The diagnosis and management of spontaneous coronary artery dissection — expert opinion of the Association of Cardiovascular Interventions (ACVI) of Polish Cardiac Society

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INTRODUCTION

Spontaneous coronary artery dissection (SCAD) has been recognized as a relatively uncommon disease for several years. The condition, although described, was poorly characterized in the era before intravascular imaging. As a result, women with SCAD were often misdiagnosed with an atheromatous acute coronary syndrome (ACS), MINOCA, or takotsubo cardiomyopathy. Increasing numbers of recent studies, including large registries, confirm that it should no longer be called a "rare" disease. These studies provided new information about the incidence, pathophysiological concepts, methods of diagnosis, and the treatment of this condition [1–9].

This paper aims to increase the awareness of SCAD among clinicians who take care of patients with acute coronary syndromes in the emergency room, through the catheterization laboratory, cardiology wards, to general practitioners. We present the recommendations regarding the identification of SCAD on angiography, the indications for the use of intravascular imaging, the methods of acute treatment, and long-term post-SCAD management. As prospective randomized trials are not available, these recommendations are based on retrospective analyses of series of patients or reflect experts' consensus.

WHAT IS SCAD?

Spontaneous coronary artery dissection is a non-atherosclerotic, non-traumatic, and non-iatrogenic disease of the coronary artery wall. It is a cause of the ACS and sudden cardiac death, especially among young and middle-aged women [1, 5, 6, 8]. Pathophysiologically, two potential mechanisms for SCAD have been proposed. First, the "inside-out" mechanism, where an intimal tear allows blood from the vessel lumen to enter the artery wall leading to dissection and false lumen formation. Second, the "outside-in" mechanism assumes that the primary event is bleeding from microvessels *(vasa vasorum)* traversing the arterial wall. With both mechanisms, the intramural hematoma causes compression

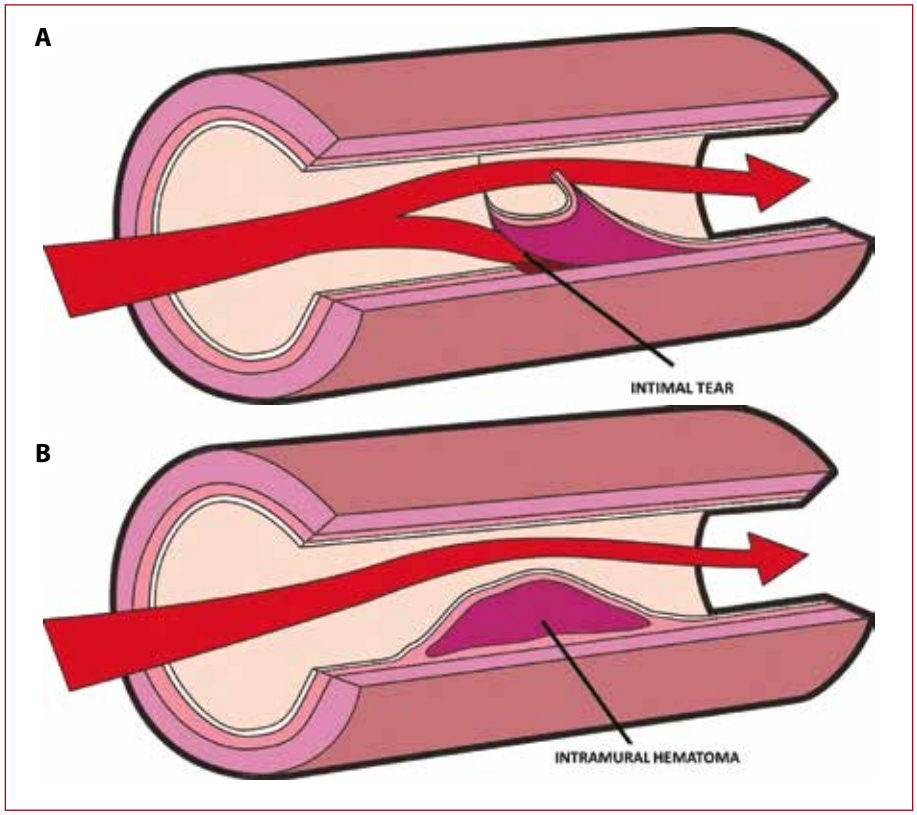

Figure 1. Pathophysiology of spontaneous coronary dissection (Images used courtesy of BeatSCAD, *www.beatscad.org.uk*)

Table 1. Spontaneous coronary artery dissection (SCAD) prevalence and baseline characteristics of patients — studies published since 2017

Author (year of publication)	Number of SCAD patients/number of all ACS patients	SCAD prevalence, %	SCAD prevalence in women ≤50 years of age	Females, %	STEMI/NSTEMI, %	Multivessel SCAD, %	Hypertension, %	Dyslipidemia, %
Motreff (2017)	36/3224	1.1	15.3	100	52.7/47.3	18.2	27.3	10.9
Meng (2017)	21/60[b]	—	35.0	100[b]	57.1/42.9	4.8	33.3	NR
Abreu (2018)	27/5002	0.5	NR	81.4	37.0/55.5	3.7	55.6	44.4
Clare (2019)	208/26598	0.78	NR	88.9	19.7/85.5	10.8	30.8	27.9
Inohara (2020)	322/68909	0.5	6.6	100[a]	NR	NR	58.7	40.1
de Roeck (2020)	27/102[b]	—	26.5	100[b]	51.9/40.7	7.4	7.4	11.1
Krittawong (2020)	375/30427	1.2	NR	64.3	NR	NR	54.7	NR

[a]Only women included; [b]Only women up to 50 years of age included.

Abbreviations: ACS, acute coronary syndrome; NR, not reported; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction

of the true lumen resulting in compromised blood flow (Figure 1). Recent intracoronary imaging studies have shown that in a large proportion of SCAD cases, an intimal tear is not present or is preceded by intramural hematoma development, supporting the "outside-in" hypothesis as the predominant mechanism for SCAD [10–13].

INCIDENCE, PRECIPITATING RISK FACTORS, COMORBIDITIES, AND CLINICAL PRESENTATION

The true prevalence of SCAD remains unknown as this is still an underdiagnosed disease. In recently published studies, SCAD accounted for 0.3%–1.2% of all ACS cases [3, 14–16] (Table 1).

This condition affects predominantly young and middle-aged women (more than 70% of cases reported in several studies) [5]. The reported prevalence of SCAD in women below 50 years of age presenting with ACS ranges from 6.6 to 35% [14, 16, 17–22]. No ethnic variations have been reported. The frequency of conventional risk factors for ischemic heart disease has often been considered minimal. Still, observational studies show these are certainly not negligible — hypertension was diagnosed in 18%–57% cases, hyperlipidemia in 10%–52%, and smoking in 11%–57% [5, 8]. Indeed, in a recent analysis of more than 30 000 patients presenting with ACS, SCAD patients (n = 375) were more often hypertensive than non-SCAD ACS patients [3]. This critical finding may potentially change the paradigm that SCAD afflicts predominantly healthy women.

The cause of SCAD remains unknown. The predominance in young and middle-aged women, together with the association with pregnancy (predominantly the 3rd trimester) and

the postpartum period, suggests a potential pathophysiological role of female sex hormones. However, the evidence of how this impacts mechanistically is still lacking [23]. Also, the following diseases or conditions were reported in case reposts or small case series, however, the potential causal relationship remains unproven: depression, hypothyroid, celiac disease, cryoglobulinemia, multiparity [5].

Spontaneous coronary artery dissection may have a genetic background in some cases (see *Genetics* section).

Among SCAD-related precipitating factors, extreme physical or emotional stress was most commonly identified [24–26]. Other potential factors, like Valsalva-type activities (sexual activity, weightlifting), use of recreational drugs (cocaine, amphetamine), high-doses of steroids, or caffeinated energy drinks binge, have been described in single-case reports [25, 27–33]. The majority of patients with SCAD present with typical symptoms of ACS [1, 5, 6, 8]. However, in some cases, the pain may be atypical (back pain, pleuritic, positional, or burning), or dyspnea may be present. If it occurs in a young, healthy woman, the symptoms may be falsely interpreted as non-cardiac, leading to a delayed or even missed diagnosis of ACS. Thus, SCAD should always be considered in the differential diagnosis of ACS presentations in this low-risk population.

In approximately 8% of patients, SCAD-ACS can also present with cardiac arrest, ventricular arrhythmia, or cardiogenic shock [1, 34, 35]. Reported ECG findings at presentation vary in terms of different proportions of ST-elevation myocardial infarction (STEMI)/non-STEMI (NSTEMI), but mainly favoring NSTEMI [8, 19, 21, 36]. In the largest cohort of a Canadian registry, including 750 patients, the proportion of NSTEMI/STEMI ACS subjects was 70% versus 30%, respectively [1].

DIAGNOSIS OF SCAD

Invasive coronary angiography

Invasive coronary angiography constitutes the primary modality for the diagnosis of SCAD [4, 5]. Coronary angiography should be performed with particular caution and using coaxial catheter alignment as an increased risk of catheter-induced iatrogenic dissections is observed in these patients [37, 38]. A Canadian study reported a 10-fold higher risk of iatrogenic dissection during angiography in SCAD patients as compared to non-SCAD angiography (2% vs 0.2%) [37].

The European Society of Cardiology (ESC) Position Paper differentiates four major angiographic types of SCAD, with type 2 further stratified into 2a and 2b subtypes [5].

Type 1 is characterized by a double linear lumen with angiographic radiolucent 'flap' and contrast staining, resulting from a connection between true and false lumen (Figure 2A). While this is considered a pathognomonic SCAD presentation, it accounts only for one-third of SCAD patients [4, 26].

The remaining types have no double-lumen appearance and sometimes may be missed or misdiagnosed by an unaware or inexperienced operator.

Type 2 is visible as diffuse and predominantly smooth stenosis, typically located in the middle or distal segments

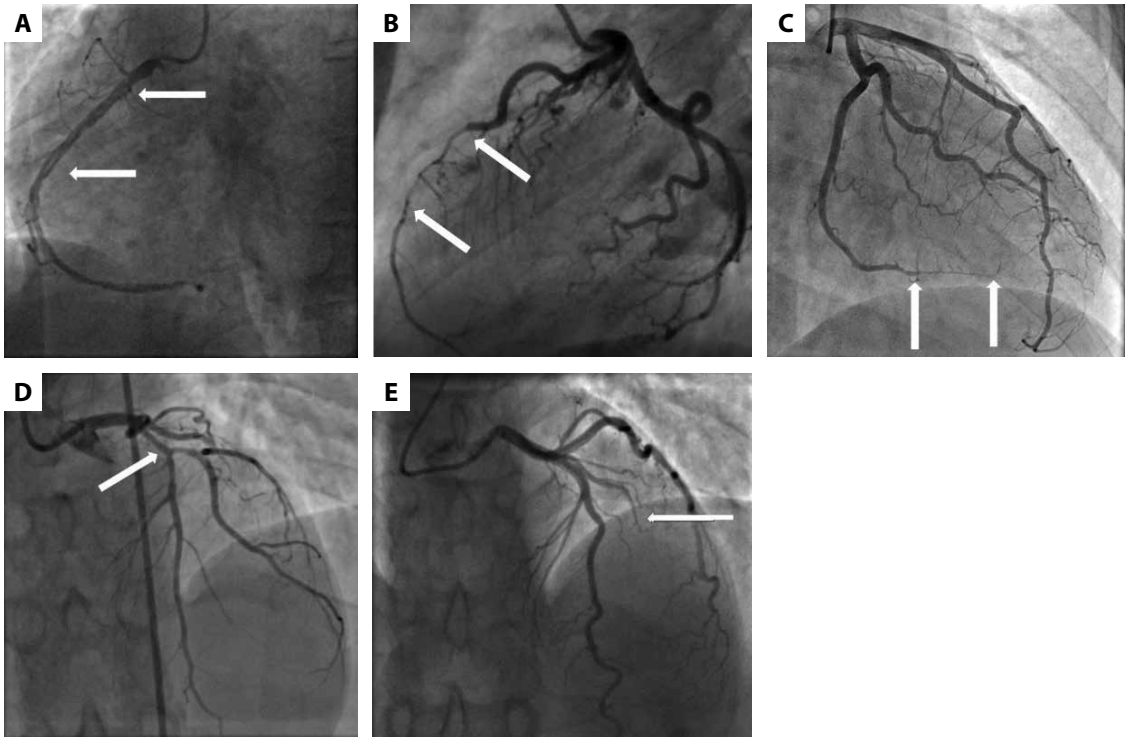

Figure 2. Angiographic types of spontaneous coronary artery dissection. **A.** Type 1. **B.** Type 2a. **C.** Type 2b. **D.** Type 3. **E.** Type 4

of the artery. The narrowing is usually long with smooth borders (usually longer than 20 mm) as a result of lumen compression by intramural hematoma with no communication between the false and true lumen and no penetration of contrast in the false lumen. It is the most frequently observed pattern reported in 55%–78% of all spontaneous dissections [1, 4, 8, 13]. Type 2 is subdivided into Type 2a, in which the narrowing reconstitutes downstream into the normal vessel, and Type 2b, in which the stenosis extends to the most distal segment (Figure 2B and 2C). In most clinical scenarios, Type 2 SCAD can be recognized based on coronary angiography alone. However, in some cases, the final diagnosis may require additional intracoronary imaging to distinguish with certainty from atherosclerotic lesions.

Type 3 mimics focal atherosclerotic lesion and can be conclusively differentiated only with intracoronary imaging (Figure 2D). The stenosis is usually shorter, being caused by focal, non-propagated mural hematoma. It has been reported in approx. 10% of patients [1, 8].

Type 4 is defined as a total occlusion, usually in a distal segment of the artery (Figure 2E). It can often only be recognized as SCAD when the flow is restored, either through coronary intervention or following vessel healing (at angiographic follow-up) and after exclusion of coronary embolism. This type is an addition to the original Yip-Saw angiographic classification of SCAD, in which only three types were distinguished [38].

The coronary distribution of SCAD has been widely investigated: the left anterior descending artery and its territory are the most commonly affected (in approximately half of the cases), the left main is less frequently involved (up to 4% of cases) [21, 36, 39, 40]. The middle and distal segments of coronary arteries are predominantly affected (more than 90%); in less than 10%, the dissection is present in proximal parts of the major coronary artery or the left main [26, 29, 30]. Other angiographic features reported in SCAD patients included increased coronary tortuosity, reduced incidence or absence of atherosclerosis, coronary fibromuscular dysplasia, association of sites of dissection with myocardial bridging [5].

Multivessel SCAD is defined as simultaneous dissections occurring in more than one artery, without continuity, and is thus distinct from continuous dissection extending into the side branch. Multivessel SCAD occurs in 5%–23% of cases with no established risk factors [11, 36, 39, 40].

Intravascular imaging

Given that angiographic diagnosis is possible in most cases, intracoronary imaging is best reserved for ambiguous lesions [6, 37, 41]. This refers particularly to patients with deceptive Type 3 SCAD, which mirrors atherosclerotic disease, and selected patients with 2 type dissection. It might also facilitate percutaneous coronary interventions (PCI) optimization and confirmation of appropriate stent expansion and apposition [4, 5].

Intravascular ultrasound (IVUS) allows for differentiation between atherosclerotic plaque and SCAD as it can depict the true and false lumen and the extent of intramural hematoma. Superior penetration ensuring complete visualization of the entire vessel wall without pressurized contrast injection are perceived as the main advantages of IVUS, compared with optical coherence tomography (OCT) [37, 42]. However, poor spatial resolution frequently limits the quality of imaging leaving significant diagnostic uncertainty and higher-resolution imaging is a better option if available.

With its superb spatial resolution (10–20 um), OCT enables detailed visualization of the intima-media complex, false lumen, presence of the thrombus, and fenestrations or connections between the true and false lumen. The benefits of OCT have to be weighed against the potential risk of further dissection propagation related to the high-pressure contrast injection required for good quality image acquisition (Figure 3). Thus, the modality should be limited to ambiguous lesions and to cases where imaging is required for clinical reasons (i.e., PCI optimization) Nevertheless, recent evidence suggests that OCT interrogation can be safely performed in SCAD patients [10, 12, 16, 42, 43].

Computed tomography coronary angiography (CCTA)

Computed tomography is a widely used tool for coronary assessment in low- and intermediate-risk patients presenting with chest pain using the triple "rule-out" protocol. However, in many cases, SCAD may be missed or undetectable on CCTA because of its lower spatial resolution (particularly in distal segments) [44–46]. Thus, a negative CCTA result cannot exclude a diagnosis of SCAD in some patients. In the case of biomarker confirmed myocardial necrosis in young or middle-aged women presenting with ACS, coronary angiography should be always considered despite a negative CCTA result.

ACUTE MANAGEMENT OF SCAD

These recommendations on SCAD management are based solely on widely accepted consensus and observational data as there are currently no randomized trials comparing revascularization and conservative strategy [4–6].

A conservative approach to revascularization is recommended in most patients, considering that observational studies showed spontaneous healing of the vessel wall in most patients and a high complication rate in the subgroup treated with PCI [21, 37, 47–49]. In a recent angiographic follow-up study, restoration of vascular architecture was observed in 86.3% of patients. This ratio increased to 95.0% when repeated coronary angiography was performed at least 30 days after the index event [48].

Multiple studies published before 2018 reported a high PCI procedural failure rate, even in patients with preserved vessel flow, reaching 30%–50% with an increased incidence

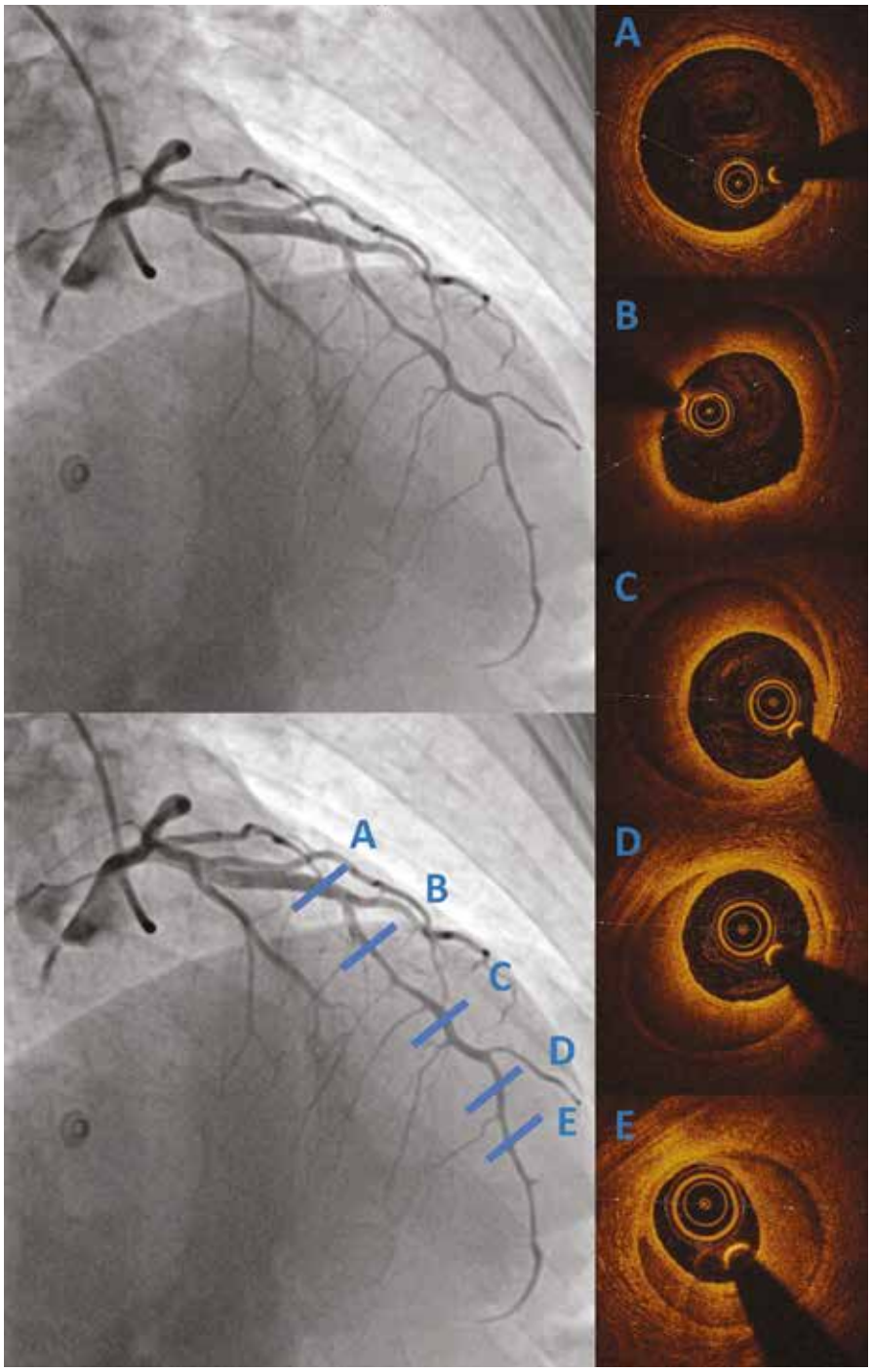

Figure 3. Optical coherence tomography in patient with SCAD. 49-year-old female without cardiovascular risk factors, hospitalized due to acute coronary syndrome without persistent ST segment elevation. Angiography depicted long smooth lumen narrowing in the mid and distal segment of left anterior descending (LAD) artery. Optical coherence tomography (OCT) revealed intramural hematoma propagating towards the distal segment of the artery (**B–E**). **A.** Healthy artery reference. SCAD type 2b has been recognized

(up to 13%) of emergency coronary artery bypass grafting [26, 36, 39]. For comparison, 90% of the conservatively managed group had an uneventful in-hospital course [4, 5]. However, revascularization is still required in some high-risk patients, and this clinical presentation is not a very rare phenomenon. It was observed in 7.6% of patients in a recently presented large Canadian SCAD population [1]. Major PCI indications included ongoing ischemia, high-risk anatomy, i.e., proximal segment dissection of large epicardial arteries, and hemodynamic/cardiac rhythm instability [4, 5, 50]. The latest studies have provided more promising results of PCI. An analysis of 144 United Kingdom patients treated percutaneously, including stenting in 72.4% of cases, plain old balloon angioplasty (POBA) in 21.1%, and wiring in 6.4%, was presented at the ESC Congress in 2020 [51]. The rate of all complications was high (38.8%). Still, the rate of significant complications, defined as flow reduction in proximal/middle segment, stent extension

into the left main artery, or iatrogenic dissection requiring PCI or coronary artery bypass grafting, was only 9%, including predominantly (77%) iatrogenic dissection. SCAD lesion length was associated with the presence of complications. Also, Lobo et al. [52] showed a 91% success rate of PCI in a relatively small group of 33 patients presented with STEMI. Those with revascularization were high-risk patients, more likely having shock, left main as a culprit lesion, proximal dissection, and initial flow grade 0 to 1.

If PCI is required, special attention should be paid to catheter maneuvers to minimize the risk of iatrogenic dissection and ensure guidewire passage into the true lumen. The risk of false lumen propagation during stent deployment or side branch occlusion by hematoma propagation also needs to be considered. Therefore, the primary goal of revascularization should be the restoration of TIMI 3 flow with the least aggressive techniques possible, including POBA, selection of either a long stent to prevent hematoma propagation or focal intervention with short stent just to seal the entry 'tear' of the dissection [25, 39, 48]. The use of bioresorbable vascular scaffolds has been considered in relatively young patients and with a non-atherosclerotic, potentially healable, underlying condition [53]. A multicenter prospective study, including 15 high-risk SCAD patients who received 34 bioresorbable vascular scaffolds, showed very satisfactory late angiographic outcomes, with no significant restenosis and an excellent minimal luminal area and optimal coronary wall healing, as assessed after 2 years by CCTA [54]. Case reports have also described the use of cutting balloons to fenestrate the intimal-medial membrane and depressurize the false lumen and drain intramural hematoma [55].

In patients with cardiogenic shock, without improvement after PCI, or with complicated PCI, mechanical circulatory support devices like intra-aortic balloon pump, left ventricular assist device, or extracorporeal membrane oxygenation may be considered as a bridge to surgical revascularization or, if required, to heart transplantation [56–58].

Coronary artery bypass grafting may be considered in patients with left-main dissection or multivessel proximal SCAD when PCI is deemed to have a very high risk (due to high-risk anatomy) or in the case of PCI failure as a bailout strategy [4, 5]. Acute management of SCAD is summarized in Figure 4.

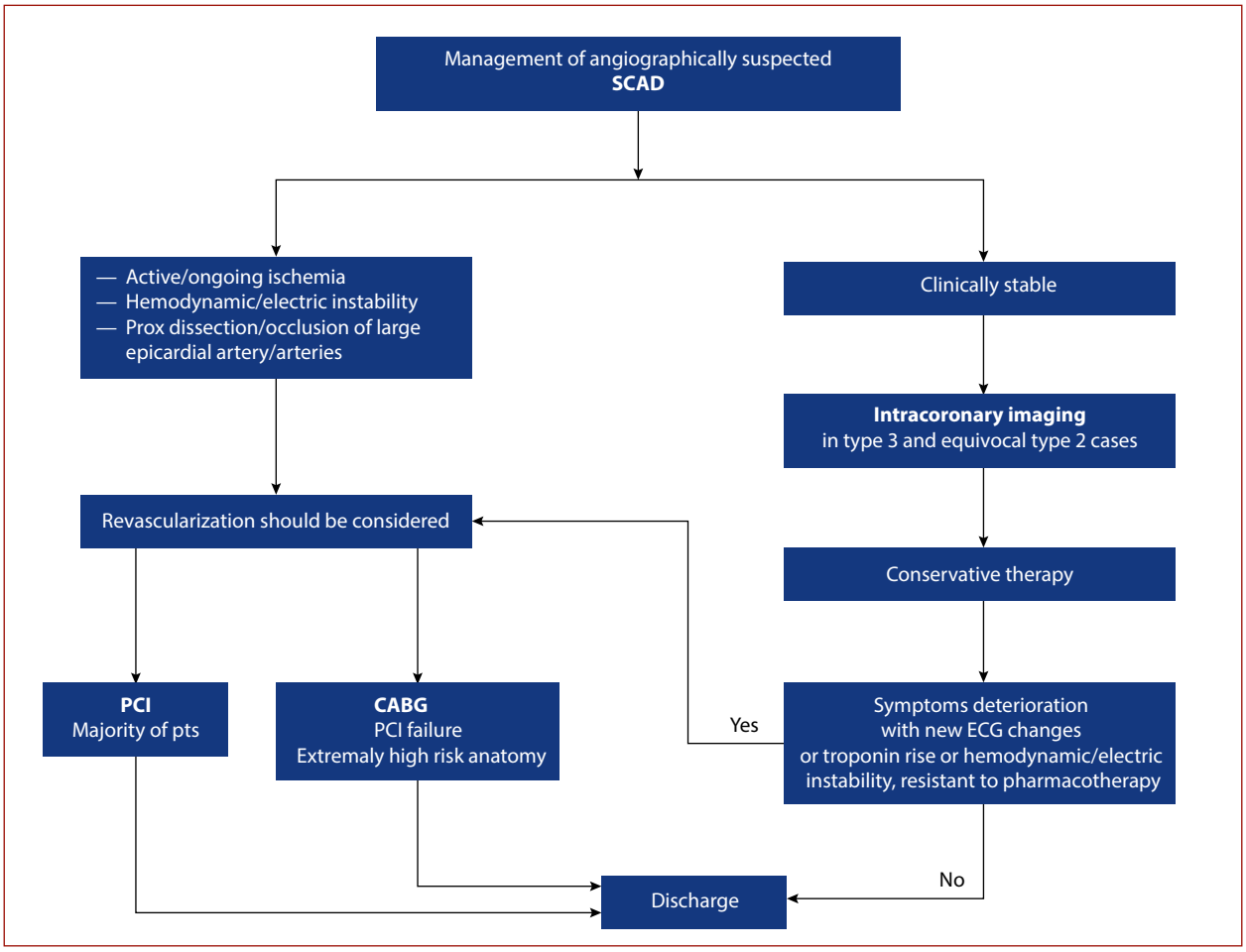

Figure 4. Acute management of spontaneous coronary artery dissection

Abbreviations: prox, proximal; pts, patients

POST-SCAD MANAGEMENT

Prognosis and post-SCAD chest pain management

The prognosis of the majority of SCAD patients is good. In-hospital mortality differs between patients treated invasively (with worse initial presentation) and those managed conservatively. The in-hospital mortality of revascularized patients ranged from 0 to 3.5% [26, 36, 39]. For comparison, in a Canadian registry, including 750 patients (86.4% treated conservatively), in-hospital mortality was 0.1% (1 patient) and mortality between discharge and 30th day was 0% [1]. However, it should be noted that 15 of 648 patients (2.3%) initially treated conservatively required revascularization during the same hospitalization. Hence, longer hospitalization should be considered in conservatively managed patients.

Long-term mortality after SCAD ranges from 1.2 to 3.1% during the median follow-up period between 22 and 37 months [14, 25, 36, 39]. In a recent study, 3-year survival after SCAD-related STEMI was 98% as compared to 84% after atheromatic STEMI [52].

Another analysis of 158 SCAD-survivors showed that the majority of patients have no or small infarctions and preserved ejection fraction as assessed in cardiac magnetic resonance imaging. Patients presenting with STEMI, TIMI 0/1 flow, or multivessel SCAD, and those with connective tissue disorders were more likely to have larger infarcts [59]. Similar data regarding the infarct size have been reported from echocardiographic follow-up of 227 SCAD patients from the Canadian registry [60].

Considering the high percentage of spontaneous healing of conservatively treated SCADs and the potential risk for iatrogenic dissection, we do not recommend routine follow-up with coronary angiography in asymptomatic patients [48]. SCAD survivors frequently report chest pain, often for several months after discharge [61, 62]. Most chest pains are nonischemic, so for symptomatic patients after proximal or middle segment dissection, when ACS is excluded, CCTA is a reasonable diagnostic modality for vessel healing assessment (Figure 5A) or exclusion of in-stent restenosis (Figure 5B) [63, 64]. In the case of distal segments or small vessel dissections, CCTA may be an

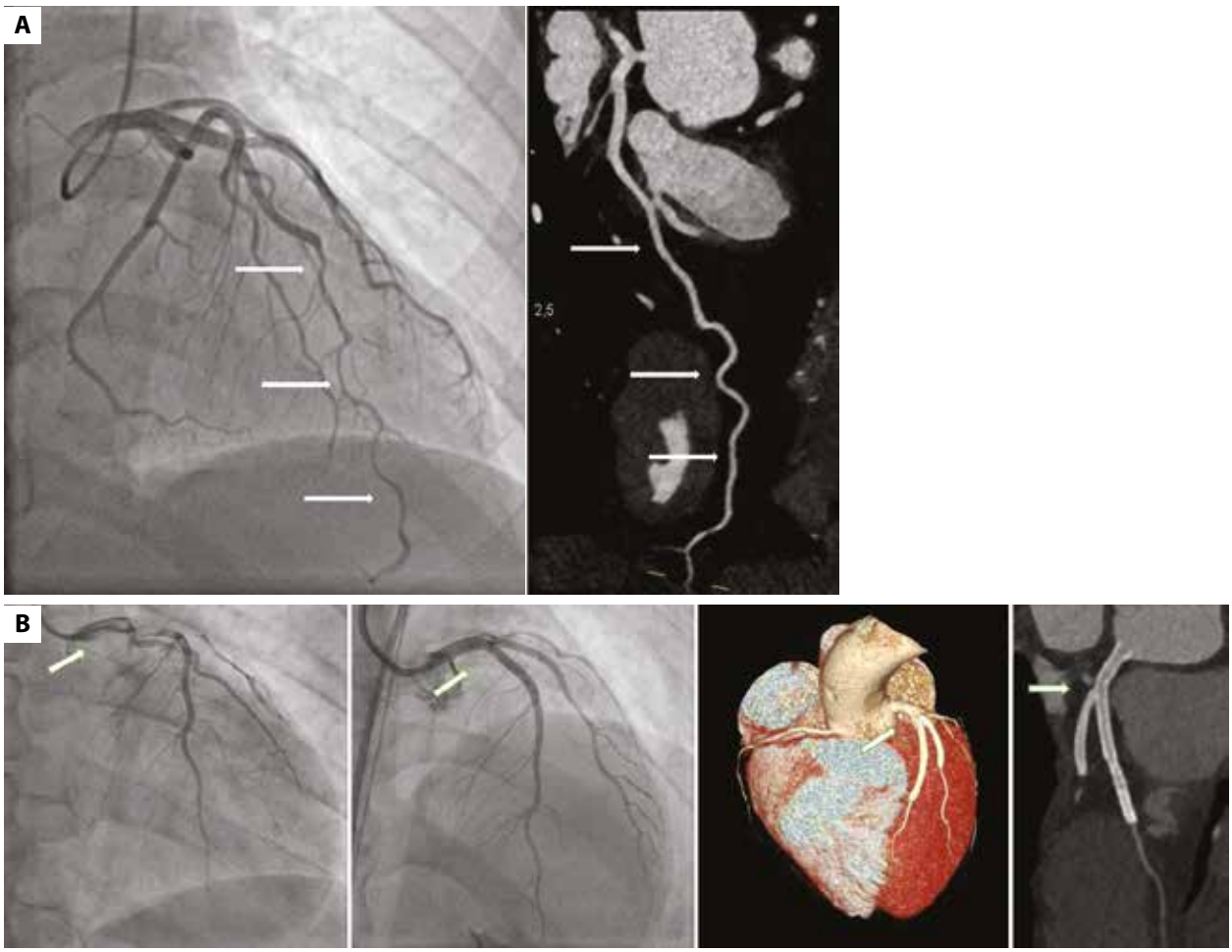

Figure 5. A. SCAD healing assessment using coronary computed tomography angiography: invasive coronary angiography with long type 2a SCAD in LAD (left), vessel healing confirmed in control CCTA (right); **B.** CCTA for in-stent restenosis exclusion. From left to right: initial angiography with left main SCAD; final angiography after stenting; CCTA during follow-up confirming favorable late result of PCI and no in-stent restenosis

Abbreviations: CCTA, computed tomography coronary angiography; LAD, left anterior descending; PCI, percutaneous coronary interventions; SCAD, spontaneous coronary artery dissection

Table 2. Prevalence and predictors of SCAD recurrence

Author (year of publication)	Patients with recurrent SCAD/all patients	Recurrence rate, %	Follow-up, months	Predictors of SCAD recurrence
Eleid (2014)	40/246	16.2	20.5	Tortuosity ↑
Nakashima (2016)	14/63	22.2[a]	34	NA
Saw (2017)	34/327	10.4	37	Hypertension ↑ β-blockers use ↓
Kok (2018)	88/585	15	31	NA[b]
Claire (2019)	22/208	10.6	56.4	Migraine ↑ Fibromuscular dysplasia ↑

[a]Half of patients experienced recurrence of SCAD within 30 days after index event.

[b]Recurrent chest pain within first 30 day after SCAD was more frequently reported in patients with migraine, however migraine was not related to 5-year SCAD recurrence

inadequate imaging method. In such cases, a functional test for ischemia may be considered. If abnormal, coronary angiography should then be considered.

Recurrence of SCAD

Recurrent SCAD is defined as the presence of new spontaneous dissection located either in another coronary segment or occurring more than 30 days after the initial episode. Recurrent SCAD reportedly occurs predominantly in a previously unaffected arterial segment [49].

The incidence of SCAD recurrence ranges from 10 to 22%, with the mean time of observation between 20 and 56 months [14, 25, 36, 40, 49]. Analysis for potential predictors of recurrence is limited by the small numbers of patients with a second SCAD. One analysis of 216 SCAD survivors revealed that coronary tortuosity was statistically borderline associated with re-SCAD [65]. In another observational study, hypertension and β-blocker use were associated with increased and decreased risk of another SCAD, respectively [25]. As this study did not provide many details about the rate of blood pressure control or the type of drugs used, the results are hypothesis-generating rather than a guide to treatment and require confirmation in other observational studies and ultimately in a randomized trial [66] A further report of Clare et al., including 208 patients, found higher recurrence risk in patients with fibromuscular dysplasia and patients with a history of migraine headaches [2]. Statin or antiplatelet therapies were not associated with the increased risk. The results of recent studies on SCAD recurrence are summarized in Table 2.

Medical therapy

There are no available clinical trials assessing the efficacy of pharmacotherapy in SCAD survivors. Optimal medical treatment remains undetermined. However, as hypertension is one of the predictors of recurrent SCAD, optimal anti-hypertensive therapy is recommended, favoring β-blocker as a first-choice drug where tolerated. Following SCAD, an assessment of left ventricular systolic function with echocardiography or cardiac magnetic resonance imaging is mandatory to guide medical therapy and to evaluate potential indications for device implantation.

In patients with heart failure, guideline-based pharmacotherapy is recommended [67]. The benefit from statin use is unknown, so we do not recommend a statin in conservatively treated patients unless they have diabetes mellitus or other conditions requiring primary prevention. In patients after stenting or with vein grafts, statins may be considered asthey can delay neo-atherosclerosis formation, at least theoretically.

The recommended length of dual antiplatelet therapy (DAPT) in patients treated with stents is the same as after atherosclerotic ACS [68, 69]. In patients treated conservatively, the benefit from the use of DAPT remains unproven. A pragmatic approach may be to use DAPT for at least 3 months in asymptomatic patients. If the vessel healing was confirmed on CCTA or angiography (if made for clinical reasons), DAPT could be stopped earlier. Clinical trials are needed to evaluate the balance between potential benefit or harm from long-term therapy with aspirin in conservatively treated patients with SCAD.

Screening for fibromuscular dysplasia (FMD) and extracoronary vascular abnormalities (EVA)

Fibromuscular dysplasia is an idiopathic, non-atherosclerotic, and non-inflammatory disease of medium-sized arteries characterized by abnormal cellular proliferation and distorted vessel wall architecture. It may affect all vascular beds, with renal and extracranial (carotid or vertebral) arteries most commonly affected and uncommon multivessel involvement (Figure 6) [70]. The typical morphological presentation includes two types of FMD: focal, which may occur in any part of the artery, and multifocal- with alternating areas of stenosis and dilation (called a 'string of beads'), which usually appears in middle and distal segments of the artery (Figure 6) [70].

The coexistence of SCAD and FMD was first reported in 2005 [71]. The prevalence of FMD in SCAD survivors reported in several studies ranged from 10% to 86%, depending on the percentage of patients undergoing full screening [5]. Systematic evaluation substantially increases the sensitivity in FMD detection. In the largest cohort of the Canadian registry, 411 of 750 included patients were systematically evaluated, and FMD was found in 56.7%

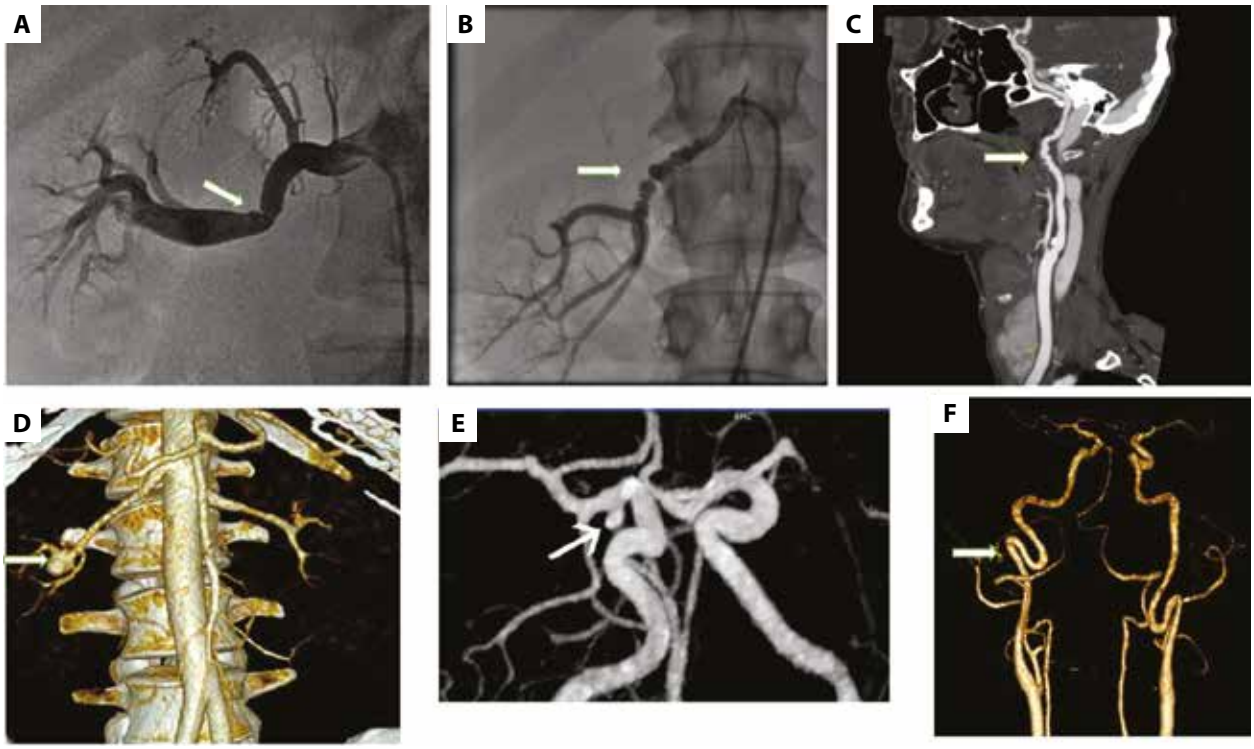

Figure 6. Extracoronary vascular abnormalities and comorbidities in patients with SCAD. **A.** Renal focal FMD. **B.** Renal multifocal FMD. **C.** Carotid FMD. **D.** Renal artery aneurysm. **E.** Carotid artery aneurysm. **F.** Tortuosity od carotid arteries

Abbreviations: FMD, fibromuscular dysplasia; SCAD, spontaneous coronary artery dissection

of them [1]. The prevalence of renal, cerebrovascular, and iliac/femoral FMD was 27.7%, 29.5%, and 21.0%, respectively. In a Mayo Clinic cohort, 335 of 585 included patients were screened and the frequency of FMD lesions was 58% [72]. Carotid/cerebral FMD was detected in 28%, body FMD in 52% of cases. FMD may also be more frequent in SCAD patients with a higher coronary tortuosity score [65]. In the ARCADIA-POL study, including 232 patients with FMD, systematic evaluation including "head-to-pelvis" computed tomography angiography resulted in detection of new FMD lesions in 34.1% of patients and previously undiagnosed vascular complications in 25% of subjects [73]. These findings require confirmation in SCAD-cohort observational studies.

The other EVAs found in patients with SCAD are aneurysms, dissections, and tortuosity, suggesting that SCAD may be the initial presentation of underlying arteriopathy (Figure 6) [4, 5]. In the abovementioned Mayo Clinic, cohort EVAs were detected in 23% of patients [72]. The prevalence of cerebral aneurysms reported in multiple studies ranged from 7.1% to 22.5% [1, 8, 72, 74]. This finding may be clinically important as some aneurysms may require intervention or systematic follow-up depending on their size or morphology [75].

Therefore, the group of experts from ACVI recommends whole-body computed tomography or magnetic resonance angiography screening (from head to pelvis) for fibromuscular dysplasia and EVA presence in all SCAD survivors.

Cardiac rehabilitation, psychotherapy

In general, there is no contraindication to usual physical activity in patients after SCAD to avoid weight gain or deconditioning. However, patients should be advised to avoid prolonged high-intensity activities, highly competitive or contact sports, and activities performed to exhaustion (racing, boot camp) [6]. Exercise training should be low resistance with high repetitions to avoid strain or Valsalva maneuver. Cardiac rehabilitation is recommended in all patients as it is safe and psychologically beneficial. It reduces symptoms of chest pain, depression, and stress [61, 76]. SCAD survivors are at the risk of posttraumatic stress disorder, depression, and anxiety, which are associated with lower quality of life [77, 78]. Given the prevalence and potential impact, screening and treatment for psychological distress are advised. Behavioral interventions targeted toward resilience training may be beneficial.

Genetics

Only a few reports of familial SCAD suggest it is not inherited disease in most cases [79, 80]. Rare causal pathogenic genetic variants occur in a minority of SCAD patients, mostly associated with known concomitant connective tissue diseases, like Ehlers-Danlos, Marfan, Loeys-Diez syndrome, or polycystic kidney disease [5].

Recently, the first common genetic variant for SCAD has been identified. In the largest study conducted, including 1055 SCAD patients and 7190 case controls, the authors found an association between rs9349379 genotype of

PHACTR1/EDN1 (phosphatase and actin regulator 1) gene on chromosome 6q24 and the incidence of SCAD [81]. Rs9349379-A allele was related to the increased risk of SCAD. This genotype was also associated with other vascular diseases, including FMD, coronary artery disease, migraine, and cervicocerebral artery dissection in previous reports [82–85].

In another report, evaluating 667 women with SCAD and 1477 female controls, the authors from Mayo Clinic identified 5 risk loci associated with SCAD, including previously described locus (1q21.3; 6p24.1; 12q13.3; 15q21.1 and 21q22.11). The alternative alleles of 3 of them have also been reported to be linked with atherosclerotic coronary artery disease. It suggests an opposite susceptibility to coronary atherosclerosis vs dissection [86].

These findings were confirmed in another trial evaluating 270 SCAD cases and 5263 controls. The authors also identified the rs12740679 allele at chromosome 1q21.2, implicating the extracellular matrix protein-encoding gene ADAMTSL4, to be significantly associated with SCAD. Moreover, the previously reported chromosome 6p24.1 PTACTR1 locus (rs9349379) and the 12q13 LRP1 locus (rs11172113) were also associated with the risk of SCAD in the meta-analysis of the genome-wide SCAD discovery and replication results. Interestingly, all three loci have been described in association with migraine headaches. The authors developed and tested a genetic risk score and demonstrated not only the association with SCAD occurrence but also opposing risks of atherosclerotic vs SCAD-related myocardial infarction [87].

In a very recent British genome sequencing study including 476 SCAD survivors and 13722 controls, pathogenic or likely rare pathogenic variants were detected in 3.5% of SCAD cases in 7 genes (PKD1, COL3A1, SMAD3, TGFB2, LOX, MYLK, and YY1AP1, with the highest association of the PKD1 gene with SCAD [88]. The results strengthen the overlap between SCAD and renal and connective tissue disorders. More studies are needed to confirm this finding.

So, at present, the group of experts does not recommend routine genetic screening. It can be considered in individuals with suspicion of connective tissue disease, extensive arteriopathies, or a strong family history of arteriopathies.

Pregnancy after SCAD and contraception

The risk of SCAD recurrence during pregnancy following a prior SCAD is poorly understood. Recently, the results of 636 women, including 23 patients who became pregnant (32 pregnancies) after SCAD, were published [89]. In the overall cohort, recurrent SCAD occurred in 122 patients. The study did not find evidence for an increased risk of SCAD recurrence in patients who became pregnant after SCAD when compared with women who did not experience pregnancy after an episode of SCAD. However, the results are limited by the small total number of women with pregnancy after SCAD, so should be interpreted with caution. So any decision on planning pregnancy should be carefully discussed with the pregnancy heart team, taking into account many aspects like left ventricular ejection fraction, maternal age, risk of recurrence, comorbidities, and teratogenic medications. In general, planned pregnancy is not contraindicated, but this decision should be individualized. Unplanned pregnancy should be avoided, and effective secure contraception is therefore important. Non-hormonal contraception is recommended such as non-hormonal intrauterine device or surgical sterilization of the patient or partner may also be a reasonable option. If hormonal contraception is required, despite the lack of studies in SCAD patients, highly effective progesterone-based approaches are preferable, including the long-acting subdermal levonorgestrel implant or levonorgestrel-releasing intrauterine device [90].

PREGNANCY-ASSOCIATED SCAD (P-SCAD)

The incidence of P-SCAD, assessed in a population-based cohort study including 4.3 million pregnancies, was 1.81 per 100 000 [91]. The following overlapping mechanisms associated with pregnancy were hypothesized to have an etiological role in P-SCAD [92]: (1) increased cardiac output with secondary increased arterial shear stress; (2) excess progesterone leading to the loss of normal corrugation of elastic fibers, a decrease in acid mucopolysaccharide ground substance and weakening the tunica media; (3) excess estrogen facilitating matrix metalloproteinases release leading to cystic medial necrosis and lack of vasa vasorum structural support; (4) impaired collagen synthesis in the peripartum period.

P-SCAD is a common cause of ACS during pregnancy and the postpartum period, reaching up to 10% of all such ACS events [93, 94]. Chronic hypertension, lipid profile abnormalities, chronic depression, and history of migraine were associated with an increased risk for P-SCAD in one study [91].

P-SCAD patients are usually characterized by a more severe clinical course, including a higher risk of cardiac arrest, ventricular arrhythmia, and cardiogenic shock. This results from increased left mainstem involvement and multivessel dissection [23, 92, 95]. Multivessel involvement supports the hypothesis of generalized arterial wall changes under hormonal changes during pregnancy. STEMI ACS is diagnosed using ECG in approximately 60% of P-SCAD patients. The long-term prognosis after P-SCAD may worsen as the left ventricle ejection fraction is lower than in patients with SCAD not related to pregnancy; they also require implantable cardiac devices more frequently [23]. On the other hand, the risk of SCAD recurrence is comparable to other SCAD patients [23].

FILLING THE GAPS AND GLIMPSE INTO THE FUTURE

We presented recommendations on the diagnosis and management of spontaneous coronary artery dissection. Many questions, like the underlying pathophysiology, the

Table 3. Summary of recommendations in SCAD management

DIAGNOSIS
SCAD should always be considered in the differential diagnosis of ACS presentations, particularly in the low-risk population of young and middle -aged women
Invasive coronary angiography remains the gold standard for the diagnosis of SCAD but should be performed with caution due to the increased risk for iatrogenic dissection
CCTA made in triple "rule-out" protocol may be false negative in SCAD patients. In case of confirmed myocardial necrosis in young or middle-aged women presenting with ACS, coronary angiography should be considered despite negative CCTA result
Intravascular imaging (preferentially OCT) is recommended in 2 primary clinical scenarios: ambiguous angiographic lesions, mainly type 3 as this is indistinguishable from atherosclerotic lesion, and in selected patients with type 2, especially when the clinical profile is not indicative for high atherothrombotic risk
TREATMENT
Conservative management should be a default strategy for low-risk patients with NSTEMI, maintained coronary flow and more distal dissection since spontaneous healing of the vessel wall is observed in the majority of patients and coronary revascularization is associated with an increased risk of complications
Coronary revascularization, preferentially PCI, is recommended in high-risk clinical and angiographic scenarios, including ongoing ischemia related to large vessel dissection, proximal dissection, hemodynamic or electrical instability
Coronary artery bypass grafting is recommended in patients with left-main dissection or multivessel proximal SCAD when PCI is considered to have a very high risk or in case of PCI failure as a bailout strategy
POST-SCAD MANAGEMENT
Optimal blood pressure control in hypertensive patients is recommended for secondary prevention of SCAD recurrence, with β-blocker preference as a first-choice drug, if not contraindicated
An assessment of left ventricular systolic is mandatory to guide medical therapy and to assess potential indications for device implantation. Guidelines-guided heart failure pharmacotherapy is recommended, if present after SCAD occurrence
The recommended length of dual antiplatelet therapy (DAPT) in patients treated with stents is the same as after atherosclerotic ACS. In patients treated conservatively, we advise using DAPT for at least 3 months in asymptomatic patients
For symptomatic patients after proximal or middle segment dissection, when ACS is excluded, CCTA is a reasonable modality for vessel healing assessment or in-stent restenosis exclusion. In the case of distal segments or small vessel dissections, CCTA may be an inadequate imaging method, and functional tests detecting ischemia are recommended. If they are abnormal, coronary angiography should be considered if revascularization is feasible and may be beneficial
Screening for fibromuscular dysplasia and the presence of extracoronary vascular abnormalities using "head-to-pelvis" CCTA arterial imaging is recommended
Usual physical activity is not contraindicated. Prolonged high-intensity activities, highly competitive or contact sports and activities performed to exhaustion should be avoided. Screening and treatment for psychological distress are strongly advised
The decision on planning pregnancy should be carefully individualized and discussed with the pregnancy heart team. Non-hormonal contraception is recommended for avoiding unplanned pregnancy — surgical sterilization may be a reasonable option. If hormonal contraception is required, highly effective mono-hormonal contraception should be used, including the long-acting subdermal levonorgestrel implant or levonorgestrel-releasing intrauterine device
Routine genetic screening is not recommended. It can be considered in individuals with suspicion of connective tissue disease, aneurysm presence, or a family history of arteriopathies

Abbreviations: ACS, acute coronary syndrome; CCTA, computed tomography coronary angiography; NSTEMI, non-ST segment elevation myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary interventions; SCAD, spontaneous coronary artery dissection

role of female sex hormones in the pathogenesis, the role and optimal duration of antiplatelet therapy, the identification of recurrence risk factors, the use of β-blockers, statins, or other potential secondary prevention drugs remain unresolved. The ESC has designed and just opened the European registry of SCAD survivors, including both prospective and retrospective subjects. Collecting data from >1000 patients will increase our knowledge and understanding of this mysterious disease. In Poland, the registry is coordinated by the National Institute of Cardiology, Warsaw. More information is available by e-mail: scad@ikard.pl

All recommendations presented in this document are summarized in Table 3.

Article information

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