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Review

What Is New in Spontaneous Coronary Artery Dissection?

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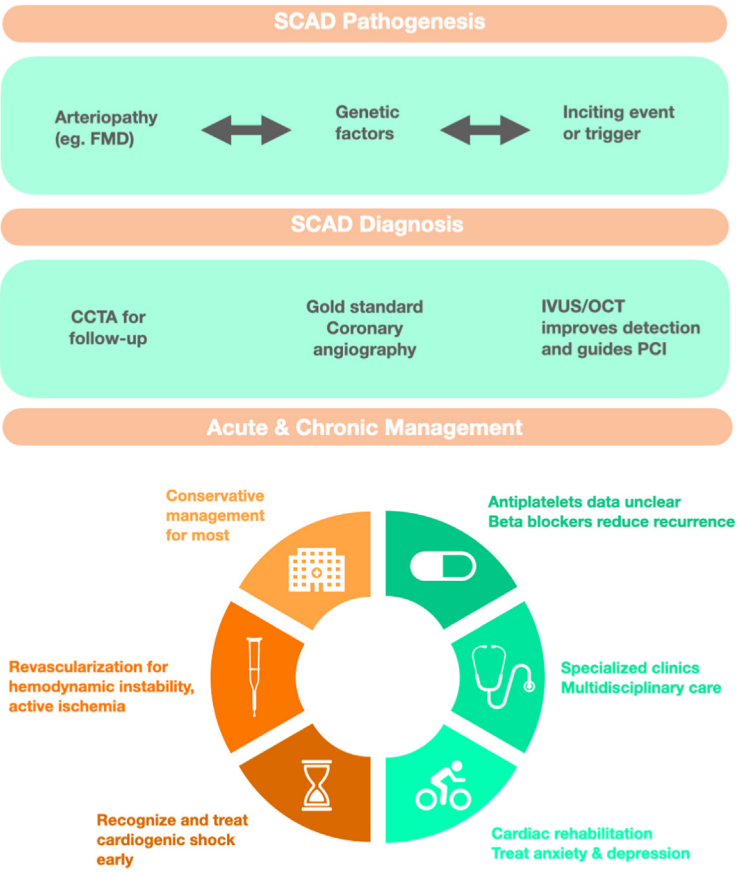

ABSTRACT

Spontaneous coronary artery dissection (SCAD) is a condition that leads to tearing of the coronary vessel wall in the absence of trauma, iatrogenic injury, or atherosclerosis. SCAD is an important cause of myocardial infarction in young women, leading to significant cardiovascular morbidity and mortality. Within cohorts of women aged around 50 years on average, who experience acute coronary syndrome, the prevalence of SCAD is 22.5%- 35%. Over the past decade, SCAD research has expanded rapidly, leading to improved understanding of this condition. In this review, we provide a summary of the

RÉSUMÉ

La dissection spontanée de l'artère coronaire (DSAC) est un trouble qui survient lorsque la paroi d'un vaisseau coronarien se déchire en l'absence de traumatisme, de lésion iatrogène ou d'athérosclérose. La DSAC est une cause importante d'infarctus du myocarde chez les jeunes femmes, menant à des taux importants de morbidité et de mortalité cardiovasculaires. Dans des cohortes de femmes âgées d'environ 50 ans, en moyenne, qui ont subi un syndrome coronarien aigu, la prévalence de DSAC était de 22,5 % à 35 %. Au cours de la dernière décennie, la recherche sur la DSAC s'est accélérée, per-

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current body of knowledge, highlight areas of ongoing research, and identify existing knowledge gaps. Specifically, we provide a focused update on the pathogenesis of SCAD, including genetic and associated conditions, clinical presentation and diagnosis, prognosis, and short-term and long-term management. Highlighted areas include the following: insights from recent genome-wide association studies; intracoronary imaging for the diagnosis of SCAD; the role of cardiac computed tomography angiography to assess for vessel healing; revascularization strategies and challenges; cardiogenic shock in SCAD; and the increasingly recognized burden of anxiety, depression, and posttraumatic stress disorder among SCAD patients.

mettant de mieux comprendre cette affection. Dans cette analyse, nous présentons un résumé du corpus de connaissances actuel, mettons l'accent sur les principaux domaines de la recherche en cours et cernons les lacunes à combler. Plus particulièrement, nous présentons une mise à jour ciblée sur la pathogenèse de la DSAC, comme les causes génétiques ou autres, les manifestations et le diagnostic cliniques, le pronostic ainsi que la prise en charge à court et à long terme. Les domaines mis de l'avant sont les suivants : résultats des récentes études d'association menées sur l'ensemble du génome; imagerie intracoronarienne pour le diagnostic de DSAC; rôle de l'angiotomodensitométrie cardiaque dans l'évaluation de la guérison des vaisseaux; stratégies et difficultés de revascularisation; choc cardiogène dans la DSAC; et fardeau croissant associé à l'anxiété, la dépression et le stress post-traumatique chez les patients atteints de DSAC.

Lay Summary

Spontaneous coronary artery dissection (SCAD) is a tear in the wall of the blood vessels that supply blood to the heart muscle. SCAD increasingly is recognized as a cause of heart attacks, particularly in young women around the age of 50 years. The exact cause of SCAD is not fully understood. In this review, we highlight the recent updates in our understanding of the causes of SCAD, its signs and symptoms, diagnosis, and short-and long-term treatment.

Spontaneous coronary artery dissection (SCAD) is a condition whereby a non-iatrogenic, nontraumatic tear of the coronary vessel wall occurs in the absence of atherosclerosis.[1] This condition leads to formation of an intramural hematoma, obstruction of coronary luminal flow, and myocardial infarction (MI). Historically, SCAD was thought to be a rare diagnosis. The population affected by this condition tends to lack traditional cardiovascular risk factors. Over the past decade, SCAD has become increasingly recognized as an important cause of acute MI, particularly among women.

Contemporary series have reported the prevalence of SCAD as ranging between 0.2% to 4% of all acute coronary syndromes (ACSs).[2-7] Within subgroups of young women with average age of around 50 years with ACS, the prevalence of SCAD has been reported to be as high as 22.5% to 35% in small single and multicentre studies.[5,6] In one single-centre study in British Columbia, SCAD was found to be the cause of ACS in 24% of cases in women aged 50 years or younger.[8] In another series examining coronary angiograms performed in women younger than 50 years at a single centre in British Columbia over a 2-year period, SCAD was diagnosed in 9% of women.[9] A large population-based analysis of acute MI between 2009 and 2014 in the United States showed that, among women with a discharge diagnosis of acute MI, 0.98% had a co-diagnosis of SCAD.[10] However, this prevalence may be an underestimate, as the diagnostic criteria for SCAD in that era likely were limited to the angiographic appearance of intimal disruption, which represents < 30% of SCAD detected on angiography.[8] The true incidence of SCAD in the population is unclear, as the diagnosis remains challenging, and a discrepancy exists between discharge database reports and studies in which angiographic review is performed by a core laboratory.

Increasing awareness and multicentre collaboration have led to the rapid expansion of SCAD research across the globe. Associations between SCAD and several conditions have been identified. Many of these conditions have a preponderance among female patients. For example, fibromuscular dysplasia, which affects women more commonly than men, is found in 31% to 72% of patients with SCAD.[8,11] Fluctuations in reproductive hormone levels also have been associated with the occurrence of SCAD, as seen during pregnancy and menopause.

SCAD is a significant cause of cardiovascular morbidity and mortality among women, particularly young women with paucity of traditional atherosclerotic risk factors. The purpose of this review article is to summarize the existing body of knowledge and highlight areas of ongoing research and development. This article will provide a focused update on the following 4 areas: pathogenesis including genetic and associated conditions; clinical presentation and diagnosis; prognosis; and short-term and long-term management of SCAD.

What Is New in Our Understanding of the Pathogenesis of SCAD?

The precise etiology and pathogenesis of SCAD remains unknown. This condition appears to affect susceptible individuals with an underlying genetic or acquired predisposition to coronary arteriopathy. Susceptible individuals include those with heritable connective tissue diseases, such as Marfan syndrome, Ehlers-Danlos syndrome, and Loeys-Dietz syndrome, as well as inflammatory arteriopathies. Whether autoimmune conditions predispose patients to SCAD is unclear. Eosinophilic periarteritis isolated to affect the coronary arteries has been reported in the literature, both with and without SCAD. An interesting finding in one case series is

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that eosinophilic coronary periarteritis without SCAD appeared mainly in men, whereas eosinophilic coronary periarteritis with SCAD appeared almost exclusively in female patients.[12] SCAD also has been reported in systemic lupus erythematosus and polyarteritis nodosa.[13,14] However, a case–control study within the Rochester Epidemiology Project, a population-based medical records database, showed no difference in the prevalence of autoimmune disease among 114 cases of SCAD and 342 matched controls. Despite adjusting for race and body mass index, the prevalences of autoimmune conditions were similar in the SCAD and control groups.[15]

Fibromuscular dysplasia (FMD) is the most common underlying arteriopathy. FMD is a nonatherosclerotic and noninflammatory vascular disease which leads to arterial stenosis, aneurysm, and dissection.[16] The prevalence of FMD has been reported to be as high as 72% among patients with SCAD.[8,11] FMD has a preponderance among female patients, with 75%-90% of FMD patients being women.[17] Clinically, FMD presents variably, depending on the arterial bed involved. For example, renal artery involvement can lead to stenosis and renovascular hypertension. By contrast, cerebrovascular FMD can lead to pulsatile tinnitus (described as "swooshing"), migraines, headaches, stroke, and transient ischemic attack. In the Canadian SCAD cohort, of 576 patients with FMD screening, 25.3% had renal artery involvement, 16.3% had femoral and/or iliac involvement, and 23.8% had cerebrovascular involvement,[18] Invasive angiography remains the gold standard for diagnosis of FMD in renal and iliac arteries, and it can show not only the classic "string of beads" appearance, but also focal stenosis, aneurysms, and dissections.[19] Computed tomography angiography is a preferred noninvasive alternative for detection of cerebrovascular FMD.

The genetic basis of SCAD is poorly understood. Recent research has led to several promising developments. Genome-wide association studies performed on over 1100 FMD patients across multiple European and North American centres identified an association between FMD and a variant in the phosphatase and actin regulator 1 gene (*PHACTR1*).[16] One variant was identified to be a risk locus for coronary artery disease (CAD), migraine, and cervical artery dissection. This report was the first of genetic evidence linking shared pathophysiology between FMD and cardiovascular disease. More recently, a genome-wide association meta-analysis of 1917 cases and 9292 controls identified 16 risk loci for SCAD.[20] These genes encoded predominantly for the regulation proteins involved in regulation of the extracellular matrix, such as ADAMTSL4, COL4A1, and TIMP3. Overall, the study provides evidence in support of SCAD being a complex polygenic disease, corroborating prior studies that show only a small proportion—about 3.5%—is due to rare genetic variants. An interesting point to note is that the study identified a novel tissue factor gene *F3*, which is part of the coagulation pathway. *F3* was shown to be associated with a higher risk for SCAD. This finding suggests that the process of intramural hematoma formation may be a potential therapeutic target in the management of SCAD.

The importance of the extracellular matrix has been demonstrated in other whole-exome sequencing studies. In one study in which over 200 SCAD patients were compared with healthy population-based controls from the United Kingdom Biobank, patients with SCAD were found to be more likely to have disruptive variants in fibrillar collagen genes.[21] The most common gene variants identified were *COL3A1* and *COL5A1*. Mice, when depleted of these genes, demonstrated an increased risk of arterial dissection. Other genome-wide association studies have identified a candidate gene in pregnancy-associated SCAD (*AFAP1*), which encodes for a protein involved in modulation of actin filament integrity in response to cellular signals. Modulation of the protein by prolactin signalling may be implicated in peripartum SCAD during the lactation period.

Among susceptible individuals, an inciting event or trigger has been reported to precede the development of SCAD. In a recent multicentre prospective registry (the Canadian SCAD Cohort Study), up to 50% of patients described having severe emotional stress preceding the SCAD event, whereas 29% reported physical stress and one-third of patients reported no precipitating factor. Valsalva-type stress is described in 12% of all patients. Extrapolating from the aortic dissection literature, raised intrathoracic pressure from Valsalva-type stress is thought to be particularly detrimental in precipitating SCAD. Although an association has been reported with many other activities, such as sneezing, retching, and use of stimulants such as cocaine, establishing any causal relationships between patient-reported triggers and the development of SCAD remains challenging, owing to cohort studies being by nature subject to recall bias.

What Is New in The Diagnosis of SCAD?

Invasive coronary angiography remains the gold standard for diagnosis of SCAD. The classic appearance of multiple radiolucent lumens is absent in over 70% of SCAD cases.[22] A novel angiographic classification of SCAD has been well described.[23] In brief, type 1 is the pathognomonic appearance of multiple arterial lumens filled with contrast. Type 2 is the most common form of SCAD on angiography, and it is frequently missed. Type 2 is a long diffuse narrowing of the artery due to intramural hematoma compression of the true lumen. Type 3 mimics atherosclerosis with focal or tubular stenosis and requires intracoronary imaging to differentiate it from atherosclerotic lesions. The classification scheme is illustrated in Figure 1.

Intracoronary imaging using intravascular ultrasound and optical coherence tomography (OCT) has improved the detection of SCAD and aids in invasive management and follow-up. OCT uses near-infrared light to generate high-resolution images. The resolution of OCT to 10-20 μm allows visualization of multiple layers of coronary vessels.[24] Compared to intravascular ultrasound, OCT offers higher spatial resolution and is able to identify intramural hematoma, endothelial tears, and dissection entry sites. One concern, however, is that OCT requires simultaneous injection of contrast and pullback of the catheter to allow image acquisition. The injection of contrast can cause propagation of dissection and worsen distal vessel flow. Small series have shown that OCT during SCAD is safe and feasible.[8,25,26] In cases of SCAD in which percutaneous coronary intervention (PCI) is indicated, OCT aids in correct stent sizing, which may be challenging in the setting of intramural hematoma, as

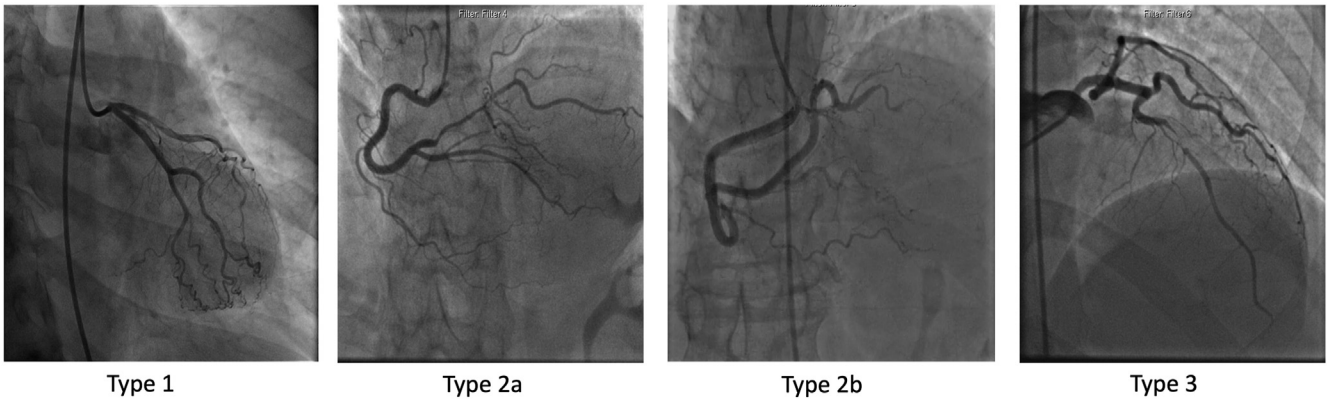

Figure 1. Angiographic classification of spontaneous coronary artery dissection. Type 1: classic multiple radioluscent lumen. Type 2a: diffuse stenosis and smooth narrowing. Type 2b: diffuse narrowing that extends to distal tip of artery. Type 3: focal or tubular stenosis that mimics atherosclerosis and requires intracoronary imaging. Adapted from Yang et al.[64] with permission from Springer Nature.

well as identification of the location of stent deployment relative to the dissection entry site.[27]

The largest international imaging series of patients with SCAD undergoing OCT included 65 patients and 68 dissected vessels.[28] This series differentiated vessels based on the presence of fenestration between the true and false lumen. A lack of fenestration appears to be associated with false lumen pressurization and compression of the true lumen. Ten patients had follow-up OCT to assess for angiography healing of SCAD at a median of 2 months post-initial OCT. In the majority of patients, recovery of the true luminal area and patchy resorption of hematoma were seen. Furthermore, an increase in vasa vasorum density was seen during the convalescence period, suggesting that neovascularization of the false lumen occurred as part of the healing process.

Cardiac computed tomography angiography (CCTA) has gained a central role in the detection, diagnosis, and prognostication of low-to-intermediate−risk stable atherosclerotic CAD.[29] In SCAD, the role of CCTA is less well established and currently is not recommended as a means of first-line investigation,[30] owing largely to its low spatial resolution. Therefore, a normal CCTA result cannot be used to confidently exclude SCAD.[31] Retrospective assessment CCTA on 14 patients with acute SCAD in the Mayo Clinic SCAD Registry identified 4 pertinent diagnostic features on CCTA: abrupt luminal stenosis, intramural hematoma, tapered luminal stenosis, and dissection.[32] This finding is in contrast to the high-risk features of atherosclerotic disease identified on CCTA, which include spotty calcifications, positive vessel remodelling, low attenuation plaque (< 30 Hounsfield units), and napkin-ring sign.[29]

Compared with invasive coronary angiography, CCTA does offer the advantage of being noninvasive and providing availability of assessment of the vessel wall and 3-dimensional reconstruction in postprocessing of images.[31] However, CCTA is limited by its lower spatial resolution and accuracy for identification of SCAD, particularly in small vessels, as well as its inability to provide simultaneous coronary intervention. An area in which CCTA may play a major role is in the follow-up of SCAD to assess for angiographic healing. This procedure allows clinicians to mitigate the risk of recurrent dissection from catheter-induced dissection. From angiographic data, the rate of spontaneous healing was 95% when repeat angiography was performed at ≥ 30 days post-SCAD in 160 dissected vessels.[33] In other studies using OCT, 90% of patients also demonstrated recovery of the true lumen diameter at a median of 80 days post-SCAD.[28] In one study of 32 patients with 38 SCAD segments, sensitivity of CCTA for assessment of dissection healing was shown to be 72%, with the optimal timing of CCTA to assess for healing being 80 days, which maximized sensitivity at 76.9% and specificity at 84%.[34] Another study showed that 20 of 24 patients undergoing follow-up CCTA at 3-to-6 months post-SCAD had a normal result.[35] One patient developed recurrent dissection at a different segment, and 2 other patients developed aneurysms in the location of the coronary dissection. One patient showed persistent dissection in the left anterior descending artery.

What Is New in the Prognosis and Acute Management of SCAD?

Patients with SCAD most commonly present with ACS. The majority of patients can be managed conservatively, unless high-risk features are present which necessitate intervention. High-risk features include evidence of ongoing ischemia to a large area of the myocardium, ST-elevation MI, cardiogenic shock, sustained ventricular arrhythmia, and left main dissection.[30,36] Conservative management is further supported by the fact that up to 95% of patients with SCAD demonstrate spontaneous healing.[33] Furthermore, ACS due to SCAD has a lower mortality rate, as compared to that for patients who develop ACS due to atherosclerotic CAD.[37] In the recently published Canadian SCAD Cohort Study that prospectively evaluated long-term outcomes of 750 SCAD patients, the 3-year mortality incidence was 0.8%, with a major adverse cardiovascular event (MACE) rate of 14.0%, which was driven largely by recurrent MI and unplanned revascularization. Overall, different observational studies have reported that between 12.5% and 55.6% of SCAD patients underwent revascularization; this wide range is likely accounted for by the variable distribution of patients in observational studies presenting with ST-elevation MI and

high-risk features, versus those with non-ST-elevation MI and a stable clinical course.[36]

Several systematic review and meta-analyses have examined long-term outcomes, comparing medical therapy vs revascularization for SCAD. One study included 17 observational studies—with 860 patients treated with medical therapy, and 509 treated with invasive therapy—and found that the relative risk of death, recurrent SCAD, and repeat revascularization was not statistically significantly different between the 2 groups. In this study, the long-term mortality incidence observed was 1%-2% among patients with SCAD, similar to that in previous reports in the literature.[37] In another pooled meta-analysis, 11 observational studies, comprised of 378 medically managed patients and 253 undergoing revascularization, also showed no significant difference between the 2 strategies in terms of either in-hospital mortality or mortality at follow-up.[38] Additionally, no difference was found in MI or SCAD recurrence between the groups. As the meta-analyses did not stratify patients with high-risk features necessitating revascularization vs stable patients, the results are limited by confounding factors in that the sicker patients were more likely to be treated with revascularization.

Urgent revascularization is most commonly performed with PCI. Observational studies have shown repeatedly that PCI for treatment of SCAD is associated with a low level of procedural success and an increased rate of complications. The PCI success rate was reported to be as low as 47% in one series. Performing PCI in patients with SCAD poses many inherent challenges, which include the risk of iatrogenic catheter-induced dissection and propagation of existing intimal dissection or intramural hematoma.[36] Furthermore, advancing the coronary wire into the true lumen also poses challenges, particularly in cases in which intimal disruption is present. In cases in which PCI is undertaken, long stents may be needed, posing a risk of restenosis. Post-PCI, as the intramural hematoma is reabsorbed, stent underexpansion is another potential issue.

Several revascularization strategies have been described in the literature in the setting of SCAD. These strategies include cutting-balloon angioplasty, using longer stents to cover the proximal and distal edges of the dissections overlapping by 5 mm, focal stenting of the proximal segment to minimize proximal extension of intramural hematoma, and use of bioabsorbable scaffolds when longer stents are required.[4,5,36,39,40] Experience with cutting-balloon angioplasty in SCAD remains limited. In the literature, 13 case reports thus far have described experience with this technique. All cases used small balloons of between 2.0 and 2.5 mm in diameter, to minimize the risk of coronary arterial wall perforation.[41-43] Shorter cutting balloons of between 6 and 10 mm in length, inflated to low pressure (4 atmospheres), are optimal.[42] Experience with use of bioresorbable scaffolds in SCAD is scarce, and long-term follow-up data are lacking.[44,45] Due to the findings of increased target-vessel revascularization and stent thrombosis in the Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II) randomized controlled trial, use of bioresorbable scaffolds has been limited.[46] A combination strategy utilizing cutting balloon and bioresorbable scaffold has been described in a 47-year-old woman with non-ST-elevation MI and SCAD of the left anterior descending artery.[47] The angiographic result after use of 2.5-mm cutting balloon alone was inadequate, and OCT-guided bioresorbable scaffold implantation with 2 overlapping scaffolds was undertaken, with good results on angiogram at 12 months' follow-up.

Cardiogenic shock (CS) and ventricular arrhythmias may complicate SCAD. The incidence of CS in SCAD is reported to be between 1.2% and 15.9%.[2,5,8,11,48-52] In the Canadian SCAD registry, analysis of a prospective cohort of 1056 patients found the incidence of CS to be 2.3%.[52] Patients with CS were significantly younger, and they were more likely to have connective tissue disorder and grand multiparity, and to be peripartum. In this cohort, 75% required mechanical circulatory support, most commonly with an intra-aortic balloon pump. Five patients received extracorporeal membrane oxygenation, and one received a left ventricular assist device. In-hospital and long-term outcomes were significantly worse in the group with CS. Those with CS also had a higher rate of cardiac arrest (58.3% vs 2.3%, $P < 0.001$). The role of use of an implantable cardioverter-defibrillator (ICD) post-SCAD is unclear. In a meta-analysis of 5 studies including 139 patients with sudden cardiac arrest post-SCAD, 20% received an ICD.[53] At a follow-up of 4.1 $\pm$ 3.3 years, 1.2% received appropriate ICD therapies, and the rate of recurrent cardiac arrest was 3.9%.

What Is New in the Long-term Management of SCAD?

The goals of long-term management of SCAD are as follows: prevent recurrent dissection; alleviate residual cardiac symptoms; develop individualized rehabilitation programs to help patients be physically active in a safe manner; and recognize and address the psychological impact of SCAD.

Experts recommend aspirin for at least 1 year and indefinitely for most patients without contraindications.[30] Those who undergo PCI should continue on dual-antiplatelet therapy (DAPT), per current national guidelines. In patients who are medically managed without percutaneous revascularization, evidence is lacking for a role for a P2Y12 inhibitor, which remains unclear. The **Di**ssezioni **S**pontanee **Co**ronariche (DISCO) study was a multicentre retrospective registry study that examined 199 patients with initially medically managed SCAD, in whom 33.7% were given single antiplatelet therapy (SAPT), and 66.3% were given DAPT. In the group using DAPT, ticagrelor was used in 36.4%, and clopidogrel was used in 62.9%. At a follow-up at 12 months, the incidence of MACEs was significantly higher in those treated with DAPT, compared to SAPT (hazard ratio 2.62, 95% confidence interaval 1.22-1.561, $P = 0.013$).[54] However, the results are confounded by the lack of randomization to receiving SAPT vs DAPT, as well as the long duration of DAPT use (12 months) in almost all patients.[55] Currently, expert recommendation for the duration of DAPT ranges between 1 month and 12 months post-ACS.[30] Observational studies have shown that beta-blocker use is associated with reduced recurrence of SCAD (hazard ratio 0.36, $P = 0.004$).[56] A meta-analysis of 14 studies, comprised of 4206 patients, examining factors associated with recurrence of SCAD, showed that hypertension (risk ratio [RR] 1.49) and FMD (RR 2.02) conferred a greater risk.[57] By contrast, the use of beta-blockers (RR 0.51) was associated with a reduced

risk of SCAD recurrence. In the recently published 3-year outcomes of the Canadian SCAD Cohort Study, recurrent de novo SCAD was seen in 2.4% of patients, and recurrent MI was seen in 5.7%.[18] A randomized multinational study, using a 2-by-2 factorial design randomizing patients to beta-blocker and short (1 month) vs prolonged (12 months) antiplatelet therapy, is underway.[58] The results are highly anticipated and will shed light on what constitutes the optimal long-term medical management.

Cardiac rehabilitation (CR) plays a critical role in the physical and emotional recovery of patients post-SCAD. Multiple studies have demonstrated the beneficial effects of CR in this setting. A study from the Mayo Clinic of 354 patients post-SCAD showed that 269 participated in CR. Of these, 82% perceived that they received physical health benefits, and 75% perceived that they received emotional health benefits. The primary barrier to patients undergoing CR was a recommendation against CR by their healthcare provider. In the Canadian context, 70 consecutive SCAD patients in a dedicated SCAD-CR program were studied at our centre. We found that after a mean duration of 12.4 $\pm$ 10.5 weeks of CR participation, the proportion of patients with recurrent chest pain was lower, and the average metabolic equivalents (METS) was higher. Also, a significant improvement occurred in the **S**creening **T**ool f**o**r **P**sychosocial **D**istress (STOP-D) score for depression screening. Furthermore, the MACE rate was lower than that for the nonrehabilitation cohort, demonstrating that SCAD-CR is both safe and beneficial.

Anxiety and depression symptoms are common in patients after SCAD. Uncertainty around the cause of SCAD, and the lack of evidence-based treatment and prevention of occurrence, likely contributes to the stress experienced by patients. This stress can be of the type resulting from a perceived lack of control. Qualitative studies have identified emotional impacts that fall into the following categories: shock and disbelief, confusion and uncertainty, unfairness, fear and anxiety, loss and grief, isolation and loneliness, guilt, invalidation and embarrassment, depression, vulnerability, and frustration. [59] In a cross-sectional study in which 158 SCAD patients were screened with the Patient Health Questionnaire-9 Depression Scale and the Generalized Anxiety Disorder-7—item scale,[60] one-third had received treatment for depression and anxiety. Younger women and those who experienced peripartum SCAD had higher scores on both of these scales, whereas those who had undergone PCI reported lower scores.

In another cross-sectional study of 14 female SCAD patients, symptoms of stress, insomnia, anxiety, depression, and post-traumatic stress disorder (PTSD) were prevalent.[61] Atlhough the incidence of PTSD in all patients post-MI was reported to be 12% in one meta-analysis,[62] among patients with SCAD, 28% reported having mild-to-moderate PTSD symptoms in an analysis of 512 patients.[63] In this study, a higher resiliency score was associated with less-severe psychological symptoms of PTSD, anxiety, and depression. This finding suggests that resiliency may be a reasonable therapeutic goal when addressing the psychological needs of patients post-SCAD.

Conclusion

Our collective knowledge of SCAD has come a long way since the first case was reported by Pretty in 1931. The increased awareness is attributed to improved diagnosis with coronary angiography and intravascular imaging, as well as the establishment of collaborative SCAD networks and research centres across the globe. However, SCAD remains a challenging condition, with a preponderance in women that is incompletely understood. Future efforts should be directed at the following aims: understanding the genetic basis of SCAD and associated conditions that predispose patients to arteriopathy and intramural hematoma formation; harnessing multimodality imaging to optimize the diagnosis and follow-up of SCAD; clarifying the role of medical therapy; identifying strategies to improve the success rate of PCI; and developing and implementing CR and counselling programs to address the long-term physical psychological recovery of patients with this unique condition.

Ethics Statement

The research reported here has adhered to the relevant clinical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article. This is a review article.

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