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Spontaneous Coronary Artery Dissection

Long-Term Follow-Up of a Large Series of Patients Prospectively Managed With a "Conservative" Therapeutic Strategy

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Objectives This study sought to assess the long-term clinical outcome of patients with spontaneous coronary artery dissection (SCD) managed with a conservative strategy.

Background SCD is a rare, but challenging, clinical entity.

Methods A prospective protocol, including a conservative management strategy, was followed. Revascularization was only considered in cases with ongoing/recurrent ischemia. Inflammatory/immunologic markers were systematically obtained.

Results Forty-five consecutive patients (incidence 0.27%) were studied during a 6-year period. Of these, 27 patients (60%) had "isolated" SCD (I-SCD), and 18 had SCD associated with coronary artery disease (A-SCD). Age was 53 ± 11 years, and 26 patients were female. Most patients presented with an acute myocardial infarction. SCD had a diffuse angiographic pattern (length: 31 ± 23 mm). In 11 patients, the diagnosis was confirmed by intracoronary imaging techniques. Sixteen patients (35%) required revascularization during initial admission. One patient died after surgery, but no additional patient experienced recurrent myocardial infarction. No significant inflammatory/immunologic abnormalities were detected. At follow-up (median 730 days), only 3 patients presented with adverse events (1 died of congestive heart failure, and 2 required revascularization). No patient experienced a myocardial infarction or died suddenly. Event-free survival was similar (94% and 88%, respectively) in patients with I-SCD and A-SCD. Notably, at angiographic follow-up, spontaneous "disappearance" of the SCD image was found in 7 of 13 (54%) patients.

Conclusions In this large prospective series of consecutive patients with SCD, a "conservative" therapeutic strategy provided excellent long-term prognosis. Clinical outcome was similar in patients with I-SCD and A-SCD. The natural history of SCD includes spontaneous healing with complete resolution. (J Am Coll Cardiol Intv 2012;5:1062–70) © 2012 by the American College of Cardiology Foundation

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Spontaneous coronary artery dissection (SCD) remains a rare, but challenging, entity. In 1931, Pretty (1) published the first case, and Forker et al. (2) reported the first angiographic diagnosis. Since then, fewer than 400 cases have been reported (3–5). Previous publications on SCD are based on single cases or relatively small series with retrospective design and without long-term follow-up (6–13).

The pathophysiology of SCD remains poorly understood (3–5). SCD may be the result of an intimal rupture with subsequent disruption of the vessel wall leading to a double lumen (true and false lumens). Alternatively, bleeding of the vasa vasorum may result in an intramural hematoma. Progressive—pressure-driven—enlargement of the false lumen or intramural hematoma may cause further separation of the dissected layers, with true lumen compression resulting in myocardial ischemia or infarction (5). SCD may occur as an isolated phenomenon (I-SCD) or associated with coronary artery disease (CAD) (A-SCD) (3–5). Coronary angiography is the most widely used diagnostic technique in this condition (2,3,5). Angiography, however, is unable to visualize the vessel wall and has a limited diagnostic accuracy. In this setting, novel tomographic techniques, such as intravascular ultrasound (IVUS), optical coherence tomography (OCT), or multislice computed tomography (MSCT), provide unique diagnostic insights (14,15).

Management of patients with SCD remains highly controversial. In particular, the value of specific medical regimens or coronary revascularization over a conservative medical management remains unsettled (6–13). In this study, we sought to assess the clinical and angiographic characteristics, management, and long-term outcome of a large cohort of consecutive patients with SCD. Findings of patients with I-SCD were compared with those of A-SCD. An exhaustive screening for immunologic and inflammatory markers was systematically performed. Finally, the value of a conservative management strategy was prospectively assessed.

Methods

Patients and definitions. From January 2004 to May 2010, 45 consecutive patients with SCD were diagnosed at our institution. During this time period, a total of 16,813 first coronary angiographies were performed, and the characteristics of individual coronary lesions were prospectively reported in a dedicated, relational database. This database specifically included the term "SCD" among the diagnostic variables. However, to avoid missing any patient with SCD, an additional retrospective search was performed, retrieving from the database all the reports that included the description of "dissection" or "filling defects." After a careful initial screening, 2 experienced interventional cardiologists jointly reviewed all corresponding coronary angiograms. Vessels with a prior coronary intervention and those with iatrogenic coronary dissections were excluded. In addition, patients with a prior myocardial infarction (with or without previous thrombolysis) presenting linear intracoronary filling defects, compatible with residual thrombus at the culprit vessel, were also excluded.

SCD was defined as a longitudinal radiolucent linear image (intimal flap) detected by angiography in at least 2 orthogonal projections and confirmed by 2 experienced observers (5). In addition, patients with the clinical suspicion of SCD and lesions not fulfilling this classical angiographic pattern but in whom the diagnosis was eventually established by a tomographic imaging technique (OCT, IVUS, MSCT) were also included (14,15). The diagnosis of SCD was confirmed in 45 consecutive patients that constitute the study population.

Coronary angiography. Coronary angiographic studies were performed by a femoral or radial approach. Intracoronary nitroglycerin was administered to all patients, and multiple angulated angiographic projections were obtained. SCD were classified according to the National, Heart, Lung, and Blood Institute (NHLBI) classification (16) and to the presence or absence of concomitant CAD. Associated CAD was defined as at least 1 coronary lesion (different from the SCD lesion) with a diameter stenosis >50% on visual assessment. The Thrombolysis In Myocardial Infarction (TIMI) flow grade classification was also used to characterize SCD lesions (17).

Offline quantitative coronary angiography (QCA) (CASS II System, Pie Medical, Maastricht, the Netherlands) was performed by experienced personnel blinded to clinical outcome, using standard methodology. At the site of dissection, the operator only corrected the path line (automatically displayed by the system) to ensure appropriate measurements of the minimal lumen diameter, disregarding the outer edge of the dissected vessel, as previously described (18). Reference segment, minimal lumen diameter, percent diameter stenosis, and lesion length were measured. In selected patients, a late angiographic follow-up was scheduled.

Other diagnostic techniques. Additional tomographic techniques were performed at the criteria of the attending cardiologist in patients with a strong clinical suspicion of SCD (suggestive clinical setting with an isolated, discrete, lumen narrowing and smooth angiographic appearance of the remaining vessels). Time-domain and frequency-domain OCT systems (Dragonfly, C7-XR, Light Lab, St. Jude Medical, St.

Abbreviations and Acronyms

A-SCD = spontaneous coronary artery dissection associated with coronary artery disease

CAD = coronary artery disease

I-SCD = isolated spontaneous coronary artery dissection

IVUS = intravascular ultrasound

MSCT = multislice computed tomography

NHLBI = National, Heart, Lung, and Blood Institute

OCT = optical coherence tomography

QCA = quantitative coronary angiography

SCD = spontaneous coronary artery dissection

TIMI = Thrombolysis In Myocardial Infarction

Paul, Minnesota) with manual injection of contrast media and the nonocclusive technique were used in 11 patients (15). IVUS studies were performed with commercially available mechanical systems (Atlantis SR Pro, 40-MHz catheter; Boston Scientific) in 3 patients. A 64-detector MSCT (Brilliance scanner, Philips Medical Systems, Best, the Netherlands) was used in 2 patients. A double-lumen morphology or an image of intramural hematoma established the diagnosis of SCD with any of these tomographic techniques (14,15).

Clinical protocol, adverse events, and follow-up. Clinical, angiographic, and biological data were prospectively collected during hospital stay. A dedicated database was designed for the purposes of the study. Serial electrocardiograms and cardiac markers were obtained in all patients. In the I-SCD group, a detailed clinical and analytical screening was systematically performed to detect any potential underlying conditions that might predispose to SCD. Specifically, these patients underwent a full blood analysis, including: blood count, coagulation profile, biochemistry, acute phase reactants (ultrasensitive C-reactive protein, erythrocyte sedimentation rate, fibrinogen, rheumatoid factor, complement, lipoprotein apolipoprotein A/B), lipid profile, thyroid function tests, and a full antibody screening (anti-nuclear, anti-DNA, anti-histone, anti-RNP, anti-SSB, anti-SSA, anti-Sm, anti-Scl 70, anti–Jo-1, anti-centromere, anti-cardiolipin, anti-myeloperoxidase, anti-protease, and anti-glomerular basement membrane antibodies). Immunoglobulins (IgG, IgA, IgM) were also assessed.

All patients with SCD were prospectively followed up with clinical interviews using a structured questionnaire. In these visits, an echocardiogram, exercise test, and blood analyses were obtained. For deceased patients, information was obtained directly by telephone from the family or responsible cardiologist. Primary clinical endpoint was a composite of cardiac death (any death that could not be attributable to a noncardiac cause), nonfatal myocardial infarction, and the need for target vessel revascularization. Myocardial infarction was defined as a rise in cardiac markers (creatine phosphokinase more than twice the upper normal value; troponin >99th percentile of the upper reference limit), associated with typical chest pain or electrocardiographic changes.

This prospective protocol, including the initial conservative management strategy, the exhaustive inflammatory-immunologic screening, the selective use of additional tomographic techniques, and the long-term clinical follow-up, was approved by the Institutional Ethics Committee. Informed consent was obtained from all patients.

Statistical analysis. Qualitative data were presented as values and percentages and continuous data as mean ± SD or median (interquartile range [IQR]) values (normality assessed with the Kolmogorov-Smirnov test). Comparison between groups (I-SCD vs. A-SCD) was performed using the chi-square or Fisher exact tests for categorical variables and the Student *t* test or the nonparametric Mann-Whitney *U* test for continuous variables. Event-free survival curves were computed according to the Kaplan-Meier method. Survival estimates were compared with the log-rank and Breslow tests. A p value <0.05 was considered statistically significant.

Results

Baseline clinical characteristics. A total of 45 consecutive patients presented with SCD. This resulted in an estimated incidence of the condition of 0.27%. Of these, 27 (60%) had I-SCD and 18 had A-SCD (Fig. 1). Table 1 displays baseline characteristics in the 2 groups. Patients were relatively young, and women were more frequently found in the I-SCD group. A high rate of classical coronary risk factors was found in the 2 groups, but especially in the A-SCD group. Interestingly, only 1 patient in the I-SCD group presented in the postpartum period, another had had early menopause, and a third patient was taking oral contraceptives. Most patients presented with an acute myocardial infarction, but ST-segment elevation myocardial infarction occurred more frequently in I-SCD patients (Table 1).

Main angiographic findings are displayed in Table 2. Half of the lesions were located in the left anterior descending coronary artery, and this vessel was more frequently involved in the I-SCD group. Mid coronary segments were often affected, but diffuse involvement of the entire vessel was found in 5 patients. Involvement of at least 2 major coronary branches was seen in 5 patients (in 1 patient, the

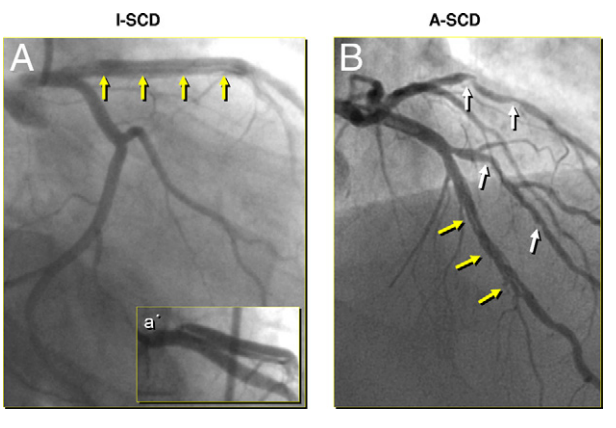

Figure 1. Angiographic Findings in a Patient With I-SCD and in a Patient With A-SCD

Angiographic findings in a patient with isolated spontaneous coronary artery dissection (I-SCD) **(A)**, and in a patient with associated coronary artery disease (A-SCD) **(B)**. **Yellow arrows** denote the angiographic intimal flap. **White arrows** denote atherosclerotic lesions. **(a')** Magnified image.

Table 1. Baseline Demographic and Clinical Characteristics

	I-SCD (n = 27)	A-SCD (n = 18)	Total (N = 45)	p Value
Age, yrs	52 ± 10	56 ± 12	53 ± 11	NS
Women	23 (85%)	3 (17%)	26 (58%)	0.001
Coronary risk factors				
Smoking	14 (52%)	14 (78%)	28 (62%)	NS
Dyslipidemia	9 (33%)	8 (44%)	17 (38%)	NS
Hypertension	10 (37%)	5 (28%)	15 (33%)	NS
Diabetes mellitus	1 (4%)	4 (22%)	5 (11%)	NS
≥3 Risk factors	1 (4%)	4 (22%)	5 (11%)	0.075
Other conditions				
Postpartum	1 (4%)	0 (0%)	1 (2%)	NS
Early menopause	1 (4%)	0 (0%)	1 (4%)	NS
Oral contraceptives	1 (4%)	0 (0%)	1 (2%)	NS
Clinical presentation				
Acute coronary syndrome	23 (85%)	11 (61%)	34 (76%)	NS
STEMI	14 (52%)	4 (22%)	18 (40%)	0.037
NSTEMI	9 (33%)	7 (39%)	16 (36%)	NS
Other	4 (15%)	7 (39%)	11 (24%)	NS
Stable angina	0 (0%)	4 (22%)	4 (9%)	NS
Dyspnea	1 (4%)	0 (0%)	1 (2%)	NS
Silent ischemia	3 (11%)	3 (17%)	6 (13%)	NS
Peak CK	947 ± 1,573	711 ± 704	853 ± 1,291	NS
Peak TnI	59 ± 217	55 ± 52	46 ± 171	NS

Values are mean ± SD or n (%).

A-SCD = spontaneous coronary artery dissection associated with coronary artery disease; CK = creatine kinase; I-SCD = isolated spontaneous coronary artery dissection; NSTEMI = non–ST-segment elevation myocardial infarction; NS = not significant; STEMI = ST-segment elevation myocardial infarction; TnI = Troponin I.

SCD affected the left main stem and the left anterior descending and circumflex coronary arteries, and in 4, involved the left anterior descending coronary artery and at least 1 diagonal branch). The NHLBI dissection classification is depicted in Table 2. Of note, 9 cases just showed a confined lumen narrowing and were considered as angiographically unclassifiable. In these 9 patients, the diagnosis of SCD could only be established using adjuvant imaging diagnostic techniques (OCT in 9, IVUS in 3, and MSCT in 2 patients) (15) (Fig. 2). In 2 additional cases, with clear angiographic intimal flaps, OCT just confirmed a previous angiographic diagnosis.

QCA analysis showed that most lesions had a diffuse pattern (length: 31 ±23 mm, with a tendency for longer lesions in the I-SCD group), and were located in relatively small vessels (Table 2). However, stenosis severity was similar in both groups. In the A-SCD group, 12 patients showed additional 1-vessel disease, and 6 had additional 2-vessel disease.

Initial management. At diagnosis, the initial therapeutic strategy was always conservative medical management. Of the 18 patients presenting with ST-segment elevation myocardial infarction (Table 1), 8 received thrombolysis in another center before the diagnosis of SCD could be established, 4 underwent primary angioplasty, and 6 were not revascularized initially: 4 were asymptomatic with angiography >12 h of symptom onset (2 of these eventually were revascularized during hospitalization), and 2 patients, with ongoing mild chest pain, were not treated as the result of very distal/diffuse disease. Medical therapy did not differ from standard therapy for patients with acute coronary syndromes. Anticoagulation was used in 35 patients (3 unfractionated heparin, 32 low-molecular-weight heparin) and IIb/IIIa glycoprotein platelet inhibitors in 12 patients (maintained for 2.1 ± 1.2 days).

Overall, 9 patients (20%) required revascularization for ongoing ischemia at the time of diagnosis: 7 were treated with stents, 1 with balloon angioplasty alone, and 1 patient, with SCD involving the left main coronary artery, required coronary surgery (Fig. 3). In a patient with an SCD at the very distal right coronary artery, stent implantation on the proximal vessel was required to seal a large, catheter-induced, remote iatrogenic dissection of the vessel. Two of

Table 2. Angiographic Findings

	I-SCD (n = 27)	A-SCD (n = 18)	Total (N = 45)	p Value
Vessel				
Left main	1 (4%)	0 (0%)	1 (2%)	NS
LAD	18 (67%)	6 (33%)	24 (53%)	0.039
LCX	4 (15%)	3 (17%)	7 (16%)	NS
RCA	4 (15%)	9 (50%)	13 (29%)	NS
Segment				
Proximal	5 (19%)	1 (6%)	6 (13%)	NS
Mid	13 (48%)	13 (72%)	26 (58%)	NS
Distal	5 (19%)	3 (17%)	8 (18%)	NS
Diffuse	4 (15%)	1 (6%)	5 (11%)	NS
Bifurcation	4 (15%)	1 (6%)	5 (11%)	NS
NHLBI classification*				
A-B-C	12 (44%)	10 (56%)	22 (49%)	NS
D-E-F	7 (26%)	7 (39%)	14 (31%)	NS
Unclassified	8 (30%)	1 (6%)	9 (20%)	
TIMI classification				
0–1	7 (15%)	3 (6%)	10 (11%)	NS
2–3	20 (74%)	15 (83%)	35 (78%)	NS
LVEF, %	55 ± 16	56 ± 18	57 ± 16	NS
Quantitative coronary angiography				
Dissection length, mm	37 ± 26	23 ± 16	31 ± 23	0,052
Reference diameter, mm	1.8 ± 0.6	2.1 ± 0.7	1.9 ± 0.6	NS
% diameter stenosis	63 ± 19	66 ± 19	64 ± 19	NS
MLD, mm	0.7 ± 0.4	0.8 ± 0.5	0.7 ± 0.5	NS

Values are n (%) or mean ± SD. *Type A, radiolucent area within the lumen, minimal/no persistence of contrast; Type B, parallel double lumen separated by a radiolucent area with minimal/no persistence of contrast; Type C, persistent presence of contrast outside the lumen; Type D, spiral luminal filling defect; Type E, dissection with persistent filling defect; Type F, dissection with total coronary occlusion.

LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LVEF = left ventricular ejection fraction; MLD = minimal luminal diameter; RCA = right coronary artery; other abbreviations as in Table 1.

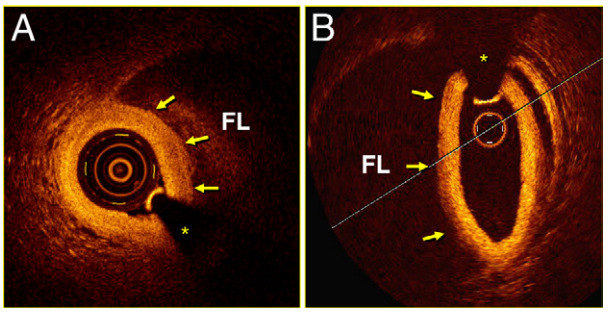

Figure 2. OCT Findings in Patients Without a Classical Intimal Flap

(A) Patient with discrete lumen narrowing in whom optical coherence tomography (OCT) unraveled the presence of an intramural hematoma. **(B)** Patient presenting with an occluded vessel in whom OCT disclosed 2 separate lumens and the intimomedial flap. **Yellow arrows** denote the intimomedial membrane. Notice the OCT catheters located within the true lumen. FL = false lumen. **Asterisk** indicates wire artifact.

these patients initially treated with stents underwent a second intervention with additional stent implantation in segments showing severe residual dissections (1 for recurrent angina and 1 for severe disease progression at the uncovered segment). Another patient had recurrent episodes of angina during hospitalization, but repeated angiography showed persistence of an excellent angiographic result of the previously implanted stent.

Seven additional patients (15%) that initially were managed conservatively required revascularization procedures during hospitalization because of recurrent ischemia. Of these, 5 underwent successful stent implantation, and 1 had a failed procedure due to the impossibility of advancing the guidewire across the target segment. The seventh patient, with A-SCD and severe 3-vessel disease, underwent elective coronary surgery. Unfortunately, this patient experienced a large perioperative myocardial infarction and died in cardiogenic shock. Altogether, 16 patients (35%) required revascularization either at diagnosis for ongoing ischemia (n = 9) or during hospitalization for recurrent ischemia (n = 7), (9 in the I-SCD group and 7 in the A-SCD group). Of the 12 patients treated with stents, 6 received bare-metal stents, 4 drug-eluting stents (all had diffuse disease in small vessels), and 2 both types of stents. In 7 of these patients treated with stents, residual, nonflow-limiting dissections were visualized distal to the stented segment.

Except for the patient dying after coronary surgery, none of these revascularization procedures was associated with recurrent myocardial infarction, and no additional patients had a myocardial infarction or died during hospitalization. Symptoms were controlled by standard antianginal medication. At discharge, 27 patients received dual antiplatelet therapy, and 3 oral anticoagulants. Thirty-six patients received beta-blockers, 3 calcium-channel blockers, and 24 angiotensin system antagonists. Medical therapy was similar in both groups.

Inflammatory and immunologic data. Major concomitant systemic medical illnesses were not found in this series. However, potentially relevant associated diseases were detected in some patients, including dilated cardiomyopathy (n = 1), hypothyroidism (n = 3), essential thrombocytosis (n = 1), hepatitis C/B (n = 4), HIV (n = 1), deep venous thrombosis (n = 3), and neoplasms (n = 2). In addition, most patients did not show any data suggestive of relevant ongoing inflammatory or immunologic processes. However, mild transient inflammatory changes were detected in 9 patients (including abnormal values of erythrocyte sedimentation rate in 4, C-reactive protein in 7, fibrinogen in 4). No patient had fever during admission, and only 1 presented transient leukocytosis with neutrophilia. Eosinophil counts were always within normal values. Finally, no relevant immunologic abnormalities were detected, although minor abnormalities were noticed in 8 patients (including rheumatoid factor in 3 and abnormal immunoglobulin levels in 5 [IgA in 1, anticardiolipin IgG in 2 or IgM in 2]).

Clinical and angiographic follow-up. Median follow-up was 730 days (IQR: 321 to 1,482 days) with no patient lost to follow-up. Only 3 patients experienced adverse events after discharge (none of them had required revascularization during initial hospitalization). A patient with I-SCD and dilated cardiomyopathy (left ventricular ejection fraction: 25%) and recurrent episodes of heart failure died of congestive heart failure 5 years after diagnosis. Two additional patients presented with ischemia and underwent successful revascularization (1 patient [I-SCD] was referred for coro-

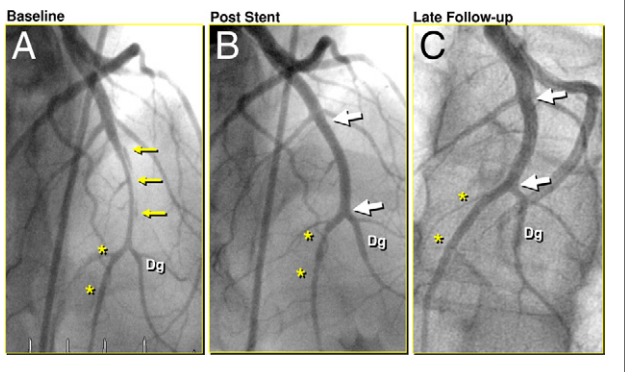

Figure 3. I-SCD in the Left Anterior Descending Coronary Artery Requiring Coronary Stenting for Ongoing Ischemia

(A) Before intervention, a clear angiographic flap is detected **(yellow arrows)** together with a smooth vessel narrowing **(asterisks)** distal to the second diagonal branch (Dg). **(B)** Result after stenting **(white arrows)**. The diagonal branch became transiently occluded and required additional stent implantation in its proximal segment. **(C)** Late angiographic follow-up. Notice the enlargement of lumen diameter at the distal vessel **(asterisks)**, suggesting resolution of intramural hematoma. I-SCD = isolated spontaneous coronary artery dissection.

nary surgery and another [A-SCD] required coronary stenting). No patient experienced sudden death or developed a myocardial infarction during follow-up. Therefore, 3 of 29 patients without initial revascularization (10%) had late events. Alternatively, none of the 15 patients revascularized during initial hospital admission (1 patient died after surgery) experienced adverse events after discharge (specifically, no patient required repeated revascularization for restenosis, and none of the 7 patients with residual "uncovered" dissections after initial stenting had late clinical events).

Event-free survival is presented in Figure 4. As described, most events were the result of myocardial infarction at presentation and revascularization procedures during hospitalization. After discharge, however, long-term clinical outcome was excellent. At 3 years, 94% and 88% of patients in the I-SCD and A-SCD groups, respectively, were free of adverse events. Clinical outcome was comparable in patients with I-SCD and A-SCD (Fig. 4). Furthermore, the angiographic type of SCD was not related with outcome. Five of 14 patients (36%) with D–E dissections required revascularization either during initial admission (n = 4) or at follow-up (n = 1), whereas revascularization was required in 13 of the 31 patients (42%) with A–C/unclassifiable dissections (12 during initial hospitalization, 1 at follow-up) (p = NS). Likewise, TIMI flow grade at presentation was not related to clinical outcome.

Late angiographic follow-up (median time: 262 days, IQR: 175 to 284 days) was obtained in 16 patients (35%) (in 4 for recurrent angina and in 12 asymptomatic patients at a scheduled late angiography). Six of these patients had been initially revascularized with stents (3 with and 3 without residual coronary dissections), and none showed images of residual dissection. Restenosis was only found in an asymptomatic patient without signs of ischemia that eventually was not treated. In the 10 patients with late angiographic follow-up that were not initially revascularized, the dissec-

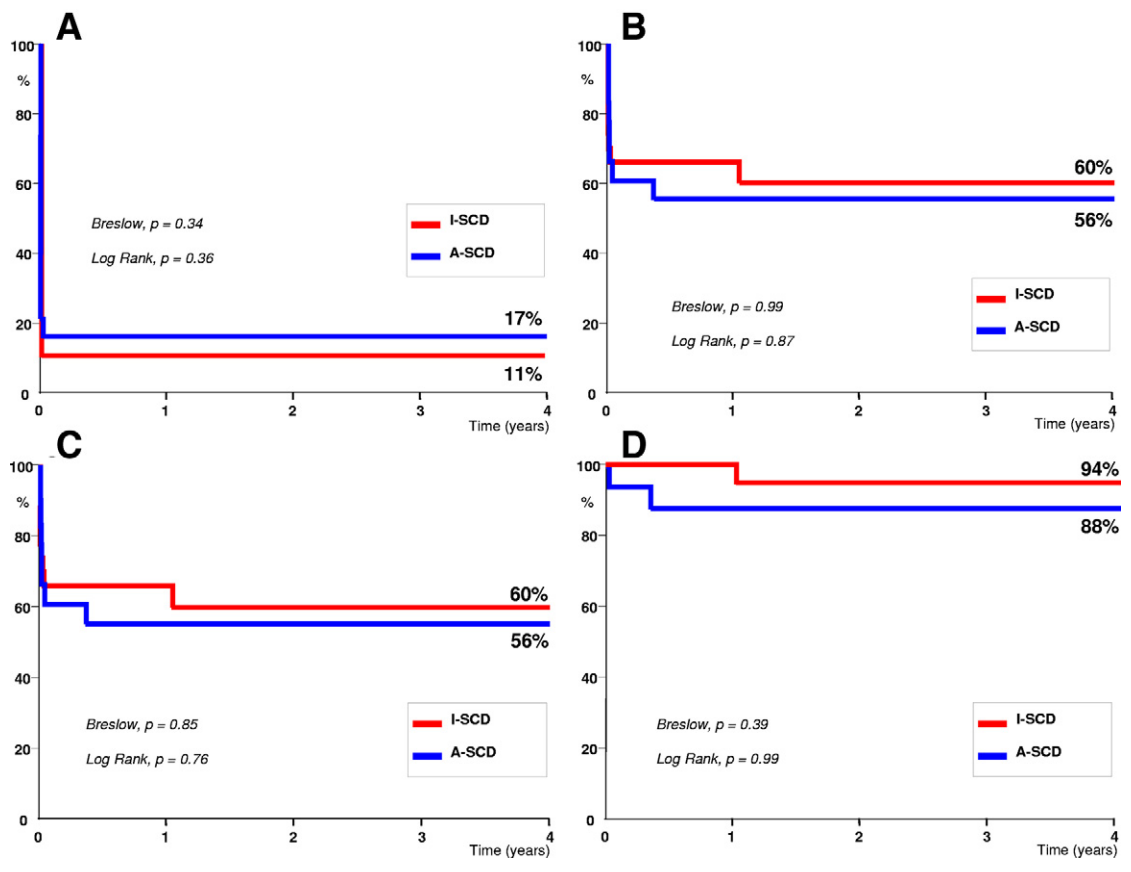

Figure 4. Clinical Outcome of Patients With SCD

(A) Event-free survival (death, myocardial infarction, and target vessel revascularization), including events at clinical presentation. **(B)** Event-free survival (death, myocardial infarction, and target vessel revascularization) from the time of diagnosis of spontaneous coronary artery dissection (SCD) (excluding the presenting clinical events). **(C)** Freedom from target vessel revascularization (most revascularizations occurred during initial hospitalization). **(D)** Event-free survival (death, myocardial infarction, target vessel revascularization) from hospital discharge (landmark analysis). After discharge, prognosis was excellent. A-SCD = SCD associated with coronary artery disease; I-SCD = isolated SCD.

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tion image disappeared in 4, improved in 1, progressed in 2 (the 2 patients requiring late revascularization), and remained unchanged in 3 patients. Eventually, of the 13 patients showing images of SCD at discharge (3 residual and 10 never treated), in 7 (54%), this image spontaneously "disappeared" at follow-up (Fig. 5).

Discussion

To the best of our knowledge, this study reports the largest series of patients with SCD (3–5). In addition, the current study provides the longest clinical follow-up currently available in patients with this rare and unique condition, with no patient lost during clinical follow-up (6–13). Furthermore, our study represents the first prospective study assessing the value of an initial conservative management strategy and including a systematic assessment of inflammatory and immunologic markers.

The main findings of the present study are as follows: 1) SCD is a serious clinical condition with significant initial morbidity mainly related to a presentation as acute myocardial infarction; 2) once the diagnosis of SCD is established, a "conservative" management strategy, defined as selecting revascularization only for patients with ongoing or recurrent ischemia, is associated with an excellent long-term prognosis; 3) in contradistinction to conventional wisdom, patients with "I-SCD" frequently have associated coronary risk factors but seldom present with conditions classically associated with this entity; 4) in most patients, data suggesting a relevant ongoing inflammatory/immune process were not identified; 5) patients with SCD may also have concomitant CAD, but the presence of associated CAD does not appear to bear clinical or prognostic implications (although the small size of the subgroups should be acknowledged); 6) in some patients with strong clinical suspicion of SCD, angiography fails to provide an accurate diagnosis, and additional imaging techniques are required to unravel the diagnosis; and 7) last, but not least, our findings demonstrate that SCD may spontaneously heal at long-term follow-up.

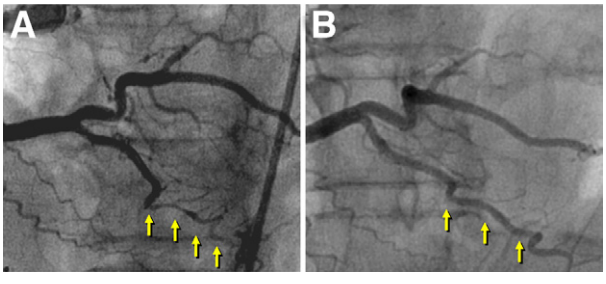

Figure 5. Spontaneous Disappearance of the SCD Image at Follow-Up

(**A**) Patient presenting with an inferior acute myocardial infarction showing an SCD **(yellow arrows)** distally in the posterior descending coronary artery. This lesion was left untreated. (**B**) Complete spontaneous disappearance of the SDC image at late angiographic follow-up.

Comparison with previous studies. The prevalence of SCD in our study is consistent with previous angiographic series, with a prevalence ranging from 0.1% to 1.1% (4,5,11–13). Most studies suggest that SCD occurs predominantly in women, with a 3-fold higher occurrence than in men (11–13). However, in series with associated CAD, the proportion of male patients has been higher (up to 80%) (8,9). We also found that the number of women was significantly higher in the I-SCD group.

Although SCD is considered to predominately affect young individuals, most previous studies have shown otherwise, with the higher prevalence in the 5th/6th decade of life (4,5). Our series, with a mean age of 53 years, is consistent with these observations. Age was similar in patients with and without associated CAD. However, it is important to recognize the existence of very young patients with this condition (12). Accordingly, we support the classical dictum emphasizing that the diagnosis of SCD should always be suspected in young females presenting with acute coronary syndromes (5).

Most studies suggest that acute myocardial infarction is the leading clinical presentation of this entity (4,5). However, some patients present with stable angina, symptomatic ventricular arrhythmias, or even sudden death (4,5). Interestingly, in our series, patients with ST-segment elevation myocardial infarction were more frequently found in the I-SCD than in the A-SCD group.

Present study. This is the first study using QCA to better characterize this condition (18). We found that most lesions were diffuse and affected relatively small vessels. Moreover, we used the NHLBI classification to assess the pattern of SCD (16). Although this classification remains the only available angiographic scheme to assess coronary dissections, it was actually devised to evaluate iatrogenic coronary dissections following interventions. As a result, this system has not been used in most previous studies of SCD (8–13). In our study, 20% of patients were considered as angiographically "nonclassifiable," due to presence of a confined angiographic lumen narrowing without an intimal flap. In these patients, (particularly frequent in the I-SCD group), with discrete coronary lesions and smooth angiographic appearance of the remaining vessels, the use of intracoronary diagnostic techniques was instrumental to confirm the diagnosis. This exhaustive diagnostic strategy, however, was not used in most previous studies. We advocate for a liberal use of these techniques in patients with strong clinical suspicion of the disease (14,15). Our data further suggest that the prognosis of SCD without a visible angiographic intimal flap is favorable and similar to that seen in classical SCD patients. However, the prognosis of "angiographically

silent" SCD (presenting as an intramural hematoma) warrants additional assessment in future studies.

In patients with I-SCD, we performed an exhaustive assessment of biomarkers and inflammatory parameters with a systematic screening for associated systemic conditions. To the best of our knowledge, this information has not been obtained in prior studies, mainly due to their retrospective design (6–13). Many systemic conditions have been associated with a "vulnerable vessel wall" leading to arterial fragility and predisposing to this complication (5). Furthermore, adventitial eosinophilic infiltrates have been reported in necropsy reports (19) However, we failed to identify relevant underlying concomitant conditions in our series. The long list of associated systemic processes has been derived from pooled analysis of sporadic cases (4–5), but clear underlying conditions were rare in most previous series where most SCD patients were classified as idiopathic (6–13). Likewise, spontaneous dissections of cervical and carotid arteries are rare, but potentially related, conditions that may also occur in the postpartum period and associated with SCD (20,21). None of our patients, however, presented with dissection in other vascular territories.

A unique finding of the current study is the presence of spontaneous healing of the vessel wall at follow-up. This phenomenon has been previously reported in anecdotal cases (13). However, our series provides robust evidence that this evolution should indeed be considered as part of the natural history of the disease. Complete disappearance of the dissection image at follow-up occurs, not only in patients with successful conservative management, but also in patients with residual (uncovered) dissections after stenting. It is tempting to speculate that the healing phenomena leading to favorable vessel remodeling in SCD might be similar to that accounting for late healing of iatrogenic dissections after interventions (22,23). Establishing whether or not a "restitutio ad integrum" of the vessel wall eventually occurs in these patients at follow-up would require further insights from intracoronary diagnostic techniques.

Finally, our data suggest that a "watchful waiting" approach should be initially recommended in stable SCD

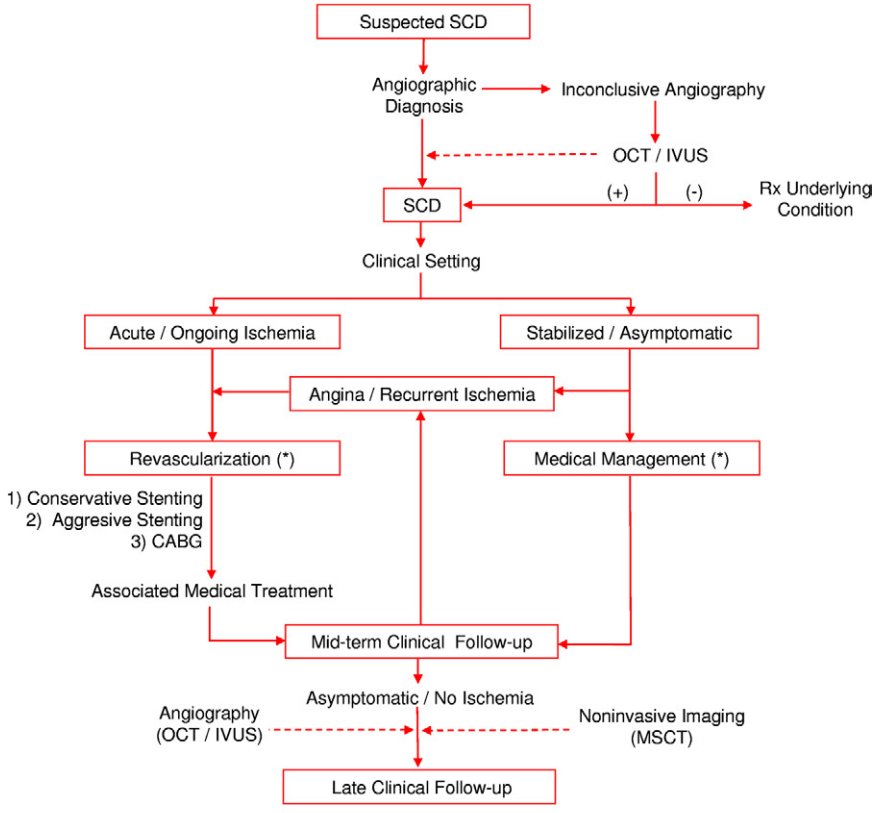

Figure 6. Suggested Algorithm for the Management of Patients With SCD

Broken arrows denote suggestions for only selected patients or with research purposes. *See text for additional considerations regarding revascularization and medical treatment (revascularization may be considered in the acute setting for asymptomatic patients with occluded vessels but should be avoided despite symptoms in small/distal vessels). CABG = coronary artery bypass grafting; IVUS = intravascular ultrasound; MSCT = multislice computed tomography; Rx = Therapy; other abbreviations as in Figures 1 and 2.

patients. A favorable clinical outcome was demonstrated when revascularization was restricted to patients with ongoing/recurrent ischemia. Although good results after a conservative strategy have been reported in selected stabilized SCD patients, previous series indicated revascularization in most patients with suitable anatomy (10–13). Conversely, we propose an initially conservative management strategy for all SCD patients (Fig. 6). However, this "watchful waiting" strategy requires a careful long-term clinical surveillance. Should ischemia recur, revascularization must be reconsidered.

Conclusions

This large prospective study suggests that a conservative initial management represents a reasonable strategy for patients with this rare, but challenging, clinical entity. After initial presentation, the long-term prognosis of SCD patients is favorable and appears to be similar for I-SCD and A-SCD. The possibility of late spontaneous vessel healing provides additional arguments supporting a conservative initial approach.

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Key Words: myocardial infarction ■ optical coherence tomography ■ revascularization ■ spontaneous coronary artery dissection ■ stents.