

Optical Coherence Tomography for *In Vivo* Identification, Characterization and Optimal Treatment of Spontaneous Recanalization of Coronary Thrombus

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Abstract. *Background/Aim: Spontaneous recanalization of coronary thrombus (SRCT) is a rare in vivo appearance, with a nonspecific angiographic aspect. The aim of this study was to investigate the importance of optical coherence tomography (OCT) use for SRCT identification, characterization of pathogenic mechanisms and optimal treatment. Patients and Methods: We retrospectively analyzed all patients with angiographic suspicion of SRCT who underwent coronary angiography for suspected coronary artery disease and afterward investigated by OCT imaging. Results: We identified 28 cases with angiographic suspicion of SCRT (0.41% of CA) and confirmed it in 4 patients (0.05% of CA). OCT provided insight about the underlying SRCT mechanism: possible complicated atherosclerotic plaques in two cases and, respectively, spontaneous coronary artery dissection in other two cases. OCT provided accurate lesion assessment and offered optimal PCI materials selection. Conclusion: Besides providing the diagnosis, OCT also improved characterization of SRCT pathogenic mechanisms, in the four confirmed SRCT cases, supporting the role of coronary wall in situ complications, namely dissection of an atherosclerotic plaque or spontaneous dissection of a normal coronary wall.*

Spontaneously recanalized coronary thrombus (SRCT) was, for the first time, observed on histopathology findings, in autopsy series, and characterized by multiple channels divided by thin septa, communicating with each other and, proximally and distally, with the normal coronary lumen (1).

The *in vivo* appearance of SRCT is a rare finding, and is possibly underdiagnosed, due to the limitations of standard coronary angiography (CA) (2). The first ever *in vivo* identification of SRCT was performed by Terashima *et al.* (3) in 2002, using intravascular ultrasound imaging (IVUS), describing a lotus-root appearance in the mid left anterior descending artery (LAD) of a 21 years old patient with suspected Kawasaki disease, with a history of sudden cardiac arrest at the age of one year. Since then, availability of intravascular imaging and the increasing awareness of interventional cardiologists brought to surface this pathology. Availability of optical coherence tomography (OCT), an intra-coronary imaging technique with a resolution 10 times higher than IVUS, further increases the possibility of SRCT identification (2).

OCT is a well recognized tool for the analysis of the atherosclerotic plaque morphology and identification of vulnerable and complicated plaques (4). OCT also has increasing clinical indications (4), with an emphasis on its role in the decision for percutaneous coronary interventions (PCI), in acute coronary syndromes (ACS) with non-significant CA lesions (5, 6). Experience concerning OCT use for optimization of PCI is also increasing (7-9).

To date, there are several reports on SRCT, regarding clinical presentation, angiographic aspect (2, 3, 10-32), OCT description (2, 10-23, 26-32) and treatment options, with imprecise data regarding its underlying pathogenic mechanisms (14, 17, 20-22, 25, 30-32). This article investigated the importance of OCT use for: (i) establishing the real-life SRCT prevalence, in patients with CA suspected SRCT; (ii) identification of the true severity of SRCT

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lesions; (iii) selection of PCI indication and optimal material selection; (iv) investigating SRCT pathogenic mechanisms, including the potential role of atherosclerotic, vulnerable and complicated plaques, as well as of in-wall spontaneous dissection.

Patients and Methods

Study population. This study retrospectively analyzed all 6,743 patients who underwent CA for suspected coronary artery disease (CAD), in a single tertiary center in Romania (Cluj County Emergency Hospital, Department of Interventional Cardiology), over a period of 7 years (January 2012 – May 2019). There were 5,605 patients with ACS: 2,177 ST segment elevation myocardial infarction (STEMI), 1,384 non-ST segment elevation myocardial infarction (NSTEMI), 2,045 unstable angina (UA) and 1137 stable CAD (stable angina pectoris or silent ischemia patients). Patients with angiographic suspicion of SRCT lesion were investigated by OCT imaging, in order to confirm SRCT diagnosis, to investigate SRCT underlying pathogenic mechanisms and to guide PCI.

Informed consent was obtained before the invasive procedure. Clinical data and angiographic examinations were stored in the hospital database and in a dedicated catheterization laboratory database, using our preexisting experience of structured databases (33-35).

CA and OCT acquisition indications, technique and analysis. CA was performed on Siemens Coroskop T.O.P and Siemens Artis Zee angiographs (Siemens Healthineers, Erlangen, Germany), in patients with suspected CAD. Severity of coronary stenosis was assessed visually and by quantitative coronary analysis (QCA). The highest degree of stenosis severity, usually the area stenosis severity provided by QCA, was considered. Angiographic criteria associated with a SRCT suspicion were pseudo-dissection, braided filling defect and haziness, with an irregular and poly-lobular artery outline and more often a combination of those (2).

OCT imaging was performed in patients with SRCT suspicion on CA. OCT images were acquired with a commercially available system (ILUMIEN OPTIS OCT Intravascular Imaging System, St. Jude Medical, St. Paul, MN, USA), using an over the wire OCT catheter (C7 Dragonfly™ and Dragonfly™ OPTIS™, St. Jude Medical, St. Paul, MN, USA). The entire length of the region of interest was scanned using the integrated automated pullback device at 20 mm/s. During image acquisition, coronary blood flow was replaced by continuous flushing of contrast medium directly from the guiding catheter. All images were recorded digitally, stored, and analyzed using proprietary software (St. Jude Medical, St. Paul, MN, USA) in concordance with standard consensus of OCT use (5).

OCT was performed freely, with no restrictions, by all three senior interventional cardiologists during working hours and, two days each week, 24/24 h, for emergency situations like ACS. OCT was performed only on the coronary vessel with CA suspicion of SRCT. SRCT was identified on OCT as a structure with multiple channels, divided by smooth, high-luminosity, strong reflection and weak attenuation septa, communicating with each other and, proximally and distally, with the normal coronary lumen (2).

In all patients in whom OCT identified SRCT as the lesion responsible for the angiographic stenotic appearance, the degree of stenosis was re-graded using OCT criteria. OCT quantification

of coronary lesion severity was made using the proprietary software, as area stenosis compared to largest pre-lesion reference area. The minimum lumen area (MLA) of SRCT was calculated as the sum of MLAs of each SRCT channels in the narrowest site of the lesion. An OCT area stenosis of at least 70% was considered as significant stenosis. An indication for PCI was made according to the presence of ischemia, objectified by symptoms, electrocardiogram and echocardiogram changes. Myocardium viability was established by echocardiogram changes: hypokinesia – suggesting viability and by Thallium scan in case of a/dyskinesia. We assessed lesion characteristics (*e.g.* length, reference vessel diameter) on OCT, in order to optimize selection of PCI materials. A comparison was made with lesion characteristics on CA.

A post-procedural detailed analysis of OCT images was performed in patients with SRCT diagnosis, in order to characterize the morphology of the underlying SRCT coronary wall. We investigated the presence of atherosclerotic markers (lipid infiltration, intimal thickening), of high-risk plaques (necrotic core, thin cap fibro-atheroma, macrophage infiltration, hypervascularization) and, respectively, of complicated plaques (intra-plaque hemorrhage, dissection, plaque rupture, erosion and ulceration) (3). The topography of these parameters, in relation to SRCT, was also studied.

In order to provide an accurate review of the literature an extensive search in the PubMed Central and MEDLINE databases was made. All known terms related to SRCT were searched for: “honey-comb like lesion”, “lotus-root lesion”, “swiss-cheese lesion” and “spider-web lesion”.

Follow-up of patients was performed at the end of this study by visits to the clinic or by phone interrogatory, with a focused interest on major adverse cardiac and cerebral events (MACCE), a composite criterion consisting of death from cardiac causes, ischemic or hemorrhagic stroke, myocardial infarction, or need for myocardial revascularization.

All procedural costs of CA, PCI and OCT imaging were supported by the Romanian National Interventional Cardiology Healthcare program.

The study complies with the Declaration of Helsinki on human research and was approved by our local Study Committee (provided in Supplementary data – original informed consent; authorized translated informed consent; official approvals from our local Study Committee).

Results

During the 7-year investigation period, there were 28 CA suspicions of SRCT, out of the 6,743 CA (0.41%). The clinical condition was represented by STEMI in 13 patients, NSTEMI in 4 patients, UA in 9 patients and stable CAD in 2 patients. OCT was performed in all 28 patients with CA suspicion of SRCT. OCT confirmed SRCT in only 4 cases (14.3%), which represent 0.05% of the total 6,743 CA and 0.09% when referred to our 4302 PCIs performed during the investigated period.

Suspected SRCT on CA were associated with significant angiographic stenosis in only 7 of the 28 patients (25%), none with OCT confirmed SRCT. Within the 21 patients'

Table I. *General clinical patient characteristics, cases 1 to 4.*

	Case no. 1	Case no. 2	Case no. 3	Case no. 4
Gender	Female	Male	Male	Male
Age	43	59	67	41
Hypertension	Yes	Yes	Yes	No
Diabetes mellitus	No	No	No	No
Dyslipidemia	No	Yes	No	No
Renal insufficiency	No	No	No	No
Overweight	No	Yes	No	No
Smoking habit	Yes	No	No	Yes
Cardiovascular history	No	No	No	No
Atrial fibrillation	No	No	No	No
Physical examination	Normal	Normal	Normal	Normal
Blood work	Normal	High troponin; hypercholesterolemia	Normal	High troponin
Electrocardiogram	Negative T waves in V1-V6	ST segment elevation in DII, DIII, aVF	Negative T waves in V3-V6	ST segment elevation in V1-V4, negative T waves in DI, aVL, V4-V6
Echocardiogram	LV anterior wall hypokinesia; 45% LVEF	LV inferior and anterior wall hypokinesia; 45% LVEF	LV lateral wall akinesia; 40% LVEF, Second grade ischaemic mitral regurgitation	LV anterior wall akinesia; LV dilatation, apical aneurysm without thrombus, 38% LVEF
Diagnosis	Unstable angina	Inferior STEMI	Unstable angina	Anterior STEMI in evolution

LV: Left ventricle; LVEF: left ventricle ejection fraction; STEMI- ST: elevated myocardial infarction.

Table II. *Angiographic characteristics, cases 1 to 4.*

	Case no. 1	Case no. 2	Case no. 3	Case no. 4
CA findings	Single vessel disease (LAD stenosis)	Two vessels disease (RCA occlusion and Diagonal stenosis)	Two vessels disease (LAD stenosis and distal LCX chronic occlusion)	Single vessel disease (LAD stenosis)
SRCT vessel	LAD	Diagonal artery	LAD	LAD
Culprit lesion	Yes	No; Culprit was RCA occlusion	Yes	Yes
Lesion severity (%)	50	40	30	50
Lesion length (mm)	15	22	20	40
TIMI flow	3	3	3	3

CA: Coronary angiography; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; SRCT: spontaneous recanalization of coronary thrombus; TIMI: thrombolysis in myocardial infarction.

subgroup with borderline lesion on CA, there were 4 OCT confirmed SRCT patients.

Clinical data of confirmed SRCT patients. Table I summarizes the relevant clinical information, for each of the 4 SRCT patients. There were 3 males and one female, with a median age of 53 years. Clinical diagnosis was UA in two patients and inferior and anterior STEMI in other two. All patients were without cardiovascular (CV) history and without atrial fibrillation. All patients had CV risk factors, ranging from one

to three CV risk factors for each patient. CV physical examination was normal in all patients. Electrocardiogram showed negative T waves in pre-cordial leads in the two UA patients, while elevated ST segment in inferior and anterior leads were present in the inferior and anterior STEMI patients. Left ventricle motion abnormalities and moderate left ventricle ejection fraction reduction were observed on three patients, while LV dilatation and anterior LV wall akinesia and apical aneurysm were observed on the fourth patient. The blood work was abnormal only in the STEMI patients.

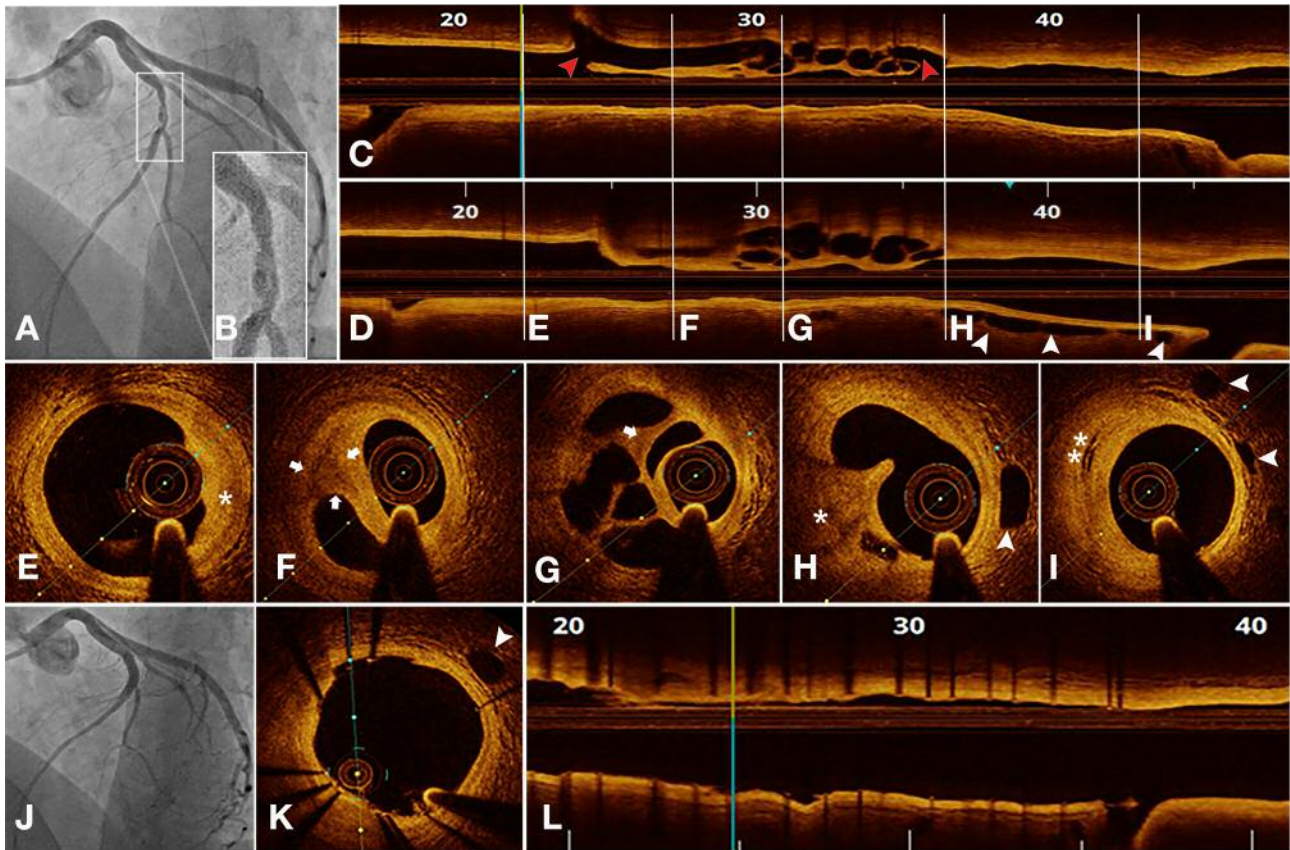


Figure 1. First spontaneous recanalization of coronary thrombus (SRCT) case. A: Angiographic view; B: Detailed angiographic view; longitudinal views: C and D, between red arrowheads; transversal views: F, G and H. OCT imaging: an SRCT structure with multiple channels divided by smooth, high-luminosity, strong reflection and weak attenuation septa; Inside septa, signal-poor, darker tissue areas are visualized (white arrows in F and G): linked by previous histopathology studies (2) to proteoglycan-rich tissue. Other signal-poor regions in the arterial wall showing some degree of posterior attenuation may correspond to lipid atherosclerotic plaques: asterisk in E and H. White arrowheads in D, H, I and K: The lesions were hypervascularized, with a large vasa vasorum. Double asterisk in I: A possible intra-plaque dissection/hemorrhage was imaged proximally to the SRCT. J: Optimal angiographic PCI result. L: Optimal post PCI OCT result.

Coronary angiography data in the SRCT confirmed patients (Table II). In both UA patients, SRCT lesions were the culprit ones, located on the mid LAD (Figures 1, 2A and 2B). In the anterior STEMI patient, the SRCT lesion, situated in the proximal and mid-LAD, was the culprit lesion as well (Figure 3). In patients no. 1 and no. 4, there was a single vessel disease. In patient no. 2, a two-vessels disease was present, due to coexisting chronic occlusion of the left circumflex artery (LCX).

In the inferior STEMI patient, in whom the acute coronary occlusion was situated on the proximal right coronary artery (RCA), the SRCT lesion was found on the first diagonal artery (Figure 4A).

The thrombolysis in myocardial infarction flow was graded normal in all SCRT arteries. The angiographic appearance of SCRT was a combination of pseudo-

dissection and braided filling defect (patients no. 1, 2 and 4) and pseudo-dissection filling defect in one case (patient no. 3). Lesion severity was graded visually and by QCA as 30, 40 and 50% for both no. 1 and 4 cases. The length of suspected SRCT was measured at 15, 20, 22 and 40 mm, respectively.

OCT data in confirmed SRCT patients (Table III). In all patients with confirmed SRCT, in whom CA revealed borderline lesions, OCT reassessed lesions as significant, with an indication for PCI. As compared to CA, lesion length was longer on OCT, while vessel diameter was similar. OCT data allowed optimal selection of stent length for PCI.

Detailed post-procedural OCT analysis provided information on the possible SRCT pathogenic mechanisms. OCT identified coronary wall *in situ* complications, namely dissection of an

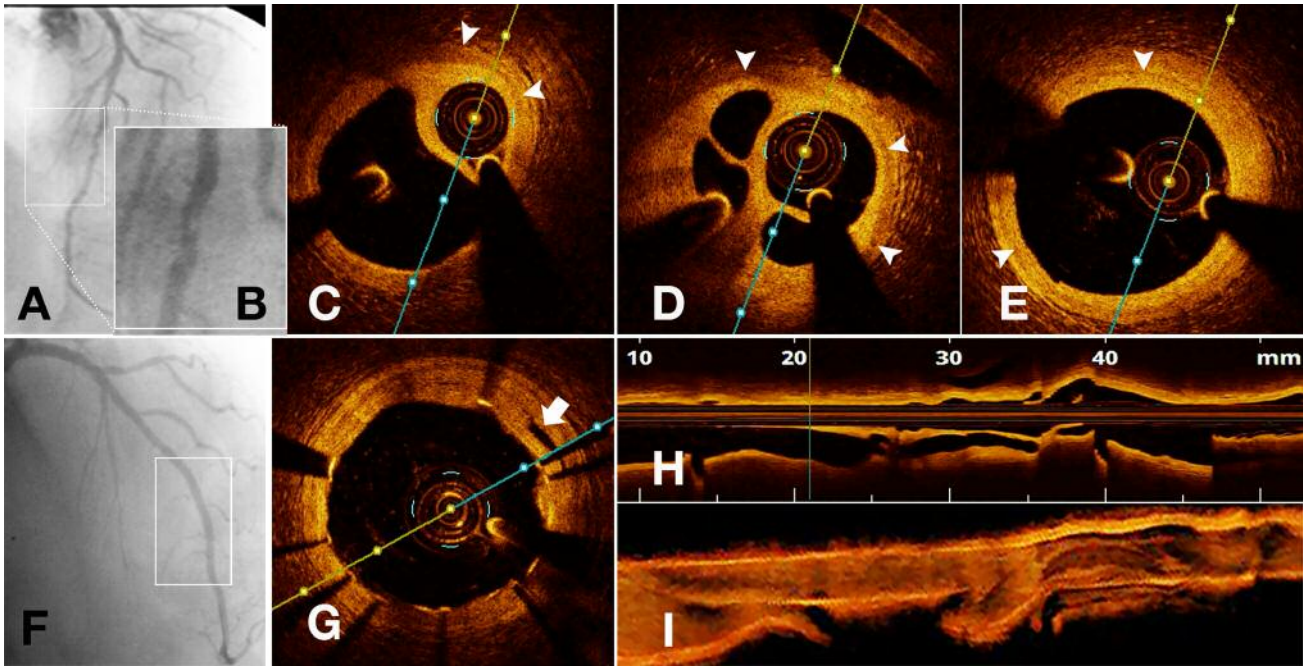


Figure 2. Third spontaneous recanalization of coronary thrombus (SRCT) case. A: Angiographic view. B: Detailed angiographic view. C to E: OCT imaging of an SRCT lesion - transversal views; C, D and E (white arrowheads): The normal, three-layered, coronary wall was observed on the entire length of SRCT, representing normal wall media, seen almost circumferentially in E, with no evidence of atherosclerosis. F: Angiographic optimal PCI result. G: OCT imaging of optimal PCI result (white arrow – SRCT remaining channel). OCT imaging of the SRCT structure: H, longitudinal view; I, three-dimensional reconstruction.

Table III. OCT characteristics, cases 1 to 4.

	Case no. 1	Case no. 2	Case no. 3	Case no. 4
OCT indication	Borderline lesion assessment	Borderline lesion assessment	Borderline lesion assessment	Borderline lesion assessment
OCT area stenosis	75	80	80	75
Lesion length	22	28	26	65
OCT description:	Yes	Yes	Yes	Yes
"Honeycomb" aspect				
Atherosclerotic plaque markers				
Lipid infiltration	Yes	Yes	No	No
Intimal thickening	Yes	Yes	No	No
Markers of high-risk plaques				
Thin cap fibro-atheroma	Possible	Possible	No	No
Macrophage infiltration	Possible	Possible	No	No
Hypervascularization	Yes	Yes	No	No
necrotic core	No	No	No	No
Markers of plaque complication				
Dissection	Possible	Possible	No	No
Plaque rupture	Possible	Possible	No	No
Plaque erosion	No	No	No	No
Plaque ulceration	No	No	No	No
Markers of coronary wall complication	No	No	Yes	Yes
OCT role for therapeutic decision	Yes; Indication for PCI	Yes; Indication for PCI	Yes; Indication for PCI	Yes; Indication for PCI
OCT role for PCI guiding	Optimizing selection of PCI devices	Optimizing selection of PCI devices	Optimizing selection of PCI devices	None
Treatment option	Direct 3/24 mm DES implantation	Direct 3.5/30 mm DES implantation	Pre-dilatation; 3/28 mm DES implantation	Conservative treatment

OCT: Optical coherence tomography; PCI: percutaneous coronary intervention; DES: drug eluting stent.

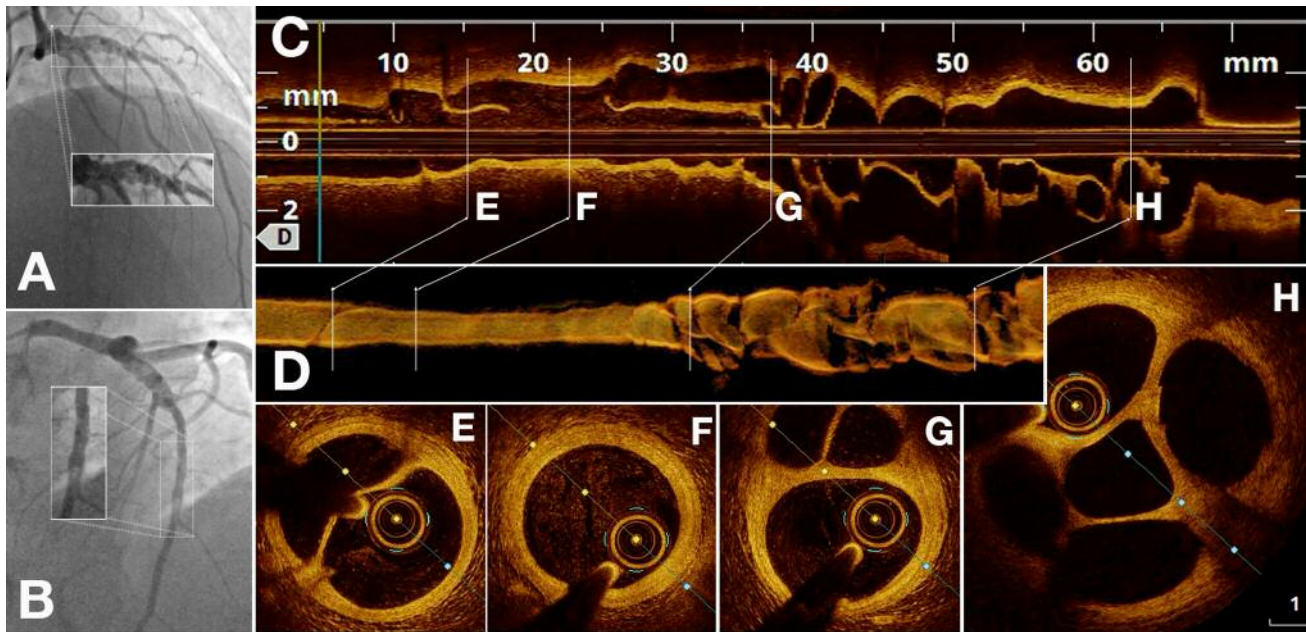


Figure 3. Fourth spontaneous recanalization of coronary thrombus (SRCT) case. A patient with a long lesion including two SRCTs, separated by a normal segment. Angiographic views with details highlighting proximal (A) and distal SRCTs (B). OCT imaging: Longitudinal view (C), 3D reconstruction (D) and transversal views at different levels – distal SRCT (E), proximal SRCT (G and H), with dilated coronary lumen (H). OCT cross-section of the normal segment between the two SRCTs is depicted in F.

atherosclerotic plaque, in the patients no. 1 and 2, and a normal coronary wall, in the patients no. 3 and 4.

In the first two patients (Figure 1E, 1F, 1H, and 4C-4H), OCT revealed, both in the area of SRCT underlying vessel wall and in adjacent coronary areas (proximal and distal to the lesion), markers of atherosclerosis (lipid infiltration and intimal thickening) and possible markers of high-risk plaques (hypervascularization). In both cases, in the area of SRCT underlying vessel wall, there were several markers of plaque complications (Figures 1 and 4). Proximal to the SRCT, in the entrance area to the SRCT lesion, OCT identified an intra-plaque hemorrhage/dissection in the first case (Figure 1I) and, respectively, a plaque rupture in the second one (Figure 4D). In this latter patient, a possible intimal rupture was also identified in the distal extremity of SRCT (Figure 4F).

In the third and fourth patients (Figures 2 and 3), OCT did not identify atherosclerotic markers. A normal, three layers, coronary wall was observed on the entire length of SRCT. After PCI (in patient no. 3), a linear signal-free space within the media raises the problem of a spontaneous coronary dissection, probable initiating the SRCT lesion. For the fourth patient, beside absence of atherosclerotic markers, the considerable length and size of the lesion may support spontaneous dissection as the nidus for thrombus formation.

Treatment options in OCT confirmed SRCT cases. PCI with DES implantation was performed in patients no. one, two and three, with direct stenting in two patients (Figure 1E, 1F and 1G; Figure 2F and 2G) and with balloon pre-dilatation in the other one (Figure 4B, 4H and 4J). There were no periprocedural complications. All three patients were discharged in a good clinical, symptom-free status, on dual antiplatelet, beta-blocker, statin, and angiotensin converting enzyme inhibitor therapy. For these three patients there was a strong clinical improvement after PCI.

For the fourth patient, a Thallium scan test was performed in order to assess the myocardium viability, which showed large areas of necrosis, making revascularization unnecessary. For this case, a conservative approach was established, with dual antiplatelet, beta-blocker, statin, angiotensin converting enzyme inhibitor, oral loop and anti-aldosterone diuretic therapy, with a good clinical condition at the last control.

A median follow-up of 29 months was made in all 4 patients (Case 1-39 months, case 2-7 months, case 3-65 months and case 4-5 months) with no MACCE reported.

Discussion

Our study confirms that SRCT is a very rare finding, with only 28 CA suspected SRCT lesions in the 6,743 patients

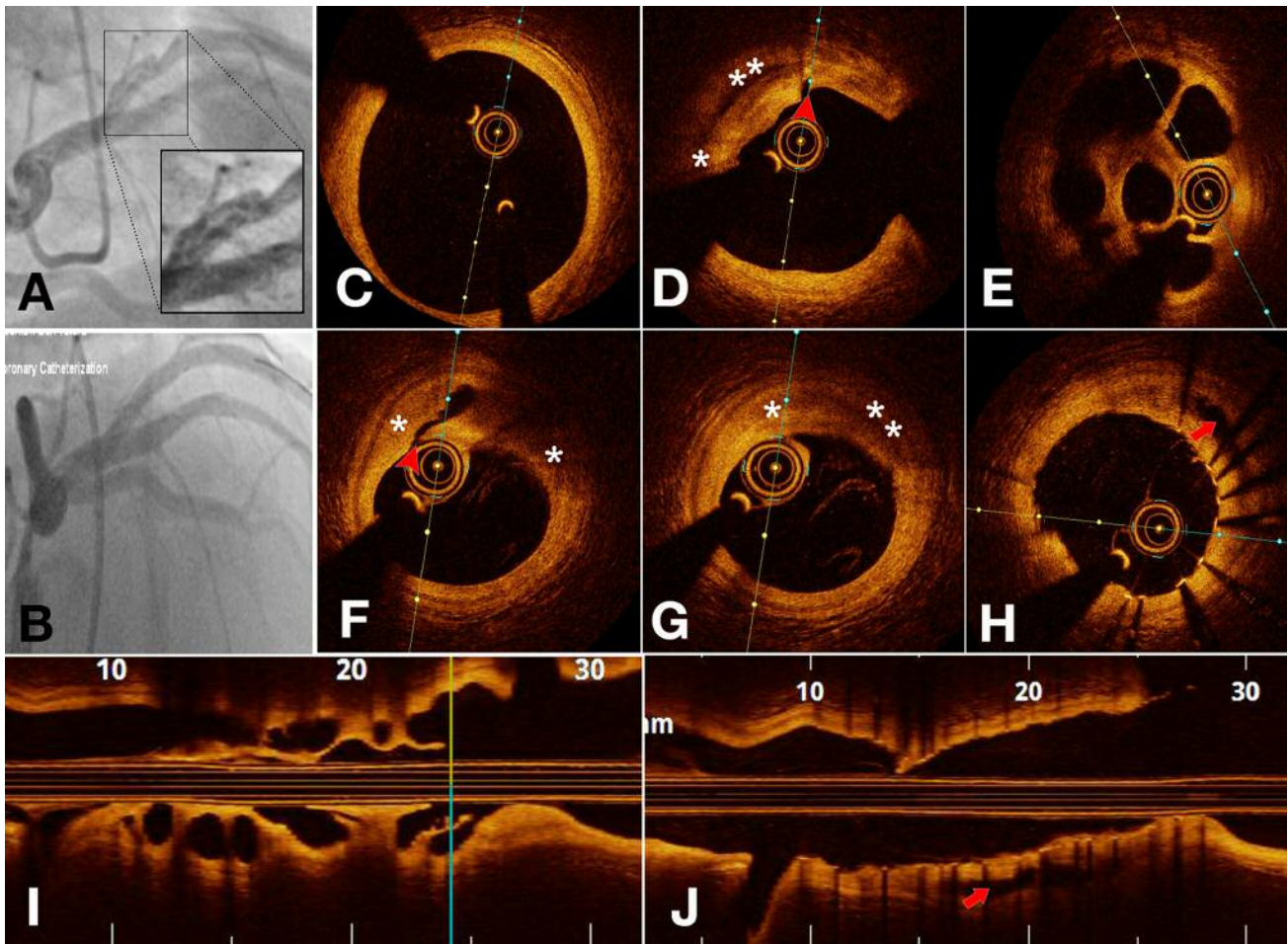


Figure 4. Second spontaneous recanalization of coronary thrombus (SRCT) case. A (with detailed view, showing the characteristic braided and pseudo-dissection aspect): Angiographic view. B: Optimal post-PCI angiography. C: Part of the coronary vessel proximal to the SRCT. Asterisk (*) in D, F and G: OCT imaging; an SRCT lesion, superimposed on an atherosclerotic plaque with signal-poor areas, representing lipid accumulation. Double asterisk (**) in D and G: A possible intra-plaque dissection/hemorrhage was imaged both proximally and distally to the SRCT. E: SRCT channels. The proximal and distal SRCT entry point can be precisely localized: D: red arrowhead - proximal entry point and F: red arrowhead, distal exit point. A part of SRCT channels were still identified on OCT, after PCI: H and J: red arrows: SRCT channels. I: OCT longitudinal view of SRCT.

with suspected CAD (0.41%) and, moreover, only 4 OCT confirmed SRCT lesions (0.05% of the CA). Prevalence of SRCT lesions was 0.09% when referred to our 4,302 PCI during the investigated period. This result is consistent with previous findings. In the largest cohort of SRCTs ever reported (10), authors identified 33 SRCT cases out of 31,500 PCIs, during a 5-year period. Considering these findings, SRCT prevalence was estimated around 0.1% of PCIs.

Besides the previous mentioned study (10), exhaustive search of the literature showed 23 case reports (3, 11-32) and one study (2) on 6 other cases reported to date, totaling 62 SRCT cases (Table IV), focusing mainly on

the clinical presentation, angiographic and intravascular imaging aspect, treatment modality and very few comments related to the mechanism for thrombus formation. Also, there are scarce data on prognostic and follow up of the SRCT patients.

It was previously believed that the true prevalence of SRCT lesions might be underestimated, due to its angiographic non-specific aspect: namely haziness, braided and pseudo-dissection filling defects. This angiographic aspect can be related to other various conditions: fresh thrombosis on plaque rupture/erosion, spontaneous dissection, aneurysm or heavy calcification (2, 36-40). The diagnosis becomes possible only by intravascular imaging.

Table IV. All SRCT-related articles published to date.

Authors	Patients (M/F)	Clinical diagnosis	SRCT vessel	Angiographic aspect	Intravascular imaging	Treatment option	Origin
Kang SJ <i>et al.</i> (2)	6 (3M/3F)	UA: 4 p SCAD: 2 p	LAD 2p RCA 4p	Haziness and pseudo-dissected: 6p	both	PCI with DES 5 Conservative 1	Plaque rupture, embolic or spontaneous dissection
Terashima M <i>et al.</i> (3)	1M	undeclared	LAD	Haziness	IVUS	Not disclosed	Not mentioned
Souteyrand G <i>et al.</i> (10)	33 (23M/10F)	STEMI: 2 p NSTEMI: 8 p SCAD: 11 p silent ischemia: 12 p	LAD 14p LCX 3p RCA 17p	Haziness: 2p; braided: 21p; pseudo-dissected: 10p; Occlusion: 1p	OCT	PCI with DES 31; Conservative 3	Not mentioned
Cho JM <i>et al.</i> (11)	1M	silent ischemia	LAD	Haziness	OCT	Not disclosed	Not mentioned
Kato M <i>et al.</i> (12)	1M	silent ischemia	RCA	Occlusion	OCT	Not disclosed	Not mentioned
Estévez-Loureiro R <i>et al.</i> (13)	1M	SCAD	LAD	Pseudo-dissected	both	Not disclosed	Not mentioned
Toutouzias K <i>et al.</i> (14)	1M	STEMI	LAD	Haziness	OCT	PCI with DES	Embolic
Gómez-Monterrosas O <i>et al.</i> (15)	1M	STEMI	LAD	Haziness	OCT	Bioresorbable scaffold	Not mentioned
Koyama K <i>et al.</i> (16)	1M	STEMI	RCA	Braided	OCT	PCI with DES	Not mentioned
Musashi M <i>et al.</i> (17)	1M	SCAD	LAD	Haziness	OCT	PCI with DES	Embolic
Yang DH <i>et al.</i> (18)	1M	UA	LAD	Occlusion	OCT	Not disclosed	Not mentioned
Watanabe Y <i>et al.</i> (19)	1M	SCAD	LAD	Haziness	OCT	Drug eluting balloon	Not mentioned
Suzuki S <i>et al.</i> (20)	1M	silent ischemia	RCA	Haziness	OCT	PCI with DES	Embolic
Kimura T <i>et al.</i> (21)	1M	SCAD	RCA	Haziness	OCT	PCI with DES	Embolic
Seike F <i>et al.</i> (22)	1M	silent ischemia	LAD	Haziness	OCT	PCI with DES	Embolic
Dai K <i>et al.</i> (23)	1M	undeclared	RCA	Occlusion	OCT	Not disclosed	Not mentioned
Karamasis GV <i>et al.</i> (24)	1M	SCAD	LAD	Haziness	IVUS	PCI with DES	Not mentioned
Haraki T <i>et al.</i> (25)	1M	SCAD	LAD	Pseudo-dissected	IVUS	PCI with DES	Embolic
Silenzi S <i>et al.</i> (26)	1M	silent ischemia	RCA	Braided	OCT	PCI with DES	Not mentioned
Niizeki T <i>et al.</i> (27)	1M	UA	RCA	Haziness	OCT	Not disclosed	Not mentioned
Khoueiry GM <i>et al.</i> (28)	1M	silent ischemia	RCA	Haziness	OCT	PCI with DES	Not mentioned
Fujino Y <i>et al.</i> (29)	1M	SCAD	LCX	Occlusion	OCT	PCI with DES	Not mentioned
Sakurai S <i>et al.</i> (30)	1M	SCAD	RCA	Braided	both	Not disclosed	Spontaneous dissection
Lin M <i>et al.</i> (31)	1M	SCAD	RCA	Haziness	both	PCI with DES	Spontaneous dissection
Kadowaki H <i>et al.</i> (32)	1M	SCAD	LAD	Haziness	OCT	PCI with DES	Embolic

M: Male; F: female; STEMI: acute ST elevated myocardial infarction; NSTEMI: acute non-ST elevated myocardial infarction; UA: unstable angina; SCAD: stable coronary artery disease; LAD: left anterior descending coronary artery; RCA: right coronary artery; LCX: left circumflex coronary artery; OCT: optical coherence tomography; IVUS: intravascular ultrasound; PCI: percutaneous coronary intervention; DES: drug-eluting stent; p: patients.

The reported angiographic aspect was described as braided in 24 cases (10, 16, 25, 30), as haziness in 18 cases (2, 3, 10, 11, 14, 15, 17, 19-22, 24, 27, 28, 31, 32), as pseudo-dissection in 15 cases (3, 10, 13, 25) and as occlusions in 5 cases (10, 12, 18, 23, 29). Our study shows that only 14.3% of the CA suspected SRCT cases (4 out of 28) were truly OCT confirmed SRCT. Another finding of our study is that the angiographic combination of braided and pseudo-dissection aspect is highly suggestive for SRCT (3 out of the 28 suspected SRCT and all 3 being confirmed as truly SRCT).

All our 4 patients with confirmed SRCT lesion had borderline CA lesions, but significant OCT stenosis. OCT also identified longer lesion length, as compared to CA

alone, therefore supporting optimal PCI material selection. We performed PCI on our first three patients based on strong clinical (ACS), ECG and echocardiogram findings suggesting ischemia and myocardium viability. Beside the acuteness of the clinical picture, our decision to perform immediate PCI was also supported by data from previous papers suggesting a greater hemodynamic impact of SRCT than that expected from stenosis severity (2). The discordance between lumen reduction and symptomatic impact may be due to the tortuosity of the channels (2). Therefore, even if SRCT lesion is not significant on CA, the blood flow might be severely impaired, due to SRCT spatial conformation (2). In the largest registry to date of SRCT lesions, PCI was performed immediately in 91% of

cases (10). The same study has shown an OCT measured lumen reduction between 20 and 93% (10). Assessment of SRCTs with fractional flow reserve (FFR) would have been of great interest because there are no data about its functional impairment. Nevertheless, there are several reports (41, 42) that suggest that the use of FFR in settings of ACS is associated with greater risks when compared to SCAD.

Besides the crucial role of OCT in providing lesion severity assessment, identification of SRCT as target lesion provided a support for immediate PCI, as mentioned above, as well as it helped us in the process of selecting PCI materials and assessment of post PCI result. It is well known the fact that sub-optimal PCI result (malposition, edge-dissection, under-expansion) is responsible for future MACCE, thus, the use of OCT for PCI guidance enriches the chances for a good immediate and late outcome (5).

In our group, there was symptomatic improvement in all these patients after revascularization. For the fourth patient a conservative treatment approach was established, due to imagistic findings of LV anterior wall and apex necrosis areas without viability at myocardial scintigraphy. There were no MACCE reported during the follow-up period.

Our treatment approach was similar to previous data, represented by the 62 reported SRCT cases, of whom most had PCIs: DES placement in 49 cases (2, 10, 14, 16, 17, 20-22, 24-26, 28, 29, 31, 32), bioresorbable vascular scaffolds implantation in one case (15) and drug eluting balloon angioplasty in another one case (19). Conservative treatment was selected for 3 cases (2, 10), suggesting a non-significant lesion, while the treatment option was not disclosed in the remaining 8 reported cases (3, 11-13, 18, 22, 27, 30).

The SRCT underlying mechanism is not known. A possible cardio-embolic origin was suggested in 7 reported cases (14, 17, 20-22, 25, 32). Post-dissection thrombus was suggested in two reported cases (30, 31). In the other reported cases, the suspected SRCT pathogenic mechanism is not mentioned.

OCT performed in our SRCT cases support the thesis of coronary wall complications as the origin for thrombus formation. We believe that in two of our four patients, OCT identified coronary wall *in situ* dissection of an atherosclerotic plaque, while a spontaneous dissection of a normal coronary wall was the nidus for thrombus formation in the third and fourth patients. Arguments for spontaneous dissection are absence of any atherosclerotic markers and embolic sources and, respectively, in the fourth case, the length and the dilatation of the coronary vessel (a lesion too long to represent an embolus or *in situ* thrombosis).

Topography of SRCT lesions, in our cases, was similar to the one in the literature, the affected coronary arteries being LAD in 26 cases (2, 10, 11, 13-15, 17-19, 22, 24, 25, 32), RCA in 32 cases (2, 10, 12, 16, 20, 21, 23, 26-28, 30, 31)

and LCX in 4 cases (10, 29). Diagonal artery is found in our study to be site for SRCT, too.

SRCT were identified, in our study, as culprit or non-culprit lesions for ACS patients. Data from the literature show that the 62 SRCT lesions may be asymptomatic - 20 cases (10-12, 20, 22, 26, 28) or symptomatic, associated with stable CAD - 23 cases (2, 10, 13, 17, 20, 21, 24, 25, 29-32), UA - 5 cases (2, 18, 27) or acute STEMI - 12 cases (2,10,14-16). Other two cases had an undeclared clinical condition (3, 23).

Gender prevalence related to SRCT is similar, in our study, to the reports in the literature. SCRT lesions has apparently a higher prevalence in men: 3 out of 4 in our study and 44 out of 62 in previously reported patients (2, 3, 10-32).

OCT was the only SRCT imaging method for our study, as it was for 56 of the 62 cases reported in the literature (2, 10-12, 14-23, 26-29, 31). IVUS was used in 3 cases (3, 24, 25), while both OCT and IVUS were used in other 3 cases (13, 30, 31). Terms used for SRCT description were "honeycomb-like structure" - 13 cases (14-17, 19-22, 25-28, 31), "lotus root structure" - 38 cases (3, 10, 12, 23, 30, 32), "swiss cheese structure" - 8 cases (2, 18, 25) and SRCT in only 3 cases (11, 13, 24).

Our study illustrates OCT real-life clinical use in SRCT management, not only for diagnosis and therapeutic decisions role, but also contribute to the understanding of SRCT lesions underlying mechanisms.

Limitations. Our study is an observational, retrospective one, with a small number of patients. We should point out that some short SRCTs, with a small number of lumens might be misconsidered as simple complicated atherosclerotic plaques, or worse, might remain simply unrecognized. Also, for the objective identification of hemodynamic lesion impairment, a fractional flow reserve assessment would have been of great interest.

OCT pitfalls. OCT has few disadvantages represented by a slightly increase in operating times, contrast agent volume and procedural complications. These disadvantages are overwhelmed by the net advantages offered by OCT use in interventional cardiology, by providing the third dimension to CA, which reflects in the correct diagnosis and, respectively, in a better procedural and clinical outcome. In the specific situation of SRCT, the stenosis severity assessed by OCT may be underestimated as the hemodynamic impact is driven also by the tortuosity of the channels (2).

Conclusion

SRCT is a very rare *in vivo* appearance, with a nonspecific angiographic aspect of haziness, braided and pseudo-dissected filling defect. OCT allowed SRCT diagnosis,

accurate lesion assessment, optimal PCI materials selection and, more important, improved characterization of SRCT pathogenic mechanisms, in the four confirmed SRCT cases, supporting the role of coronary wall *in situ* complications, namely dissection of an atherosclerotic plaque or spontaneous dissection of a normal coronary wall.

Conflicts of Interest

The Authors declare that no conflicts of interest exist with regard to the present study.

Authors' Contributions

Conceptualization: Mihail Spinu and Dan Mircea Olinic; Data curation: Mihail Spinu and Calin Homorodean; Formal analysis: Calin Homorodean and Maria Olinic; Investigation: Calin Homorodean, Mihai Claudiu Ober and Dan Mircea Olinic; Methodology: Calin Homorodean, Mihai Claudiu Ober, Maria Olinic and Dan Mircea Olinic; Project administration: Mihail Spinu and Petru Adrian Mircea; Resources: Maria Olinic; Software, Mihail Spinu, Calin Homorodean and Mihai Claudiu Ober; Supervision: Petru Adrian Mircea and Dan Mircea Olinic; Validation: Petru Adrian Mircea and Dan Mircea Olinic; Visualization: Petru Adrian Mircea; Writing – original draft: Mihail Spinu; Writing – review & editing: Dan Mircea Olinic.

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