better ultrasound penetration, allowing better appreciation of the extent of IMH. Overall, OCT is preferred for imaging SCAD due to its superiority and ease in visualizing IMH, intimal disruption, and double lumens, especially because there is no clinical need to evaluate the full depth and extent of IMH. Moreover, OCT is superior in visualizing stent strut apposition, thus allowing stent optimization if intervention is pursued. However, there are potential risks with intracoronary imaging in the setting of SCAD (Table 2), including the risks of extending dissection with the wire or imaging catheter, hydraulic extension with OCT contrast injection, catheter-induced occlusion, and guide catheter iatrogenic dissection. Thus, the utmost care and meticulous techniques should be used when performing intracoronary imaging.

CARDIAC CTA. Cardiac CTA has much lower spatial resolution compared with conventional angiography and has challenges in evaluating the lumens and walls of small coronary arteries (especially those <2.5 mm diameter). Because most of SCAD affects nonproximal arteries and does not have extraluminal contrast staining, cardiac CTA has limited capacity to diagnose SCAD. Moreover, the often subtle demarcation from normal to stenosis observed on coronary angiography is frequently not appreciated on cardiac CTA. Thus, despite its noninvasiveness, cardiac CTA is not recommended as a first-line imaging for SCAD due to the concerns of missed diagnoses in small and nonproximal arteries (2). However, it may be useful as an alternative to angiography to assess for arterial healing after SCAD of larger proximal-mid arteries. In a small series of 34 patients, 24 patients underwent cardiac CTA at a median of 4 months, and complete healing was observed in 83% (14).

MANAGEMENT OF SCAD

The optimal management of SCAD remains undetermined because no randomized trials have compared medical therapies or revascularization strategies, unlike atherosclerotic disease. Standard guideline-indicated medical therapies administered for ACS have not been specifically studied for SCAD, and it is unclear if they are beneficial in this unique population (56). Current recommendations on management are largely used on the basis of expert opinions from observational series (Table 3) (2,39,57).

MEDICAL THERAPY. Beta-blockers. There is general consensus that beta-blockers play an important role in the pharmacological armamentarium for SCAD. Beta-blockade reduces arterial shear stress and is instrumental in the management of aortic dissection (58). Such benefit may be extrapolated to SCAD with reduction of coronary arterial wall stress, and thus, beta-blockers are usually administered

TABLE 3 Demographics, Presentation, and Cardiovascular Outcomes in Contemporary SCAD Series

First Author (Ref. #)	Year	N	Age (yrs)	Women	ACS	STEMI	NSTEMI	Revasc, PCI*	PCI Success	In-hosp Death	In-hosp MI	In-hosp Urgent Revasc	Median F/U Time	F/U Death	F/U MI	F/U SCAD	F/U Revasc	F/U HF
Alfonso (8)	2012	27	53.0 ± 11.0	85.0	85.0	52.0	33.0	55.6, 100.0	80.0	0.0	0.0	7.4	730 days	0.0	0.0	NR	3.7	3.7
Saw (9)	2014	168	52.1 ± 9.2	92.3	100.0	26.1	73.9	20.2, 82.3	63.6	0.0	4.8	4.8	6.9 yrs	2.4	15.5	13.1	6.5	0.0
Tweet† (10)	2014	189	44.0 ± 9.0	92.0	100.0	37.0	63.0	50.3, 93.7	47.0	0.5	0.0	7.0	2.3 yrs	2.0	19.6	27.0	25.0	13.0
Lettieri (11)	2015	134	52.0 ± 11.0	81.0	93.0	49.2	40.3	42.0, 91.1	72.5	2.2	5.2	5.8	22 days	3.1	1.6	4.7	4.6	3.9
Rogowski (12)	2015	64	53.0 ± 11.2	94.0	100.0	69.0	30.0	12.5, 87.5	66.7	1.5	0.0	0.0	4.5 yrs	0.0	6.3	6.3	0.0	0.0
Roura (14)	2015	34	47.0 ± 12.0	94.1	100.0	55.0	45.0	23.5, 100.0	75.0	0.0	0.0	0.0	121 days	0.0	5.9	2.9	0.0	0.0
Rashid (13)	2016	21	53.3 ± 8.8	95.2	100.0	34.8	56.5	28.6, 100.0	66.7	0.0	0.0	NR	NR	NR	NR	NR	NR	NR
Nakashimi (15)	2016	63	46.0 ± 10.0	94.0	100.0	87.0	13.0	55.6, 97.1	91.0	NR	NR	NR	2.8 yrs	1.6	28.6	22.0	NR	NR

Values are % or mean ± SD. *The first percentage is those who had revascularization, and the second percentage is the proportion of those who underwent revascularization that was PCI. †Follow-up events for this study are Kaplan-Meier estimates.

ACS = acute coronary syndrome; F/U = follow-up; HF = heart failure; In-hosp = in-hospital; MI = myocardial infarction; NR = not reported; NSTEMI = non–ST-segment elevation myocardial infarction; Revasc = revascularization; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Tables 1 to 3.

acutely and long-term after SCAD. Furthermore, beta-blockers reduce ventricular arrhythmias and improve long-term survival, and are routinely recommended post-MI (56,59). Despite our preference for routine beta-blockade for SCAD patients, the efficacy of this therapy has not been specifically studied in this patient population.

Antiplatelet therapy. The role of antiplatelet therapy for SCAD is unknown, but on the basis of the totality of evidence for aspirin in ACS and secondary prevention, together with its low side effect profile, aspirin appears reasonable to use for acute and long-term SCAD management (60). Clopidogrel for acute management of SCAD patients not treated with stents is of uncertain benefit. However, considering that a proportion of SCAD involves intimal tears, which can be prothrombotic, dual antiplatelet therapy (DAPT) could be empirically beneficial. Reducing the false lumen thrombus burden with DAPT can also theoretically reduce true lumen compression (61). Therefore, clopidogrel is often administered for 1 to 12 months post-SCAD, and then it is typically discontinued if there is no further ischemic pain or if angiographic healing is subsequently demonstrated, although there is no supportive evidence for this approach. The role of novel $P2Y_{12}$ antagonists (ticagrelor and prasugrel) for SCAD management is undefined. Glycoprotein IIb/IIIa inhibitors have also not been evaluated for SCAD; however, they are not recommended because of their greater potency, higher bleeding risk, and a potential risk of extending the dissection (2).

Anticoagulant and thrombolytic therapy. The role of anticoagulation for SCAD is controversial and has not been studied. Heparin agents are routinely administered for ACS management in hospital, but the clinical benefit has not been established for SCAD. There is a potential risk of extending the dissection with anticoagulation, which is balanced by the potential benefit of resolving overlying thrombus and improving true lumen patency. Heparin should likely be discontinued once the SCAD diagnosis is made; however, this practice remains controversial and lacks supportive data. Thrombolytic therapy should be avoided in SCAD because there have been reports of harm and clinical deterioration due to extension of IMH and dissection (62,63). In a retrospective review of 87 SCAD patients who received thrombolysis, 60% had clinical deterioration that required rescue PCI or coronary artery bypass grafting (CABG) (62). There are anecdotal reports of successful thrombolysis with SCAD that may be related to lysis of false lumen thrombi (64); however, the bulk of the data suggest harm with thrombolysis for SCAD.

Angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker. These agents are standardly recommended after an MI (class IIa indication), especially in the presence of significant left ventricular dysfunction (ejection fraction ≤40%, class 1 indication) (65). However, because these agents have not been studied in SCAD patients, they tend to only be administered to SCAD patients with significant left ventricular dysfunction. There is a small, ongoing, randomized controlled study comparing angiotensin-converting enzyme inhibitors and statins versus placebo in SCAD patients (SAFER-SCAD [Statin and Angiotensin-converting Enzyme Inhibitor on Symptoms in Patients With SCAD]; NCT02008786) that is assessing symptomatic outcome.

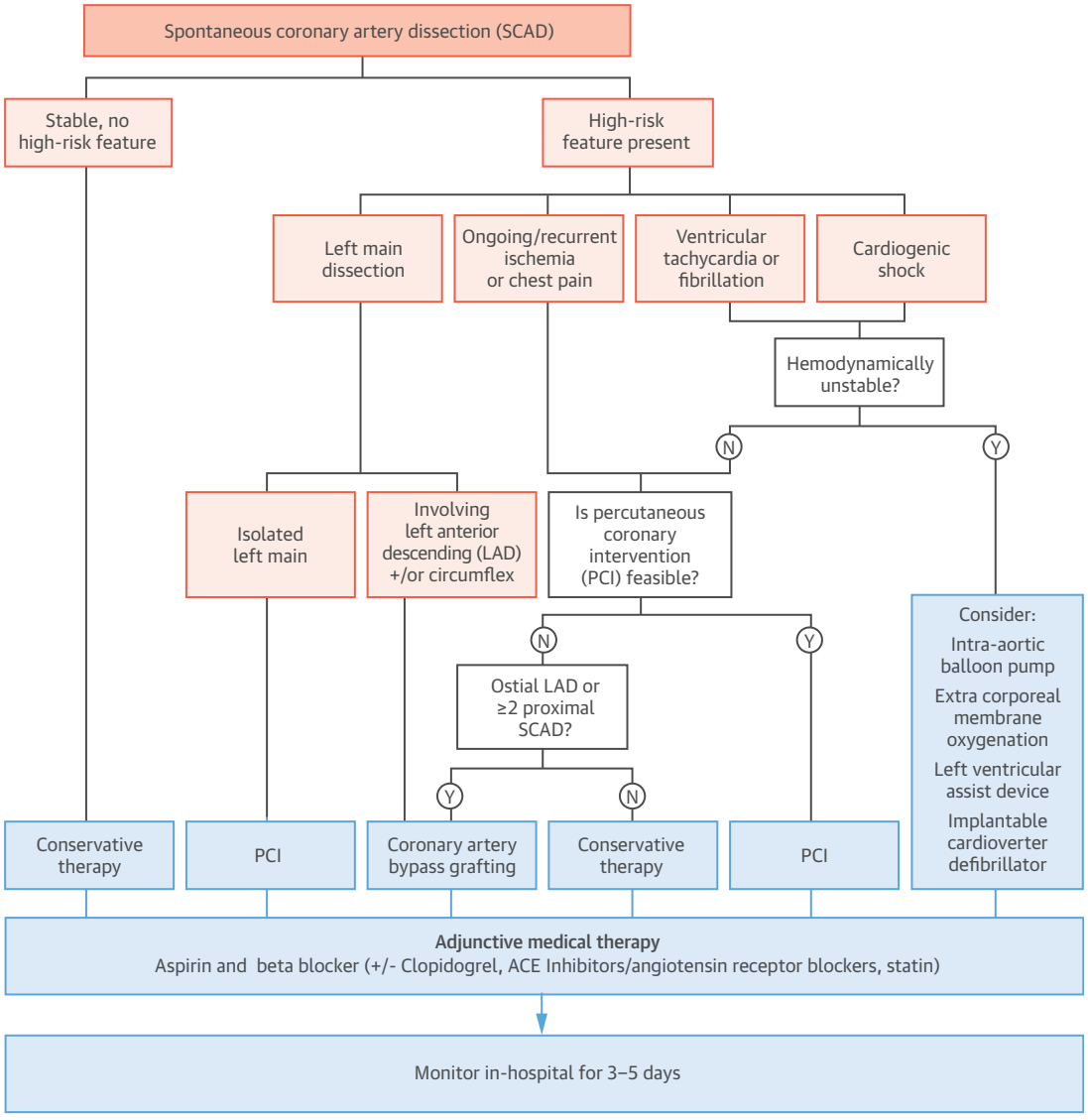
Lipid-lowering therapy. The use of statins for SCAD is controversial. A small retrospective study demonstrated potentially higher SCAD recurrence with statins (7); however, the bulk of data for ACS demonstrates significant benefit with lipid lowering, and statins are routinely recommended post-MI (59). Because of the uncertainty and the general lack of atherosclerosis in SCAD patients, statins tend to only be administered to patients with pre-existing dyslipidemia. One series reported a high rate of statin use without apparent safety concerns (12).

INVESTIGATION AND/OR SCREENING. Following diagnosis of SCAD, it has become routine practice in several centers specializing in SCAD to screen for predisposing arteriopathies associated with SCAD. Because of the strong association with FMD, we routinely image the renal and iliac arteries for FMD during baseline coronary angiography with nonselective abdominal and iliac aortograms when SCAD is diagnosed at our institution. The use of digital subtraction enhances diagnosis of mild FMD changes. As an alternative, noninvasive CTA FMD screening may be performed (9,47); however, the sensitivity of diagnosing FMD is much lower than that with invasive angiography (66). We also advocate CTA of the head and neck to assess for cerebrovascular FMD and intracranial aneurysm (the latter occurs in 14% to 25% of SCAD patients) (9,47). Although this screening approach is standard at our institution, this strategy has not been evaluated to assess if there is an impact on outcomes. A detailed history to assess for potential underlying connective tissue disorders, systemic inflammatory disease, pregnancy history, hormonal therapy, and precipitating factors should also be obtained. In terms of genetic screening, the yield for connective tissue disorders with routine genetic testing is very low (only 5% of 59 patients who have had genetic testing) (67). In addition, familial inheritance of SCAD was only identified in a minority of cases (1.2%; 5 of 412 mother–daughter, sisters, aunt–niece, or first cousins) (68). Thus, further studies that evaluate the genetic predispositions should be performed, but routine genetic screening is not currently recommended because of the low yield. Likewise, blood work to screen for inflammatory disease is of low yield and is not routinely performed (8).

REVASCULARIZATION. Conservative therapy. An overall conservative approach is preferred on the basis of expert opinions derived from observational data (2,8–11). This recommendation relies on observations that SCAD arteries heal spontaneously in most cases, and that revascularization is associated with high failure rates. In prospective series in which repeat coronary angiograms were performed, spontaneous angiographic healing was observed in most of the cases with conservative management: 73% (43 of 59 cases) (10); 90% (79 of 88) (9); and 97% (29 of 30) (12). There appears to be a time requirement for angiographic healing to occur; when repeat angiography was performed ≥26 days post-dissection, angiographic healing was observed in all cases (100%; 79 of 79) in this series (9). However, others have observed a small proportion of cases with residual dissections at late follow-up. Resorption of IMH appeared to start within days of the dissection on OCT (69); however, complete vessel healing probably takes about a month in most cases.

Indications for revascularization. Although conservative therapy is usually recommended according to expert opinions, therapy is not administered based on any randomized trial because no data are available. Nevertheless, a small proportion of patients should be considered for revascularization, including those with ongoing or recurrent ischemia, hemodynamic instability, ventricular arrhythmias, or left main dissection (**Central Illustration**). PCI should be performed in these cases if the anatomy is suitable; otherwise, CABG should be considered. In the Vancouver cohort, of the 80% who were treated conservatively (134 of 168 patients), the recurrent MI rate in-hospital was 4.5% (55). In the recently presented updated Vancouver cohort of 280 prospectively followed patients, 83% were treated conservatively, and subsequent revascularization in-hospital in this group was only 3.5% (2.9% PCI and 0.6% CABG) (70). In the Mayo Clinic series, 9 of 94 (10%) patients who were treated conservatively had SCAD progression that required revascularization (10). Therefore, inpatient monitoring for several days (3 to 5 days) is recommended, the duration of which depends on symptoms and the location of the dissection.

CENTRAL ILLUSTRATION **Management Algorithm for Spontaneous Coronary Artery Dissection**



Saw, J. et al. J Am Coll Cardiol. 2016;68(3):297–312.

Conservative therapy is typically pursued in stable patients and in patients monitored in-hospital for 3 to 5 days. Revascularization should be considered for those with high-risk features, including PCI, if feasible. Consider intra-aortic balloon pumps, extracorporeal membranous oxygenation, left ventricular assist devices, or implantable cardioverter-defibrillators in hemodynamically unstable patients. ACE = angiotensin-converting enzyme; LAD = left anterior descending; PCI = percutaneous coronary intervention; SCAD = spontaneous coronary artery dissection.

PCI outcomes. Several series have reported poor technical success with PCI for SCAD. In the Vancouver cohort of 168 patients, successful or partially successful PCI was achieved in only 64% (57% had extension of dissections during PCI, 12% required urgent CABG, and 6% had stent thrombosis), with long-term durable results in only 30% (9). In the Mayo Clinic series of 189 patients, PCI failure occurred in 53%, and emergency CABG was required in 13% (10). In the Italian series of 134 patients, successful PCI was achieved in 72.5% (9% required urgent CABG, and 5% had stent thrombosis), and patients treated conservatively had lower in-hospital major cardiac adverse events (MACEs) compared with those treated with revascularization (3.8% vs. 16.1%; p = 0.028) (11).

PCI challenges. These suboptimal results are a consequence of multiple challenges with PCI in this anatomy (Table 4). These arteries are typically architecturally weakened by the underlying arteriopathies, and are prone to iatrogenic dissections and extension of dissections during PCI. In a retrospective review of 348 angiographic studies in SCAD patients, iatrogenic catheter-induced dissections occurred in 3.4% (in addition to their presenting SCAD arteries), with a much higher occurrence in ad hoc PCI cases (14.3%) (71). Thus, PCI has to be undertaken cautiously with meticulous techniques, but may still result in suboptimal outcomes. It may be challenging to enter the true lumen with the coronary guidewire, especially in the presence of type 1 angiographic SCAD with intimal disruption. With wiring, angioplasty, or stenting, the IMH can often propagate anterogradely or retrogradely, further compromising the true lumen and extending the dissection. Long stents are typically required because dissections are extensive, with a higher risk of restenosis. Furthermore, SCAD often involves distal coronary segments that are too small for stents. Moreover, with the natural resorption of IMH over time, there may be subacute and late strut malapposition, which can increase the risk of stent thrombosis (69).

TABLE 4 Challenges and Suggestions With SCAD PCI

Challenges during PCI of SCAD
Risk of iatrogenic catheter-induced dissection
Difficulty advancing coronary wire into distal true lumen
Propagating IMH anterograde and retrograde with angioplasty/stenting, extending dissection and further compromising true lumen arterial flow
Dissection tends to extend into distal arteries, which are too small for stents
Often extensive dissected segments require long stents, increasing stent restenosis
Risk of stent malapposition after resorption of IMH, with risk of late stent thrombosis
Suggestions if PCI is pursued for SCAD
Meticulous guide catheter manipulation, preferably through femoral access approach
OCT/IVUS guidance to ensure wire in true lumen (or over-the-wire catheter injections) and optimize stent apposition
Long stents covering 5–10 mm of proximal and distal edges of IMH
Placing short stents at proximal and distal edges first, before placing long stent in the middle
Consider bioabsorbable stents (temporary scaffold to avoid long-term malapposition)
Possible and careful use of cutting balloon (to fenestrate IMH)
Consider follow-up OCT to assess for malapposed/uncovered struts before stopping DAPT

DAPT = dual antiplatelet therapy; IMH = intramural hematoma; IVUS = intravascular ultrasound; PCI = percutaneous coronary intervention; other abbreviations as in Tables 1 and 2.

PCI approach. If PCI has to be pursued, there are a few strategies that may improve the outcome. A femoral access approach is preferred, because the radial approach has been associated with higher iatrogenic dissection in these patients (3-fold higher risk) (9,71). OCT/IVUS guidance should be considered to ensure true lumen access and adequate stent strut apposition. Long stents are suggested to provide adequate coverage for both proximal and distal edges of the IMH (5 to 10 mm longer on both edges) to accommodate extension of the IMH compressed by the stent. For longer lesions that require multiple stents, a multistep approach of stenting the distal edge, followed by the proximal edge, and then stenting the middle, may be useful in preventing IMH propagation (72). The use of bioresorbable stents also has the theoretical benefits of providing a temporary scaffold, and yet avoiding late stent malapposition and possibly stent thrombosis after resorption of IMH (69,73). There have also been recent successful case reports of using cutting balloons to fenestrate the IMH to allow decompression of the false lumen into the true lumen (74,75). This may prevent propagation of IMH if stenting is subsequently required; however, there is a theoretical risk of coronary rupture in the setting of SCAD. Thus, this should be performed cautiously with an undersized balloon. Follow-up OCT should also be considered to assess for malapposed or uncovered struts before cessation of DAPT.

CABG. Emergent CABG should be considered for patients with left main dissections, extensive dissections involving proximal arteries, or in patients in whom PCI failed or who are not anatomically suitable for PCI. Only small observational studies are available, but most show good acute survival following CABG, which is encouraging because these are typically emergency operations in unstable SCAD patients (9–11). Acute unsuccessful graft bypass was reported in 6% of grafts (2 of 34) in a 20-patient series (10). However, long-term results with CABG appears suboptimal, with reported graft patency of 27% in a small series (7), which may be related to spontaneous arterial healing, with subsequent competitive flow causing graft thrombosis. Nevertheless, CABG is an important temporizing strategy, providing coronary blood flow and myocardial perfusion for these critically ill patients in whom PCI is unsuitable.

POST-DISCHARGE RECOMMENDATIONS. At our institution, long-term medical management routinely consists of aspirin and beta-blockers, with the addition of angiotensin-converting enzyme inhibitors and statins as required. Cardiac rehabilitation is also highly encouraged, especially if a dedicated program for SCAD patients is available. A dedicated program

inclusive of exercise rehabilitation, psychosocial counseling, and peer group support was shown to be safe and beneficial for SCAD patients (76). Patients are advised to avoid lifting weights >20 pounds, and to have a low target exercise heart rate and systolic blood pressure with this program. SCAD patients who participated in the dedicated rehabilitation program had lower long-term MACEs compared with those who did not participate (76). For men with SCAD, the threshold of weightlifting was increased to 50 pounds (51), although it is not known if such weight restrictions will reduce the risk of recurrent SCAD. In terms of hormonal therapy, continued use should generally be avoided, because of the higher risk of recurrent MI (45). Among women of childbearing age, future pregnancy should also likely be avoided because the risk of recurrent SCAD among patients who subsequently became pregnant in a small series was 1 of 7 (14%) (77).

CARDIOVASCULAR OUTCOMES

The in-hospital outcomes of SCAD patients are reasonably good in contemporary prospective series (**Table 3**). Acute in-hospital mortality was <5% in modern series, and in-hospital recurrent MI, need for urgent revascularization in conservatively managed patients, or other MACEs were 5% to 10% (7,9,11). However, following hospital discharge, a significant proportion of patients can have recurrent chest pains and MACEs. Subacute MACEs were reported in 10% to 20% of patients at 2-year follow-up, with recurrent SCAD occurring in ~15% (9). Longer-term recurrent SCAD rates at 4 to 5 years were reported at ~27% (10,15). Although overall long-term survival is good in this cohort (>95%), long-term MACE rates can be high, and were reported to be 15% to 37% at 5 to 7 years and estimated at ~50% at 10 years (7,9,11,15). In the updated prospectively followed cohort of 280 patients, MACEs were 20.4% at a median 2.3-year follow-up; recurrent MI was 19.0%, with a recurrent SCAD rate of 12.2% (70). Such high long-term MACE rates emphasize the importance of close follow-up of SCAD survivors by cardiovascular specialists. Of note, patients with post-partum SCAD may have worse prognoses than other SCAD cohorts. In a small retrospective series, post-partum patients had larger infarcts, lower mean left ventricular ejection fractions, and tended to have more proximal artery dissections (78).

CONCLUSIONS

SCAD is an infrequent cause of ACS, but is not as rare as previously thought, especially in young women presenting with MI. It is frequently associated with predisposing and precipitating factors, such as FMD, and isometric and emotional stresses. Conservative therapy is favored, except for patients with unstable symptoms, hemodynamic instability, or left main dissection. Acute survival is good; however, long-term MACEs are frequent, including recurrent SCAD. Thus, SCAD patients should be closely followed for cardiac events, and further prospective studies exploring strategies to improve cardiovascular outcomes are needed.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Jacqueline Saw, Division of Cardiology, Vancouver General Hospital, 2775 Laurel Street, Level 9, Vancouver, BC, V5Z1M9, Canada. E-mail: jsaw@mail.ubc.ca.

REFERENCES

1. Pretty HC. Dissecting aneurysm of coronary artery in a woman aged 42: rupture. BMJ 1931;1:667.

2. Saw J. Spontaneous coronary artery dissection. Can J Cardiol 2013;29:1027–33.

3. Vrints CJ. Spontaneous coronary artery dissection. Heart 2010;96:801–8.

4. Poon K, Bell B, Raffel OC, et al. Spontaneous coronary artery dissection: utility of intravascular ultrasound and optical coherence tomography during percutaneous coronary intervention. Circ Cardiovasc Interv 2011;4:e5–7.

5. Saw J, Poulter R, Fung A, et al. Spontaneous coronary artery dissection in patients with fibromuscular dysplasia: a case series. Circ Cardiovasc Interv 2012;5:134–7.

6. Saw J, Ricci D, Starovoytov A, et al. 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.

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

8. 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.

9. 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.

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

11. Lettieri C, Zavalloni D, Rossini R, et al. Management and long-term prognosis of spontaneous coronary artery dissection. Am J Cardiol 2015;116:66–73.

12. Rogowski S, Maeder MT, Weilenmann D, et al. Spontaneous coronary artery dissection: angiographic follow-up and long-term clinical outcome in a predominantly medically treated population. Catheter Cardiovasc Interv 2015 Dec 28 [E-pub ahead of print].

13. Rashid HN, Wong DT, Wijesekera H, et al. Incidence and characterisation of spontaneous coronary artery dissection as a cause of acute coronary syndrome - a single-centre Australian experience. Int J Cardiol 2016;202:336–8.

14. Roura G, Ariza-Solé A, Rodriguez-Caballero IF, et al. Noninvasive follow-up of patients with spontaneous coronary artery dissection with CT angiography. J Am Coll Cardiol Img 2015 Oct 6 [E-pub ahead of print].

15. Nakashima T, Noguchi T, Haruta S, et al. Prognostic impact of spontaneous coronary artery dissection in young female patients with acute myocardial infarction: a report from the Angina Pectoris-Myocardial Infarction Multicenter Investigators in Japan. Int J Cardiol 2016;207:341–8.

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

17. Inspire. 2016. Available at: https://www.inspire.com. Accessed May 23, 2016.

18. 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.

19. Mortensen KH, Thuesen L, Kristensen IB, et al. Spontaneous coronary artery dissection: a Western Denmark Heart Registry study. Catheter Cardiovasc Interv 2009;74:710–7.

20. Hering D, Piper C, Hohmann C, et al. [Prospective study of the incidence, pathogenesis and therapy of spontaneous, by coronary angiography diagnosed coronary artery dissection] [in German]. Z Kardiol 1998;87:961–70.

21. 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 2016;5:263–70.

22. Hill SF, Sheppard MN. Non-atherosclerotic coronary artery disease associated with sudden cardiac death. Heart 2010;96:1119–25.

23. Saw J, Aymong E, Mancini GBJ, et al. Non-atherosclerotic coronary artery disease in young women. Can J Cardiol 2014;30:814–9.

24. Elkayam U, Jalnapurkar S, Barakkat MN, et al. Pregnancy-associated acute myocardial infarction: a review of contemporary experience in 150 cases between 2006 and 2011. Circulation 2014;129: 1695–702.

25. Maehara A, Mintz GS, Castagna MT, et al. Intravascular ultrasound assessment of spontaneous coronary artery dissection. Am J Cardiol 2002;89:466–8.

26. Isner JM, Donaldson RF, Fortin AH, et al. Attenuation of the media of coronary arteries in advanced atherosclerosis. Am J Cardiol 1986;58: 937–9.

27. Saw J, Mancini GB, 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.

28. 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.

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

30. Olin JW, Gornik HL, Bacharach JM, et al., American Heart Association Council on Peripheral Vascular Disease, Council on Clinical Cardiology, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Disease in the Young, Council on Cardiovascular Radiology and Intervention, Council on Epidemiology and Prevention, Council on Functional Genomics and Translational Biology, Council for High Blood Pressure Research, Council on the Kidney in Cardiovascular Disease, and Stroke Council. Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association. Circulation 2014;129:1048–78.

31. Lie JT, Berg KK. Isolated fibromuscular dysplasia of the coronary arteries with spontaneous dissection and myocardial infarction. Hum Pathol 1987;18:654–6.

32. Mather PJ, Hansen CL, Goldman B, et al. Postpartum multivessel coronary dissection. J Heart Lung Transplant 1994;13:533–7.

33. Brodsky SV, Ramaswamy G, Chander P, et al. Ruptured cerebral aneurysm and acute coronary artery dissection in the setting of multivascular fibromuscular dysplasia: a case report. Angiology 2007;58:764–7.

34. Saw J, Poulter R, Fung A. Intracoronary imaging of coronary fibromuscular dysplasia with OCT and IVUS. Catheter Cardiovasc Interv 2013; 82:E879–83.

35. Michelis KC, Olin JW, Kadian-Dodov D, et al. Coronary artery manifestations of fibromuscular dysplasia. J Am Coll Cardiol 2014;64:1033–46.

36. Saw J, Bezerra H, Gornik HL, et al. Angiographic and intracoronary manifestations of coronary fibromuscular dysplasia. Circulation 2016; 133:1548–59.

37. Eleid MF, Guddeti RR, Tweet MS, et al. Coronary artery tortuosity in spontaneous coronary artery dissection: angiographic characteristics and clinical implications. Circ Cardiovasc Interv 2014;7: 656–62.

38. Vijayaraghavan R, Verma S, Gupta N, et al. Pregnancy-related spontaneous coronary artery dissection. Circulation 2014;130:1915–20.

39. Yip A, Saw J. Spontaneous coronary artery dissection-a review. Cardiovasc Diagn Ther 2015;5: 37–48.

40. Sheikh AS, O'Sullivan M. Pregnancy-related spontaneous coronary artery dissection: two case reports and a comprehensive review of literature. Heart Views 2012;13:53–65.

41. Koller PT, Cliffe CM, Ridley DJ. Immunosuppressive therapy for peripartum-type spontaneous coronary artery dissection: case report and review. Clin Cardiol 1998;21:40–6.

42. 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.

43. Manalo-Estrella P, Barker AE. Histopathologic findings in human aortic media associated with pregnancy. Archiv Pathol 1967;83:336–41.

44. Labbok MH. Effects of breastfeeding on the mother. Pediatr Clin North Am 2001;48:143–58.

45. Eng L, Starovoytov A, Heydari M, et al. Abstract 18913: Spontaneous coronary artery dissection in women and association with hormonal stressors (abstr). Circulation 2015;132: A18913.

46. Kamran M, Guptan A, Bogal M. Spontaneous coronary artery dissection: case series and review. J Invasive Cardiol 2008;20:553–9.

47. 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.

48. Lempereur M, Grewal J, Saw J. Spontaneous coronary artery dissection associated with β-HCG injections and fibromuscular dysplasia. Can J Cardiol 2014;30:464.e1–3.

49. Sivam S, Yozghatlian V, Dentice R, et al. Spontaneous coronary artery dissection associated with coughing. J Cyst Fibros 2014;13:235–7.

50. Keir ML, Dehghani P. Corticosteroids and spontaneous coronary artery dissection: a new predisposing factor? Can J Cardiol 2016;32:395. e7–8.

51. Fahmy P, Prakash R, Starovoytov A, et al. Predisposing and precipitating factors in men with spontaneous coronary artery dissection. J Am Coll Cardiol Intv 2016;9:866–8.

52. Luong C, Starovoytov A, Heydari M, et al. Clinical presentation of patients with spontaneous coronary artery dissection. Paper presented at: SCAI 2016; May 4-7, 2016; Orlando, FL.

53. Franco C, Starovoytov A, Mancini GB, et al. Spontaneous resolution of LV dysfunction post SCAD: a case series. Paper presented at: SCAI 2015, May 6–9, 2015; San Diego, CA.

54. Rogers JH, Lasala JM. Coronary artery dissection and perforation complicating percutaneous coronary intervention. J Invasive Cardiol 2004;16:493–9.

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

56. Mehta LS, Beckie TM, DeVon HA, et al., American Heart Association Cardiovascular Disease in Women and Special Populations Committee of the Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council on Cardiovascular and Stroke Nursing, and Council on Quality of Care and Outcomes Research. Acute Myocardial Infarction in Women: A Scientific Statement From the American Heart Association. Circulation 2016;133:916–47.

57. Alfonso F, Bastante T, Rivero F, et al. Spontaneous coronary artery dissection. Circ J 2014;78: 2099–110.

58. Nienaber CA, Powell JT. Management of acute aortic syndromes. Eur Heart J 2012;33:26–35b.

59. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;64:2645–87.

60. Antithrombotic Trialists Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death,

myocardial infarction, and stroke in high risk patients. BMJ 2002;324:71–86.

61. Choi JW, Davidson CJ. Spontaneous multivessel coronary artery dissection in a long-distance runner successfully treated with oral antiplatelet therapy. J Invasive Cardiol 2002;14:675–8.

62. Shamloo BK, Chintala RS, Nasur A, et al. Spontaneous coronary artery dissection: aggressive vs. conservative therapy. J Invasive Cardiol 2010;22:222–8.

63. Zupan I, Noc M, Trinkaus D, et al. Double vessel extension of spontaneous left main coronary artery dissection in young women treated with thrombolytics. Catheter Cardiovasc Interv 2001;2001:226–30.

64. Leclercq F, Messner-Pellenc P, Carabasse D, et al. Successful thrombolysis treatment of spontaneous left main coronary artery dissection without subsequent surgery. Eur Heart J 1996;17:320–1.

65. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. J Am Coll Cardiol 2007;50:e1–157.

66. Rayner-Hartley E, Verma T, Starovoytov A, et al. Catheter angiography versus computed tomography angiography for the diagnosis of extracardiac fibromuscular dysplasia in patients with spontaneous coronary artery dissection. Paper presented at: SCAI 2016; May 4-7, 2016; Orlando, FL.

67. Henkin S, Negrotto SM, Tweet MS, et al. Spontaneous coronary artery dissection and its association with heritable connective tissue disorders. Heart 2016;102:876–81.

68. Goel K, Tweet M, Olson TM, et al. Familial spontaneous coronary artery dissection: evidence for genetic susceptibility. JAMA Intern Med 2015;175:821–6.

69. 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.

70. Saw J, Prakash R, Starovoytov A, et al. Cardiovascular outcomes in a large prospectively followed single-center cohort of spontaneous coronary artery dissection patients (abstr). J Am Coll Cardiol 2016;67:457.

71. Prakash R, Starovoytov A, Heydari M, et al. TCT-386: iatrogenic catheter-induced dissection during angiography of patients with spontaneous coronary artery dissection (abstr). J Am Coll Cardiol 2015;66 Suppl B:B155–6.

72. Walsh SJ, Jokhi PP, Saw J. Successful percutaneous management of coronary dissection and extensive intramural haematoma associated with ST elevation MI. Acute Card Care 2008;10:231–3.

73. Cockburn J, Yan W, Bhindi R, et al. Spontaneous coronary artery dissection treated with bioresorbable vascular scaffolds guided by optical coherence tomography. Can J Cardiol 2014;30:1461.e1–3.

74. Yumoto K, Sasaki H, Aoki H, et al. Successful treatment of spontaneous coronary artery dissection with cutting balloon angioplasty as evaluated with optical coherence tomography. J Am Coll Cardiol Intv 2014;7:817–9.

75. Alkhouli M, Cole M, Ling FS. Coronary artery fenestration prior to stenting in spontaneous coronary artery dissection. Catheter Cardiovasc Interv 2015 Sep 2 [E-pub ahead of print].

76. Chou AY, Prakash R, Rajala J, et al. The first dedicated cardiac rehabilitation program for patients with spontaneous coronary artery dissection: description and initial results. Can J Cardiol 2016;32:554–60.

77. Tweet MS, Hayes SN, Gulati R, et al. The risk of pregnancy after spontaneous coronary artery dissection (abstr). J Am Coll Cardiol 2014;63:A28.

78. Ito H, Taylor L, Bowman M, et al. Presentation and therapy of spontaneous coronary artery dissection and comparisons of postpartum versus nonpostpartum cases. Am J Cardiol 2011;107:1590–6.

KEY WORDS fibromuscular dysplasia, myocardial infarction, women