ESC European Society of Cardiology

European Heart Journal (2018) **0**, 1–21
doi:10.1093/eurheartj/ehy080

CURRENT OPINION

European Society of Cardiology, acute cardiovascular care association, SCAD study group: a position paper on spontaneous coronary artery dissection

ESC-ACCA Position Paper on spontaneous coronary artery dissection

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Received 31 July 2017; revised 19 October 2017; editorial decision 31 January 2018; accepted 7 February 2018

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The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal* or of the European Society of Cardiology.

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Introduction

Spontaneous coronary artery dissection (SCAD) has long been recognized as a cause of acute coronary syndromes (ACS). Initially considered very rare and associated primarily with pregnancy and the peripartum period, the use of higher sensitivity Troponin assays and early angiography in ACS, coupled with greater awareness of the condition, has led to increased diagnosis, and it is now understood that SCAD represents a significant cause of ACS in predominantly young to middle-aged women, with most cases occurring outside the context of recent pregnancy.[1,2] Although there are no randomized controlled trials in SCAD, knowledge has further advanced in the last 5-years as a result of an international research effort primarily focused on building and studying national SCAD registries.[3–19] These studies have demonstrated, not only that SCAD is a distinct pathophysiological entity, but that there are key differences in management and outcomes compared to ACS of atherosclerotic aetiology. This position paper aims to set-out current knowledge on SCAD for the benefit of practicing clinicians caring for patients with this condition. It presents the consensus on contemporary management and areas of controversy and uncertainty, which remain a focus of ongoing research. The information is provided to support clinical care providers but is not intended to replace individualized decision-making by clinicians and other health care professionals.

Definition

For the purposes of this article, SCAD refers to the acute development of a false lumen within the coronary artery wall which may compromise coronary flow by external compression of the true lumen. Dissections arising from coronary instrumentation (iatrogenic), trauma and as a consequence of a penetrating ulcer or plaque rupture secondary to atherosclerotic disease or primary aortic dissection are not considered here.

Pathology

Spontaneous coronary artery dissection is a recognized, relatively rare cause of sudden cardiac death, presumably as a result of ventricular arrhythmia triggered by myocardial ischaemia or infarction.[20] Accurate diagnosis at autopsy can be challenging and the condition is likely under-represented in post mortem series.[21,22] A high index of suspicion for SCAD is recommended in all potential cases with careful assessment of coronary histopathology, particularly of the mid-distal vessels which are predominantly affected in SCAD and examination of the peripheral arterial system for associated arteriopathies [such as fibromuscular dysplasia (FMD)].

Spontaneous coronary artery dissection results from the development of a false lumen, generally in the outer third of the tunica media (*Figure 1A*).[21–27] The primary cause of false lumen formation is unclear with two potential mechanisms proposed: the 'inside-out' model (*Figure 1B*), where the causal event is the development of an endothelial and intimal discontinuity or 'tear', allowing blood to cross the internal elastic lamina and accumulate in the media; and the 'outside-in' mechanism (*Figure 1C*) where the causal event is the primary disruption of a vasa vasorum micro-vessel leading to haemorrhage directly into the tunica media.[1,28,29] In either case blood propagates axially as the false lumen extends leading to compression of the true lumen. It remains unclear if there is a single dominant mechanism in SCAD or if both causal events are possible. However, a recent intracoronary imaging study with high resolution optical coherence tomography (OCT) has shown case examples where there is no demonstrable communication between false and true lumens,[13,30,31] suggesting the 'outside-in' mechanism is likely in at least some cases.

Histologically, fibrin-rich haematoma is present in the false lumen (*Figure 2*) with a neutrophil infiltrate extending into the media. There are frequent reports of a peri-adventitial inflammatory infiltrate with a predominance of eosinophils.[21,23–25,27,32–36] The clot reorganizes and attaches to the media with granulation tissue formation and recanalization. Although this may not be specific to SCAD, it can be useful in distinguishing SCAD from post mortem artefact where

Key Messages

- Spontaneous coronary artery dissection should be actively considered in the post-mortem differential diagnosis of unexplained sudden cardiac death with careful assessment of the entire coronary tree.

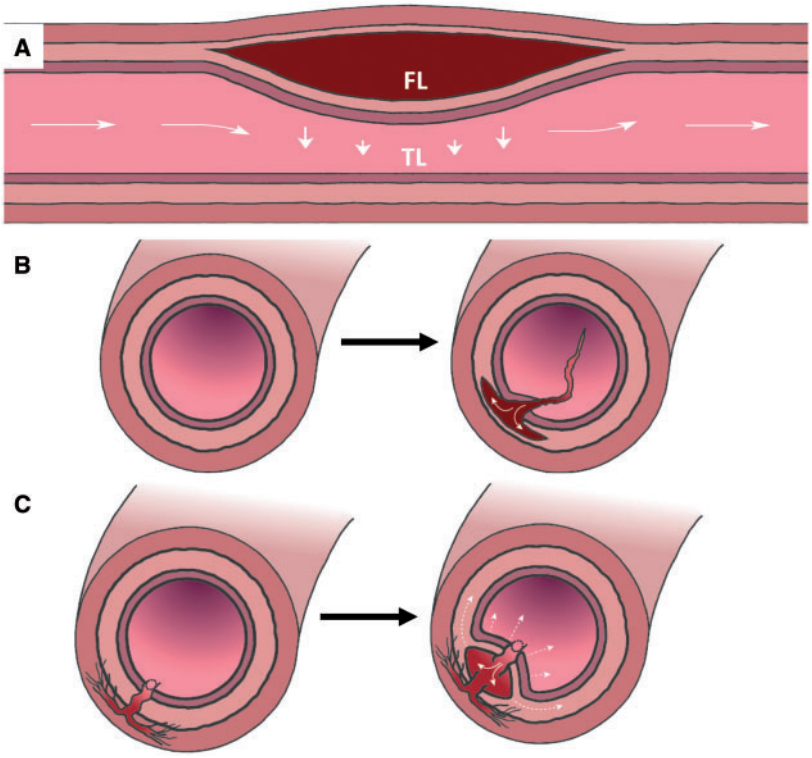

Figure 1 Schematic illustration of spontaneous coronary artery dissection. Accumulation and axial propagation of blood forms a false lumen in the outer third of the tunica media leading to external compression of the true lumen (*A*). Blood may enter through an endothelial-intimal disruption or 'tear' (*B*) or as a result of bleeding from a microvessel within the vessel wall (*C*) leading to an expanding and compressing false lumen (dotted arrows).

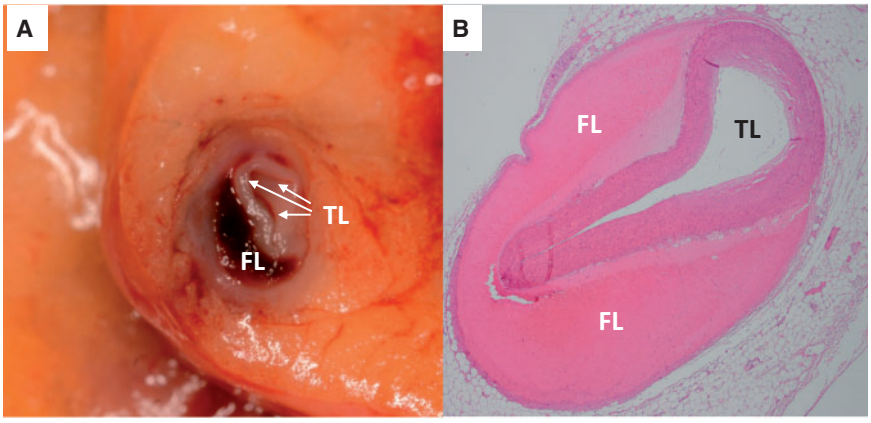

Figure 2 Gross pathology (*A*) and histopathology (*B*) showing spontaneous coronary artery dissection with external compression of the true lumen by blood within a false lumen in the outer third of the tunica media.

Table 1 Demographics and risk factors of patients with spontaneous coronary artery dissection (SCAD) in contemporary case series (studies with $n > 20$)

	Max N	Age (years)	Gender (female, %)	HTN (%)	Chol (%)	Smoking (%)	DM (%)	FH (%)	P-SCAD (%)
Mayo Clinic[3]	189	44 ± 9	92	31	22	15	2	NA	15
Saw[4]	168	52 ± 9	92	39	24	13	5	29	2
Lettieri[5]	134	52 ± 11	81	51	33	34	2	25	NA
Faden[6]	79	33 ± 5	100	17	18	17	11	NA	100
Rogowski[7]	64	53 ± 11	94	45	52	28	0	19	5
Nakashima[8]	63	46 ± 10	94	33	23	32	0	8	8
Motreff[13]	55	50	100	27	11	22	4	22	4
McGrath-Cadell[9]	40	45 ± 10	95	18	10	8	5	28	8
Roura[10]	34	47 ± 12	94	NA	NA	NA	NA		15
Alfonso[11]	27	52 ± 10	85	37	33	52	4	NA	4
Ito[12]	23	45 ± 11	100	57	22	30	4	NA	30
Vanzetto[14]	23	46 ± 9	74	26	39	43	13	13	0
Mortensen[15]	22	49 ± 9	81	38	NA	57	0	40	10
Rashid[16]	21	53 ± 9	95	48	48	47	5	24	0

Data are given as mean ± standard deviation or percentages.
HTN, hypertension; Chol, dyslipidaemia; DM, diabetes mellitus; FH, family history of coronary artery disease; NA, not available; P-SCAD, pregnancy-associated coronary artery dissection.

fissure formation may occur but only red blood cells are present.[21] Some early cases report features of cystic medial necrosis[37–39] but more recent reports do not concur.[32,34,40] Significant co-existent atherosclerotic coronary artery disease in SCAD is uncommon.[21]

Epidemiology

Incidence

The true incidence of SCAD is unknown as this condition remains under-diagnosed.[2] Spontaneous coronary artery dissection was historically considered very rare but contemporary angiographic series report SCAD diagnosis rates of 0.07–0.2% of all angiograms and 2–4% of angiograms performed for ACS[14,41,42] (although the study with the highest ACS prevalence did not exclude all atherosclerotic cases[42]). Furthermore, in younger women SCAD is reported to account for a much higher proportion of ACS presentations. In a Canadian series of women less than 50 years with myocardial infarction, SCAD accounted for 24% of cases.[43] Likewise a Japanese registry reported SCAD in 35% of females patients under 50 years presenting with acute myocardial infarction (AMI),[8] a French series reported SCAD in 36% of women under 60 years with ACS and one or fewer conventional cardiovascular risk factors[13] and a smaller Australian series describes a SCAD prevalence of 23% in women under 60 years presenting with ACS.[16] Pregnant and peripartum cases (P-SCAD) account for a minority of these cases (around 10% in most contemporary series)[3–11,13–16,18,44,45] and SCAD should no longer be considered primarily a peripartum condition. However, 21–27% of myocardial infarctions in pregnancy and 50% of post-partum coronary events are reportedly due to SCAD.[18,46]

Demographics

Previously considered primarily a disease of young adults, SCAD has now been described in patients aged 18–84 years[4,44] with the mean age in large contemporary series ranging from 44 to 53 years.[3–5,7–16]

No ethnic variations have been reported but there is a strong female predominance (female sex and pregnancy section). The demographics of SCAD patients from 14 contemporary series with at least 20 patients are summarized in *Table 1*.[3–16]

Key Messages

- Whilst SCAD has been described across a broad demographic, it is a frequent cause of ACS in young- to middle-aged women and patients with myocardial infarction in egnancy or post-partuprm.
- Pregnancy-associated SCAD accounts for a minority of cases.

Pathophysiology: risk factors and associations

The pathophysiology of SCAD remains unknown. It is likely that a combination of predisposing factors increase susceptibility such that a relatively minor trigger event is sufficient to precipitate SCAD. There are a large number of reported associations with SCAD (Supplementary material online, *Table S2*).[4,8,9,33,38,44,47–91,117–124,127–133,140–143] For some (e.g. female sex, pregnancy, and FMD), a link with SCAD has been established in multiple series. Other associations are based on anecdotal case reports, and in this context causality is harder to determine.

Female sex and pregnancy

The vast majority of SCAD patients (~90%) are women.[3–11,14–18] There is some evidence from a Canadian series that male SCAD patients are different from female cases, being slightly younger and with higher rates of preceding isometric exercise and lower prior emotional stress levels.[92] The predilection of SCAD for female patients and the association with pregnancy suggest a pathophysiological role for female sex hormones. The precise nature of this association

remains to be elucidated but may relate to hormonal influences on vascular connective tissue and/or the vessel microvasculature.

Data from most contemporary SCAD series suggest that P-SCAD represents approximately 10% of SCAD cases. Multi-parity, fertility hormones and pre-eclampsia may increase risk.[45,93–95] Pregnant and peripartum cases has been reported antepartum as early as the 5th week of pregnancy,[96] although most events reported during pregnancy are in the third trimester.[97–99] It also occurs in the early (<6 weeks), late (6 weeks to 12 months), and very late post-partum (12 to 24 month) periods, with the peak occurring in the early post-partum period.[95,97–99] Anecdotally, late post-partum SCAD may occur in association with breastfeeding.[96]

A Canadian study identified 79 P-SCAD cases from a nationwide cohort study of 4.4 million pregnancies between 2008 and 2012 (incidence 1.8 SCAD cases per 100 000 pregnancies),[6] a higher incidence of P-SCAD compared to the historical literature. This study suggested the P-SCAD presentation may be more severe than SCAD outside the context of pregnancy, with ST-elevation myocardial infarction (STEMI) in 64%, cardiogenic shock in 24%, cardiac arrest in 14%, and maternal death in 4.5%. Moreover, P-SCAD was more likely to involve the proximal coronaries and was associated with a reduction in post-infarct ejection fraction. A recent report of P-SCAD cases from the US Mayo Clinic Series also reported increased STEMI, proximal or mutivessel disease and worse left ventricular function compared to non-P-SCAD. The findings of a more severe P-SCAD phenotype were confirmed in an analysis of contemporary published cases[99] and a small retrospective study comparing 7 P-SCAD and 16 SCAD cases.[12]

Fibromuscular dysplasia

Spontaneous coronary artery dissection has been associated with various predisposing arteriopathies (*Figure 3*).[1,2,92] The most frequent is FMD, a non-atherosclerotic, non-inflammatory disease of arterial walls, which also occurs predominantly in middle-aged females with few cardiovascular risk factors. Fibromuscular dysplasia may lead to stenosis, dissections, and aneurysms of medium-sized arteries, including but not limited to renal, cervico-cephalic, and visceral arteries.[100,101] It is currently classified by angiography into two subtypes, multifocal and (uni)-focal. Multifocal FMD, with the typical 'string-of-beads' pattern, is the

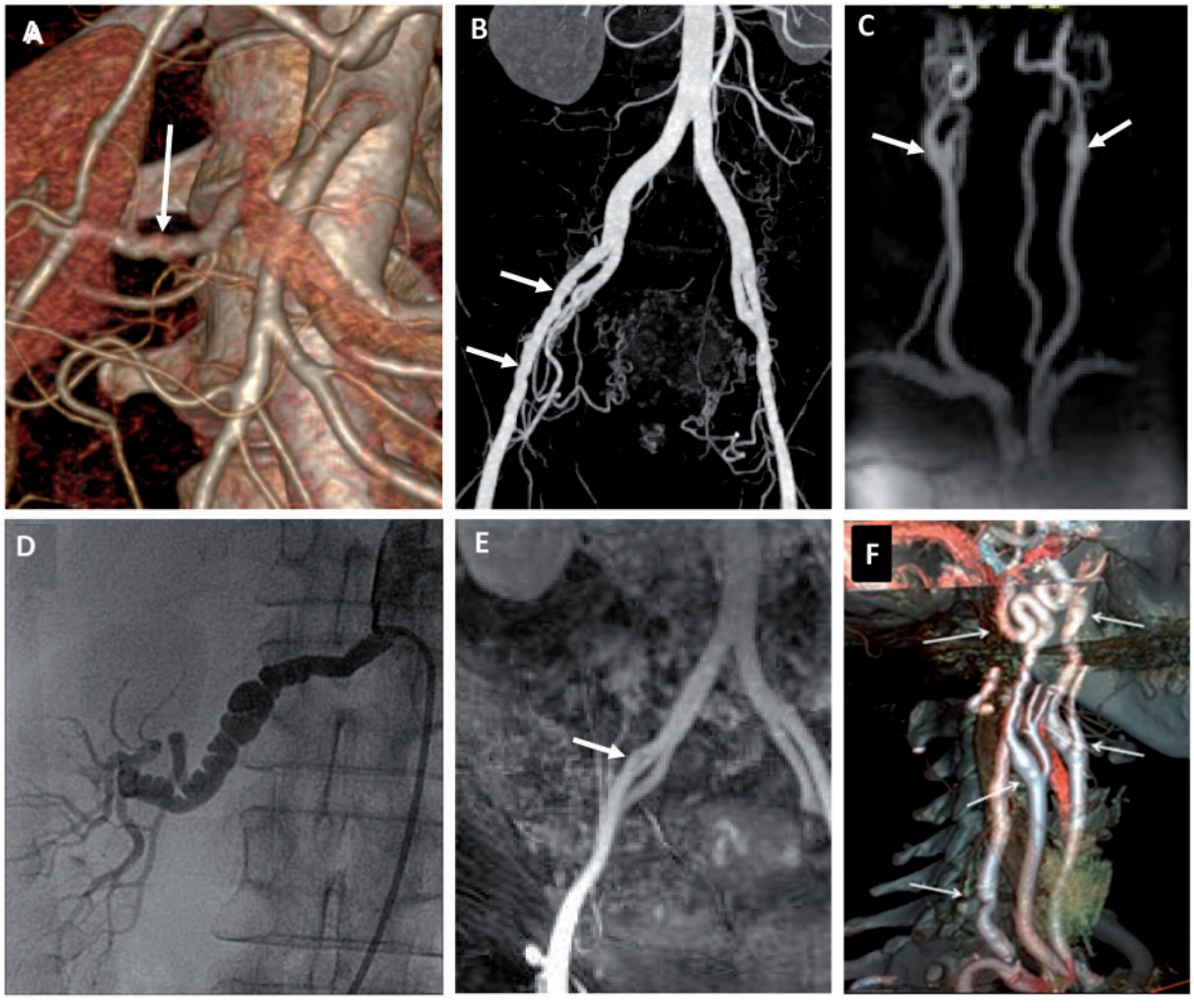

Figure 3 Extracoronary abnormalities in spontaneous coronary artery dissection including renal (*A* and *D*) and femoral (*B*) fibromuscular dysplasia, carotid and vertebrobasilar aneurysms and tortuosity (*C* and *F*) and a localised iliac dissection (*E*).

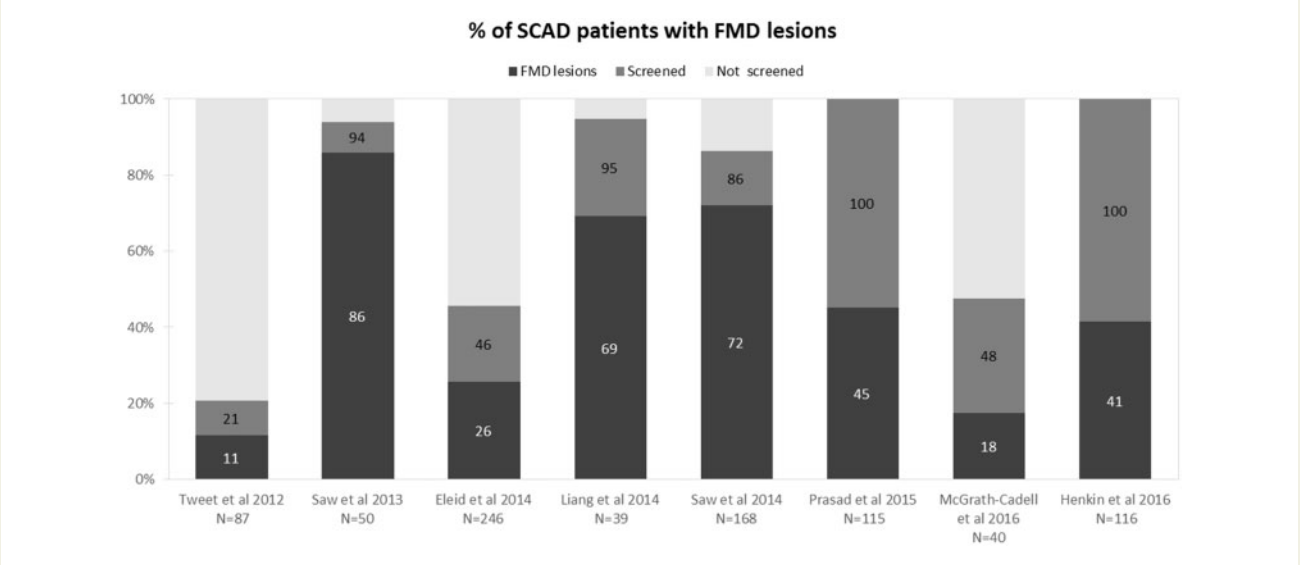

Figure 4 Prevalence of extracoronary lesions of fibromuscular dysplasia in contemporary series of spontaneous coronary artery dissection patients.

angiographic presentation of medial FMD and is at least four times more frequent than unifocal FMD.[101–103]

Since the first case series reporting the association of SCAD with extra-coronary FMD in 2012,[104,105] FMD of extra-coronary vascular beds has been documented in 11–86% of patients with SCAD,[4,9,44,47,50,106–108] with a narrower range of 41–86% after exclusion of three studies in which <50% of patients were screened[9,44,47] (*Figure 4*). The prevalence of extra-coronary FMD in various cohorts may differ according to the proportion of patients screened, the screening protocol used (e.g. imaging technique, vascular beds, screening according to symptoms vs. systematic assessment etc.) and diagnostic criteria of FMD. Fibromuscular dysplasia of extra-coronary vascular beds may also be more frequent in SCAD patients with a higher coronary tortuosity score.[47]

In current series, the most commonly affected vascular beds are renal, cervico-cephalic and iliac arteries.[4,50,106–108] In three studies in which the information was available,[104,106,107] 29–70% of SCAD patients with extra-coronary FMD had involvement of two or more vascular beds. While Saw *et al.*[4] focused their analysis on the presence of the 'string-of-beads' appearance, almost pathognomonic of multifocal FMD, Prasad *et al.*[107] extended vascular screening to isolated stenosis possibly due to unifocal FMD. Notably however, the 52 cases of extra-coronary FMD documented in their series of 115 SCAD patients were exclusively of the multifocal subtype. Finally, besides typical FMD lesions, other extra-coronary vascular abnormalities (EVAs) such as aneurysms, dissections, irregularities, undulations, and/or tortuosity have been reported.[106,107] Whether the latter correspond to subtle forms of FMD or a different process such as a form of connective tissue disorder remains to be established[107] The clinical implications of the association between EVAs and SCAD are described in the 'Computed tomography-peripheral angiography or magnetic resonance-angiography section' below.

In view of the high prevalence of extra-coronary FMD in patients with SCAD, it is tempting to speculate that SCAD is a complication of underlying coronary FMD in a substantial proportion of cases.[108] Pathological demonstration of coronary FMD lesions in at least four cases of SCAD[37,109–111] adds weight to this hypothesis. However, at present, a degree of caution is required in equating SCAD with FMD, as (i) current data on the association of SCAD with extra-coronary FMD mostly derive from two centres in Canada[4,104] and the USA,[44,47,50,106,107] with repeat publications from the same group likely representing different stages of recruitment and exploration of these two cohorts; (ii) typical FMD coronary lesions are rare[112,113] and description of the angiographic characteristics of coronary FMD is only in its infancy[114,115]; (iii) the prevalence of coronary artery dissection is very low (<3%) in the US FMD registry[116]; and (iv) a proportion of cases of SCAD remain idiopathic or are associated with other vascular diseases.

Inflammatory conditions

Spontaneous coronary artery dissection has been associated with systemic inflammatory conditions (Supplementary material online, *Table S2*).[33,68–77,117–124] While the prevalence of inflammatory systemic diseases was 8.9% in a Canadian series of 168 cases,[4] this is not yet widely corroborated in other series.[11] A clear mechanistic link between systemic inflammation and SCAD remains to be elucidated.

Atherosclerotic risk factors

Significant atherosclerosis is rare in typical SCAD (although this may partly reflect the criteria used to define cases). Spontaneous coronary artery dissection patients have fewer traditional cardiovascular risk factors for ischaemic heart disease than patients with atherosclerotic coronary artery disease,[44] and some patients have no such risk factors at all. However, in contrast to the previous perception, many patients do have some risk factors for ischaemic heart disease including hypertension, smoking, and dyslipidaemia[3–18] (*Table 1*), although there is no evidence these contribute directly to the risk of SCAD. For example, the mean low-density lipoprotein cholesterol (LDL-C) plasma concentration in the case series by Rogowski *et al.*[7] was 3.3 mmol/L and some

cases of SCAD have been reported in patients with severe hypertension.[125,126] In contrast, diabetes seems to be rare in SCAD patients. In keeping with the wider population, coronary risk factors tend to be more prevalent in older patients with SCAD.

Mechanical stressors and exercise

A number of mechanical triggers have been linked to SCAD events, including extreme Valsalva-type manoeuvres and the provocation of coronary spasm (Supplementary material online, *Table S2*).[4,9,79–91,127–133] Dissections have also been reported following isometric or extreme exercise,[134–138] reported in 11.9% of cases in a recent prospective series[19] and occurring more commonly in men.[92] A mechanism linked to increased coronary wall shear stress has been proposed. There are also patients in whom there is a significant lag time between the last exercise event and the onset of symptoms suggesting a higher exercise performance capability may be a feature of the SCAD phenotype in some patients (potentially relating to a mild connective tissue phenotype).[139]

Emotional stressors

Antecedent emotional stresses such as a bereavement or major personal crisis have been reported in a higher than expected proportion of SCAD cases, particularly in women.[4,8,92]

Inherited connective tissue disorders

Although SCAD has frequently been reported in association with connective tissue disorders (Supplementary material online, *Table S2*),[38,44,50–58,140–143] large contemporary series suggest such cases constitute a tiny minority of prevalent cases (around 1–2% in the US, Canadian, and Japanese series)[4,107] and until now the yield from genetic screening of SCAD-survivors for associated genes has been reported to be very low.[50]

Genetics

The genetics of SCAD remains to be clearly elucidated with very few focused studies to date. Whilst a number of sibling–sibling pairs and mother–daughter pairs have been described,[144] SCAD outside the rare context of known connective tissue disorders does not appear to be a strongly inherited condition, with only 1.2% of 412 patients in one series describing a family history of SCAD.[144] Hence whilst a thorough clinical assessment for rare connective tissue disorders is required in all SCAD-survivors, whether more systematic genetic screening is useful and cost-effective remains to be demonstrated.[50,115]

Key Messages

- The strong female predisposition and association with pregnancy suggest a role for female sex-hormones in the pathogenesis of SCAD but the mechanism remains unknown.
- Spontaneous coronary artery dissection is frequently associated with extra-coronary arteriopathies including FMD.
- Spontaneous coronary artery dissection is not a strongly inherited condition.
- Research is needed to better understand the pathophysiology of SCAD.

Clinical presentation

There is considerable evidence that SCAD remains under-diagnosed.[2] Some patients fail to act on their symptoms and never present to medical services and a few cases may present with sudden cardiac death (see pathology section). However, of those who do present to medical services, missed or delayed diagnosis is common.[1,145] Some patients are not referred for coronary investigations, primarily because most acute medical and cardiology services are focused on the identification of patients at high risk of obstructive atherosclerotic ACS and patients with SCAD typically fall into the lowest risk groups on the basis of traditional risk scores for ischaemic heart disease. A high index of suspicion in typical patients, coupled with familiarity with the angiographic variants of SCAD is key to minimizing missed or delayed diagnoses.

Patients with SCAD usually present with an ACS associated with positive biomarkers of myocardial necrosis (e.g. high sensitivity troponin). The proportion of cases presenting with STEMI (26–55%) vs. non-ST-elevation myocardial infarction (NSTEMI) varies in the larger published series.[3–5,8,13,45] This likely reflects differences in patient selection for these registries. A minority present with ventricular arrhythmia (2.8–10%),[3–5,8,45] Chest pain is the most frequently described presenting symptom,[15,44,146] an association which may be more common in SCAD than atherosclerotic ACS patients (chest pain reported in 60–90% of SCAD patients).[146] This may be because, in addition to pain arising from myocardial ischaemia and infarction, dissection *per se* is inherently painful.[145] In the Canadian series, chest pain was reportedly associated with radiation to the arm (49.5%) and neck (22.1%), nausea and vomiting (23.4%), diaphoresis (20.9%), dyspnoea (19.3%), and back pain (12.2%).[146] Despite the strong association with chest pain, the nature of the pain may be atypical with 'burning' (9%), 'pleuritic' (3.0%), 'tearing' (1.0%), and 'positional' (1%) descriptors in a minority of patients.[146]

Key Messages

- Patients with SCAD usually present with ACS.
- Delayed diagnosis is common and SCAD should be actively considered in the differential diagnosis of ACS presentations in low risk patients.

Diagnosis

The differential diagnosis for SCAD includes atherosclerotic ACS, coronary artery spasm, Takotsubo cardiomyopathy, coronary thromboembolism, and myocardial infarction with non-obstructed coronary arteries (MINOCA). There are no currently identified specific blood biomarkers for SCAD. Coronary angiography represents the principal tool for the diagnosis of SCAD in clinical practice.[1,145,147] Intracoronary nitroglycerin should be given, where blood pressure allows, to ensure complete vasodilation and to rule out the possibility of associated coronary spasm. With experience most SCAD cases can be diagnosed on angiography alone, with intracoronary imaging reserved for cases where diagnostic uncertainty exists.[145] However, it is important to appreciate that the appearances of a radiolucent flap, dual lumen, and contrast hold-up seen with

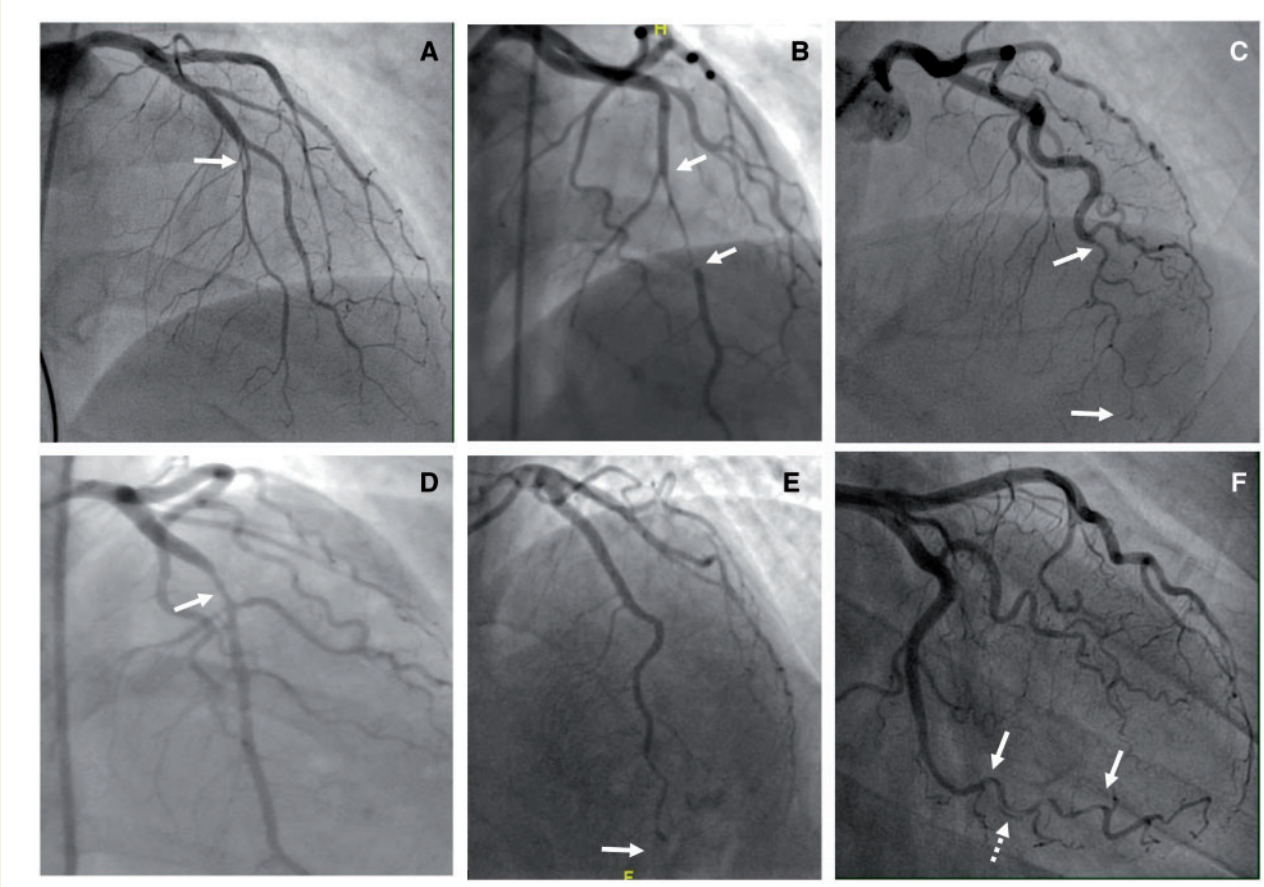

Figure 5 Angiographic classification of spontaneous coronary artery dissection. Type 1 spontaneous coronary artery dissection (*A*), Type 2A spontaneous coronary artery dissection (*B*), Type 2B spontaneous coronary artery dissection (*C*), Type 3 spontaneous coronary artery dissection (*D*), Type 4 spontaneous coronary artery dissection (*E*), and Intermediate Type1/2 spontaneous coronary artery dissection (*F*).

iatrogenic dissections[148] and familiar to most interventional cardiologists are present in only a minority of SCAD angiograms.

Coronary angiographic classification

The most commonly used angiographic classification of SCAD has been adapted from Saw *et al.*[149,150] (*Figure 5*), although other approaches are also proposed (Supplementary material online, *Figure S6*).[13] From the Saw classification, Type 1 represents the classical angiographic radiolucent 'flap' and linear double lumen often associated with contrast hold-up (*Figure 5A*). This reportedly occurs in 29–48% of cases.[4,7,8] However these features are absent in the commoner Type 2 pattern (52–67%)[4,7,8] characterized by a long diffuse and smooth stenosis predominantly located in mid-to-distal segments. This has been divided into Type 2a (*Figure 5B*) where there is recrudescence of a normal calibre distal vessel and Type 2b (*Figure 5C*) where the stenosis extends angiographically to the end of the vessel. Intermediate appearances (between Type 1 and 2) are also seen where a typical Type 2 pattern is seen but with a short segment of dual lumen or contrast hold-up in keeping with a localized fenestration between true and false lumen (*Figure 5F*). Type 3 lesions (*Figure 5D*) are defined as angiographically indistinguishable from a focal atherosclerotic stenosis requiring diagnostic confirmation by intracoronary imaging (see intracoronary imaging section). However, these account for a small minority of cases (0–3.9%).[4,7,8] Type 4 SCAD is described as a total occlusion, usually of a distal vessel (*Figure 5E*).[145] In this uncommon circumstance, the diagnosis is particularly challenging and frequently can only be established during an ensuing coronary intervention once coronary flow is re-established or inferred by subsequent vessel healing and the exclusion of an embolic cause.

Additional possible angiographic findings

Other angiographic features reported in association with SCAD include:

- Increased coronary tortuosity[47]
- Predilection for more distal coronary segments (in contrast to atherosclerotic disease)[4,5,44,45]
- Predominant involvement of the left anterior descending coronary artery and its branches reported in most[4,5,8,13,44] but not all[45] series
- False lumen starting and/or ending at a side branch[13]
- Absence or reduced incidence of co-existent atherosclerosis—unaffected coronaries are usually normal or near-normal[13]
- Coronary FMD (see fibromuscular dysplasia section)
- Association of sites of dissection with myocardial bridging.[151]

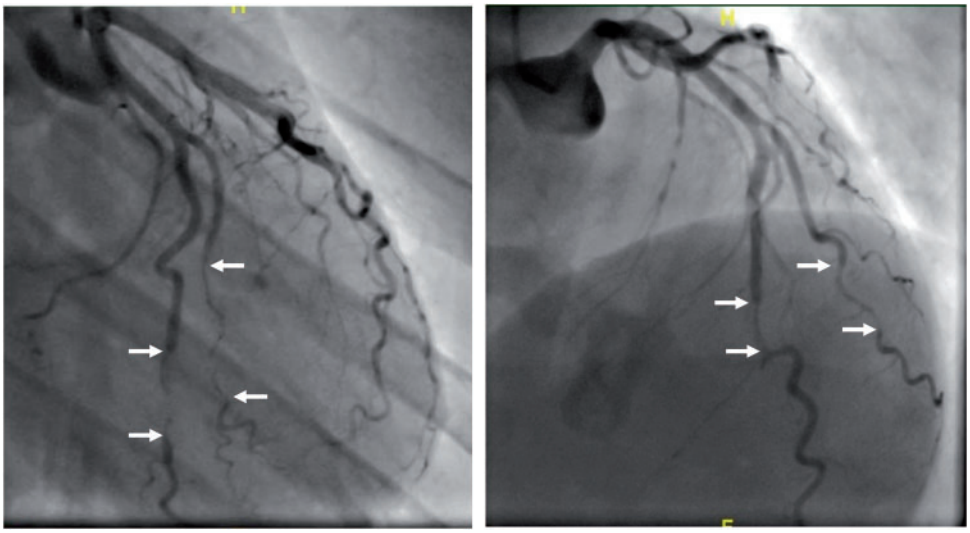

Figure 6 Multivessel spontaneous coronary artery dissection affecting two branches of the circumflex coronary artery, the left anterior descending coronary artery and its diagonal branch (arrows).

Multi-vessel spontaneous coronary artery dissection

Multi-vessel SCAD (*Figure 6*) is defined as simultaneous dissections occurring in more than one artery, without continuity, and is thus distinct from recurrent SCAD or a continuous dissection which extends into different coronary territories. It is well recognized[152–156] with a reported frequency of 5–13%[3–5,8,13,45] in the larger series and careful angiographic assessment of apparent non-culprit vessels during index angiography is recommended. There are no current specific studies of multi-vessel SCAD; however, the approach to management for multi-vessel SCAD should not differ from single vessel disease with each lesion being assessed for intervention on its individual merits and a preference for conservative management where possible (see conservative management section).

Secondary iatrogenic dissection in spontaneous coronary artery dissection

A single study has reported an increased risk of secondary iatrogenic dissections during angiography and percutaneous coronary intervention (PCI) in SCAD patients (2% risk during coronary angiography vs. 0.2% during non-SCAD angiography, 14.3% during PCI).[157] High rates of secondary iatrogenic dissection were also reported in a second series (11 of 189 SCAD cases) but without a comparator population.[3] For this reason, a meticulous co-axial catheter technique and avoidance of aggressive or deeply engaging guiding catheter designs is advised.

Intracoronary imaging

Most SCAD can be diagnosed angiographically and in scenarios where a conservative approach to management is feasible, coronary instrumentation should, if possible, be avoided.[19,106,108] However, where diagnostic uncertainty exists or to guide coronary intervention when required, careful intracoronary imaging can be invaluable and appears safe.[13,30] Because SCAD frequently affects more distal coronary segments, complete imaging of the axial extent of the false lumen may not be possible (e.g. for Type 2b SCAD). In one series only 5/11 affected cases could be imaged across the entire affected length.[30] However imaging of shorter proximal segments may be sufficient for diagnostic purposes.[30] Intravascular ultrasound (IVUS) and OCT provide tomographic images of the vessel wall and the coronary lumen that have proved to be of major value in the diagnosis of SCAD.[13,30,31,158,159] Intracoronary imaging can also help to guide decision-making on stent size. The length of the stent may be planned according to the longitudinal extent of the false lumen with the aim of minimizing propagation of intramural haematoma (see percutaneous coronary intervention section). The reported risk of late malapposition on haematoma resorption due to stent under-sizing in the presence of extensive haematomas[160] can also potentially be minimized by careful assessment of proximal and distal vessel dimensions with IVUS/OCT. Although there are relative advantages to each technology, OCT is generally favoured for SCAD imaging because of its higher spatial resolution.[1,145]

Intravascular ultrasound

Intravascular ultrasound (axial resolution 150 μm) is able to differentiate atherosclerotic plaques from SCAD (*Figure 7A*).[31,158,159,161–165] This technique readily depicts the true and the false coronary lumens and is able to demonstrate the extent of false lumen thrombosis. The principal advantage of IVUS over OCT is firstly, that blood clearance (and therefore pressurized contrast injection) is not required and secondly, IVUS has superior depth penetration, enabling complete visualization of the vessel wall to the external elastic lamina, including imaging through thrombus. The main limitation is poor spatial resolution which can limit identification of small structures associated with SCAD such as the intimal-medial membrane and localized fenestrations connecting true and false lumens.[145]

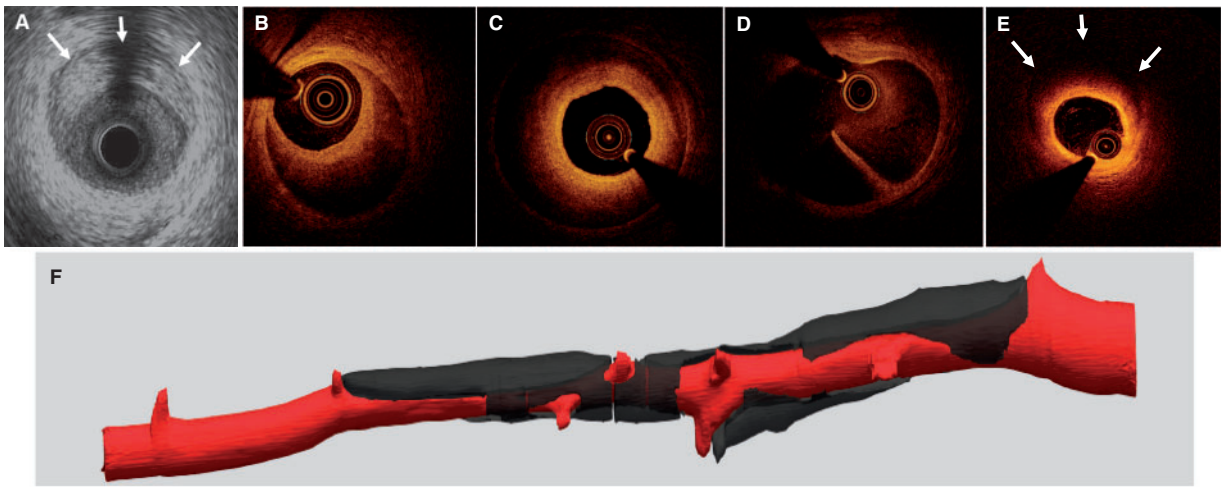

Figure 7 Intracoronary imaging of spontaneous coronary artery dissection by intravascular ultrasound (with outer border of false lumen arrowed, *A*), and optical coherence tomography showing partial (*B*) and circumferential (*C*) false lumens; the site of a fenestration (*D*) connecting true and false lumens and reduced light penetration through the false lumen (*E*). Three-dimensional image derived from segmentation of optical coherence tomography image showing how the false lumen tracks around the true lumen and is influenced (and frequently bounded) by side branches (*F*).

Optical coherence tomography

Optical coherence tomography has the advantage of much higher spatial resolution (axial resolution 15 μm), and characteristic images of SCAD are well described (*Figure 7B–E*).[30,42,150,159,166] Imaging with OCT necessitates blood clearance requiring a high pressure contrast injection which carries a potential risk of extension of the false lumen, especially in proximal Type I SCAD. However, reports to date suggest, with care, OCT imaging in SCAD can be conducted safety.[13,30,150] Depth penetration is more limited with OCT, exacerbated by shadowing or attenuation e.g. by thrombus or haematoma. However this generally does not limit accurate diagnosis.

Optical coherence tomography enables detailed characterization of: the true lumen including any associated thrombus; the size, nature, and extent of the false lumen including points where the false lumen surrounds the true lumen circumferentially; the relationship of the false lumen with side-branches; fenestrations or the more classical 'entry tear' connecting true and false lumens.[30] Accurate measurement of key features is also practical including the thickness of the intimal-medial membrane (mean 350 μm)[30] and the dimensions of the compressed true lumen. Optical coherence tomography has also been used to report areas characterized as 'coronary FMD' (see fibromuscular dysplasia section). It is important to recognize that the light attenuation (blackness) of the false lumen is highly variable (presumably reflecting phases in the maturation of the intramural thrombus and variability in contrast penetration of the false lumen).[145] Careful assessment of the images is required to identify the classical crescentic semi-lunar false lumen (*Figure 7B–E*) and ensure an accurate OCT diagnosis.

Optical coherence tomography is also of value in the subset of SCAD patients requiring coronary revascularization.[30,167] Before any intervention it is critical to confirm, if there is any uncertainty, that the guidewire is located in the true lumen (*Figure 8*) as stenting into the false lumen can have serious consequences.[168–170] Long-term follow-up OCT has also been reported in a few cases showing the stages of vessel healing. In most cases restitutio ad integrum of the previously affected vessel wall can be appreciated.[171] One report described an increase in the vasa vasorum density during the healing phase (median 44 days after presentation) of SCAD.[172] Given the reported increased risk of iatrogenic dissection in SCAD patients, repeat imaging should only be considered where clinically necessary.

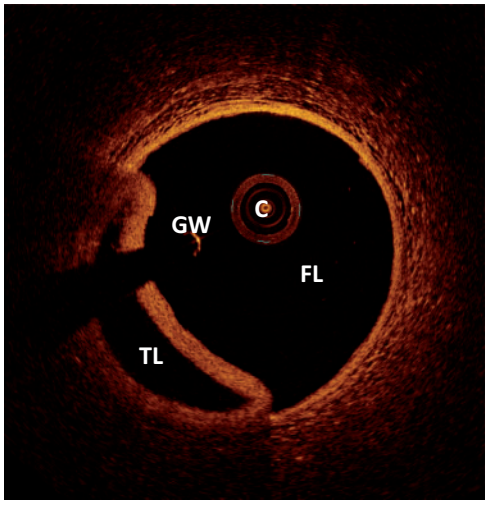

Figure 8 Guidewire passage into the false lumen demonstrated by optical coherence tomography, with both wire (GW) and optical coherence tomography catheter (C) seen in the false lumen outside the compressed true lumen.

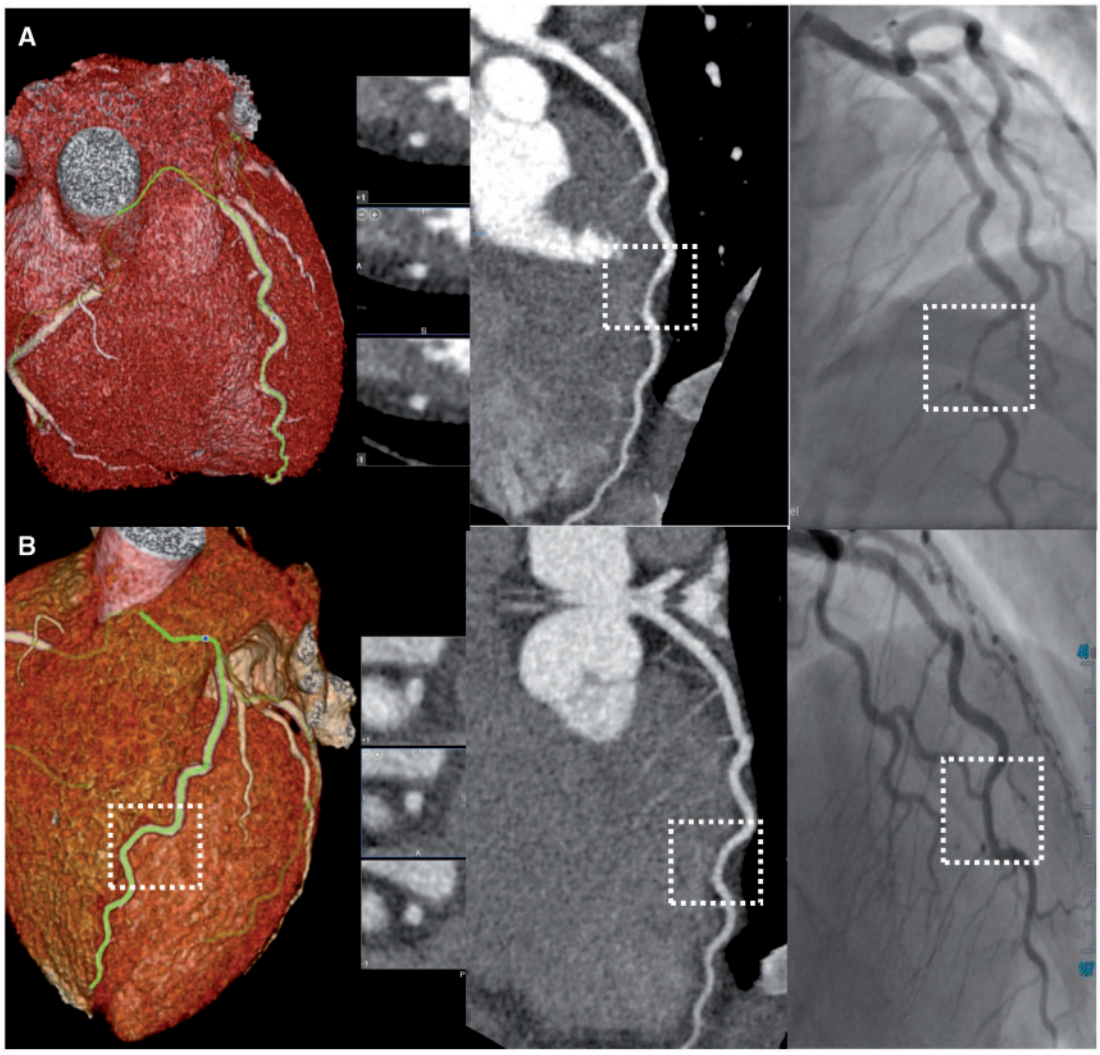

Figure 9 Coronary computed tomography findings with parallel angiographic images for a Type 2A dissection of the left anterior descending coronary artery at presentation (*A*) and following healing after 3-months follow-up (*B*).

Computed tomography coronary angiography

There is currently limited data to support the use of computed tomography coronary angiography (CTCA) for the diagnosis of acute SCAD. However, this imaging modality is increasingly used clinically to assess acute chest pain presentations. For SCAD, it has the advantage of being non-invasive (allowing coronary assessment without the increased risk of iatrogenic dissection reported with invasive angiography. However it is limited by lower spatial resolution, of particular importance for accurate assessment and interpretation of the smaller mid-to-distal coronary territories for which SCAD has a predilection.[173] Typical CTCA appearances have been described[147,174] (*Figure 9A*) and are consistent with angiographic and OCT findings where some cases show clear-cut contrast penetration of the false lumen leading to a 'classical' dual lumen but many show compression of the true-lumen by haematoma but without contrast penetration. The sensitivity and specificity of CTCA as a primary diagnostic investigation for SCAD are not known and false negative findings are reported.[173,175] In this context at present, patients in whom SCAD is suspected (e.g. low atherosclerotic risk young- to middle-aged females with typical symptoms and positive biomarkers) are recommended to undergo coronary angiography as the primary diagnostic investigation of choice. CTCA may however have a role in the follow-up assessment of SCAD (*Figure 9B*, see coronary angiography or computed tomography-coronary angiography section).

Key Messages

- Most SCAD can be diagnosed by coronary angiography and a working knowledge of the typical angiographic findings is key.
- Intracoronary imaging with OCT appears safe and should be considered where there is diagnostic uncertainty.
- Multi-vessel SCAD is common and careful assessment for this is required during angiography.

Acute management

Conservative management

There is good evidence that the majority of SCAD will first stabilize and then heal completely over time if managed conservatively (Supplementary material online, *Figure S6*).[3,4,7,8,11] Revascularization in patients with SCAD is very challenging due to the presence of an underlying disrupted and friable coronary vessel wall. This is widely reported to lead to worse outcomes for PCI than in atherosclerotic coronary disease.[3–5,7,8] For this reason where revascularization is not mandated (i.e. in haemodynamically stable patients with maintained distal flow in the culprit coronary and without demonstrable ongoing ischaemia) a conservative strategy is generally favoured.[1,2,145]

The proportion of healed cases described in contemporary series depends on the number of cases undergoing follow-up angiography and the timing and indication for repeat assessment. The US Mayo Clinic series reported on 59 patients (from 95 managed conservatively) who underwent repeat angiography for a range of reasons a median of 2.4 years after the index event. In all, 73% (43/59) were described as 'healed'.[3] Likewise, the Canadian series reported late revascularization in 3/134 conservatively managed cases but complete healing in all 79 of the remaining cases who underwent repeat angiography[73]; a Japanese series reported 68% healing in 28 conservatively managed patients assessed early by CTA a median of 3.4 months post event[8]; a Swiss series reported healing in all but one of 36 from 56 conservatively managed patients who underwent repeat angiography 6 months after the event.[7] It does appear that a small number of cases initially managed conservatively subsequently require revascularization. In a recent prospective series, 9 of 272 (3.3%) patients managed conservatively required subsequent in-hospital revascularization.[19] This may depend in part on the threshold for repeat investigation and intervention. It should be noted that dissections are often inherently painful and careful consideration should be given as to whether ongoing symptomatic chest pain is ischaemic in origin before proceeding to repeat angiography or intervention on a symptomatic basis.[145] As the majority of cases failing a conservative management strategy occur early during follow-up, prolonged inpatient monitoring (~5 days) in conservatively managed SCAD is suggested.[1,2,148] Further prospective research is required to better understand vascular healing after SCAD and the characteristics and management approach to delayed or failed healing.

Percutaneous coronary intervention

Published studies consistently show an increased risk of coronary complications with PCI.[3–5,7,8] In the Canadian series, revascularization procedural success was only achieved in 64% of patients and, in addition to that, only 30% of patients maintained durable results at long-term follow-up.[4] In the large series from the Mayo Clinic, most patients (2/3 of the total cohort) underwent coronary revascularization during initial hospitalization.[3] Coronary interventions, however, were associated with high complication rates. Procedural success was only achieved in 57% of cases. Furthermore revascularization was not associated with a reduced long-term risk of repeated revascularization or recurrent SCAD.[3,8] Where ongoing ischaemia or infarction mandates intervention, interventional cardiologists should be mindful of specific additional risks associated with SCAD interventions. These include:

- Increased risk of secondary iatrogenic dissection
- Guidewire passage into the false lumen[3,168–170] (*Figure 8*)
- Proximal and/or distal false lumen propagation during stent deployment[33,36,38,39,41] (*Figure 10*)
- Persistent distal dissection
- Major side branch restriction or occlusion by propagation of haematoma

Where stents are deployed, second generation drug-eluting stents (DES) are advised. Significant rates of in-stent restenosis are reported in one retrospective series [23/44 target vessel revascularization (TVR) from 87 patients managed by PCI and followed-up for a median 2.3 years], although the drug elution status of the stents used is not described.[3] In a recent retrospective multicentre study of 238 SCAD patients,[176] 108 underwent PCI with DES or bare metal stents

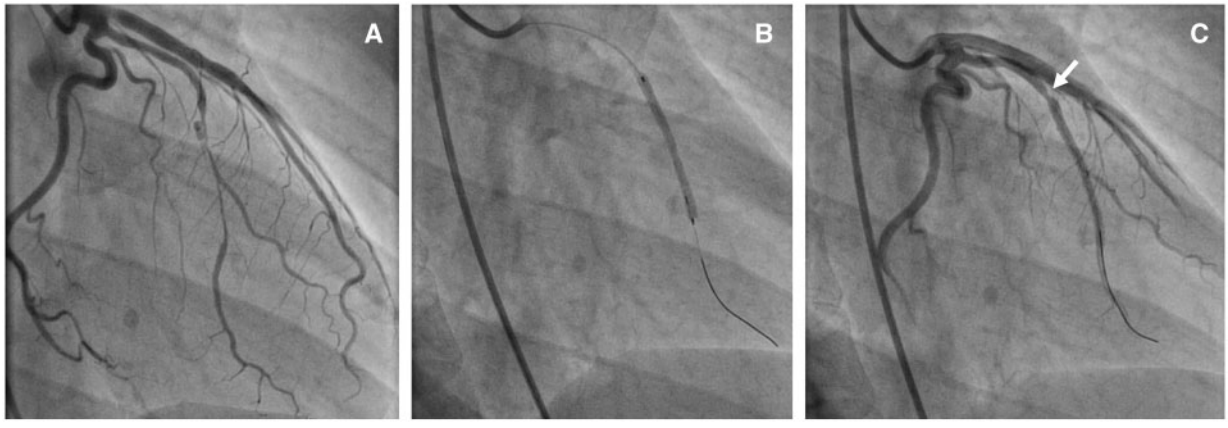

Figure 10 False lumen propagation during stenting. A Type 2A dissection affecting a high obtuse marginal branch of the circumflex but with maintained distal flow (*A*). Stenting (*B*) leads to proximal haematoma migration (arrowed *C*). Two further stents were required in this case to fully exclude the haematoma from luminal restriction.

(BMS). Overall, 24 patients (22.2%) suffered procedural-related complications. After a median follow-up of 3 years there was a trend towards a reduction in major adverse cardiac events after DES compared with BMS (26 vs. 39%, $P = 0.14$) mainly driven by TVR (4 vs. 18%, $P = 0.08$). Although the differences did not achieve statistical significance, the trends are consistent with existing knowledge about the relative risk of BMS vs. DES in non-SCAD PCI. A recent meta-analysis also suggested an additional TVR risk of 6.3% in patients treated with revascularization.[177] A single case has been reported of late strut mal-apposition purportedly due to the effects of haematoma resorption[160] although to date an increased incidence of stent thrombosis has not been confirmed. Adequate stent sizing and expansion is therefore likely to be important but stent post-dilation/optimization is a balance between the risk of haematoma propagation and ensuring optimal strut expansion.

Given the increased risk of adverse outcomes with PCI in SCAD, a number of less conventional interventional approaches have been reported. These include:

- Minimal plain old balloon angioplasty (POBA) to restore flow followed by a conservative strategy[178]
- Extended stent lengths to reduce the chances of proximal or distal haematoma propagation
- Sealing the proximal and distal extremes of the affected segments with short stents to restrict the haematoma before stenting the intermediate segments.[179,180]
- Targeting an intimal tear or 'flap' for focal stenting or stenting just the proximal extent of the dissection to prevent proximal propagation.[8,181]
- Cutting balloon inflation to fenestrate the intimal-medial membrane and depressurize the false lumen as a stand-alone strategy or prior to stenting.[182–185]
- Use of bioresorbable coronary scaffolds.[184,186–188]

These anecdotal case reports are subject to publication bias. Additionally, the role of bioresorbable coronary scaffolds more generally has been the subject of recent scrutiny.[189] In the absence of randomized data, no specific alternative PCI strategy can at present be specifically recommended.

Coronary artery bypass grafting

Coronary artery bypass grafting (CABG) in SCAD is generally used as a bail-out strategy either for a failure of PCI with ongoing ischaemia or infarction of a significant at-risk myocardial territory (e.g. failure to wire the true lumen distal to a SCAD occlusion) or because the site and extent of the dissection (usually involving the left main stem or the presence of multiple dissections in different vessels) is felt to pose a prohibitive risk with either a conservative or a PCI strategy. Successful grafting may be challenging where the dissection extends beyond the graft anastomosis site and great care must be taken to ensure anastomosis to the true lumen.[190] Coronary artery bypass grafting using arterial or venous conduits and both off-pump and robotic techniques are described but the literature on CABG in SCAD is limited to case reports and small case series (5–23 cases).[3,6,12,14] Early outcomes from these limited data on CABG are reported to be good but the Mayo Clinic Series reported high rates of graft failure at follow-up, perhaps due to healing of the native coronary leading to competitive flow and conduit thrombosis.[3]

Adjunctive supportive devices and transplant

For details, see Supplementary material online.[191–208]

Medical management

There are to date no randomized controlled trials comparing different pharmacological treatment strategies for SCAD. Current practice is therefore based on case and registry observations, clinical experience and the extrapolation (where appropriate) of guidelines for non-SCAD ACS treatment.

Thrombolysis

Although individual historical cases of SCAD managed apparently successfully with thrombolysis have been described,[209] there are also reports of dissection extension and even coronary rupture leading to cardiac tamponade following lytic therapy.[210–213] Thrombolysis is therefore contraindicated for the acute management of SCAD.

Antiplatelet therapies

The use of antiplatelet therapies and the duration of treatment remains an area of controversy and divergent practice in SCAD. This results from an apparent conflict between the strength of existing data of efficacy from non-SCAD ACS vs. an inherent concern (albeit unproven) about using medications that prolong bleeding time for a condition whose primary pathophysiology may be an intramural bleed.[145] This may be further complicated by problematic menorrhagia which can be an issue in SCAD-survivors of menstrual age taking antiplatelet therapies.[214] Patients who undergo stenting should receive dual antiplatelet therapy for 12 months and prolonged or lifelong monotherapy (usually with aspirin) in accordance with current ACS guidelines.[206,207] In patients managed conservatively, there is evidence from OCT studies of high grade stenosis sometimes with true luminal thrombus in association with SCAD.[30,166] This provides justification for antiplatelet therapy in the acute phase and most authors advocate acute dual antiplatelet therapy (usually with aspirin and clopidogrel rather than the newer P2Y12 inhibitors and avoiding intravenous antiplatelet therapies).[19,106,108] The optimal duration of dual and subsequent monotherapy remains unknown with some authors advocating lifelong aspirin[19,108] and others questioning this approach.[106]

Anticoagulant therapies

The same concerns about the potential adverse impact described for antiplatelet therapies also apply to anticoagulant treatments. Anticoagulation should probably be limited to acute administration during revascularization procedures while chronic use should be restricted to situations where there is an unequivocal clinical indication (such as left ventricular thrombus or thromboembolism) which should over-ride what is at present a theoretical risk.[145]

Angiotensin converting enzyme inhibitors, angiotensin receptor antagonists, mineralocorticoid receptor antagonists, beta-blockers, and vasodilator therapies

Medical management of SCAD patients with significant impairment of left ventricular systolic function should follow current guidelines aimed at maximizing angiotensin converting enzyme (ACE) or angiotensin receptor blocker (ARB) and β-blocker doses and adding in a

mineralocorticoid receptor antagonist (MRA) as indicated,[206,207] although hypotension frequently limits dose escalation in this younger population. More controversial is the management of SCAD-survivors without significant impairment of left ventricular systolic function. One recent multivariate analysis from a prospective cohort reported an association between hypertension and an increased risk of recurrent SCAD and β-blocker treatment with a reduced risk of recurrence.[19] These findings are not from a randomized study and await validation in other cohorts[215] but if confirmed provide the first evidence that SCAD recurrence risk may be reduced therapeutically. Vasodilatory therapies (e.g. nitrates or calcium channel blockers) are reserved for the empirical treatment of chest pain during the acute phase and recurrent chest pain following the index event (see post-spontaneous coronary artery dissection chest pain and its management section).

Statins

The rationale for prescribing statins for a condition whose pathophysiology has no known association with cholesterol is unclear. One small study reported higher statin use in patients with SCAD recurrence[44] but this non-randomized finding should be interpreted with caution and an adverse signal was not reported in a larger prospective cohort.[19] In general, statins are reserved for patients with conventional indications for treatment independent of their SCAD event.

Contraception and hormone replacement therapy

Concerns about hormonal contraception[62,63] and hormone replacement therapy[30] following SCAD are largely based on the presumed pathophysiological association between SCAD and female sex hormones arising from the female sex predominance and the known association of SCAD with the peripartum period.[1,2] However, the exact nature of this association remains to be elucidated. A number of cases have been reported of SCAD in association with exogenous sex hormones but given the high prevalence of use in the population, a causative link has yet to be determined. At present a reasonable strategy may be to avoid hormonal contraception where possible. In patients with recurrent cyclical chest pain following SCAD, low dose local hormone delivery intrauterine contraceptive devices have been anecdotally reported to be helpful.[145] The use of the levonorgestrel releasing intra uterine system (LNG-IUS) or endometrial ablation may also be considered in women with prolonged, severe menorrhagia (e.g. where antiplatelet therapies are mandated in the context of previous stenting).

Key Messages

- Coronary revascularization is associated with an increased risk of complications and adverse outcomes compared with atherosclerotic coronary disease.
- Conservatively (without revascularization) managed SCAD usually heals completely over a few months.
- Where flow is maintained and in the absence of ongoing ischaemia or infarction, a conservative approach should be considered followed by a period of inpatient observation.
- Further research is needed to clarify the optimal PCI strategy in cases where revascularization is necessary.
- The acute and convalescent medical strategy in SCAD may have key differences from post atherosclerotic AMI and further research is needed to establish the optimal treatment approach.

Pregnancy

Pregnancy-associated spontaneous coronary artery dissection: special considerations

Special considerations for the management of P-SCAD include the avoidance of teratogenic drugs, minimization of exposure of the unborn foetus to ionizing radiation[216] and timing of delivery to minimize as much as possible risk to both mother and baby. Obstetric issues are reviewed elsewhere[96] and are not considered in detail here but coronary management should not differ greatly from other SCAD patients with diagnosis by limited coronary angiography and a management preference for a conservative approach to revascularization where practical.

Pregnancy after spontaneous coronary artery dissection

There is a single published report of nine pregnancies in SCAD-survivors with one recurrence occurring in a patients whose first event was not peripartum.[217] The degree of left ventricular impairment post-SCAD will also contribute independently to the risk. Some authors have advocated a blanket recommendation to avoid pregnancy in SCAD-survivors.[1,2] Patients should certainly be carefully counselled before contemplating pregnancy, potentially teratogenic drugs discontinued, and any planned or un-planned pregnancy should be considered high risk and monitored accordingly.

Key Messages

- P-spontaneous coronary artery dissection should be managed by a multidisciplinary team with individualized cardiovascular and obstetric management.
- There is limited data on the risk of pregnancy in SCAD-survivors but at present pregnancy should be considered high risk pending further research to better quantify this risk.

Outcomes and follow-up

Follow-up imaging

Echocardiography/cardiac magnetic resonance imaging

Following SCAD, as with myocardial infarction of other causes, an assessment of left ventricular systolic function is mandatory to guide medical and potentially device therapy.[206,207]

Computed tomography-peripheral angiography or magnetic resonance-angiography

In view of the association between SCAD, FMD and other underlying EVAs, affecting multiple vascular beds (see fibromuscular dysplasia

section) and the potential implications for patient management and follow-up,[106] imaging of extra-coronary vascular beds in patients with SCAD is advised.[101,103,106] Saw *et al.*[1] have advocated non-selective angiography of the corresponding arteries with a pigtail catheter on the occasion of the index coronary angiography. However, this strategy has the potential risks of additional vascular imaging, catheter manipulation and prolonged procedural times in unstable patients, with possibly increased vascular fragility.[106] Furthermore, this approach requires separate non-invasive imaging of cerebral aneurysms, which have been identified in 8 to 14% of cases despite a low screening rate, sometimes in the absence of typical FMD lesions.[4,104,107] Alternatively, Liang *et al.*[106] have shown the feasibility of a dedicated CTA protocol from the neck to the pelvis, with low-osmolar contrast agents and radiation dose-limiting techniques. While the sensitivity of CTA is lower than that of conventional angiography, it is unlikely to miss clinically relevant FMD lesions. MR-angiography leads to a further decrease in spatial resolution but remains a reasonable, radiation-free alternative,[105] and may be preferred in case of diabetes, renal insufficiency or iodine-contrast intolerance. There is currently no specific data on follow-up of EVAs identified in SCAD patients and therefore currently this should follow best practice for similar conditions in non-SCAD patients.

Coronary angiography or computed tomography-coronary angiography

Whilst it is clear that the majority of conservatively managed SCAD heals completely over time, some cases of persistent dissection are reported (see conservative management section). The value of follow-up coronary imaging to determine SCAD-healing and how this should be used to guide subsequent management remains unclear. It may be relevant, for decision-making about the duration of anti-platelet therapy (see antiplatelet therapies section) or in symptomatic patients where the diagnosis is not clear (see post-spontaneous coronary artery dissection chest pain and its management section). Non-invasive imaging is attractive as invasive angiography in SCAD patients has been associated with an increased risk of iatrogenic dissections (see secondary iatrogenic dissection in spontaneous coronary artery dissection section). Computed tomography coronary angiography has been proposed as an alternative although current data are limited to single case discussions and one small series. Although the issue of spatial resolution in the smaller, more distal, SCAD coronary sites is still relevant (see computed tomography coronary angiography section), CT may have greater utility in assessing healing where the site of dissection has already been determined by angiography (*Figure 9B*).[147,218] Roura *et al.*[10] reported the largest series of patients with SCAD studied by multislice CT (MSCT) at follow-up (24 cases). In 83% of cases, complete resolution of SCAD was shown. Further data is required before CTCA can be recommended for follow-up SCAD imaging. Where essential, invasive angiography should be performed with meticulous attention to minimize the risk of iatrogenic dissection.

Prognosis: mortality, recurrence risk, and major adverse cardiac events

Outcomes following SCAD are summarized in Supplementary material online, *Table S3*.[3,5,7,8,19] In patients surviving SCAD, long-term mortality is low. In the US Mayo Clinic series 10-year survival from Kaplan-Meier estimates is reported at 92%.[44] Similarly an Italian series reported 94.4% 6-year survival,[5] whilst a Swiss series reported no deaths after the index event in 63 patients followed-up to a median 4.5 years,[7] a Japanese series reported one death from 63 patients followed up for a median 34 months[8] and a prospective Canadian series report 1.2% mortality at median follow-up 3.1 years.[19] However this masks significant morbidity. The overall major adverse cardiac events (MACE) rate in SCAD patients is significant but with considerable variation between published series (47.4% MACE over 10-years from Kaplan–Meier estimates in the US series;[44] MACE in the prospective Canadian series was 19.9% over median 3.1 years follow-up;[19] 5-year MACE in the Japanese series was 37%;[8] in the Italian series 6-year MACE was 14.6%).[5] This is primarily driven by recurrent dissections and a high rate of target vessel failure in patients undergoing PCI (see percutaneous coronary intervention section).[3] Recurrence in SCAD has been widely reported.[1,3–5,7,8,44] The US series reported SCAD recurrence in 17% of patients across a median follow-up period of 47 months with a 10-year recurrence rate of 29.4% [the median time to a second event was 2.8 years (ranging from 3 days to 12 years)][44]; the Canadian prospective series report recurrent *de novo* SCAD in 10.4% of 327 patients followed up for a median 3.1 years and a recurrent MI rate of 16.8% in the same cohort[19]; the Japanese series reported seven recurrent SCAD after the first 30-days from the index event from 63 patients followed up for a median 34 months[8]; the Swiss series report 3/63 recurrent SCAD followed-up for a median 4.5 years[7]; the Italian series report 4.7% recurrence over a median 22 month follow-up].[5] Recurrence often appears to affect new territories (e.g. in 12/15 patients in the US series)[44] and stenting at the time of the first event does not appear to be protective. Although reported rates may represent a slight overestimation of true recurrence rates due to the selection bias inherent to self-referral based cohort studies and prospective data is needed, recurrences are certainly a justified concern in SCAD patients. One study has reported a borderline association between recurrence and increased coronary tortuosity, although it is unclear if tortuosity is a marker of an underlying vasculopathy or provides a mechanism for arterial injury.[47] Apart from the potential benefit of betablockers and control of hypertension previously described, no current treatment strategy has, to date, been shown to reduce rates of recurrence.

Post spontaneous coronary artery dissection chest pain and its management

Recurrent chest pain, often with associated hospital admission, is common after SCAD. In some patients symptoms occur cyclically, usually pre-menstrually.[219] Given the SCAD recurrence risk, patients presenting with recurrent chest pain require careful assessment with serial electrocardiography (ECG) and high sensitivity troponin measurement. However, given the reported increased risk of secondary iatrogenic dissection in SCAD patients (see secondary iatrogenic dissection in spontaneous coronary artery dissection section), invasive angiography should be reserved for patients with hard evidence of ischaemia or myocardial necrosis. A role for CTCA to rule out recurrent SCAD, when evaluating post SCAD chest pain, although potentially attractive, remains to be clearly elucidated (see coronary angiography or computed tomography-coronary angiography

section). Anecdotally, where recurrent SCAD has been excluded, symptoms may respond to a treatment strategy aimed at reducing vasospasm with vasodilator therapies (where left ventricular function is normal reducing blood pressure lowering medications may be necessary to allow the initiation of vasodilators).[145] Likewise it has been reported that cyclical symptoms may respond to low dose contraception (e.g. the progesterone hormonal coil).[145]

Cardiac rehabilitation and exercise

For details, see Supplementary material online.[220,221]

Post-traumatic stress disorder and the emotional and psychological consequences of spontaneous coronary artery dissection

For details, see Supplementary material online.[220,222]

Key Messages

- Although the prognosis following SCAD appears good, recurrent SCAD is well recognized.
- Assessment for extra-coronary arteriopathies is advised in SCAD-survivors.
- Cardiac rehabilitation should be considered in SCAD patients and a return to full-activity with an avoidance of extreme or isometric exercise encouraged.
- Recurrent chest pain after SCAD is common and requires careful assessment and management.

Management considerations

Whilst there are several areas in the management of patients with SCAD where the optimal approach remains uncertain and research is needed to provide evidence to justify firm recommendations (see research priorities section), the following considerations may be useful for clinicians:

- Early coronary angiography should be considered to exclude the diagnosis of SCAD in patients presenting with clinical features of ACS but at low risk of atherosclerotic AMI, in particular young to middle aged women
- Where angiographic diagnosis of SCAD is uncertain, intracoronary imaging with OCT should be considered
- In clinically stable patients with maintained coronary flow, a conservative management strategy is preferred because of the increased risk of adverse outcomes with revascularization
- In patients with confirmed SCAD imaging for extra-coronary arteriopathies is advised
- A diagnosis of SCAD should be actively sought at post mortem in unexplained cases of sudden cardiac death by careful assessment of the full length of the coronary tree

Research priorities

Despite huge progress in the clinical characterization of SCAD from an international effort to register, assess and follow-up patients, this remains a condition for which the pathophysiology is poorly understood and for which, despite a significant recurrence risk, there is no specific disease-modifying therapy. Current international efforts are focused on building large prospectively recruited multicentre cohorts, phenotyped by state-of-the-art imaging for pathophysiological (including genetic) and clinical studies. For example, the European Observational Research Platform (EORP) SCAD study will open for recruitment in the summer of 2018. Prospective studies (including ultimately randomized studies) assessing the best medical therapies (e.g. role and duration of antiplatelet therapy, use of beta-blockers and other secondary prevention drugs) as well as the optimal coronary intervention strategy are urgently needed. It is hoped these ongoing collaborative research efforts will shed new light and expand knowledge on this relatively rare, elusive and challenging clinical entity.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Acknowledgements

We wish to acknowledge our European patients with SCAD, EURODIS, BeatSCAD; the ESC-ACCA SCAD Study Group and the ACCA secretariat—in particular Eugenie Delaveau and Celine Serio; Dr J. Cade for the image in *Figure 9*, Dr S Parsons for *Figure 2*. A Persu is grateful to Prof. Patrick Chenu (Cardiology Department, Cliniques Universitaires Saint Luc, UCL, Brussels, Belgium) for sharing his knowledge and experience on Spontaneous Coronary Artery Dissection (SCAD) and to Mr Xiang Li, medical student at the same University for his contribution to *Figure 4* and literature review.

Funding

British Heart Foundation, the NIHR RD-TRC and the Leicester NIHR Biomedical Research Centre to D.A.

Conflict of interest: D.A. declares grants from Astra Zeneca and St Jude Medical (now part of Abbott Vascular) as well as grants from the British Heart Foundation, NIHR RD-TRC and BeatSCAD. H.B. reports grants and personal fees from ASTRA ZENECA, personal fees from DAICHII-SANKYO, personal fees from ELI-LILLY, personal fees from BAYER, personal fees from SANOFI, during the conduct of the study; personal fees from NOVARTIS, personal fees from BMS-PFIZER, from SERVIER, outside the submitted work.

References

1. Saw J, Mancini GB, Humphries KH. Contemporary review on spontaneous coronary artery dissection. *J Am Coll Cardiol* 2016;**68**:297–312.
2. Tweet MS, Gulati R, Hayes SN. Spontaneous coronary artery dissection. *Curr Cardiol Rep* 2016;**18**:60.
3. Tweet MS, Eleid MF, Best PJ, Lennon RJ, Lerman A, Rihal CS, Holmes DR, Jr., Hayes SN, Gulati R. Spontaneous coronary artery dissection: revascularization versus conservative therapy. *Circ Cardiovasc Interv* 2014;**7**:777–786.
4. Saw J, Aymong E, Sedlak T, Buller CE, Starovoytov A, Ricci D, Robinson S, Vuurmans T, Gao M, Humphries K, Mancini GB. Spontaneous coronary artery dissection: association with predisposing arteriopathies and precipitating stressors and cardiovascular outcomes. *Circ Cardiovasc Interv* 2014;**7**:645–655.
5. Lettieri C, Zavalloni D, Rossini R, Morici N, Ettori F, Leonzi O, Latib A, Ferlini M, Trabattoni D, Colombo P, Galli M, Tarantini G, Napodano M, Piccaluga E, Passamonti E, Sganzerla P, Ielasi A, Coccato M, Martinoni A, Musumeci G, Zanini R, Castiglioni B. Management and long-term prognosis of spontaneous coronary artery dissection. *Am J Cardiol* 2015;**116**:66–73.

6. Faden MS, Bottega N, Benjamin A, Brown RN. A nationwide evaluation of spontaneous coronary artery dissection in pregnancy and the puerperium. *Heart* 2016;**102**:1974–1979.
7. Rogowski S, Maeder MT, Weilenmann D, Haager PK, Ammann P, Rohner F, Joerg L, Rickli H. Spontaneous coronary artery dissection: angiographic follow-up and long-term clinical outcome in a predominantly medically treated population. *Catheter Cardiovasc Interv* 2017;**89**:59–68.
8. Nakashima T, Noguchi T, Haruta S, Yamamoto Y, Oshima S, Nakao K, Taniguchi Y, Yamaguchi J, Tsuchihashi K, Seki A, Kawasaki T, Uchida T, Omura N, Kikuchi M, Kimura K, Ogawa H, Miyazaki S, Yasuda S. 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**:341–348.
9. McGrath-Cadell L, McKenzie P, Emmanuel S, Muller DW, Graham RM, Holloway CJ. Outcomes of patients with spontaneous coronary artery dissection. *Open Heart* 2016;**3**:e000491.
10. Roura G, Ariza-Sole A, Rodriguez-Caballero IF, Gomez-Lara J, Ferreiro JL, Romaguera R, Teruel L, de Albert M, Gomez-Hospital JA, Cequier A. Noninvasive follow-up of patients with spontaneous coronary artery dissection with CT angiography. *JACC Cardiovasc Imaging* 2016;**9**:896–897.
11. Alfonso F, Paulo M, Lennie V, Dutary J, Bernardo E, Jiménez-Quevedo P, Gonzalo N, Escaned J, Bañuelos C, Pérez-Vizcayno MJ, Hernández R, Macaya C. Spontaneous coronary artery dissection: long-term follow-up of a large series of patients prospectively managed with a "conservative" therapeutic strategy. *JACC Cardiovasc Interv* 2012;**5**:1062–1070.
12. Ito H, Taylor L, Bowman M, Fry ET, Hermiller JB, Van Tassel JW. Presentation and therapy of spontaneous coronary artery dissection and comparisons of postpartum versus nonpostpartum cases. *Am J Cardiol* 2011;**107**:1590–1596.
13. Motreff P, Malcles G, Combaret N, Barber-Chamoux N, Bouajila S, Pereira B, Amonchot A, Citron B, Lusson JR, Eschalier R, Souteyrand G. How and when to suspect spontaneous coronary artery dissection: novel insights from a single-centre series on prevalence and angiographic appearance. *EuroIntervention* 2017;**12**:e2236–e2243.
14. Vanzetto G, Berger-Coz E, Barone-Rochette G, Chavanon O, Bouvaist H, Hacini R, Blin D, Machecourt J. 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**:250–254.
15. Mortensen KH, Thuesen L, Kristensen IB, Christiansen EH. Spontaneous coronary artery dissection: a Western Denmark Heart Registry Study. *Catheter Cardiovasc Intervent* 2009;**74**:710–717.
16. Rashid HN, Wong DT, Wijesekera H, Gutman SJ, Shanmugam VB, Gulati R, Malaipan Y, Meredith IT, Psaltis PJ. 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**:336–338.
17. Barber-Chamoux N, Souteyrand G, Combaret N, Ouedraogo E, Lusson JR, Motreff P. Contribution of optical coherence tomography imaging in management of iatrogenic coronary dissection. *Cardiovasc Revasc Med* 2016;**17**:138–142.
18. Elkayam U, Jalnapurkar S, Barakkat MN, Khatri N, Kealey AJ, Mehra A, Roth A. Pregnancy-associated acute myocardial infarction: a review of contemporary experience in 150 cases between 2006 and 2011. *Circulation* 2014;**129**:1695–1702.
19. Saw J, Humphries K, Aymong E, Sedlak T, Prakash R, Starovoytov A, Mancini GBJ. Spontaneous coronary artery dissection: clinical outcomes and risk of recurrence. *J Am Coll Cardiol* 2017;**70**:1148–1158.
20. Basso C, Aguilera B, Banner J, Cohle S, d'Amati G, de Gouveia RH, di Gioia C, Fabre A, Gallagher PJ, Leone O, Lucena J, Mitrofanova L, Molina P, Parsons S, Rizzo S, Sheppard MN, Mier MPS, Kim Suvarna S, Thiene G, van der Wal A, Vink A, Michaud K. Association for European Cardiovascular P. Guidelines for autopsy investigation of sudden cardiac death: 2017 update from the Association for European Cardiovascular Pathology. *Virchows Arch* 2017;**471**:691–705.
21. Desai S, Sheppard MN. Sudden cardiac death: look closely at the coronaries for spontaneous dissection which can be missed. A study of 9 cases. *Am J Forensic Med Pathol* 2012;**33**:26–29.
22. Hill SF, Sheppard MN. Non-atherosclerotic coronary artery disease associated with sudden cardiac death. *Heart* 2010;**96**:1119–1125.
23. Mandal R, Brooks EG, Corliss RF. Eosinophilic coronary periarteritis with arterial dissection: the mast cell hypothesis. *J Forensic Sci* 2015;**60**:1088–1092.
24. Melez İE, Arslan MN, Melez DO, Akçay A, Büyük Y, Avşar A, Kumral B, Şirin G, Karayel FA, Daş T, Dokudan YE, Şam B. Spontaneous coronary artery dissection: report of 3 cases and literature review hormonal, autoimmune, morphological factors. *Am J Forensic Med Pathol* 2015;**36**:188–192.
25. Stoukas V, Dragovic LJ. Sudden deaths from eosinophilic coronary monoarteritis: a subset of spontaneous coronary artery dissection. *Am J Forensic Med Pathol* 2009;**30**:268–269.
26. Basso C, Morgagni GL, Thiene G. Spontaneous coronary artery dissection: a neglected cause of acute myocardial ischaemia and sudden death. *Heart* 1996;**75**:451–454.
27. Robinowitz M, Virmani R, McAllister HAJ. Spontaneous coronary artery dissection and eosinophilic inflammation: a cause and effect relationship? *Am J Med* 1982;**72**:923–928.
28. Alfonso F, Bastante T. Spontaneous coronary artery dissection: novel diagnostic insights from large series of patients. *Circ Cardiovasc Interv* 2014;**7**:638–641.
29. Vrints CJ. Spontaneous coronary artery dissection. *Heart* 2010;**96**:801–808.
30. Alfonso F, Paulo M, Gonzalo N, Dutary J, Jimenez-Quevedo P, Lennie V, Escaned J, Banuelos C, Hernandez R, Macaya C. Diagnosis of spontaneous coronary artery dissection by optical coherence tomography. *J Am Coll Cardiol* 2012;**59**:1073–1079.
31. Paulo M, Sandoval J, Lennie V, Dutary J, Medina M, Gonzalo N, Jimenez-Quevedo P, Escaned J, Banuelos C, Hernandez R, Macaya C, Alfonso F. Combined use of OCT and IVUS in spontaneous coronary artery dissection. *JACC Cardiovasc Imaging* 2013;**6**:830–832.
32. Fengping Y, Jue H, Qingchun Y, Fangxing H. A case of sudden death due to spontaneous coronary artery dissection. *Am J Forensic Med Pathol* 2011;**32**:312–313.
33. Kanaroglou S, Nair V, Fernandes JR. Sudden cardiac death due to coronary artery dissection as a complication of cardiac sarcoidosis. *Cardiovasc Pathol* 2015;**24**:244–246.
34. Lunebourg A, Letovanec I, Eggenberger P, Lehr HA. Images in cardiovascular medicine. Sudden cardiac death due to triple vessel coronary dissection. *Circulation* 2008;**117**:2038–2040.
35. Wei JP, Kay D, Fishbein MC. Spontaneous dissection of the distal obtuse marginal coronary artery: a rare cause of sudden death. *Am J Forensic Med Pathol* 2008;**29**:199–201.
36. Carreon CK, Esposito MJ. Eosinophilic coronary monoarteritis. *Arch Pathol Lab Med* 2014;**138**:979–981.
37. Asuncion CM, Hyun J. Dissecting intramural hematoma of the coronary artery in pregnancy and the puerperium. *Obstet Gynecol* 1972;**40**:202–210.
38. Conraads VM, Vorlat A, Colpaert CG, Rodrigus IE, De Paep RJ, Moulijn AC, Vrints CJ. Spontaneous dissection of three major coronary arteries subsequent to cystic medial necrosis. *Chest* 1999;**116**:1473–1475.
39. Madu EC, Kosinski DJ, Wilson WR, Burket MW, Fraker TD, Jr, Ansel GM. Two-vessel coronary artery dissection in the peripartum period. Case report and literature review. *Angiology* 1994;**45**:809–816.
40. Makino Y, Inokuchi G, Yokota H, Hayakawa M, Yajima D, Motomura A, Chiba F, Torimitsu S, Nakatani Y, Iwase H. Sudden death due to coronary artery dissection associated with fibromuscular dysplasia revealed by postmortem selective computed tomography coronary angiography: a case report. *Forensic Sci Int* 2015;**253**:e10–e15.
41. Mortensen KH, Thuesen L, Kristiensen IB, Christiansen EH. Spontaneous coronary artery dissection - a western Denmark heart registry study. *Eur Heart J* 2009;**30**:787–787.
42. Nishiguchi T, Tanaka A, Ozaki Y, Taruya A, Fukuda S, Taguchi H, Iwaguro T, Ueno S, Okumoto Y, Akasaka T. Prevalence of spontaneous coronary artery dissection in patients with acute coronary syndrome. *Eur Heart J Acute Cardiovasc Care* 2016;**5**:263–270.
43. Saw J, Aymong E, Mancini GB, Sedlak T, Starovoytov A, Ricci D. Nonatherosclerotic coronary artery disease in young women. *Can J Cardiol* 2014;**30**:814–819.
44. Tweet MS, Hayes SN, Pitta SR, Simari RD, Lerman A, Lennon RJ, Gersh BJ, Khambatta S, Best PJ, Rihal CS, Gulati R. Clinical features, management, and prognosis of spontaneous coronary artery dissection. *Circulation* 2012;**126**:579–588.
45. Rogowski S, Maeder MT, Weilenmann D, Haager PK, Ammann P, Rohner F, Joerg L, Rickli H. Spontaneous coronary artery dissection: angiographic follow-up and long-term clinical outcome in a predominantly medically treated population. *Catheter Cardiovasc Interv* 2017;**89**:59–68.
46. Bush N, Nelson-Piercy C, Spark P, Kurinczuk JJ, Brocklehurst P, Knight M. Myocardial infarction in pregnancy and postpartum in the UK. *Eur J Prev Cardiol* 2013;**20**:12–20.
47. Eleid MF, Guddeti RR, Tweet MS, Lerman A, Singh M, Best PJ, Vrtiska TJ, Prasad M, Rihal CS, Hayes SN, Gulati R. Coronary artery tortuosity in spontaneous coronary artery dissection: angiographic characteristics and clinical implications. *Circ Cardiovasc Interv* 2014;**7**:656–662.
48. Huikuri HV, Mallon SM, Myerburg RJ. Cardiac arrest due to spontaneous coronary artery dissection in a patient with coronary ectasia—a case report. *Angiology* 1991;**42**:148–151.
49. Mieghem CA, Ligthart JM, Cademartiri F. Images in cardiology. Spontaneous dissection of the left main coronary artery in a patient with Osler-Weber-Rendu disease. *Heart* 2005;**92**:394.
50. Henkin S, Negrotto SM, Tweet MS, Kirmani S, Deyle DR, Gulati R, Olson TM, Hayes SN. Spontaneous coronary artery dissection and its association with heritable connective tissue disorders. *Heart* 2016;**102**:876–881.

51. Sato C, Wakabayashi K, Suzuki H. Natural course of isolated spontaneous coronary artery dissection in Marfan syndrome. *Int J Cardiol* 2014;**177**:20–22.
52. Fattori R, Sangiorgio P, Mariucci E, Ritelli M, Wischmeijer A, Greco C, Colombi M. Spontaneous coronary artery dissection in a young woman with Loeys-Dietz syndrome. *Am J Med Genet A* 2012;**158A**:1216–1218.
53. Hampole CV, Philip F, Shafii A, Pettersson G, Anesi GL, Patel JB, Menon V. Spontaneous coronary artery dissection in Ehlers-Danlos syndrome. *Ann Thorac Surg* 2011;**92**:1883–1884.
54. Giugliano GR, Sethi PS. Spontaneous left anterior descending coronary artery dissection in a patient with neurofibromatosis. *J Invasive Cardiol* 2009;**21**: e103–e105.
55. Sibon I, Sommer P, Lamaziere JM, Bonnet J. Lysyl oxidase deficiency: a new cause of human arterial dissection. *Heart* 2005;**91**:e33.
56. Martín Dávila F, Delgado Portela M, García Rojo M, González García J, Puig Rullán AM, López Pérez R, Carbajo Vicente M. Coronary artery dissection in alpha-1-antitrypsin deficiency. *Histopathology* 1999;**34**:376–378.
57. Diez-del Hoyo F, Sanz-Ruiz R, Diez-Villanueva P, Nunez-Garcia A, Casado-Plasencia A, Angulo-Llanos R, Clavero-Olmos M, Elizaga Corrales J, Fernandez-Aviles F. A novel cardiovascular presentation of Alport Syndrome: spontaneous coronary artery dissection. *Int J Cardiol* 2014;**177**:e133–e134.
58. Itty CT, Farshid A, Talaulikar G. Spontaneous coronary artery dissection in a woman with polycystic kidney disease. *Am J Kidney Dis* 2009;**53**:518–521.
59. Marcoff L, Rahman E. Menstruation-associated spontaneous coronary artery dissection. *J Invasive Cardiol* 2010;**22**:E183–E185.
60. Iltumur K, Karahan Z, Ozmen S, Danis R, Toprak N. Spontaneous coronary artery dissection during hemodialysis in the post-abortion period. *Int J Cardiol* 2008;**127**:e45–e47.
61. Luceri S, Paolillo V,D, Benedictis M, Scrocca I. Spontaneous dissection of the left coronary tree after an interruption of pregnancy treated with extensive stenting. *J Invasive Cardiol* 2006;**18**:E117–E120.
62. Azam MN, Roberts DH, Logan WF. Spontaneous coronary artery dissection associated with oral contraceptive use. *Int J Cardiol* 1995;**48**:195–198.
63. Zehir R, Karabay CY, Kocabay G. Myocardial infarction and spontaneous dissection of coronary artery due to oral contraceptive. *J Cardiovasc Med (Hagerstown)* 2011;**12**:448–450.
64. Pan AL, Fergusson D, Hong R, Badawi RA. Spontaneous coronary artery dissection following topical hormone replacement therapy. *Case Rep Cardiol* 2012; **2012**:1.
65. Abuzeyad FH, Ibnaouf ES, Farras MA. Clomiphene associated inferior STEMI in a young female due to right coronary artery Dissection. *Case Rep Emerg Med* 2017;**2017**:1.
66. Lempereur M, Grewal J, Saw J. Spontaneous coronary artery dissection associated with beta-HCG injections and fibromuscular dysplasia. *Can J Cardiol* 2014; **30**:464 e1–463.
67. Mirra M, Kola N, Mattiello G, Morisco C, Spinelli L. Spontaneous coronary artery dissection in a young woman with polycystic ovarian syndrome. *Am J Emerg Med* 2017;**35**:936 e5–936 e7.
68. Aldoboni AH, Hamza EA, Majdi K, Ngibzadhe M, Palasaidi S, Moayed DA. Spontaneous dissection of coronary artery treated by primary stenting as the first presentation of systemic lupus erythematosus. *J Invasive Cardiol* 2002;**14**:694–696.
69. Srinivas M, Basumani P, Muthusamy R, Wheeldon N. Active inflammatory bowel disease and coronary artery dissection. *Postgrad Med J* 2005;**81**:68–70.
70. Chu KH, Menapace FJ, Blankenship JC, Hausch R, Harrington T. Polyarteritis nodosa presenting as acute myocardial infarction with coronary dissection. *Cathet Cardiovasc Diagn* 1998;**44**:320–324.
71. Hunsaker JC 3rd, O'Connor WN, Lie JT. Spontaneous coronary arterial dissection and isolated eosinophilic coronary arteritis: sudden cardiac death in a patient with a limited variant of Churg-Strauss syndrome. *Mayo Clin Proc* 1992;**67**: 761–766.
72. Shah AH, Kinnaird TD. Recurrent ST elevation myocardial infarction: what is the aetiology? *Heart Lung Circ* 2015;**24**:e169–e172.
73. Saw J, Aymong E, Sedlak T, Buller CE, Starovoytov A, Ricci D, Robinson S, Vuurmans T, Gao M, Humphries K, Mancini GBJ. Spontaneous coronary artery dissection: association with predisposing arteriopathies and precipitating stressors and cardiovascular outcomes. *Circulation* 2014;**7**:645–655.
74. Gerede DM, Yüksel B, Tutar E, Küçükşahin O, Uzun Ç, Atasoy KÇ, Düzgün N, Bengisun U. Spontaneous coronary artery dissection in a male patient with Takayasu's arteritis and antiphospholipid antibody syndrome. *Case Rep Rheumatol* 2013;**2013**:1.
75. Ionescu CN, Chrissoheris M, Caraccciolo EA. Spontaneous coronary artery dissection and severe hypothyroidism. *J Invasive Cardiol* 2009;**21**:E60–E62.
76. Bayar N, Çağırcı G, Üreyen ÇM, Kuş G, Küçükseymen S, Arslan Ş. The relationship between spontaneous multi-vessel coronary artery dissection and celiac disease. *Korean Circ J* 2015;**45**:242–244.
77. Kay IP, Williams MJ. Spontaneous coronary artery dissection: long stenting in a patient with polycythemia vera. *Int J Cardiovasc Intervent* 1999;**2**:191–193.
78. Tsujita K, Miyazaki T, Kaikita K, Chitose T, Takaoka N, Soejima H, Tayama S, Hokimoto S, Sugiyama S, Ogawa H. Premenopausal woman with acute myocardial infarction caused by spontaneous coronary artery dissection and potential association with coronary vasospasm. *Cardiovasc Interv Ther* 2012;**27**:121–126.
79. Jaffe BD, Broderick TM, Leier CV. Cocaine-induced coronary-artery dissection. *N Engl J Med* 1994;**330**:510–511.
80. Suh SY, Kim JW, Choi CU, Kim EJ, Rha SW, Park CG, Seo HS, Oh DJ. Spontaneous coronary dissection associated with sleep deprivation presenting with acute myocardial infarction. *Int J Cardiol* 2007;**115**:e78–e79.
81. Velusamy M, Fisherkeller M, Keenan ME, Kiernan FJ, Fram DB. Spontaneous coronary artery dissection in a young woman precipitated by retching. *J Invasive Cardiol* 2002;**14**:198–201.
82. Schifferdecker B, Pacifico L, Ramsaran EK, Folland ED, Spodick DH, Weiner BH. Spontaneous coronary artery dissection associated with sexual intercourse. *Am J Cardiol* 2004;**93**:1323–1324.
83. Tsimikas S, Giordano FJ, Tarazi RY, Beyer RW. Spontaneous coronary artery dissection in patients with renal transplantation. *J Invasive Cardiol* 1999;**11**: 316–321.
84. Mallon DH, McKenzie D, Dayer M. A spontaneous coronary arterial dissection associated with a calcineurin inhibitor. *BMJ Case Rep* 2012;**2012**: bcr2012006414.
85. Abbott JD, Curtis JP, Murad K, Kramer HM, Remetz MS, Setaro JF, Brennan JJ. Spontaneous coronary artery dissection in a woman receiving 5-fluorouracil—a case report. *Angiology* 2003;**54**:721–724.
86. Goli AK, Koduri M, Haddadin T, Henry PD. Spontaneous coronary artery dissection in a woman on fenfluramine. *Rev Cardiovasc Med* 2007;**8**:41–44.
87. Keir ML, Dehghani P. Corticosteroids and spontaneous coronary artery dissection: a new predisposing factor? *Can J Cardiol* 2016;**32**:395 e7–398.
88. Mahmood MM, Wright RA. Spontaneous coronary artery dissection in a patient on methylphenidate for attention deficit hyperactivity disorder. *Int J Cardiol* 2016;**222**:830–831.
89. Garcia Garcia C, Casanovas N, Recasens L, Miranda F, Bruguera J. Spontaneous coronary artery dissection in ergotamine abuse. *Int J Cardiol* 2007;**118**:410–411.
90. Saunders SL, Ford SE. Primary coronary artery dissection possibly related to drug hypersensitivity in a male. *Can J Cardiol* 1991;**7**:138–140.
91. Karabinos I, Papadopoulos A, Koulouris S, Kranidis A, Korovesis S, Katritsis D. Spontaneous coronary artery dissection during a dobutamine stress echocardiography. *Echocardiography* 2006;**23**:232–234.
92. Fahmy P, Prakash R, Starovoytov A, Boone R, Saw J. Pre-disposing and precipitating factors in men with spontaneous coronary artery dissection. *JACC Cardiovasc Interv* 2016;**9**:866–868.
93. Vijayaraghavan R, Verma S, Gupta N, Saw J. Pregnancy-related spontaneous coronary artery dissection. *Circulation* 2014;**130**:1915–1920.
94. Cade JR, Szarf G, de Siqueira ME, Chaves A, Andrea JC, Figueira HR, Gomes MM Jr, Freitas BP, Filgueiras Medeiros J, Dos Santos MR, Fiorotto WB, Daige A, Goncalves R, Cantarelli M, Alves CM, Echenique L, de Brito FS Jr, Perin MA, Born D, Hecht H, Caixeta A. Pregnancy-associated spontaneous coronary artery dissection: insights from a case series of 13 patients. *Eur Heart J Cardiovasc Imaging* 2017;**18**:54–61.
95. Tweet MS, Hayes SN, Codsi E, Gulati R, Rose CH, Best PJM. Spontaneous coronary artery dissection associated with pregnancy. *J Am Coll Cardiol* 2017;**70**: 426–435.
96. Codsi E, Tweet MS, Rose CH, Arendt KW, Best PJ, Hayes SN. Spontaneous coronary artery dissection in pregnancy: what every obstetrician should know. *Obstet Gynecol* 2016;**128**:731–738.
97. Appleby CE, Barolet A, Ing D, Ross J, Schwartz L, Seidelin P, Silversides C, Horlick E. Contemporary management of pregnancy-related coronary artery dissection: a single-centre experience and literature review. *Exp Clin Cardiol* 2009;**14**:e8–e16.
98. Koul AK, Hollander G, Moskovits N, Frankel R, Herrera L, Shani J. Coronary artery dissection during pregnancy and the postpartum period: two case reports and review of literature. *Catheter Cardiovasc Interv* 2001;**52**:88–94.
99. Havakuk O, Goland S, Mehra A, Elkayam U. Pregnancy and the risk of spontaneous coronary artery dissection: an analysis of 120 contemporary cases. *Circ Cardiovasc Interv* 2017;**10**:e004941.
100. Olin JW, Gornik HL, Bacharach JM, Biller J, Fine LJ, Gray BH, Gray WA, Gupta R, Hamburg NM, Katzen BT, Lookstein RA, Lumsden AB, Newburger JW, Rundek T, Sperati CJ, Stanley JC; American Heart Association Council on Peripheral Vascular Disease, American Heart Association Council on Clinical Cardiology, American Heart Association Council on Cardiopulmonary Critical Care, Perioperative and Resuscitation, American Heart Association Council on Cardiovascular Disease in the Young, American Heart Association Council on Cardiovascular Radiology and Intervention, American Heart Association Council on Epidemiology and Prevention, American Heart Association Council on Functional Genomics and Translational Biology, American Heart Association Council for High Blood Pressure Research, American Heart Association

Council on the Kidney in Cardiovascular Disease, American Heart Association Stroke Council. Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association. *Circulation* 2014;**129**:1048–1078.
101. Persu A, Giavarini A, Touze E, Januszewicz A, Sapoval M, Azizi M, Barral X, Jeunemaitre X, Morganti A, Plouin PF, de Leeuw PESH Working Group Hypertension and the Kidney. European consensus on the diagnosis and management of fibromuscular dysplasia. *J Hypertens* 2014;**32**:1367–1378.
102. Savard S, Steichen O, Azarine A, Azizi M, Jeunemaitre X, Plouin PF. Association between 2 angiographic subtypes of renal artery fibromuscular dysplasia and clinical characteristics. *Circulation* 2012;**126**:3062–3069.
103. Persu A, Van der Niepen P, Touze E, Gevaert S, Berra E, Mace P, Plouin PF, Jeunemaitre X. Revisiting fibromuscular dysplasia: rationale of the European fibromuscular dysplasia initiative. *Hypertension* 2016;**68**:832–839.
104. Saw J, Poulter R, Fung A, Wood D, Hamburger J, Buller CE. Spontaneous coronary artery dissection in patients with fibromuscular dysplasia: a case series. *Circ Cardiovasc Interv* 2012;**5**:134–137.
105. Toggweiler S, Puck M, Thalhammer C, Manka R, Wyss M, Bilecen D, Corti R, Amann-Vesti BR, Lüscher TF, Wyss CA. Associated vascular lesions in patients with spontaneous coronary artery dissection. *Swiss Med Wkly* 2012;**142**:w13538.
106. Liang JJ, Prasad M, Tweet MS, Hayes SN, Gulati R, Breen JF, Leng S, Vrtiska TJ. A novel application of CT angiography to detect extracoronary vascular abnormalities in patients with spontaneous coronary artery dissection. *J Cardiovasc Comput Tomogr* 2014;**8**:189–197.
107. Prasad M, Tweet MS, Hayes SN, Leng S, Liang JJ, Eleid MF, Gulati R, Vrtiska TJ. Prevalence of extracoronary vascular abnormalities and fibromuscular dysplasia in patients with spontaneous coronary artery dissection. *Am J Cardiol* 2015;**115**:1672–1677.
108. Saw J, Ricci D, Starovoytov A, Fox R, Buller CE. Spontaneous coronary artery dissection: prevalence of predisposing conditions including fibromuscular dysplasia in a tertiary center cohort. *JACC Cardiovasc Interv* 2013;**6**:44–52.
109. Lie JT, Berg KK. Isolated fibromuscular dysplasia of the coronary arteries with spontaneous dissection and myocardial infarction. *Hum Pathol* 1987;**18**:654–656.
110. Brodsky SV, Ramaswamy G, Chander P, Braun A. Ruptured cerebral aneurysm and acute coronary artery dissection in the setting of multivascular fibromuscular dysplasia: a case report. *Angiology* 2007;**58**:764–767.
111. Mather PJ, Hansen CL, Goldman B, Inniss S, Pina I, Norris R, Jeevanandam V, Bove AA. Postpartum multivessel coronary dissection. *J Heart Lung Transplant* 1994;**13**:533–537.
112. Camuglia A, Manins V, Taylor A, Hengel C. Case report and review: epicardial coronary artery fibromuscular dysplasia. *Heart Lung Circ* 2009;**18**:151–154.
113. Pate GE, Lowe R, Buller CE. Fibromuscular dysplasia of the coronary and renal arteries? *Catheter Cardiovasc Interv* 2005;**64**:138–145.
114. Michelis KC, Olin JW, Kadian-Dodov D, d'Escamard V, Kovacic JC. Coronary artery manifestations of fibromuscular dysplasia. *J Am Coll Cardiol* 2014;**64**:1033–1046.
115. Saw J, Bezerra H, Gornik HL, Machan L, Mancini GB. Angiographic and intracoronary manifestations of coronary fibromuscular dysplasia. *Circulation* 2016;**133**:1548–1559.
116. Kadian-Dodov D, Gornik HL, Gu X, Froehlich J, Bacharach JM, Chi YW, Gray BH, Jaff MR, Kim ES, Mace P, Sharma A, Kline-Rogers E, White C, Olin JW. Dissection and aneurysm in patients with fibromuscular dysplasia: findings from the U.S. Registry for FMD. *J Am Coll Cardiol* 2016;**68**:176–185.
117. Buccheri D, Piraino D, Andolina G. Behcet disease and spontaneous coronary artery dissection: the chicken or the egg? *Int J Cardiol* 2016;**215**:504–505.
118. Reddy S, Vaid T, Ganiga Sanjeeva NC, Shetty RK. Spontaneous coronary artery dissection as the first presentation of systemic lupus erythematosus. *BMJ Case Rep* 2016;doi:10.1136/bcr-2016-216344.
119. Rekik S, Lanfranchi P, Jacq L, Bernasconi F. Spontaneous coronary artery dissection in a 35 year-old woman with systemic lupus erythematosus successfully treated by angioplasty. *Heart Lung Circ* 2013;**22**:955–958.
120. Nisar MK, Mya T. Spontaneous coronary artery dissection in the context of positive anticardiolipin antibodies and clinically undiagnosed systemic lupus erythematosus. *Lupus* 2011;**20**:1436–1438.
121. Kothari D, Ruygrok P, Gentles T, Occleshaw C. Spontaneous coronary artery dissection in an adolescent man with systemic lupus erythematosus. *Intern Med J* 2007;**37**:342–343.
122. Sharma AK, Farb A, Maniar P, Ajani AE, Castagna M, Virmani R, Suddath W, Lindsay J. Spontaneous coronary artery dissection in a patient with systemic lupus erythematosis. *Hawaii Med J* 2003;**62**:248–253.
123. Canpolat U, Dural M, Atalar E. Acute inferior myocardial infarction in a young female patient with polyarteritis nodosa. *Herz* 2012;**37**:461–463.
124. Fernández-Gutiérrez B, Zamorano J, Batlle E, Alfonso F, Conde A, Sánchez-Harguindey L, Jover JA. Coronary dissection associated with hepatitis C virus-related cryoglobulinaemia. *Rheumatology (Oxford)* 1999;**38**:1299–1301.
125. Iyisoy A, Agac MT, Celik T, Jata B. Spontaneous dissection of left main coronary artery associated with hypertensive crisis: a probable fatal complication detected by intravascular ultrasound. *Int J Cardiol* 2010;**139**:e5–e7.
126. Greenblatt JM, Kochar GS, Albornoz MA. Multivessel spontaneous coronary artery dissection in a patient with severe systolic hypertension: a possible association. A case report. *Angiology* 1999;**50**:509–513.
127. Sivam S, Yozghatlian V, Dentice R, McGrady M, Moriarty C, Di Michiel J, Bye PT, Rees D. Spontaneous coronary artery dissection associated with coughing. *J Cyst Fibros* 2014;**13**:235–237.
128. Afzal AM, Sarmast SA, Weber NA, Schussler JM. Spontaneous coronary artery dissection in a 22-year-old man on lisdexamfetamine. *Proc (Bayl Univ Med Cent)* 2015;**28**:367–368.
129. Ijsselmuiden A, Verheye S. Cocaine-induced coronary artery dissection. *JACC Cardiovasc Interv* 2009;**2**:1031.
130. Kanwar M, Gill N. Spontaneous multivessel coronary artery dissection. *J Invasive Cardiol* 2010;**22**:E5–E6.
131. Katikaneni PK, Akkus NI, Tandon N, Modi K. Cocaine-induced postpartum coronary artery dissection: a case report and 80-year review of literature. *J Invasive Cardiol* 2013;**25**:E163–E166.
132. Wickremaarachchi C, Olinga J, Ooi SY, Cranney G. Complete angiographic resolution of cocaine induced coronary artery dissection within eight days without coronary stenting—a case report. *Heart Lung Circ* 2016;**25**:e24–e28.
133. Reriani M, Sara JD, Flammer AJ, Gulati R, Li J, Rihal C, Lennon R, Lerman LO, Lerman A. Coronary endothelial function testing provides superior discrimination compared with standard clinical risk scoring in prediction of cardiovascular events. *Coron Artery Dis* 2016;**27**:213–220.
134. Balakrishnan K, Scott P, Oliver L. A confluence of circumstances: a case of IVF, extreme exercise and spontaneous coronary artery dissection. *Int J Cardiol* 2016;**203**:76–77.
135. El-Sherief K, Rashidian A, Srikanth S. Spontaneous coronary artery dissection after intense weightlifting UCSF Fresno Department of Cardiology. *Catheter Cardiovasc Interv* 2011;**78**:223–227.
136. Ellis CJ, Haywood GA, Monro JL. Spontaneous coronary artery dissection in a young woman resulting from an intense gymnasium "work-out". *Int J Cardiol* 1994;**47**:193–194.
137. 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**:675–678.
138. Aghasadeghi K, Aslani A. Spontaneous coronary artery dissection in a professional body builder. *Int J Cardiol* 2008;**130**:e119–e120.
139. Adlam D, Cuculi F, Lim C, Banning A. Management of spontaneous coronary artery dissection in the primary percutaneous coronary intervention era. *J Invasive Cardiol* 2010;**22**:549–553.
140. Basile C, Lucarelli K, Langialonga T. Spontaneous coronary artery dissection: one more extrarenal manifestation of autosomal dominant polycystic kidney disease? *J Nephrol* 2009;**22**:414–416.
141. Grover P, Fitzgibbons TP. Spontaneous coronary artery dissection in a patient with autosomal dominant polycystic kidney disease: a case report. *J Med Case Rep* 2016;**10**:62.
142. Klingenberg-Salachova F, Limburg S, Boereboom F. Spontaneous coronary artery dissection in polycystic kidney disease. *Clin Kidney J* 2012;**5**:44–46.
143. Nakamura M, Yajima J, Oikawa Y, Ogasawara K, Uejima T, Abe K, Aizawa T. Vascular Ehlers-Danlos syndrome–all three coronary artery spontaneous dissections. *J Cardiol* 2009;**53**:458–462.
144. Goel K, Tweet M, Olson TM, Maleszewski JJ, Gulati R, Hayes SN. Familial spontaneous coronary artery dissection: evidence for genetic susceptibility. *JAMA Intern Med* 2015;**175**:821–826.
145. Al-Hussaini A, Adlam D. Spontaneous coronary artery dissection. *Heart* 2017;
146. Luong C, Starovoytov A, Heydari M, Sedlak T, Aymong E, Saw J. Clinical presentation of patients with spontaneous coronary artery dissection. *Catheter Cardiovasc Interv* 2017;
147. Tweet MS, Gulati R, Williamson EE, Vrtiska TJ, Hayes SN. Multimodality imaging for spontaneous coronary artery dissection in women. *JACC Cardiovasc Imaging* 2016;**9**:436–450.
148. Rogers JH, Lasala JM. Coronary artery dissection and perforation complicating percutaneous coronary intervention. *J Invasive Cardiol* 2004;**16**:493–499.
149. Saw J. Coronary angiogram classification of spontaneous coronary artery dissection. *Catheter Cardiovasc Interv* 2014;**84**:1115–1122.
150. Saw J, Mancini GB, Humphries K, Fung A, Boone R, Starovoytov A, Aymong E. Angiographic appearance of spontaneous coronary artery dissection with intramural hematoma proven on intracoronary imaging. *Catheter Cardiovasc Interv* 2016;**87**:E54–E61.
151. De-Giorgio F, Grassi VM, Abbate A, d'Aloja E, Arena V. Causation or coincidence? A case of sudden death due to spontaneous coronary artery dissection in presence of myocardial bridging. *Int J Cardiol* 2012;**159**:e32–e34.

152. Burke AP, Kutys R, Fowler D, Virmani R. Multiple spontaneous coronary artery dissections in association with anomalous origin of right coronary and intramural coronary artery dysplasia. *Cardiovasc Pathol* 2004;**13**:173–175.
153. Degrauwe S, Zuffi A, Muller O, Schiele F, Eeckhout E, Iglesias JF. Very late multiple recurrent spontaneous coronary artery dissection in a young woman with recidivating acute myocardial infarction. *Int J Cardiol* 2016;**223**:168–170.
154. Motreff P, Souteyrand G, Dauphin C, Eschalier R, Cassagnes J, Lusson JR. Management of spontaneous coronary artery dissection: review of the literature and discussion based on a series of 12 young women with acute coronary syndrome. *Cardiology* 2010;**115**:10–18.
155. Sanchez-Recalde A, Guzman G, Armada E, Moreno R. Multiple spontaneous coronary artery dissection associated with a left main coronary artery lesion treated by stenting. Late multiple stent fractures detected by multislice CT. *Rev Esp Cardiol* 2009;**62**:225–226.
156. Sharma AM, Herrera B, Aronow HD. Simultaneous spontaneous coronary and vertebral artery dissection in a postpartum woman. *J Invasive Cardiol* 2010;**22**:E229–E232.
157. Prakash R, Starovoytov A, Heydari M, Mancini GB, Saw J. Catheter-induced iatrogenic coronary artery dissection in patients with spontaneous coronary artery dissection. *JACC Cardiovasc Interv* 2016;**9**:1851–1853.
158. Arnold JR, West NE, van Gaal WJ, Karamitsos TD, Banning AP. The role of intravascular ultrasound in the management of spontaneous coronary artery dissection. *Cardiovasc Ultrasound* 2008;**6**:24.
159. Poon K, Bell B, Raffel OC, Walters DL, Jang IK. Spontaneous coronary artery dissection: utility of intravascular ultrasound and optical coherence tomography during percutaneous coronary intervention. *Circ Cardiovasc Interv* 2011;**4**:e5–e7.
160. Lempereur M, Fung A, Saw J. Stent mal-apposition with resorption of intramural hematoma with spontaneous coronary artery dissection. *Cardiovasc Diagn Ther* 2015;**5**:323–329.
161. Haraki T, Uemura R, Masuda S, Lee T. Progressed multivessel spontaneous coronary artery dissection that naturally healed in a male patient with non-st segment elevation myocardial infarction. *Case Rep Cardiol* 2016;**2016**:4109496.
162. Auer J, Punzengruber C, Berent R, Weber T, Lamm G, Hartl P, Eber B. Spontaneous coronary artery dissection involving the left main stem: assessment by intravascular ultrasound. *Heart* 2004;**90**:e39.
163. Danzi GB, Sesana M, Capuano C, Baglini R. Intravascular ultrasound assessment of a spontaneous coronary artery dissection causing acute myocardial infarction. *Ital Heart J* 2004;**5**:796–797.
164. Kearney P, Erbel R, Ge J, Zamorano J, Koch L, Gorge G, Meyer J. Assessment of spontaneous coronary artery dissection by intravascular ultrasound in a patient with unstable angina. *Cathet Cardiovasc Diagn* 1994;**32**:58–61.
165. Maehara A, Mintz GS, Castagna MT, Pichard AD, Satler LF, Waksman R, Suddath WO, Kent KM, Weissman NJ. Intravascular ultrasound assessment of spontaneous coronary artery dissection. *Am J Cardiol* 2002;**89**:466–468.
166. Alfonso F, Canales E, Aleong G. Spontaneous coronary artery dissection: diagnosis by optical coherence tomography. *Eur Heart J* 2009;**30**:385.
167. Satogami K, Ino Y, Kubo T, Shiono Y, Nishiguchi T, Matsuo Y, Orii M, Yamano T, Yamaguchi T, Hirata K, Tanaka A, Akasaka T. Successful stenting with optical frequency domain imaging guidance for spontaneous coronary artery dissection. *JACC Cardiovasc Interv* 2015;**8**:e83–e85.
168. Bento AP, Fernandes RG, Neves DC, Patricio LM, de Aguiar JE. Spontaneous coronary dissection: "Live Flash" optical coherence tomography guided angioplasty. *Case Rep Cardiol* 2016;**2016**:5643819.
169. Mori H, Kutys R, Romero M, Virmani R, Finn AV. Stenting of spontaneous coronary artery dissection from a pathological point of view. *Circ Cardiovasc Interv* 2016;**9**:e004549.
170. Combaret N, Souteyrand G, Amonchot A, Coupez E, Motreff P. Contribution of guidance by optical coherence tomography (OCT) in rescue management of spontaneous coronary artery dissection. *Eur Heart J Cardiovasc Imaging* 2013;**14**:714.
171. Cade J, Mintz GS, Silva RMF, Caixeta A. Spontaneous coronary artery dissection and healing documented by optical coherence tomography. *Einstein (Sao Paulo)* 2016;**14**:435–436.
172. Kwon TG, Gulati R, Matsuzawa Y, Aoki T, Guddeti RR, Herrmann J, Lennon RJ, Ritman EL, Lerman LO, Lerman A. Proliferation of coronary adventitial vasa vasorum in patients with spontaneous coronary artery dissection. *JACC Cardiovasc Imaging* 2016;**9**:891–892.
173. Eleid MF, Tweet MS, Young PM, Williamson E, Hayes SN, Gulati R. Spontaneous coronary artery dissection: challenges of coronary computed tomography angiography. *Eur Heart J Acute Cardiovasc Care* 2017;2048872616687098.
174. Torres-Ayala SC, Maldonado J, Bolton JS, Bhalla S. Coronary computed tomography angiography of spontaneous coronary artery dissection: a case report and review of the literature. *Am J Case Rep* 2015;**16**:130–135.
175. Alzand BS, Vanneste L, Fonck D, Van Mieghem C. Spontaneous coronary artery dissection undissolved using cardiac computed tomography. *Int J Cardiol* 2016;**222**:1040–1041.
176. Conrotto F, D'Ascenzo F, Cerrato E, Fernandez-Ortiz A, Gonzalo N, Macaya F, Tamburino C, Barbanti M, van Lavieren M, Piek JJ, Applegate RJ, Latib A, Spinnler MT, Marzullo R, Iannaccone M, Pavani M, Crimi G, Fattori R, Chinaglia A, Presbitero P, Varbella F, Gaita F, Escaned J. Safety and efficacy of drug eluting stents in patients with spontaneous coronary artery dissection. *Int J Cardiol* 2017;**238**:105–109.
177. Martins JL, Afreixo V, Santos L, Costa M, Santos J, Goncalves L. Medical treatment or revascularisation as the best approach for spontaneous coronary artery dissection: a systematic review and meta-analysis. *Eur Heart J Acute Cardiovasc Care* 2017;2048872617706502.
178. Arrivi A, Milici C, Bock C, Placanica A, Boschetti E, Dominici M. Idiopathic, serial coronary vessels dissection in a young woman with psychological stress: a case report and review of the literature. *Case Rep Vasc Med* 2012;**2012**:1.
179. Dashwood AM, Saw J, Dhillon P, Murdoch D. Use of a three-stent technique for a case of spontaneous coronary artery dissection. *Can J Cardiol* 2017;**33**:830.e13–830.e15.
180. 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**:231–233.
181. Alfonso F, Bastante T, Garcia-Guimaraes M, Pozo E, Cuesta J, Rivero F, Benedicto A, Antuna P, Alvarado T, Gulati R, Saw J. Spontaneous coronary artery dissection: new insights into diagnosis and treatment. *Coron Artery Dis* 2016;**27**:696–706.
182. Ito T, Shintani Y, Ichihashi T, Fujita H, Ohte N. Non-atherosclerotic spontaneous coronary artery dissection revascularized by intravascular ultrasonography-guided fenestration with cutting balloon angioplasty. *Cardiovasc Interv Ther* 2017;**32**:241–243.
183. Alkhouli M, Cole M, Ling FS. Coronary artery fenestration prior to stenting in spontaneous coronary artery dissection. *Catheter Cardiovasc Interv* 2016;**88**:E23–E27.
184. Motreff P, Barber-Chamoux N, Combaret N, Souteyrand G. Coronary artery fenestration guided by optical coherence tomograhy before stenting: new interventional option in rescue management of compressive spontaneous intramural hematoma. *Circ Cardiovasc Interv* 2015;**8**:e002266.
185. Yumoto K, Sasaki H, Aoki H, Kato K. Successful treatment of spontaneous coronary artery dissection with cutting balloon angioplasty as evaluated with optical coherence tomography. *JACC Cardiovasc Interv* 2014;**7**:817–819.
186. Watt J, Egred M, Khurana A, Bagnall AJ, Zaman AG. 1-year follow-up optical frequency domain imaging of multiple bioresorbable vascular scaffolds for the treatment of spontaneous coronary artery dissection. *JACC Cardiovasc Interv* 2016;**9**:389–391.
187. Sengottuvelu G, Rajendran R. Full polymer jacketing for long-segment spontaneous coronary artery dissection using bioresorbable vascular scaffolds. *JACC Cardiovasc Interv* 2014;**7**:820–821.
188. Panoulas VF, Ielasi A. Bioresorbable scaffolds and drug-eluting balloons for the management of spontaneous coronary artery dissections. *J Thorac Dis* 2016;**8**:E1328–E1330.
189. Serruys PW, Chevalier B, Sotomi Y, Cequier A, Carrié D, Piek JJ, Van Boven AJ, Dominici M, Dudek D, McClean D, Helqvist S, Haude M, Reith S, de Sousa Almeida M, Campo G, Iñiguez A, Sabaté M, Windecker S, Onuma Y. Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial. *Lancet* 2016;**388**:2479–2491.
190. Wehman B, Lehr EJ, Mukherjee R, Grigore A, Griffith B, Bonatti J. Robotic totally endoscopic coronary artery bypass grafting for spontaneous coronary artery dissection. *Int J Med Robot* 2012;**8**:166–168.
191. Abu-Laban RB, Migneault D, Grant MR, Dhingra V, Fung A, Cook RC, Sweet D. Extracorporeal membrane oxygenation after protracted ventricular fibrillation cardiac arrest: case report and discussion. *CJEM* 2015;**17**:210–216.
192. Aliyary S, Mariani MA, Verhorst PM, Hartmann M, Stoel MG, von Birgelen C. Staged therapeutic approach in spontaneous coronary dissection. *Ann Thorac Surg* 2007;**83**:1879–1881.
193. Farhat F, Sassard T, Maghiar A, Jegaden O. Primary spontaneous coronary artery dissection complicated by iatrogenous aortic dissection: from David procedure to full arterial coronary revascularization. *Interact Cardiovasc Thorac Surg* 2006;**5**:149–152.
194. Jacob JC, Kiernan FJ, Patel N, Rock J, Hammond J, Jr., Wencker D, Lasala AF. SCAD: a rare case of cardiac arrest in a young female. *Conn Med* 2011;**75**:147–152.
195. Jorge-Pérez P, García-González MJ, Ávalos-Pinto RM, G-Cosio-Carmena MD, Renes-Carreño E, Delgado JF, Yanes-Bowden G, Ferrer-Hita JJ. Spontaneous coronary dissection and cardiogenic shock requiring mechanical circulatory support in a non-transplant center. *Int J Cardiol* 2016;**221**:629–630.
196. Julia I, Tauron M, Munoz-Guijosa C. Postpartum acute coronary syndrome due to intramural hematoma and coronary artery dissection. *Thorac Cardiovasc Surg* 2012;**61**:085–087.
197. Paez M, Buisan F, Herrero E. Spontaneous dissection of the left coronary artery trunk during the postpartum period treated with revascularization surgery,

ventricular assistance and a successful heart transplant. *Acta Anaesthesiol Scand* 2007;**51**:960–961.
198. Rahman S, Abdul-Waheed M, Helmy T, Huffman LC, Koshal V, Guitron J, Merrill WH, Lewis DF, Dunlap S, Shizukuda Y, Weintraub NL, Meyer C, Cilingiroglu M. Spontaneous left main coronary artery dissection complicated by pseudoaneurysm formation in pregnancy: role of CT coronary angiography. *J Cardiothorac Surg* 2009;**4**:15.
199. Weinberg L, Ong M, Tan CO, McDonnell NJ, Lo C, Chiam E. Spontaneous coronary artery dissection in pregnancy requiring emergency caesarean delivery followed by coronary artery bypass grafting. *Anaesth Intensive Care* 2013;**41**:251–255.
200. Bashir M, Mustafa H, Singh H, Bonser R. Cardiac transplantation for spontaneous coronary artery dissection. *Interact Cardiovasc Thorac Surg* 2013;**16**:91–92.
201. Evans R. Post-partum spontaneous coronary artery dissection and the use of veno-arterial extra-corporeal membrane oxygenation. *Nurs Crit Care* 2014;**19**: 304–309.
202. Knapp KE, Weis RA, Cubillo EI, Chapital AB, Ramakrishna H. Spontaneous, postpartum coronary artery dissection and cardiogenic shock with extracorporeal membrane oxygenation assisted recovery in a 30-year-old patient. *Case Rep Cardiol* 2016;**2016**:1.
203. Martins RP, Leurent G, Corbineau H, Fouquet O, Seconda S, Baruteau AE, Moreau O, Le Breton H, Bedossa M. Coronary angiography of pregnancy-associated coronary artery dissection: a high-risk procedure. *Cardiovasc Revasc Med* 2010;**11**:182–185.
204. Patane F, Boffini M, Sansone F, Campanella A, Rinaldi M. ECMO as a bridge to transplantation in biventricular dysfunction due to primary spontaneous coronary artery dissection. *Transpl Int* 2009;**22**:500–502.
205. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, Gonzalez-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P. Authors/Task Force M. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;**37**:2129–2200.
206. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S, Baumgartner H, Gaemperli O, Achenbach S, Agewall S, Badimon L, Baigent C, Bueno H, Bugiardini R, Carerj S, Casselman F, Cuisset T, Erol C, Fitzsimons D, Halle M, Hamm C, Hildick-Smith D, Huber K, Iliodromitis E, James S, Lewis BS, Lip GY, Piepoli MF, Richter D, Rosemann T, Sechtem U, Steg PG, Vrints C, Luis Zamorano J. Management of Acute Coronary Syndromes in Patients Presenting without Persistent STSEotESoC. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2016;**37**:267–315.
207. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimsky P. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Rev Esp Cardiol (Engl Ed)* 2017;**70**:1082.
208. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck K-H, Hernandez-Madrid A, Nikolaou N, Norekvål TM, Spaulding C, Van Veldhuisen DJ. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J* 2015;**36**:2793–2867.
209. Jovic Z, Obradovic S, Djenic N, Mladenovic Z, Djuric P, Spasic M, Tavicovski D. Does thrombolytic therapy harm or help in ST elevation myocardial infarction (STEMI) caused by the spontaneous coronary dissection? *Vojnosanit Pregl* 2015; **72**:536–540.
210. Andreou AY, Georgiou PA, Georgiou GM. Spontaneous coronary artery dissection: report of two unsuspected cases initially treated with thrombolysis. *Exp Clin Cardiol* 2009;**14**:e89–e92.
211. Shamloo BK, Chintala RS, Nasur A, Ghazvini M, Shariat P, Diggs JA, Singh SN. Spontaneous coronary artery dissection: aggressive vs. conservative therapy. *J Invasive Cardiol* 2010;**22**:222–228.
212. Zupan I, Noc M, Trinkaus D, Popovic M. Double vessel extension of spontaneous left main coronary artery dissection in young women treated with thrombolytics. *Catheter Cardiovasc Interv* 2001;**52**:226–230.
213. Goh AC, Lundstrom RJ. Spontaneous coronary artery dissection with cardiac tamponade. *Tex Heart Inst J* 2015;**42**:479–482.
214. Maas AH, Euler M, Bongers MY, Rolden HJ, Grutters JP, Ulrich L, Schenck-Gustafsson K. Practice points in gynecardiology: abnormal uterine bleeding in premenopausal women taking oral anticoagulant or antiplatelet therapy. *Maturitas* 2015;**82**:355–359.
215. Tweet MS, Olin JW. Insights into spontaneous coronary artery dissection: can recurrence be prevented? *J Am Coll Cardiol* 2017;**70**:1159–1161.
216. Colletti PM, Lee KH, Elkayam U. Cardiovascular imaging of the pregnant patient. *AJR Am J Roentgenol* 2013;**200**:515–521.
217. Tweet MS, Hayes SN, Gulati R, Rose CH, Best PJ. Pregnancy after spontaneous coronary artery dissection: a case series. *Ann Intern Med* 2015;**162**:598–600.
218. Guo LQ, Wasfy MM, Hedgire S, Kalra M, Wood M, Prabhakar AM, Ghoshhajra BB. Multimodality imaging of spontaneous coronary artery dissection: case studies of the Massachusetts General Hospital. *Coron Artery Dis* 2016;**27**:70–71.
219. Bhatt DD, Kachru R, Gupta S, Kaul U. Recurrent chest pain after treatment of spontaneous coronary artery dissection: an enigma. *Indian Heart J* 2015;**67**: S18–S20.
220. Chou AY, Prakash R, Rajala J, Birnie T, Isserow S, Taylor CM, Ignaszewski A, Chan S, Starovoytov A, Saw J. The first dedicated cardiac rehabilitation program for patients with spontaneous coronary artery dissection: description and initial results. *Can J Cardiol* 2016;**32**:554–560.
221. Krittanawong C, Tweet MS, Hayes SE, Bowman MJ, Gulati R, Squires RW, Hayes SN. Usefulness of cardiac rehabilitation after spontaneous coronary artery dissection. *Am J Cardiol* 2016;**117**:1604–1609.
222. Liang JJ, Tweet MS, Hayes SE, Gulati R, Hayes SN. Prevalence and predictors of depression and anxiety among survivors of myocardial infarction due to spontaneous coronary artery dissection. *J Cardiopulm Rehabil Prev* 2014;**34**:138–142.