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Role of Invasive and Non-invasive Imaging Tools in the Diagnosis and Optimal Treatment of Patients with Spontaneous Coronary Artery Dissection

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Abstract

Purpose of Review Spontaneous coronary artery dissection (SCAD) is a serious non-atherosclerotic disease, most frequently presenting as an acute coronary syndrome and affecting female patients. Considering that diagnosis of SCAD is often elusive, and its interventional treatment is associated to a higher rate of complications than obstructive atherosclerotic disease, we aim to review all the imaging tools currently available for the optimal diagnosis and treatment of this condition.

Recent Findings The developments in both invasive and non-invasive imaging alternatives to coronary angiography, such as intravascular ultrasound, optical coherence tomography, and computed coronary angiography, have largely contributed to appraise the epidemiology of SCAD, understand its causative pathophysiological mechanisms, and improve our ability to confirm doubtful cases of SCAD. Intracoronary imaging is also a valuable in deciding the best therapeutic approach and in guiding interventions in those patients requiring percutaneous treatment. Furthermore, non-invasive imaging is a key tool in ruling out significant extracoronary vascular abnormalities which frequently occur in patients with underlying conditions like fibromuscular dysplasia who develop SCAD.

Summary Main imaging tools employed in SCAD cases could have advantages and drawbacks. Focusing on different types of SCAD, operators should be able to choose the best imaging technique for diagnosis, management, and follow-up.

Keywords Spontaneous coronary artery dissection · Acute coronary syndrome · Coronary angiography · Optical coherence tomography · Intravascular ultrasound · Invasive imaging tools

Introduction

Spontaneous coronary artery dissection (SCAD) is a frequent cause of acute coronary syndrome (ACS) in women caused by the separation between the layers of the coronary artery wall. SCAD may affect also men, although in a much lower proportion (around one in ten). By definition, SCAD is not related to external trauma, coronary involvement of aortic dissection, iatrogenic causes, or complicated atherosclerosis [1••, 2]. This particular pathogenesis implies the development of an intramural hematoma (IMH) compressing the true lumen of the vessel: the new "false" lumen may rapidly expand reducing or even blocking the coronary flow, therefore leading to myocardial ischemia. Clinical presentation is often classic ACS but some cases present as ventricular arrhythmias or cardiac arrest.

Although SCAD has been known for a long time, it was considered a rare cause of myocardial infarction. However, over the last 10 years, dedicated registries confirmed that SCAD is an underdiagnosed disorder with a much higher incidence than traditionally thought, occurring especially among young women without or with few

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conventional cardiovascular risk factors (accounting for 15–35% of ACS in young women) [1••, 3, 4]. A key aspect of this shift in the epidemiology of SCAD has been the increased recognition of its angiographic appearance, which has derived from the insights gained from the use of intracoronary imaging. The widespread use of optical coherence tomography (OCT) and intravascular ultrasound (IVUS), in addition to the improved pathophysiological and clinical knowledge about the disease, has made it possible to increase the number of properly diagnosed cases, highlighting the urgent need to define the best diagnostic, therapeutic, and follow-up pathways. Scientific societies have generated consensus documents on SCAD in an attempt to disseminate current knowledge on its diagnosis and treatment [1••, 3]. The following sections provided an expanded and updated review on the use of imaging to SCAD diagnosis and personalized treatment of this condition.

Mechanisms of Spontaneous Coronary Artery Dissection: Implications for Imaging-Based Diagnosis

There are two proposed mechanisms for SCAD pathogenesis, which may present with different angiographic patterns. The first is the "inside-out" model, based on the development of an intimal tear, while the second is the "outside-in" model, which implies a disruption of the coronary vasa vasorum [5].

Although the final result is always an intramural hematoma (IMH), the angiographic appearance differs according to the pathophysiological cause [6]: the *inside-out* mechanism often leads to the typical multiple radiolucent lumens and contrast dye stains in the arterial wall, or even slow clearing or hang-up of contrast dye is visible; the *outside-in* on the contrary may appear only as luminal narrowing due to the external compression, which if focal, may be misinterpreted as atherosclerotic disease. Sometimes instead, other causes of misdiagnosis are mild and smooth-walled stenoses as well as the involvement of distal and small arteries [6].

Imaging has a fundamental role in diagnosing and following up of SCAD. The pretest likelihood of SCAD is increased in patients presenting with relevant clinical features such as young age, female gender, peripartum, and few or no conventional risk factors. First assessment is always based on angiographic appearance, but only through imaging is it possible to eventually confirm the diagnosis and classify SCAD. There are SCAD variants that mimic atherosclerotic lesions or overlying spasms: for this reason, the current diagnostic algorithm for SCAD is based on different tools such as OCT and IVUS in addition to the coronary angiography that still represents the main diagnostic technique [4, 6].

Depending on the angiographic features, three different types of SCAD were originally described [2, 7]:

- Type 1: Typical radiolucent "flap" with a double-lumen image due to a linear filling defect, often associated with contrast retention
- Type 2: Long smooth stenosis which is mainly located in the mid or distal segments of the artery. It is divided into two subtypes:

  - Type 2a: The distal vessel maintains a normal caliber
  - Type 2b: The stenosis angiographically reaches the distal tip of the vessel, respecting more or less the normal anatomical tapering

- Type 3: Angiographically indistinguishable from focal or tubular atherosclerotic stenosis and requiring OCT or IVUS to demonstrate the presence of IMH and/or double lumen or repeating coronary angiogram to document healing

The 2018 ESC position paper has introduced an additional type 4 [1••] which is described as the total occlusion of a vessel (usually a distal one) where sources of coronary embolism have been excluded: for this type, there is a need for documenting vessel healing, in keeping with the natural history of SCAD. However, in some of these cases, the diagnosis will remain tentative.

Types 2 and 3 are the most challenging to differentiate from atherosclerosis: the most common SCAD features are lack of atherosclerosis in other territories, long lesions, and linear stenosis. Even though the clinical and angiographical suspicion is fundamental, the only way to immediately confirm diagnosis is through an intracoronary imaging device, if feasible and worthwhile. In other cases, a provisional diagnosis is assumed until vessel healing or transformation into a type 1 is seen in a repeat angiogram.

Notably, any proposed flowchart for SCAD treatment implies to perform, as a first step, a coronary angiogram. However, in patients with SCAD, the coronary tree is prone to develop iatrogenic dissections, even when catheters are carefully manipulated. For this reason, the potential role of non-invasive techniques such as cardiac tomography was also investigated by several authors. The cardiac computed tomography angiography (CCTA) is acquiring more and more importance as an efficient diagnostic tool in low- and intermediate-risk patients with ACS. Actually, the computed tomography may be beneficial by assessing coronary wall thickness and plaque constitution in addition to the presence of a double lumen [8]. Moreover, it is a non-invasive tool which avoids the risk of iatrogenic dissection often reported with angiography. Nevertheless, at present, CCTA cannot be recommended as a first-line exam to rule out SCAD [1••, 6, 9]: firstly, it has a lower spatial resolution than coronary angiography, and SCAD usually affects mid-to-distal coronary segments, which are more difficult to visualize. Also, lumen compression by IMH and contrast staining may not be well visualized even with this non-invasive imaging tool [10]. The role of the computed tomography is to date limited to the follow-up assessment of SCAD, as presented in Fig. 1. As invasive imaging techniques have been associated with a higher rate of iatrogenic complications, the non-invasive tools are preferred for follow-up. CCTA have recently been demonstrated to have greater utility in assessing healing where the site of dissection has already been determined by angiography. Furthermore, a Spanish prospective register conducted by Roura et al. has actually pointed out CCTA benefits in showing the vessel wall healing especially for those patients who did not undergo percutaneous coronary intervention (PCI) [11]. MR angiography represents a radiation-free alternative to CCTA for those patients presenting with renal insufficiency, diabetes, or iodine contrast intolerance [12]; however, concerns regarding its resolution to depict coronary arteries may impede its establishment as a standard technique for follow-up. The use of cardiac magnetic resonance (CMR) in SCAD patients has to date only been anecdotally described. It may be useful to confirm myocardial infarction and assess the extent of myocardial involvement but also to evaluate for other concurrent etiologies and sequelae [13–15]. Future investigations to elucidate the prognostic value of CMR parameters after acute SCAD are warranted.

Therefore, in the current review, we will focus on the invasive imaging techniques, moving from diagnostic process to PCI planning/optimization and follow-up.

Invasive Imaging Techniques

Coronary Angiography

In spite of being a bidimensional imaging tool not capable of imaging the arterial walls, coronary angiography represents today the first opportunity to diagnose a SCAD thanks to the typical angiographic and clinical features. As mentioned before, SCAD is currently classified by using other angiographic criteria than solely the presence of an angiographically visible

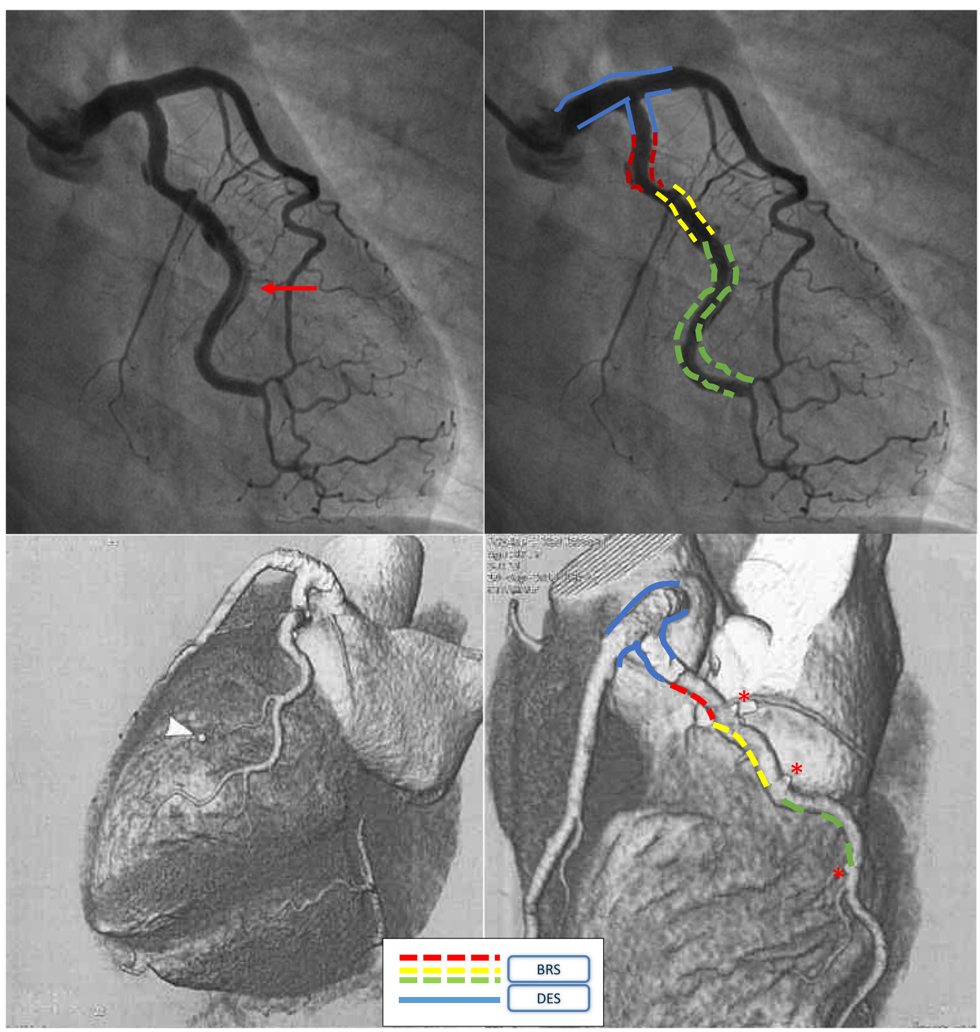

Fig. 1 46-year-old woman presenting with ACS/NSTEMI. After a conservative strategy treatment, the patient was readmitted few days after the discharge. Angiography showed a proximal and distal propagation of the SCAD requiring an extensive treatment with a hybrid DES and BRS DESSOLVE. However, residual dissection with hematoma persists in the mid-distal part of the circumflex (red arrow) (upper panel). Clinical follow-up was free of recurrences. AngioTC follow-up was performed 1 year later showing an excellent result with hematoma reabsorption and healing of the mid-distal part of the circumflex. DESSOLVE BRS markers were visible by angioTC (red asterisk)

intraluminal flap. The performance of a coronary angiogram always entails a definite risk for adding iatrogenic dissection in SCAD patients, because of the intrinsic frailty of the coronary walls [16] and because the injection of contrast may cause hydraulic extension of the dissection, particularly when made forcefully or with a tight engagement of the guiding catheter in the coronary ostium.

Intravascular Imaging Techniques

Intravascular imaging techniques are used for many purposes due to the possibility of showing the structure of the arterial wall. These tools have led to greater imaging definition and diagnostic accuracy but also entail additional costs and risk of complications [3, 17]. Their advantages and limitations are summarized in Supplemental Figure A. The two main imaging modalities are intravascular ultrasound (IVUS) and optical coherence tomography (OCT).

IVUS has a lower spatial resolution but a deeper penetration than OCT (4–8 rather than 1–2 mm) enabling the visualization of the entire vessel wall and an accurate measure of the depth and extent of the IMH [3, 9], which is not always possible with OCT [6]. Unfortunately, its lower resolution limits IVUS capacity to detect intimal disruptions.

OCT, on the other hand, is a more recent tool in the clinical setting, which benefits include improved ability to detect intimal disruptions, intraluminal clots, false lumens, and IMH, but requires blood clearance and has a limited optical penetration and shadowing [1••, 2]. Although most operators would prefer OCT for SCAD imaging, local expertise and weighed risk of additional contrast injections should determine the selection between OCT and IVUS.

Intravascular imaging has additional modalities that may be useful in order to better depict the false lumen and the intramural hematoma. In particular, ChromaFlo is an IVUS modality capable of identifying true and false lumens with a color interpolation: it compares sequential IVUS images and represents the two lumens with different colors by exploiting the echogenicity of blood particles [18].

Co-registration of OCT or IVUS with angiography is another modality often applied in order to better identify vessel anatomy. This allows assessing catheter position along the vessel by using a series of frames acquired at the same time as the OCT or IVUS pullback. The result is a precise correspondence of the angiogram with the intravascular imaging frames that will help delineate the dissected and healthy segments, as depicted in Fig. 2.

Although both IVUS and OCT are safe techniques in most patients, it is clear that SCAD intracoronary instrumentation may cause extension of the dissection with the wire, the imaging catheter, or the contrast injection (the latter for OCT only), causing catheter-induced iatrogenic dissections and catheter-induced occlusion of the true lumen [2, 3, 19]. Occasionally, complications of intracoronary imaging may develop well after intracoronary interrogation was performed [17]. Thus, these investigations are usually recommended only for those uncertain cases which require a confirmatory diagnosis (Fig. 2).

Diagnostic Process

The recognition of typical angiographic features and a more standardized use of intracoronary imaging improve diagnostic accuracy in SCAD [7]. The potential risk of instrumenting an acutely dissected vessel should be carefully weighed, especially when the angiogram is characteristic of SCAD.

As mentioned before, for those angiographically ambiguous cases of SCAD, i.e., types 2 and 3, a supplementary tool is required. The type 2 variants are usually very long and can easily be recognized after getting acquainted with its characteristics. OCT/IVUS or repeating angiography more than 1 month later should be considered in case of uncertainty (Fig. 3). There is a higher risk of misdiagnosis for the type 3 because it may be mistaken for atherosclerosis unless intracoronary imaging is performed. This diagnostic difficulty was first noted by Maehara et al. whose study showed 5 patients with IVUS-proven SCAD had a medial dissection with an intramural hematoma occupying the dissected false lumen but none had intimal tears [20]. More recently, these findings were confirmed by Alfonso et al. who focused on the role of OCT [21]: among 11 patients with confirmed SCAD, only three patients presented a classical angiographic intimal flap although a relatively diffuse lumen compromise was detected in all cases. In addition, mild stenosis, smooth-walled stenosis, and involvement of distal and small arteries have also been reported in misdiagnosis by angiography of SCAD [6]. Taruya et al. recently demonstrated the recognition by OCT of high-risk features may help in stratifying patients with a poorer outcome [22].

An example of a diagnostic algorithm for SCAD that highlights the role of intracoronary imaging is presented in Supplemental Figure B.

OCT may provide clearer images of the dissection site than IVUS and, when available, is preferred for diagnostic purposes owing to its greater resolution for depicting SCAD morphologic features (such as intimal flap and entry tear, double-lumen morphology, intramural hematoma, or associated thrombus) [23].

Problems arise when the SCAD is distally located. The anatomical location may hamper or impede appropriate OCT acquisition [7] (Supplemental Figure C). Furthermore, when the vessel is large or the intramural hematoma is rich in red thrombi, the tissue behind cannot be clearly seen with OCT [24]. In these cases, IVUS may provide real-time imaging and

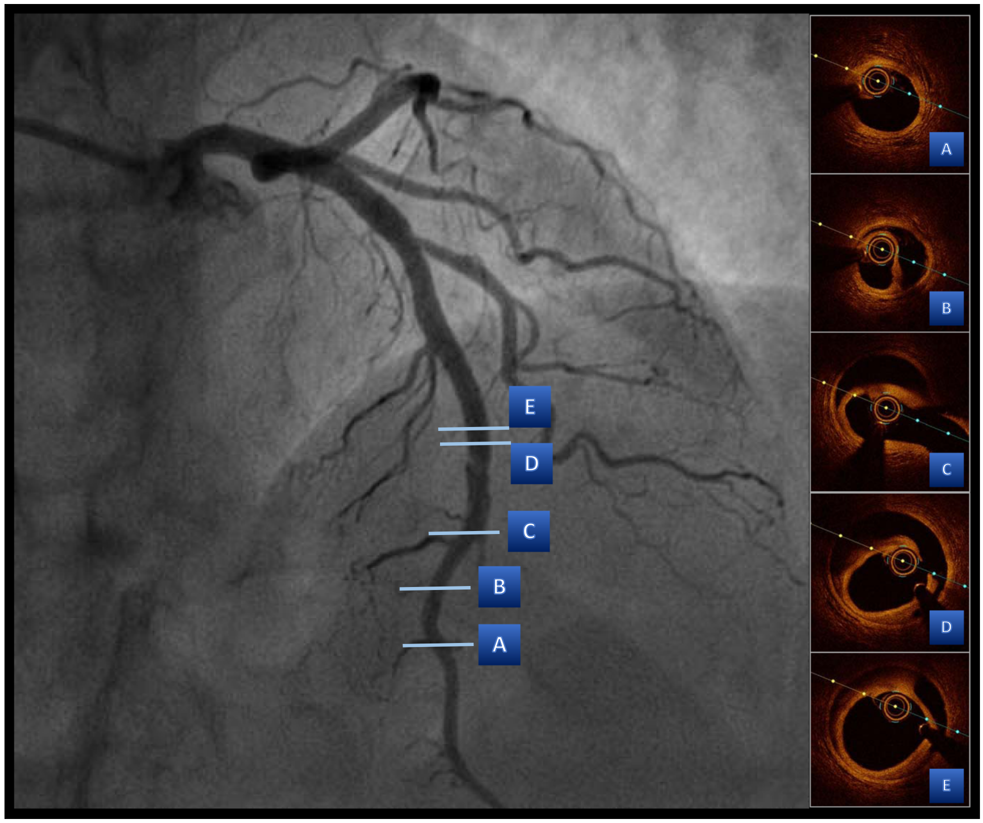

Fig. 2 50-year-old woman presenting with ACS/NSTEMI. Angiographic finding was unclear. Optical coherence tomography interrogation allowed to clearly identify the position of the guidewire in the true lumen identifying the true lumen on the vessel in course of SCAD

the ChromaFlo modality may identify the site where the true and false lumens are connected.

Some authors suggest a combined use of both the intravascular techniques [25] because they may provide unique diagnostic details on SCAD pathophysiological mechanism. These studies have demonstrated that both tools have same sensitivity in detecting the IMH but OCT still has a better ability to recognize intimal ruptures and flaps [25]. There is no need to say that the combination of both techniques implies a longer procedure with higher procedural costs and risks.

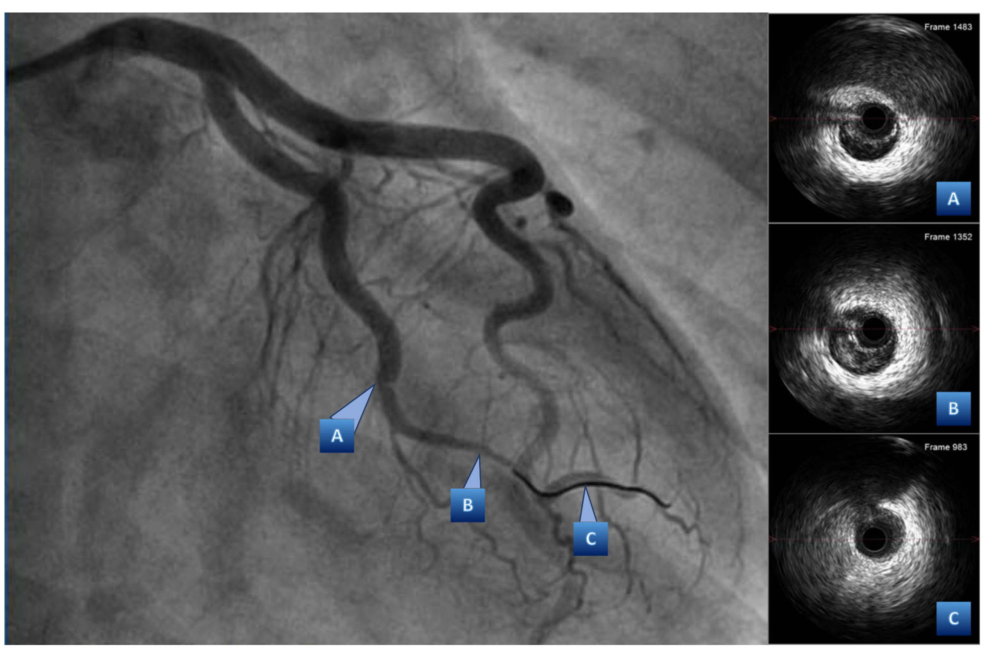

Fig. 3 51-year-old woman presenting with ACS/NSTEMI. Angiographic finding suspected for type 2 SCAD was confirmed by intravascular ultrasound imaging (IVUS)

PCI Planning and Optimization

An interventional management is nowadays discouraged as first line due to the evidence of good prognosis with the conservative approach [26] coupled with the significant rate of complications associated with the interventional approach [27]. Stenting may be followed by tear of the disrupted flap (resulting in extension of the dissection), "squeezing" of the intramural hematoma with obstruction of the vessel at either proximal or distal edges of the stent, or even vessel rupture [28]. Bioresorbable stents have been proposed as a less aggressive way of scaffolding dissection coronary arteries, with the potential advantage of their disappearance from the coronary arteries of typically young individuals [29, 30] (Fig. 1).

In any case, revascularization is to date advised only for those patients presenting with risk features such as STEMI presentation, hemodynamic instability, ventricular tachycardia or fibrillation, ongoing or recurrent episodes of angina, or left main dissection [31•].

Even during PCI, imaging plays a fundamental role to avoid complications and optimize the interventional strategy. Both IVUS and OCT may be used to ascertain the positioning of the guidewire within the true lumen: one of the most feared complications is the stent deployment in the false lumen.

Many studies focused on the role of OCT during PCI in spontaneous coronary artery dissection [21, 24, 32]: in particular, OCT gives unique insights on the extension of hematoma and on the vessel diameter which aids to appropriately select size and device type. This could be useful for example in case of an extensive self-contained hematoma, where the use of cutting balloon may be considered to decompress the hematoma as described in few reports [33]. Finally, the hematoma resorption could lead to stent/scaffold malposition, which may be fixed by staging an intracoronary imaging study to optimize the previous PCI [34].

An excellent example of intravascular tools' utility in PCI planning is shown in Supplemental Figure D.

Follow-up

The latest studies on SCAD have highlighted the importance of angiographic follow-up. In the vast majority of SCAD patients selected for conservative therapy, the dissection heals within months [35, 36•]. Most stable cases during the acute phase healed completely at least after 26 days from the index event [7]. These results support the "conservative whenever possible" approach.

An angiographic follow-up may be used at first to confirm SCAD diagnosis after an initial conservative treatment. Besides, it represents a way to ascertain the long-term result after extensive stenting/scaffolding. In particular, the evaluation of SCAD healing may be relevant for decision-making on the duration of the antiplatelet therapy or to exclude abnormal healing or recurrent SCAD in symptomatic patients.

Likewise, intracoronary imaging may be used for the follow-up: OCT is usually preferred to IVUS owing to its better spatial resolution. It may be considered to assess the mid-term result of PCI and guide antiplatelet therapy [2].

In most cases a complete restitutio in integrum occurs and may be appreciated only through OCT [21]; notwithstanding, this tool must be reserved only for those clinical situations that require a strong confirmation as the potential risks often outweigh the benefits [37].

Extracardiac Arteriopathies

Most reports show a high prevalence in SCAD patients of the so-called "extracoronary vascular abnormalities" (EVAs) arousing suspicion SCAD could be a located manifestation of a systemic vascular disorder [3, 4]. The most commonly reported is fibromuscular dysplasia (FMD) (Supplemental Figure E), but it also encompasses coronary tortuosity, focal stenoses, and intracranial aneurisms, with an associated risk involved [38], which warrants the need for a screening protocol for EVAs in case of SCAD. Furthermore, patients presenting with marked coronary tortuosity are usually at a higher risk of SCAD recurrence [39].

Saw et al. suggest looking for these abnormalities during the index coronary angiography [2], but the high risks related to additional invasive imaging, especially for unstable patients, prompt operators to postpone it [12, 40]. Liang et al. [40] published a screening protocol based on CT using low-osmolar contrast agents and low radiation doses. Macaya et al. reported the use of contrast-enhanced magnetic resonance angiography as a possible alternative to CCTA and angiography for the screening of EVAs [15, 41].

Conclusions

In conclusion, imaging tools play a key role in the diagnosis and management of SCAD during the acute phase of its clinical presentation. While coronary angiography constitutes to date the initial approach to diagnose or suspect the presence of SCAD, in many cases, the use of intravascular imaging provides a robust approach to confirm SCAD and to better characterize its particular endotype. Non-invasive imaging, used particularly in the subacute phase, can be also used to confirm SCAD by documenting involution of compressed coronary lumina in the mid-term or to disclose associated non-coronary vascular abnormalities which should rise the diagnosis of systemic vasculopathy.

Intracoronary techniques may support the interventional management by providing unique insights on IMH extension and morphology as well as confirming, in case of needed invasive treatment, the presence of the guidewire in the true lumen and stent/scaffold apposition.

Finally, in the follow-up, the imaging techniques (including the non-invasive options) help to assess the long-term result in case of extensive stenting/scaffolding, provide information about the spontaneous healing when it is not performed, and rule out extracardiac arteriopathy.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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