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Diagnosis of Spontaneous Coronary Artery Dissection by Optical Coherence Tomography

Fernando Alfonso, MD, PHD, Manuel Paulo, MD, Nieves Gonzalo, MD, PHD, Jaime Dutary, MD, Pilar Jimenez-Quevedo, MD, PHD, Vera Lennie, MD, Javier Escaned, MD, PHD, Camino Bañuelos, MD, Rosana Hernandez, MD, PHD, Carlos Macaya, MD, PHD

Madrid, Spain

Objectives This study sought to assess the diagnostic value of optical coherence tomography (OCT) in patients with suspected spontaneous coronary artery dissection (SCAD).

Background SCAD is a rare but challenging clinical entity.

Methods Following a prospective protocol, OCT was performed in 17 consecutive patients with a clinical and angiographic suspicion of SCD from a total of 5,002 patients undergoing coronary angiography. A conservative management strategy was followed.

Results OCT ruled out the diagnosis of SCAD in 6 patients with coronary artery disease (atherosclerotic plaques and/or intracoronary thrombus). In 11 patients (age 48 ± 9 years, 9 female), OCT confirmed the presence of SCAD. A double-lumen or intramural hematoma image was visualized in all cases. However, only 3 patients presented an intimal "flap" on angiography. OCT readily identified the intimal rupture site (n = 7), the thickness (348 ± 84 μm) and length (31 ± 9 mm) of the intimomedial membrane, the area of the true (1.1 ± 0.5 mm^2) and false lumen (5.9 ± 2.1 mm^2), the associated intramural hematoma (n = 9), and thrombi in the true or false lumens (n = 11). Most of these findings were angiographically silent. After stenting (n = 4), OCT disclosed adequate stent coverage, expansion, and apposition, but also residual intramural hematoma at the stented site (abluminal) and at the distal vessel.

Conclusions OCT provides unique insights in patients with SCAD that allow an early diagnosis and adequate management. Most of these findings are undetectable by angiography. (J Am Coll Cardiol 2012;59:1073–9) © 2012 by the American College of Cardiology Foundation

Spontaneous coronary artery dissection (SCAD) is a rare clinical entity that frequently presents as an acute coronary syndrome (1–4). SCAD is thought to be caused by hemorrhage within the vessel wall, leading to separation of its layers. An intimal rupture may precipitate bleeding into the wall with free communication between the true and false lumens (1–4). Alternatively, rupture of the *vasa vasorum* may generate a wall hemorrhage without communication with the lumen (2–4). Myocardial ischemia results from the compromise of the true lumen.

Currently, clinical diagnosis of SCAD relies on the visualization of a radiolucent intimal "flap" on coronary angiography (2–4). Angiography, however, is unable to visualize the coronary wall, and therefore, its diagnostic accuracy is limited (2–4). Recent reports suggest the value of tomographic techniques, as intravascular ultrasound, in the diagnosis of SCAD (5). Optical coherence tomography (OCT) is a new technique that provides accurate visualization of the coronary artery wall with an unprecedented resolution (15 μm) (6–9). OCT provides unique insights on coronary atherosclerosis and results of coronary interventions (6–9). However, its value in the diagnosis of SCAD remains unsettled.

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In this prospective study, we sought to assess the diagnostic value of OCT in patients with suspected SCAD.

Methods

Patients. From February 2009 to February 2011, 17 consecutive patients with the clinical and angiographic suspi-

From the Interventional Cardiology Unit, Cardiovascular Institute, IdISSC, Complutense University, Clínico San Carlos, University Hospital, Madrid, Spain. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Abbreviations and Acronyms

OCT = optical coherence tomography

SCAD = spontaneous coronary artery dissection

cion of SCAD were studied with OCT. Patients with a radiolucent intimal flap were included (1–5). In addition, young patients with discrete lumen narrowing, but otherwise smooth coronary vessels, were also investigated (1–5). This prospective OCT protocol was devised after the unexpected OCT diagnosis of SCAD in a young woman presenting with an occluded vessel after a myocardial infarction (6). During the study period, 5,002 patients underwent a first diagnostic coronary angiography at our center. Patients with previous interventions were excluded. No additional patients with angiographic intimal flaps, suggestive of SCAD, were encountered during this time. The protocol was approved by the Institutional Review Board, and all patients gave informed consent.

Angiographic analysis. Adequate views of the region of interest, avoiding vessel foreshortening and side-branch overlap, were obtained after intracoronary nitroglycerin (200 μg) administration. Classical qualitative angiographic criteria were used (10). Off-line, quantitative coronary angiography (CASS II, Pie Medical, Maastricht, the Netherlands) was performed by experienced personnel using standard methodology (10).

Optical coherence tomography. Before imaging 5,000 IU of unfractionated heparin and an additional bolus of intracoronary nitroglycerin were administered. Care was taken to gently navigate the guidewire across the target coronary segment. Likewise, great attention was paid during contrast media flushing to avoid any vessel injury. Guiding catheter damping was systematically ruled out. Initial studies were performed with time-domain technology (Image wire, M3, Light Lab Imaging, Inc, Westford, Massachusetts). Later on, Fourier-domain (frequency domain) OCT systems (C7-XR) and refined catheters (Dragon Fly, LightLab, St. Jude Medical, St. Paul, Minnesota), were used. The nonocclusive flushing technique was used to remove blood from the vessel (9). Before imaging, the catheter tip was advanced 10 mm distal to the target segment. When poor image quality was obtained, the pullback was repeated after modifying the flushing intensity or probe position. In patients with long diseased segments on small vessels, only the proximal aspect of the diseased segment was imaged.

Atherosclerotic plaque and thrombus were classified according to conventional criteria (9). The diagnosis of SCAD required the visualization of an intimomedial flap generating a double-lumen or an intramural hematoma (6–9). Intramural hematoma was considered when the intima was separated from the outer vessel wall by a relatively homogeneous material with high backscatter and variable attenuation. Quantitative, off-line OCT measurements were performed using proprietary computer software (LightLab Imaging) after readjusting the z-offset for calibration. The thickness, arc (°), and longitudinal extent of the dissection membrane were measured. True and false lumen areas were analyzed to determine longitudinal extent, true lumen minimal area, false lumen largest area, and the smaller true/false lumen ratio. These features were carefully reviewed (frame by frame) for the entire longitudinal extension of the acquired images.

Management and follow-up. By protocol, a conservative "watchful waiting" strategy was initially followed in all patients with SCAD (2–5). Medical management consisted of blood pressure control, dual antiplatelet therapy, and beta blockers. Coronary revascularization was only indicated in patients with favorable anatomy and ongoing/recurrent ischemia. Furthermore, in patients with diffuse SCAD, a conservative stenting approach was favored, restricting treatment to the most proximal segment of the disease, but ensuring adequate sealing of the intimal tear (6,10–13). Residual distal dissections were left untreated if they caused no significant lumen narrowing and were associated with normal flow or when located in small vessels (10–13).

Serial electrocardiograms and cardiac enzyme measurements were obtained. A comprehensive screening for inflammatory/immunologic abnormalities (C-reactive protein, C3-C4, rheumatoid factor, cryoglobulins, immunoglobulin G/A/M, antinuclear, anti-cardiolipin antibodies) was systematically performed. All patients were prospectively followed up, and a late angiographic follow-up was recommended.

Statistical analysis. Continuous data were presented as mean ± SD or median (interquartile range) values. Paired *t* tests were used to evaluate changes after interventions. $p < 0.05$ was considered statistically significant.

Results

In 6 patients with a confined angiographic lumen narrowing/linear filling defect, OCT ruled out the presence of SCAD. All of these patients presented with an acute myocardial infarction. Three patients had a localized intracoronary red thrombus (inducing partial dorsal shadowing), and 3 patients had severe atherosclerotic coronary artery disease. In 1 patient with mild haziness at the left anterior descending coronary artery that evolved as a Takotsubo syndrome, OCT disclosed a nonruptured calcified nodule.

In 11 patients, OCT confirmed the diagnosis of SCAD (Figs. 1 and 2). Baseline clinical characteristics are presented in Table 1. Interestingly, a classical angiographic intimal flap was only detected in 3 patients (1 type B, 2 type C), but all patients showed a relatively diffuse lumen compromise (Table 1). All other epicardial vessels were normal and showed a smooth angiographic appearance.

OCT readily visualized the affected coronary wall along the entire vessel (Table 2) (Figs. 1, 2, and 3). The length of the diseased segment was 32 ± 12 mm (double lumen, 8.4 ± 6.7 mm; intramural hematoma, 21.9 ± 15 mm; the full length of the angiographic disease could be interrogated in 7 patients). All patients showed an intimomedial flap (Table 2). The true and false lumens were

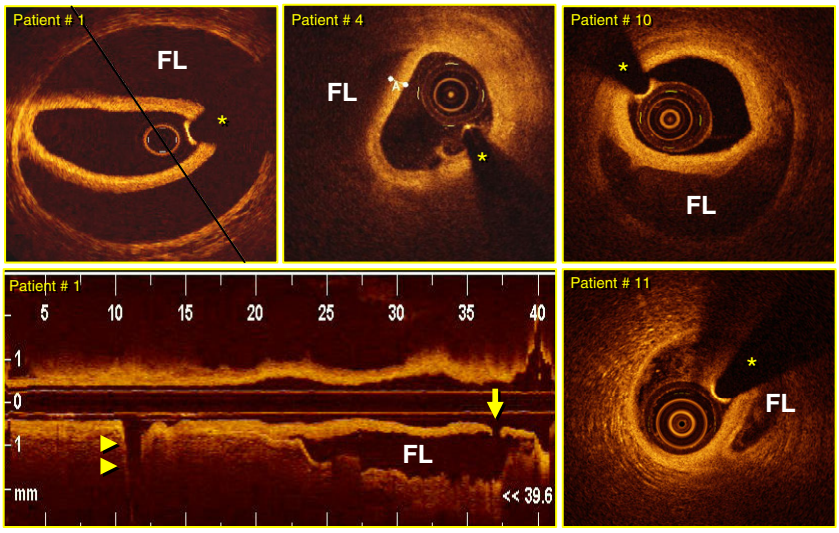

Figure 1 **OCT Images of the Intimomedial Membrane in Different Patients**

The thickness and extent of the intimomedial dissection, separating the true lumen (where the imaging probe is located) from the false lumen (FL), are clearly visualized. A longitudinal view is displayed at the **bottom left panel**. **Arrow** = entry tear; **arrowheads** = side branch originating from the true lumen; * = shadow caused by the wire artifact; OCT = optical coherence tomography.

readily recognized (Table 2). Associated thrombus was detected in all patients, including 3 patients with significant dorsal shadowing (length 12 ± 4 mm) from a red thrombus within the true lumen. Partial or complete thrombosis of the false lumen was detected in all cases (Fig. 3). A confined intimal tear was identified in 7 patients. The edges of the intimal rupture site were particularly thin (Table 2) (Fig. 2).

Four patients required coronary stenting for ongoing/recurrent ischemia with abnormal coronary flow. After stenting the most severe angiographic narrowing improved (minimal lumen diameter: 0.8 ± 0.4 mm to 2.4 ± 0.2 mm; p = 0.028), and all patients obtained a Thrombolysis In Myocardial Infarction flow grade 3. In 1 patient, stent deployment induced dissection propagation with temporal occlusion of a major side branch that was successfully treated with

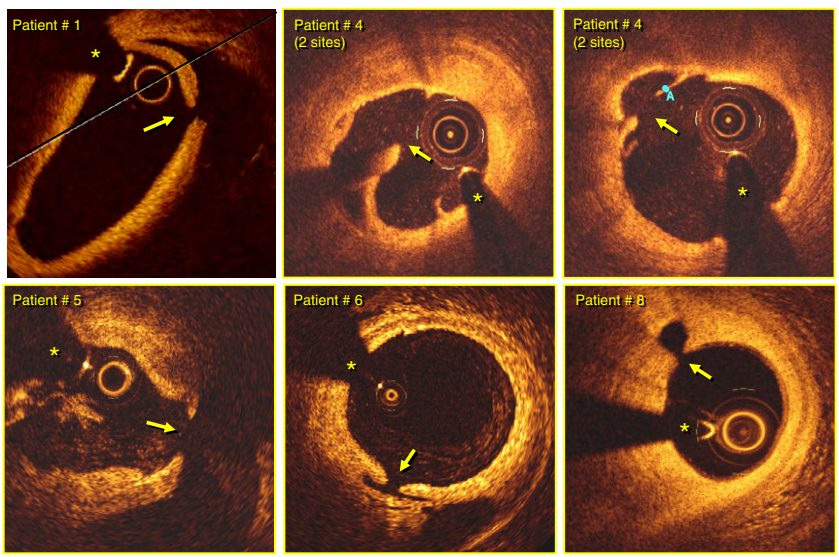

Figure 2 **OCT Images Showing the Variable Morphology and Characteristics of the Intimal Tear**

Patient #4 had 2 separate ruptures. **Arrows** = rupture sites; * = shadow caused by the wire artifact. Abbreviation as in Figure 1.

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Table 1 Clinical and Angiographic Characteristics

Age, yrs	48 ± 9
Female	9 (82%)
Risk factors	
Smoking	8 (73%)
Diabetes mellitus	0 (0%)
Hypertension	3 (27%)
Dyslipidemia	4 (36%)
Early menopause	1 (9%)
Associated diseases*	3 (27%)
Clinical presentation	
STEMI	9 (82%)
NSTEMI	2 (18%)
Myocardial infarction	
Q-wave	8 (73%)
CPK (IU)/TnI (ng/ml) peak	1,703 ± 2,232/128 ± 337
Time from symptoms to angiography, h†	24 (4–48)
TIMI grade (3/2/1–0)	6/3/2
Therapy before diagnosis	
Thrombolysis/IIb IIIa inhibitors	3 (27%)/1 (9%)
Quantitative coronary angiography	
Proximal reference diameter, mm	2.7 ± 0.4
Interpolated reference diameter, mm	1.8 ± 0.4
Minimal lumen diameter, mm	0.76 ± 0.3
Diameter stenosis, %	58 ± 10
Lesion length, mm	36 ± 17

Values are mean ± SD or n (%). *Hypothyroidism, n = 1; hepatitis C, n = 1, HIV infection, n = 1. †In 3 patients, the spontaneous coronary artery dissection diagnosis was obtained by optical coherence tomography during a second, elective, angiography. No patient had previously had strenuous exercise, had taken oral contraceptives, had toxic drugs consumption, or was in the peripartum period.

CPK = creatine phosphokinase; NSTEMI = Non–ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction; TnI = troponin I.

another stent. After stenting, OCT revealed sealing of entry tear and adequate stent expansion and apposition (Table 2). However, at the stented site, a persistent abluminal hematoma (space between the intimomedial membrane and the adventitia) was detected in the 4 patients (Fig. 4), whereas in 3 patients, a residual intramural hematoma distal to the stent was visualized (Fig. 4). The diseased segment length was reduced (from 32 ± 11 mm to 7.5 ± 6 mm; p = 0.06) (Table 2). No patient developed any clinical complication attributable to OCT imaging.

Relevant immunologic, inflammatory abnormalities (2 patients had mild elevation of anticardiolipin antibody titers) were not detected. Systemic collagen disease was ruled out in all cases. No patient developed additional events during hospitalization (7.2 ± 3.2 days). At late clinical follow-up (median 17.4 months), no patient experienced adverse events or required revascularization. Late angiographic follow-up (median 7.7 months) was obtained in 6 patients. Of these, 4 showed improvement in angiographic findings (2 complete normalization) (Fig. 5), whereas 2 patients, initially treated with stents, were free from restenosis, and 1 experienced marked enlargement of the distal vessel. In 2 patients, late OCT examinations revealed a completely normal vessel wall at the target site (Fig. 5).

Discussion

Diagnosis and management of SCAD is very challenging. However, an accurate and early diagnosis remains of paramount importance (1–5). Only anecdotal case reports have suggested the potential value of OCT in this condition (6–8). The present series represents the first prospective and systematic effort to assess the value of OCT in this exceedingly rare disease. Our findings demonstrate that OCT provides unique insights in patients with a clinical/angiographic suspicion of SCAD where angiography alone has limited diagnostic value. OCT was very useful to rule out the diagnosis in patients with images mimicking SCAD. This allowed an early triage with conventional management for patients with severe underlying coronary artery disease or large intracoronary thrombi.

Unique diagnostic insights provided by OCT. OCT was able to readily visualize the double-lumen morphology characteristic of this entity and to identify the entry tear, the circumferential and longitudinal extent of the disease, and the involvement of related side branches. The compromise of the true lumen and the distribution of the false lumen were also clearly visualized. Interestingly, most of these striking findings were undetectable by angiography. OCT was especially of value in patients with the suspicion of intramural hematoma (smooth, diffuse, narrowing but otherwise normal vessels). Notably, the diagnosis of SCAD would have been missed by angiography alone in most patients.

Table 2 Optical Coherence Tomography Findings

OCT system (time/frequency domain)	5/6
OCT pre-intervention (n = 11)	
No. of imaging runs	3.0 ± 1.7
Total image length, mm	48.1 ± 10.0
Mild atheroma seen at proximal (unrelated) sites	3 (27%)
Total length of the diseased segment, mm	32 ± 12
Intimomedial membrane	
Thickness	
Maximal, μm	348 ± 84
Minimal, μm	175 ± 63
At the rupture site, μm	99 ± 66
Length, mm	31 ± 9
Arc, °	212 ± 112
Rupture site identification*	7 (74%)
True-lumen minimal area, mm^2	1.1 ± 0.5
False-lumen maximal area, mm^2	5.9 ± 2.1
Smallest true/false lumen area ratio	0.29 ± 0.1
Intramural hematoma	9 (82%)
Associated thrombus	11 (100%)
No. of related side-branches	3.5 ± 0.7
OCT post-stenting (n = 4)†	
Minimal stent area, mm^2	7.8 ± 2.7
Stent expansion (% of reference)	90 ± 10
Abluminal residual hematoma (distance), mm	0.56 ± 0.60
Distal residual hematoma (length), mm	10 ± 5

Values are mean ± SD or n (%). *One patient had 2 distinct rupture sites. †Two drug-eluting stents, 2 bare-metal stents.

OCT = optical coherence tomography.

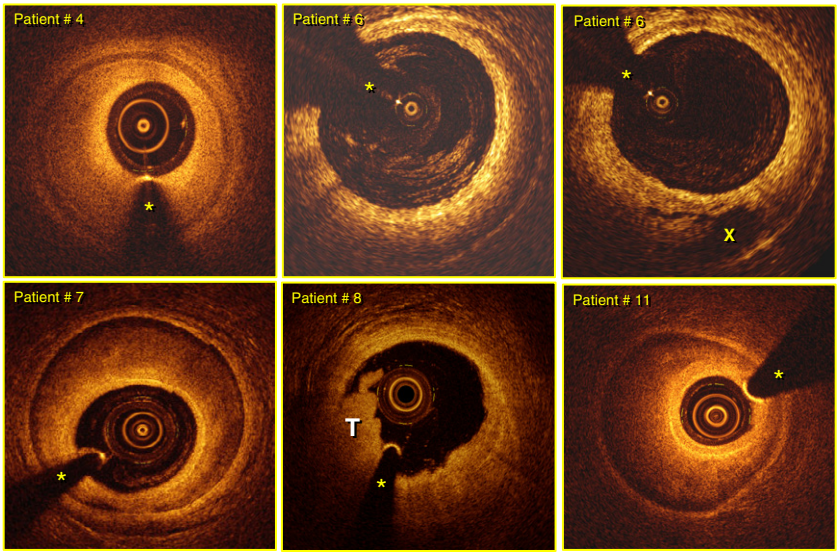

Figure 3 **OCT Images of Intramural Hematoma**

In Patient #6, the transition from the intramural hematoma to a double-lumen morphology (X) is depicted. In Patient #8, a red thrombus (T) partially shadows the underlying vessel wall. * = shadow caused by the wire artifact. Abbreviation as in Figure 1.

A striking finding of the present study was the thickness of the intimal flap (Fig. 1). Our results suggest that in most patients, this membrane is relatively thick (348 ± 84 μm) and actually consists of intima-plus-media. These findings are consistent with classical pathological reports (1,4). Accordingly, we propose to use the term *intimomedial dissection* in this condition. The intimal tear (intimal rupture or "entry door") could be identified in 7 patients (Fig. 2). To our knowledge, this diagnosis is unique to this high-resolution technique and may have major clinical implications. The thickness of the intimomedial membrane was the thinnest precisely at the edges of the intimal tear. An accurate diagnosis of the intimal tear not only has pathophysiologic interest, but also might bear important clinical consequences. Indeed, sealing the entry door appears warranted to ensure a favorable outcome in patients with iatrogenic coronary left dissections (10–14). However, dissections induced during coronary interventions are usually generated in diseased coronary segments, whereas the hallmark of SCAD remains separation of the vessel wall layers in segments free from atherosclerotic disease. In fact, the absence of atherosclerotic plaque may explain not only the relative diffuse appearance, but also the risk of further extension of the disease should the presence of hemodynamic stimuli persist. This provides a rationale for a restrictive therapeutic approach, namely sealing exclusively the proximal part of the SCAD when long coronary segments are involved to stabilize the clinical picture and allow spontaneous healing of the residual dissection (10–14).

OCT is also able to identify the presence of associated thrombus, which, in our experience, frequently occurs in the

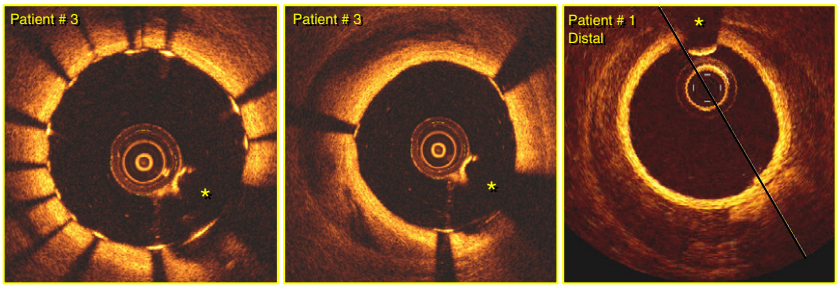

Figure 4 **OCT Findings After Coronary Stenting**

(Left) Well-expanded and apposed stent. **(Middle)** Residual abluminal hematoma at the stented segment. **(Right)** Residual intramural hematoma distal to the stented segment. * = shadow caused by the wire artifact. Abbreviation as in Figure 1.

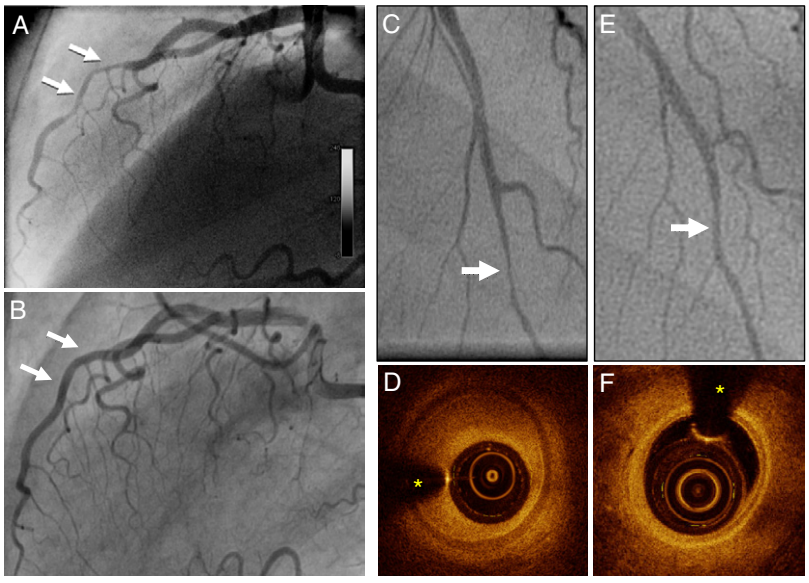

Figure 5 **Late Spontaneous Resolution of Angiographic Images Corresponding to SCAD on OCT**

(A) Diffuse, confined lesion in the mid left anterior descending coronary artery **(arrows)** (note normal proximal and distal segments) with complete resolution at late angiographic follow-up **(B). (C)** Diffuse lesion **(arrow)** on the distal left anterior descending coronary artery where OCT revealed an intramural hematoma **(D). (E)** At late follow-up, the angiographic image significantly improved, and a normal vessel wall was demonstrated by OCT **(F)**. * = shadow caused by the wire artifact; SCAD = spontaneous coronary artery dissection. Abbreviation as in Figure 1.

acute setting, and its location within the true/false lumen. Whether individual thrombus characteristics or the presence of thrombus in the false lumen have prognostic implications remains to be elucidated.

OCT during coronary interventions. OCT was of unique value to guide coronary interventions in these complex patients. Firstly, OCT was instrumental to confirm that the guidewire was located in the true lumen. Furthermore, adequate stent coverage, expansion, and apposition were readily identified. In most patients, OCT disclosed residual disease at the stented site and also in the distal segment (Fig. 4). We selected a conservative strategy even in patients requiring revascularization regarding stent expansion and length (6,10–13). Extrusion of thrombus in the false lumen may cause propagation of the dissection toward unaffected coronary segments. Finally, although drug-eluting stents are attractive in this setting, the consequences of the eluted drug on the vessel wall healing process remain unsettled (13).

Clinical outcome. Revascularization (percutaneous or surgical) for SCAD may be shadowed by the fragility of the vessel wall. Therefore, we selected a conservative strategy, restricting revascularization to patients with refractory ischemia, with favorable acute and long-term clinical outcome. Furthermore, we were able to demonstrate that, at least in some patients, SCAD completely heals during follow-up. Although anecdotal, our OCT findings strongly suggest that a *restitutio ad integrum* of the arterial wall may be expected in this entity.

Study limitations. First, our series is limited in size as a result of the rarity of SCAD. Second, the use of invasive techniques in this highly unstable anatomic substrate may be risky. Therefore, clinical prudence, paying major attention to technical details, can not be overemphasized. Third, OCT has a limited penetration into the vessel wall, and red thrombus produces signal-free shadowing hampering visualization of potentially relevant features. Finally, a complete analysis of the SCAD length may be inappropriate in long SCAD. Despite these caveats, the information provided by OCT was sufficient to gain a highly comprehensive appraisal of the complex underlying anatomical substrate.

Conclusions

Coronary angiography is unable to establish the correct diagnosis of SCAD, even in patients with strong clinical suspicion. Conversely, OCT provides unique insights on most relevant morphologic features of the condition including entry tear, intimomedial flap, double-lumen morphology, intramural hematoma, and associated thrombus.

Reprint requests and correspondence: Dr. Fernando Alfonso, Interventional Cardiology, Cardiovascular Institute, IdISSC, Complutense University, Clínico "San Carlos" University Hospital, Madrid 28040, Spain. E-mail: falf@hotmail.com.

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Key Words: optical coherence tomography ■ spontaneous coronary artery dissection.