

Clinical outcomes by angiographic type of spontaneous coronary artery dissection

Ricardo Mori¹, MD; Fernando Macaya^{1*}, MD; Federico Giacobbe², MD; Pablo Salinas¹, PhD; Marco Pavani³, MD; Alberto Boi⁴, MD; Luca Bettari⁵, MD; Cristina Rolfo⁶, MD; Italo Porto⁷, PhD; Nieves Gonzalo¹, PhD; Ferdinando Varbella², MD; Enrico Cerrato⁶, PhD; Javier Escaned¹, PhD

1. Hospital Clínico San Carlos, IdiSSC, Universidad Complutense de Madrid, Madrid, Spain; 2. San Luigi Gonzaga University Hospital, Orbassano, Italy; 3. Ospedale Maggiore SS. Annunziata, Savigliano, Italy; 4. Azienda Ospedaliera Brotzu, Cagliari, Italy; 5. Fondazione Poliambulanza Istituto Ospedaliero, Brescia, Italy; 6. San Luigi Gonzaga University Hospital, Rivoli, Italy; 7. Ospedale Policlinico San Martino, Genoa, Italy

R. Mori, F. Macaya, F. Giacobbe and E. Cerrato contributed equally to this manuscript.

A list of study collaborators can be found in the Appendix paragraph.

This paper also includes supplementary data published online at: <https://eurointervention.pconline.com/doi/10.4244/EIJ-D-20-01275>

KEYWORDS

- ACS/NSTE-ACS
- spontaneous dissection
- STEMI

Abstract

Background: Spontaneous coronary artery dissection (SCAD) is an increasingly diagnosed cause of myocardial infarction. Although different SCAD angiographic classifications exist, their clinical impact remains unknown.

Aims: The aim of this study was to evaluate the relationship between an angiographic classification and the development of adverse clinical events during the follow-up of a large, unselected cohort of patients with SCAD.

Methods: We conducted an observational study of consecutive SCAD patients from 26 centres across Italy and Spain. Cases were classified into five different angiotypes according to the latest classification endorsed by the European Society of Cardiology. The main composite endpoint included all-cause death, non-fatal myocardial infarction (MI), and any unplanned revascularisation.

Results: In total, 302 SCAD patients (mean age 51.8±19 years) were followed up for a median of 22 months (IQR 12-48). At 28 days, the composite outcome was higher for the angiotypes with a circumscribed contained intramural haematoma (2A and 3): 20.0% vs 5.4%, $p<0.001$ (non-fatal MI: 11.0% vs 3.5%, $p=0.009$; unplanned revascularisation: 11.0% vs 2.5%, $p<0.001$). This was sustained during follow-up (24.5% vs 9.9%, $p=0.001$). There were no differences in mortality (0.3% overall). The presence of an angiotype 2A or 3 was an independent predictor of a higher incidence of the composite outcome (adjusted HR 2.44, CI: 1.24-4.80, $p=0.010$).

Conclusions: The SCAD angiographic classification correlates with outcome. Those presenting with an angiographically circumscribed contained intramural haematoma (angiotypes 2A and 3) showed an increased risk of short-term adverse clinical events that was maintained during follow-up.

*Corresponding author: Hospital Clínico San Carlos, Calle del Prof Martín Lagos s/n, 28040 Madrid, Spain.
E-mail: fernando@macaya.eu

Abbreviations

ACCA	Acute Cardiovascular Care Association
ESC	European Society of Cardiology
IMH	intramural haematoma
IVUS	intravascular ultrasonography
MACE	major adverse cardiovascular events
MI	myocardial infarction
PCI	percutaneous coronary intervention
SCAD	spontaneous coronary artery dissection
TIMI	Thrombolysis In Myocardial Infarction

Introduction

Spontaneous coronary artery dissection (SCAD) is a condition that predominantly affects middle-aged women, causing myocardial infarction (MI), cardiac arrest, and cardiac death¹. SCAD can be defined as the acute and spontaneous development of a false lumen within the coronary artery wall that leads to flow limitation by compression of the true coronary lumen (with this definition excluding dissections caused by complicated atherosclerotic disease, iatrogenic factors or related to direct trauma)². Although SCAD has largely been overlooked as a cause of acute coronary syndromes, the expanded use of coronary angiography and intracoronary imaging techniques in patients presenting with acute coronary syndrome has led to an increased awareness of this condition³.

From a pathological perspective, the hallmark of SCAD is the intimomedial flap that separates the true and false lumens. Two different patterns have been identified: the communicated double lumen – fenestrated SCAD – and the contained intramural haematoma (IMH) – non-fenestrated SCAD¹. On the other hand, the angiographic manifestation of these two pathological substrates is more diverse. In a study by Waterbury et al on conservatively managed SCAD, angiographic presentation as IMH entailed a greater risk of early clinical progression compared to the angiographic radiolucent flap and linear double lumen (intimomedial tear with communication between false and true lumens) after adjusting by several confounders⁴. García-Guimaraes et al reported similar findings from a large multicentre registry, in which type 2 SCAD, defined by the presence of long contained IMH (>20 mm), resulted in being an independent predictor of in-hospital MACE⁵.

Different classifications have been developed to depict the rich angiographic spectrum of SCAD^{2,6,7}, which has contributed to the knowledge of this entity. However, we are still uncertain whether the use of these classification systems has clinical or therapeutic implications. In this study, we aimed to evaluate the relationship between an angiographic classification and the development of adverse clinical events during the follow-up of a large, unselected cohort of patients with SCAD.

Editorial, see page 447

Methods

STUDY DESIGN AND POPULATION

DISCO-IT/SPA (Dissezioni Spontanee COronariche Italian-SPANish) (ClinicalTrials.gov identifier: NCT04415762) was an

observational, international, multicentre, retrospective registry which enrolled SCAD patients from 23 centres in Italy and Spain. Details regarding eligibility and data collection are provided in **Supplementary Appendix 1**.

ANGIOGRAPHIC ANALYSIS AND CLASSIFICATION

Diagnosis confirmation and subsequent classification into five angiographic categories or angiotypes (**Figure 1**) was performed through a two-step core lab process. A detailed description is provided in **Supplementary Appendix 2**.

FOLLOW-UP AND OUTCOMES

Patients were followed up routinely after discharge by telephone/office contact at 1, 6, and 12 months, and annually thereafter. Follow-up was censored at four years. Clinical outcomes included all-cause death, non-fatal MI (fourth universal definition of myocardial infarction⁸), any unplanned revascularisation, stroke, or Bleeding Academic Research Consortium (BARC) bleeding events. Only BARC type 2 or greater bleeding events were considered. The latter outcome was only collected for the first four weeks. The primary outcome was a composite of major adverse cardiovascular events (MACE), which consisted of all-cause death, non-fatal MI, and any unplanned revascularisation. MACE were analysed and reported at 28 days (4 weeks) and at a maximum of 4 years of follow-up. Percutaneous coronary intervention (PCI) success was defined as Thrombolysis In Myocardial Infarction (TIMI) flow 2-3 with residual stenosis <30% (after stent/scaffold implantation) or <50% (after simple balloon angioplasty).

STATISTICAL ANALYSIS

This section is reported in **Supplementary Appendix 3**.

Results

PATIENT CLINICAL CHARACTERISTICS

We retrospectively enrolled 302 patients with complete follow-up at a minimum of six months. Overall, mean age was 51.8±10 years (range 23-84 years) and there was a female preponderance (88.4%). Among women with SCAD, 13.2% were receiving hormonal therapy. No significant differences were noted among the different groups with regard to baseline characteristics (**Table 1**), except that more patients with angiotype 1 presented with a recent pregnancy and that more patients with angiotype 2B presented with a postmenopausal status. With regard to clinical presentation (**Table 2**), 48.0% presented with ST-elevation MI (STEMI) and 45.0% with non-ST-elevation MI (NSTEMI). Patients with angiotype 4 (TIMI 0) presented more often with STEMI than the other angiotypes (71.6% angiotype 4 vs 39.3% non-angiotype 4, $p<0.001$).

ANGIOGRAPHIC FEATURES, MANAGEMENT, AND PROCEDURAL OUTCOME

Angiographic characteristics are described in **Table 2**. Half of the 302 patients included had angiotype 2 (49.3%), these being 26.5% 2A and 22.8% 2B. The other half comprised angiotype 4

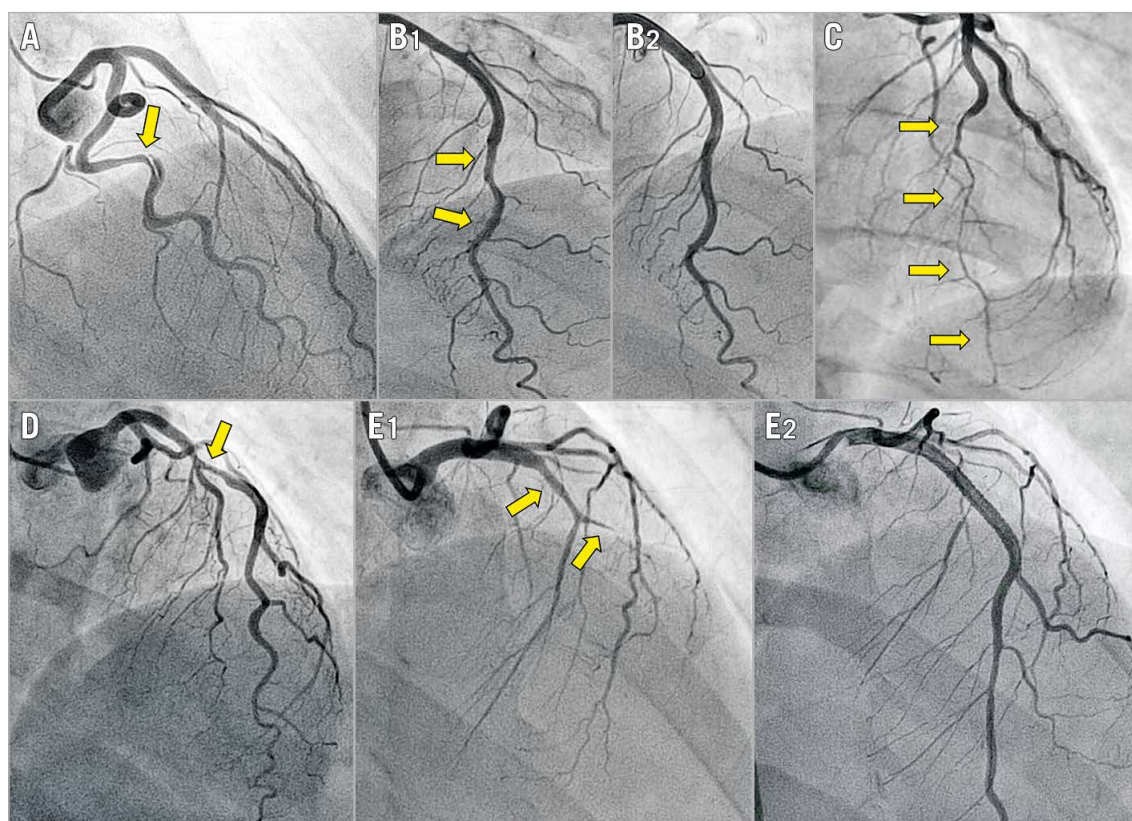


Figure 1. Angiographic classification of SCAD. Arrows indicate the dissected segments. A) Angiotype 1, radiolucent flap or dual lumen. B1) Angiotype 2A, long (>20 mm) narrowing with distal calibre recovery. B2) Vessel restoration three months after conservative management of B1. C) Angiotype 2B, long (>20 mm) narrowing involving the main distal vessel. D) Angiotype 3, focal (<20 mm), sometimes tubular stenosis. E1) Angiotype 4, total occlusion of the main vessel. E2) Flow restoration after stenting.

(26.8%), followed by angiotype 1 (17.2%) and, lastly, angiotype 3 (6.6%). The majority of SCAD involved a single coronary artery territory (88.1%), the most common one being the left anterior descending artery and/or its branches (54.3%). However, angiotype 3 was seen more often in the left circumflex artery (65%). Mean angiographic stenosis was 85.7% (SD±17.4%) and mean dissection length was 40.3 mm (SD±24.3 mm). Procedural characteristics and management are described in **Table 3**. Most patients (n=198, 65.6%) were managed conservatively as the initial strategy, with significant differences among angiotypes (more revascularisation in angiotypes 1 and 4). Intracoronary imaging was used in 27.8% (n=84) of the patients. Optical coherence tomography (OCT) was used more frequently in patients with angiotypes 2A and 3 (22.0% vs 10.3%, p=0.03). Moreover, 100 patients underwent *ad hoc* PCI (33.1%), 78% of which were adjudicated as successful in the core laboratory. Common complications included false lumen stenting and proximal and/or distal dissection propagation. Four patients (1.3%) underwent coronary artery bypass graft (CABG) surgery as first therapeutic option.

SHORT- AND LONG-TERM CLINICAL EVENTS

The median hospital stay was 6 (IQR 5-8) days. At the time of discharge, a total of 120 patients (39.7%) had undergone

revascularisation (38.4% PCI and 1.3% CABG). Most patients were discharged home on aspirin (96.6%), and P2Y₁₂ inhibitors (76.8%) – with 75.5% on a dual antiplatelet regimen, beta-blockers (81.3%) and statins (70.5%). **Supplementary Table 1** shows the pharmacological treatment according to the initial management strategy; there were no differences except in antiplatelet treatment. **Table 4** shows clinical outcomes during the first 28 days and in the long term. The occurrence of 28-day MACE was significantly different among angiotypes, mainly due to a higher incidence in patients with a circumscribed contained IMH (angiotypes 2A and 3) than in the others (20.0% vs 5.4%, p<0.001), particularly in the first two weeks (**Figure 2**). This was driven mainly by an increase in non-fatal MI (11.0% vs 3.5%, p=0.009) and unplanned revascularisation (11.0% vs 2.5%, p<0.001) in those patients. Among patients undergoing unplanned revascularisation, chest pain with evidence of ischaemia on the electrocardiogram (ECG) was the most common cause (n=14, 87.5%), while angiographic progression of the initial dissection with flow worsening was the most common finding (n=13, 81.3%). Of this latter subgroup, the majority (n=8, 61.5%) were initially managed conservatively.

Patients were followed up for a median of 22 months (minimum 6 months, maximum 4 years, IQR 12-48 months). There was only one death that occurred during hospitalisation in a patient admitted

Table 1. Study population characteristics.

Patients, n	Total	Type 1	Type 2A	Type 2B	Type 3	Type 4	p-value
	302 (100)	52 (17.2)	80 (26.5)	69 (22.8)	20 (6.6)	81 (26.8)	
Date of diagnosis*	April 2017 (March 2015, May 2018)	July 2016 (Dec. 2010, August 2017)	Dec. 2016 (Nov. 2014, Nov. 2017)	October 2017 (Feb 2015, Sept. 2018)	Dec. 2016 (Oct. 2014, June 2018)	Nov.2017 (Dec. 2015, Nov. 2018)	0.431
Female	267 (88.4)	42 (80.7)	73 (91.3)	62 (89.9)	17 (85.0)	73 (90.1)	0.381
Age, years	51.8±10	50.6±11.2	50.6±8.9	53.6±9.7	50.9±9.1	52.6±10.7	0.369
Cardiovascular risk factors							
Diabetes	8 (2.6)	0	2 (2.5)	4 (5.8)	0	2 (2.5)	0.451
Dyslipidaemia	108 (35.8)	15 (28.8)	28 (40.6)	28 (40.6)	6 (30)	31 (38.3)	0.613
Hypertension	104 (34.4)	15 (28.8)	23 (28.8)	33 (47.8)	7 (35)	26 (32.1)	0.096
Current smoker	85 (28.1)	20 (38.5)	19 (23.8)	17 (24.6)	6 (30)	23 (28.4)	0.629
Family history of CAD	86 (28.5)	14 (26.9)	20 (25)	24 (34.8)	3 (15)	25 (30.8)	0.385
Other medical history							
Hypothyroidism	33 (10.9)	4 (7.7)	13 (16.3)	7 (10.1)	1 (5.1)	8 (9.9)	0.471
Migraine	57 (18.9)	10 (19.2)	16 (20)	16 (23.2)	2 (10)	13 (16)	0.690
Anxiety	82 (27.2)	11 (21.2)	22 (27.5)	18 (26.1)	8 (40)	23 (28.4)	0.418
Depression	45 (14.9)	6 (11.5)	12 (15.0)	12 (17.4)	3 (15)	12 (14.8)	0.885
OB/GYN history							
Post-menopausal	96 (31.8)	9 (17.3)	26 (32.5)	30 (43.5)	5 (25)	26 (32.1)	0.029
Hormonal therapy	40 (13.2)	8 (15.4)	13 (16.3)	6 (8.7)	2 (10)	11 (13.6)	0.675
Recent pregnancy	6 (2.0)	4 (7.7)	2 (2.5)	0	0	0	0.023
Precipitating factors							
Emotional stress	77 (29.5)	12 (27.2)	21 (30.9)	17 (30.3)	9 (47.7)	18 (25.2)	0.398
Physical stress	28 (10.7)	4 (9.2)	12 (18.0)	5 (8.9)	3 (15.9)	4 (5.6)	0.127

Data are presented as means±SDs for continuous variables or median ±interquartile range if required, and numbers (%) for categorical variables. *Dates are described with mean and interquartile range. CAD: coronary artery disease; OB/GYN: obstetrics and gynaecology

with cardiac arrest (cardiac death). MACE occurred in 48 (15.9%) patients in the whole cohort with a different incidence among the five angiotypes (**Table 4, Supplementary Figure 1**): angiotype 1: 21.2%, angiotype 2A: 25.0%, angiotype 2B: 8.7%, angiotype 3: 25.0% and angiotype 4: 7.4% (log-rank=13.30, p=0.010). The excess of MACE observed in patients with angiotype 2A and 3 compared with the rest was maintained in the follow-up: 24.5% versus 9.9% (log-rank=10.67, p=0.001) (**Figure 2**). Looking at the MACE components, non-fatal MI was significantly higher in angiotypes 2A and 3 (20.0% vs 7.9% in other SCAD angiotypes, log-rank=8.55, p=0.003) as was unplanned revascularisation (15.0% vs 7.9%, log-rank=4.26, p=0.039), with no differences in mortality (**Supplementary Figure 2**). On the other hand, angiotype 4 had a lower rate of MACE compared to the other angiotypes (7.4% vs 19.0%, p=0.015).

After multivariate adjustment in Cox regression analysis, circumscribed IMH (types 2A and 3) was confirmed as an independent predictor of MACE (adjusted hazard ratio [HR] 2.44, 95% CI: 1.24-4.80, p=0.010). Conversely, single antiplatelet therapy was identified as a protective factor (HR 0.31, 95% CI: 0.11-0.87, p=0.027) (**Supplementary Table 2**). MACE rates according to the initial therapeutic strategy and each angiotype during follow-up

are reported in **Supplementary Table 3**. No significant differences were found between the revascularisation strategy and the conservative management groups (18.3% vs 14.7%, respectively, p=0.426); however, in the angiotype 4 subgroup there was a higher incidence of events in those who underwent revascularisation (13.9% vs 0%, p=0.027).

Discussion

In this multicentre, international study we found that angiographic presentations of SCAD suggesting a circumscribed contained IMH – angiotypes 2A and 3 – showed a higher incidence of MACE, notably during the first 28 days (including hospital admission). This excess of adverse events relates mainly to recurrent MI and unplanned PCIs during hospitalisation, being unrelated to initial treatment (conservative vs revascularisation).

SCAD is increasingly recognised as an important cause of acute coronary syndrome among young and middle-aged women. The demographic data derived from this large SCAD series are very much in keeping with the most recent and largest reports from other registries and countries^{5,9,10}, confirming again that SCAD presents predominantly in middle-aged patients, with a female preponderance and few, but not absent, cardiovascular risk

Table 2. Clinical and angiographic presentation.

Patients, n		Total	Type 1	Type 2A	Type 2B	Type 3	Type 4	p-value
		302 (100)	52 (17.2)	80 (26.5)	69 (22.8)	20 (6.6)	81 (26.8)	
Clinical presentation	STEMI	145 (48)	26 (50)	33 (41.2)	21 (30.4)	7 (35)	58 (71.6)	<0.001
	NSTEMI	136 (45)	20 (38.5)	39 (48.8)	44 (63.8)	12 (60)	21 (25.9)	<0.001
	Angina	8 (2.7)	4 (7.7)	4 (5)	0	0	0	0.181
	Cardiac arrest	13 (4.3)	2 (3.8)	4 (5)	4 (5.8)	1 (5)	2 (2.5)	0.409
Culprit vessel	Left main	8 (2.6)	5 (9.6)	2 (2.5)	0	0	1 (1.2)	0.066
	LAD	164 (54.3)	26 (50)	51 (63.8)	36 (52.2)	6 (30)	45 (55.5)	0.090
	LCX	77 (25.5)	10 (19.2)	18 (22.5)	18 (26.1)	13 (65)	18 (2.2)	0.004
	RCA	53 (17.5)	11 (21.2)	9 (11.3)	15 (21.7)	1 (5)	17 (20.9)	0.266
Multivessel disease (MVD)		36 (11.9)	11 (21.2)	8 (10)	5 (7.2)	2 (10)	10 (12.3)	0.420
LAD involved		25 (69.4 of MVD)	10 (19.2)	9 (11.3)	2 (2.9)	0	4 (4.8)	0.024
Angiographic stenosis (%)		85.7±17.4	79.3±17	83.2±17.7	80.1±20.2	79.6±12.1	100	<0.001*
SCAD length (mm)		40.3±24.3	35.2±25.8	38.6±18.6	52.8±26.2	18±7.4	37.8±23.4	<0.001
OCT use (%)		43 (14.1)	8 (15.4)	16 (20.0)	7 (10.1)	6 (30.0)	6 (7.4)	0.026
IVUS use (%)		48 (16.0)	9 (17.3)	13 (16.3)	5 (7.2)	4 (20.0)	17 (20.9)	0.188
TIMI flow baseline	0	89 (29.4)	3 (5.8)	1 (1.3)	4 (5.8)	0	81 (100)	<0.001
	1	19 (6.3)	5 (9.6)	8 (10)	5 (7.4)	1 (5)	0	0.809*
	2	58 (17.6)	15 (28.9)	19 (23.8)	13 (19.1)	6 (30)	0	0.458*
	3	136 (45.2)	27 (51.9)	52 (65)	44 (64.7)	13 (65)	0	0.485*
Most proximally affected segment	Proximal	52 (17.2)	17 (32.7)	15 (18.8)	6 (14.7)	2 (10)	12 (15)	0.012
	Medium	73 (24.2)	17 (32.7)	23 (28.8)	13 (18.8)	3 (15)	17 (21)	0.262
	Distal	92 (30.5)	11 (21.2)	23 (28.8)	26 (37.7)	3 (15)	29 (35.8)	0.045
	Secondary branches	85 (28.1)	7 (13.5)	19 (23.8)	24 (34.8)	12 (60)	23 (28.4)	<0.001

Data are presented as means±SDs for continuous variables and numbers (%) for categorical variables. *p-values calculated excluding angiotype 4. IVUS: intravascular ultrasonography; LAD: left anterior descending artery; LCX: left circumflex; NSTEMI: non-ST-elevation myocardial infarction; OCT: optical coherence tomography; RCA: right coronary artery; SCAD: spontaneous coronary artery dissection; STEMI: ST-elevation myocardial infarction

Table 3. Management and procedural outcomes.

Patients, n		Total	Type 1	Type 2A	Type 2B	Type 3	Type 4	p-value
		302 (100)	52 (17.2)	80 (26.5)	69 (22.8)	20 (6.6)	81 (26.8)	
Vascular access (n=264)	Radial	218 (82.6)	33 (70.2)	54 (79.4)	56 (90.3)	17 (94.4)	58 (84.1)	0.042
	Femoral	46 (17.4)	14 (29.8)	14 (20.6)	6 (9.7)	1 (5.6)	11 (15.9)	0.026
Management (first treatment choice)	PCI	100 (33.1)	23 (45.1)	18 (22.5)	9 (13)	7 (35)	43 (53.8)	<0.001
	CABG	4 (1.3)	2 (3.4)	1 (1.3)	1 (1.5)	0	0	0.704
	Conservative	198 (65.6)	27 (51)	61 (76.3)	59 (85.5)	13 (65)	37 (46.3)	<0.001
PCI (n=100)			N=23	N=18	N=9	N=7	N=43	
Only guidewire		13 (13)	2 (8.7)	1 (5.6)	2 (22.2)	1 (14.3)	12 (27.9)	0.228
Predilatation		42 (42)	5 (21.7)	8 (44.4)	3 (33.3)	4 (57.1)	22 (51.2)	0.127
Cutting balloon		1 (1)	0	0	0	0	1	1
Stenting*		78 (78)	20 (87)	15 (57.7)	6 (48.2)	6 (85.7)	31 (72.1)	0.248
TIMI flow post procedure	3	78 (78)	19 (82.6)	14 (77.7)	7 (77.8)	7 (100.0)	23 (54.4)	0.004
	<3	22 (22)	4 (17.4)	4 (22.2)	2 (22.2)	0	20 (45.6)	
Successful PCI	Yes	78 (78)	19 (82.6)	17 (94.4)	7 (77.8)	6 (85.7)	29 (67.4)	0.558

Data are presented as means±SDs for continuous variables and numbers (%) for categorical variables. *These include 50 drug-eluting stents, 20 bare metal stents and 8 bioresorbable scaffolds. CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention

Table 4. Cardiovascular events during follow-up according to the angiotype.

Patients, n	Total	Type 1	Type 2A	Type 2B	Type 3	Type 4	p-value
	302 (100)	52 (17.2)	80 (26.5)	69 (22.8)	20 (6.6)	81 (26.8)	
28-day cardiovascular events							
Hospital stay, days	6 (5-8)	6 (5-7)	7 (5-10)	6 (5-9)	6.5 (5-7)	6 (5-8)	0.490
28-day MACE	31 (10.3)	6 (11.5)	15 (18.8)	3 (4.3)	5 (25)	2 (2.5)	0.030
All-cause death*	1 (0.3)	0	0	0	1 (5.6)	0	0.250
Non-fatal MI*	18 (6)	3 (5.8)	9 (11.3)	2 (2.9)	2 (10)	2 (2.5)	0.166
Any unplanned revascularisation*	16 (5.3)	3 (5.8)	9 (11.3)	2 (2.9)	2 (10)	0 (0)	0.004
Stroke	1 (0.3)	0	0	0	0	1 (1.2)	1
Bleeding events	4 (1.2)	1 (1.9)	2 (2.5)	1 (1.4)	0	0	0.632
Cardiovascular events up to 4 years							(log-rank)
4-year MACE	48 (15.9)	11 (21.2)	20 (25)	6 (8.7)	5 (25)	6 (7.4)	0.083
All-cause death*	1 (0.3)	0	0	0	1 (5)	0	0.411
Non-fatal MI*	36 (11.9)	8 (15.4)	16 (20)	5 (7.25)	4 (20)	3 (3.7)	0.054
Any unplanned revascularisation*	31 (10.3)	8 (15.4)	13 (16.3)	3 (4.4)	2 (10)	5 (6.2)	0.237
Recurrent SCAD	10 (3.3)	2 (3.8)	2 (2.5)	3 (5.2)	1 (5.1)	2 (2.7)	0.899
Stroke	2 (0.7)	0	0	1 (1.8)	0	1 (1.2)	0.980

Data are presented as means±SDs for continuous variables or median±interquartile range if required and numbers (%) for categorical variables. *MACE components. MI: myocardial infarction

factors. Mood disorders such as anxiety or depression were frequent, as were hormonal stress situations. The clinical presentation, essentially as a classic acute coronary syndrome, was often

accompanied by an identifiable triggering stressor. STEMI was the predominant presentation in cases of SCAD type 4, as expected. In keeping with other SCAD angiographic series, angiotype 3 was the least common presentation, probably underrepresented owing to underdiagnosis.

This article informs on detailed short- and long-term outcomes in patients with a confirmed SCAD diagnosis. Survival to discharge and during follow-up was particularly good, with only one in-hospital cardiac death (mortality 0.3%). With the majority being treated conservatively as the initial treatment strategy, most patients were discharged without MACE. Of note, in-hospital recurrent MI occurred in 6.0% and any unplanned revascularisation in 5.3%, highlighting the importance of monitoring for recurrent ischaemia which requires urgent revascularisation in these patients.

In our study, patients with an angiographic SCAD presentation that denotes the presence of circumscribed haematoma with preserved patency in the distal vessel (angiotypes 2A and 3) – as opposed to those with double lumen (angiotype 1), distal haematoma (angiotype 2B) or blocked vessel (angiotype 4) – underwent unplanned revascularisation due to reinfarction during admission more often. We opted to merge angiotypes 2A and 3 into one single group based on a similar pathological substrate (contained haematoma circumscribed to a vessel segment) and on similar clinical behaviour. In the Spanish national SCAD registry, García-Guimaraes et al⁵ found that IMH was an independent predictor of in-hospital events. Similarly, Waterbury et al⁴ reported data from the Mayo Clinic registry showing that patients with SCAD experiencing clinical progression over hospital admission frequently presented initially with isolated IMH (without intimal dissection).

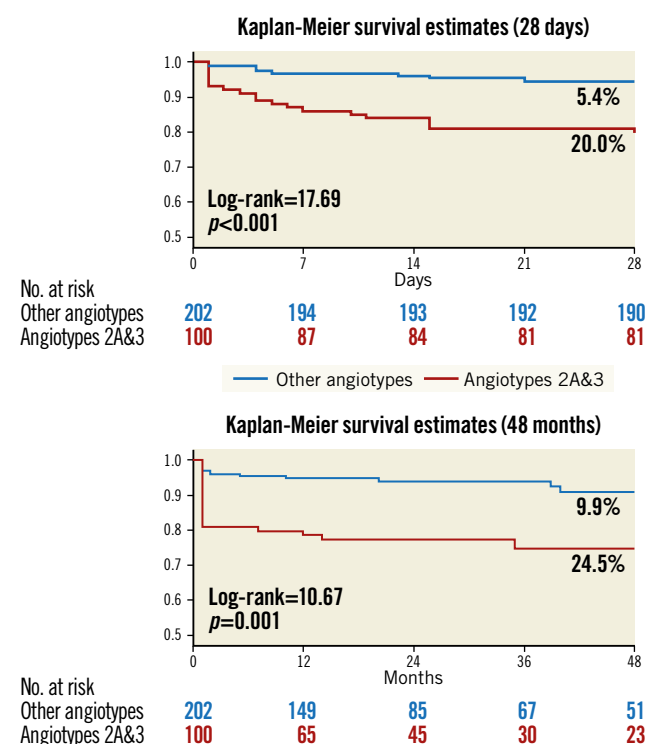


Figure 2. Kaplan-Meier curves for MACE in angiotypes 2A and 3 versus other angiotypes during the first 28 days and long-term follow-up.

Circumscribed IMH is an unstable structure that may progress in length and degree of luminal obstruction, causing clinical ischaemia. It has been suggested that fenestrated and non-fenestrated spontaneous dissections may be two distinct pathological manifestations of the same substrate¹¹. Hypothetically, an initial haemorrhage leads to different angiotypes that correspond to distinct stages of the natural history of SCAD. Thus, when a focal IMH starts the process, this may result in either an intimal rupture (angiotype 1) or a contained haematoma, which can be circumscribed (angiotype 3 or 2A) or propagated through the distal vessel (angiotype 2B). Furthermore, any of these may potentially occlude the vessel (angiotype 4). We hypothesise that an angiographically circumscribed IMH may correspond to an early pathological phase of SCAD and, for this reason, would suggest a more unstable lesion with higher likelihood of changing, including progression into a more severe stenosis or vessel occlusion that can cause recurrent ischaemia, non-fatal MI and may lead to unplanned revascularisation. Supporting this hypothesis, the observed protective role of single antiplatelet therapy compared to a dual antiplatelet regimen may be explained by a lower risk of IMH progression. For these reasons, this subset of patients may benefit most from a prolonged admission with close surveillance and monitoring.

Patients with angiotype 1 SCAD also showed a high rate of adverse events in this series (21.2%). We believe that this finding may carry a degree of temporal bias. As a result of the fact that a radiolucent flap was virtually the only angiographic feature used to diagnose SCAD, earlier cases in our series belong mostly to angiotype 1 (diagnosis dates are shown in **Table 1**). Besides, as conservative management of SCAD did not become the standard of treatment until recently, these earlier angiotype 1 SCAD cases were treated more frequently with PCI (PCI rate of 45%). Of note, early angiotype 1 cases had proximal vessel involvement more often than those with other angiotypes (32.7% vs 14.1%, $p=0.01$), which after all reflects a higher-risk cohort. The limited spatial resolution of angiography may add some classification bias here, i.e., small intimomedial flaps are less likely to be detected in mid and distal segments and therefore those lower-risk cases may be classified into other angiotypes.

Interestingly, patients with an angiotype 4 SCAD showed the best MACE-free survival curve, with a low event rate during admission and long-term follow-up. This association was significant despite being the group with the highest rate of PCI (53.8%), with no events in those managed conservatively. A more favourable evolution of these patients may be explained by the fact that angiotype 4 constitutes an advanced phase of the dynamic process of SCAD in some cases, with already established MI and free from the instability of angiotypes 2A and 3. Distal or secondary branch involvement was predominant in most cases with angiotype 4 which implies a limited extension of the necrosis, whereas in those cases with more proximal occlusions and a significant territory at risk patients would receive immediate revascularisation.

Along the same lines, patients with angiotype 2B SCAD also showed a low incidence of MACE, all these cases involving predominantly distal segments of a coronary artery or branch. The latter highlights the importance of breaking down angiotype 2 into 2A and 2B, which gives a clear sense not only of diagnosis but also of prognosis, and even questions the sense of grouping these different presentations under the same category. Based on our findings, the angiographic classification of SCAD could be simplified to reflect the clinical significance of the various angiotypes.

Moreover, despite the fact that intracoronary imaging has an important role for diagnosing SCAD when angiography is inconclusive, these techniques should be used sensibly in this clinical scenario. We believe that the relatively low usage of intracoronary imaging reported in this study (27.8%) and in other large contemporary cohorts^{5,9} testifies to an increasing acquaintance with the characteristic angiotypes of SCAD as well as to the understanding of the risks of coronary instrumentation in these patients¹².

Taken together, we found that patients with SCAD presenting with angiographic patterns suggesting a circumscribed contained IMH were more prone to present in-hospital reinfarction and to require urgent unplanned revascularisation. This association with worse outcomes was maintained in the long-term follow-up and was demonstrated to be independent after multivariable adjustment. The data presented support a strategy of prolonged admission and monitoring in those SCAD patients presenting with high-risk angiotypes. In general, a clinically guided approach should be followed. However, for the surveillance of selected patients with proximal vessel involvement or proximal residual stenosis following PCI, computed tomography is our preferred imaging modality. The implications of these findings for tailoring treatment in patients with SCAD need to be elucidated in future studies.

Limitations

This study has the limitations of a retrospective analysis. Given the shifts in diagnosis and therapies of SCAD since 2009, an inherent temporal bias may potentially affect the results of this study. The clinical indications that may have accounted for the decision on revascularisation were not protocolised, and therefore probably heterogeneous among the different participating centres. Furthermore, the angiography-based definition of “contained IMH” is somewhat imprecise as small fenestrations of the intimomedial lamina (disclosable by pathology or OCT) cannot be excluded. Notwithstanding this, this study was designed to evaluate an angiography-based classification and therefore its findings are applicable to the mere use of this imaging modality. Finally, this study was not designed or powered to assess the impact of treatment strategies among the different angiotype groups. Future studies are needed to assess this matter.

Conclusions

The use of an angiographic classification of SCAD discriminated patients with different rates of events. Patients with SCAD presenting with an angiographically circumscribed and contained

haematoma (angiotypes 2A and 3) showed an increased risk of adverse clinical events during admission that was maintained during long-term follow-up.

Impact on daily practice

SCAD may manifest in a variety of angiographic patterns (angiotypes). Those with a circumscribed intramural haematoma were found to be at higher risk of adverse clinical events in the short term, driven by a fourfold increased risk of unplanned revascularisation and a threefold greater risk of reinfarction. These poorer outcomes were sustained during long-term follow-up. These patients may benefit from prolonged monitoring and hospital stay to identify early ischaemic relapses.

Appendix. Study collaborators

Ivan Núñez-Gil, PhD, Hernán Mejía-Rentería, PhD, Luis Nombela-Franco, PhD, Pilar Jiménez-Quevedo, PhD, Gabriela Tirado-Conte, MD, Antonio Fernández-Ortiz, PhD, Carlos Macaya, PhD; *Hospital Clínico San Carlos, IdiSSC, Universidad Complutense de Madrid, Madrid, Spain*. Giorgio Quadri, MD, Francesco Tomassini, MD, Fabio Ferrari, MD, Fabio Mariani, MD, Alfonso Franzè, MD; *Interventional Cardiology Unit, San Luigi Gonzaga University Hospital, Orbassano, and Rivoli Infermi Hospital, Rivoli, Turin, Italy*. Matteo Bianco, MD, Laura Montagna, MD; *Division of Cardiology, A.O.U San Luigi Gonzaga, Orbassano, Turin, Italy*. Luca Lo Savio, MD; *Division of Cardiology, Infermi Hospital, Rivoli, Turin, Italy*. Angelica Rossi, MD, Bruno Loi, MD; *Azienda Ospedaliera Brotzu, Cagliari, Italy*. Gianmarco Annibali, MD; *A.O. Ordine Mauriziano, Ospedale Umberto I, Turin, Italy*. Massimiliano Scappaticci, MD; *Santa Maria Goretti Hospital, Latina, Italy*. Umberto Barbero, MD, Michele De Benedictis, MD; *Ospedale Maggiore Ss. Annunziata - Savigliano (CN), Italy*. Mario Iannacone, MD; *Ospedale San Giovanni Bosco, Turin, Italy*. Gianluca Campo, MD, Andrea Erriquez, MD; *Azienda Ospedaliero Universitaria di Ferrara, Ferrara, Italy*. Dario Buccheri, MD; *Sant'Antonio Abate Hospital, Trapani, Italy*. Chiara Cavallino, MD, Fabrizio Ugo, MD; *Cardiology Division, Sant'Andrea Hospital, Vercelli, Italy*. Primiano Lombardi, MD, Alessandra Truffa Giachet, MD; *Cardinal Massaia Civil Hospital, Asti, Italy*. Chiara Bernelli, MD, Annamaria Nicolino, MD; *Santa Corona Hospital, Pietra Ligure (SV), Italy*. Andrea Rognoni, MD, Marco Mennuni, MD, Giuseppe Patti, MD; *Cardiology Department, Ospedale Maggiore Della Carità, Novara, Italy*. Elisabetta Bordoni, MD; *Ospedale Santa Maria della Misericordia, Perugia, Italy*. Vincenzo Infantino, MD, Angelo Di Leo, MD; *Division of Cardiology, Ospedale Civile di Ciriè (TO), Italy*. Alfonso Gambino, MD, Giuseppe Pietro Greco Lucchina, MD; *Santa Croce Hospital, Moncalieri (TO), Italy*. Sebastian Cinconze, MD; *Azienda Ospedaliera S. Croce e Carle, Cuneo, Italy*. Giuseppe Musumeci, MD; *A.O. Ordine Mauriziano, Ospedale Umberto I, Turin, Italy*. Francesco Cassano, MD; *Ospedale SS Annunziata, Taranto, Italy*. Federico Beqaraj, MD, Luca Gaido, MD; *Division of Cardiology, Maria Vittoria Hospital,*

Turin, Italy. Fabrizio D'Ascenzo, MD, Francesco Bruno, MD; *Cardiology Department, AOU Città della Salute e della Scienza di Torino, Turin, Italy*.

Funding

R. Mori received a training grant from the European Society of Cardiology (APP000019660). F. Macaya received a grant from Fundación Interhospitalaria para la Investigación Cardiovascular to conduct research on SCAD. The Fundación Interhospitalaria para la Investigación Cardiovascular provided financial support for the creation and maintenance of the SCAD online database at Hospital Clínico San Carlos and receives manuscript publication fees derived from related projects.

Conflict of interest statement

The authors/study collaborators have no conflicts of interest to declare.

References

- Macaya F, Salinas P, Gonzalo N, Fernández-Ortiz A, Macaya C, Escaned J. Spontaneous coronary artery dissection: contemporary aspects of diagnosis and patient management. *Open Heart*. 2018;5:e000884.
- Adlam D, Alfonso F, Maas A, Vrints C, al-Hussaini A, Bueno H, Capranzano P, Gevaert S, Hoole SP, Johnson T, Lettieri C, Maeder MT, Motreff P, Ong P, Persu A, Rickli H, Schiele F, Sheppard MN, Swahn E. European Society of Cardiology, acute cardiovascular care association, SCAD study group: a position paper on spontaneous coronary artery dissection. *Eur Heart J*. 2018;39:3353-68.
- Alfonso F, Paulo M, Gonzalo N, Dutary J, Jimenez-Quevedo P, Lennie V, Escaned J, Bañuelos C, Hernandez R, Macaya C. Diagnosis of spontaneous coronary artery dissection by optical coherence tomography. *J Am Coll Cardiol*. 2012;59:1073-9.
- Waterbury TM, Tweet MS, Hayes SN, Eleid MF, Bell MR, Lerman A, Singh M, Best PJM, Lewis BR, Rihal CS, Gersh BJ, Gulati R. Early natural history of spontaneous coronary artery dissection. *Circ Cardiovasc Interv*. 2018;11:e006772.
- García-Guimaraes M, Bastante T, Macaya F, Roura G, Sanz R, Alvarado JCB, Tizón H, Flores-Ríos X, Moreu J, Ojeda S, Nogales JM, Veiga G, Masotti M, Camacho-Freire SJ, Jimenez-Valero S, Jiménez-Kocher M, Lozano I, González-Ferreiro R, Velásquez M, Avanzas P, Rivero F, Alfonso F. Spontaneous coronary artery dissection in Spain: clinical and angiographic characteristics, management, and in-hospital events. *Rev Esp Cardiol (Engl Ed)*. 2021;74:15-23.
- Motreff P, Malcles G, Combaret N, Barber-Chamoux N, Bouajila S, Pereira B, Amonchot A, Citron B, Lussion JR, Eschaliere R, Souteyrand G. How and when to suspect spontaneous coronary artery dissection: novel insights from a single-centre series on prevalence and angiographic appearance. *EuroIntervention*. 2017;12:e2236-43.
- Saw J. Coronary angiogram classification of spontaneous coronary artery dissection. *Catheter Cardiovasc Interv*. 2014;84:1115-22.
- Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD; Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. Fourth Universal Definition of Myocardial Infarction (2018). *Circulation*. 2018;138:e618-51.
- Saw J, Starovoytov A, Humphries K, Sheth T, So D, Minhas K, Brass N, Lavoie A, Bishop H, Lavi S, Pearce C, Renner S, Madan M, Welsh RC, Lutichmedial S, Vijayaraghavan R, Aymong E, Har B, Ibrahim R, Gornik HL, Ganesh S, Buller C, Matteau A, Martucci G, Ko D, Mancini GBJ. Canadian spontaneous coronary artery dissection cohort study: in-hospital and 30-day outcomes. *Eur Heart J*. 2019;40:1188-97.
- Clare R, Duan L, Phan D, Moore N, Jorgensen M, Ichiuji A, Shen AY, Lee MS. Characteristics and Clinical Outcomes of Patients With Spontaneous Coronary Artery Dissection. *J Am Heart Assoc*. 2019;8:e012570.
- Jackson R, Al-Hussaini A, Joseph S, van Soest G, Wood A, Macaya F, Gonzalo N, Cade J, Caixeta A, Hlinomaz O, Leinveber P, O'Kane P, García-Guimaraes M, Cortese B, Samani NJ, Escaned J, Alfonso F, Johnson T, Adlam D. Spontaneous Coronary Artery Dissection: Pathophysiological Insights From Optical Coherence Tomography. *JACC Cardiovasc Imaging*. 2019;12:2475-88.

12. Macaya F, Salazar CH, Pérez-Vizcayno MJ, Salinas P, Jiménez-Quevedo P, Nombela-Franco L, Del Trigo M, Nuñez-Gil I, Fernández-Ortiz A, Macaya C, Escaned J, Gonzalo N. Feasibility and Safety of Intracoronary Imaging for Diagnosing Spontaneous Coronary Artery Dissection. *JACC Cardiovasc Imaging*. 2019;12:763-4.

Supplementary data

Supplementary Appendix 1. Study design and population.

Supplementary Appendix 2. Angiographic analysis and classification.

Supplementary Appendix 3. Statistical analysis.

Supplementary Figure 1. Kaplan-Meier curves for MACE in all angiotypes (Adlam's classification) during the first 28 days and long-term follow-up.

Supplementary Figure 2. Breakdown of the components of the composite major adverse cardiovascular events (MACE) in angiotypes 2A and 3 versus other angiotypes.

Supplementary Table 1. Pharmacologic treatment in the studied population according to the initial therapeutic strategy.

Supplementary Table 2. MACE predictor analysis.

Supplementary Table 3. MACE during 48 months of follow-up according to the initial therapeutic strategy in each angiotype.

The supplementary data are published online at:
[https://eurointervention.pcronline.com/
doi/10.4244/EIJ-D-20-01275](https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-20-01275)



Supplementary data

Supplementary Appendix 1. Study design and population

Patients were enrolled in the registry from January 2009 to December 2019. We included patients with clinical presentation compatible with acute coronary syndrome and meeting criteria for SCAD [1,2]. Patients with significant ($\geq 50\%$) atherosclerotic disease in other coronary arterial segments or with an underlying complicated plaque as revealed by intracoronary imaging were excluded. Data on demographics, clinical presentation, treatment modality, angiographic findings, management, and early and late outcomes were extracted from clinical source documents or collected via medical records, patient interviews, and follow-up visits. A dedicated data manager (L. Lo Savio) was in charge of source verification, quality control, and queries generation from the coordinating centre to the participating sites to minimise bias. Follow-up data were collected by each centre through review of medical records or during outpatient visits and/or telephone contacts. The study was conducted in accordance with the Declaration of Helsinki.

Supplementary Appendix 2. Angiographic analysis and classification

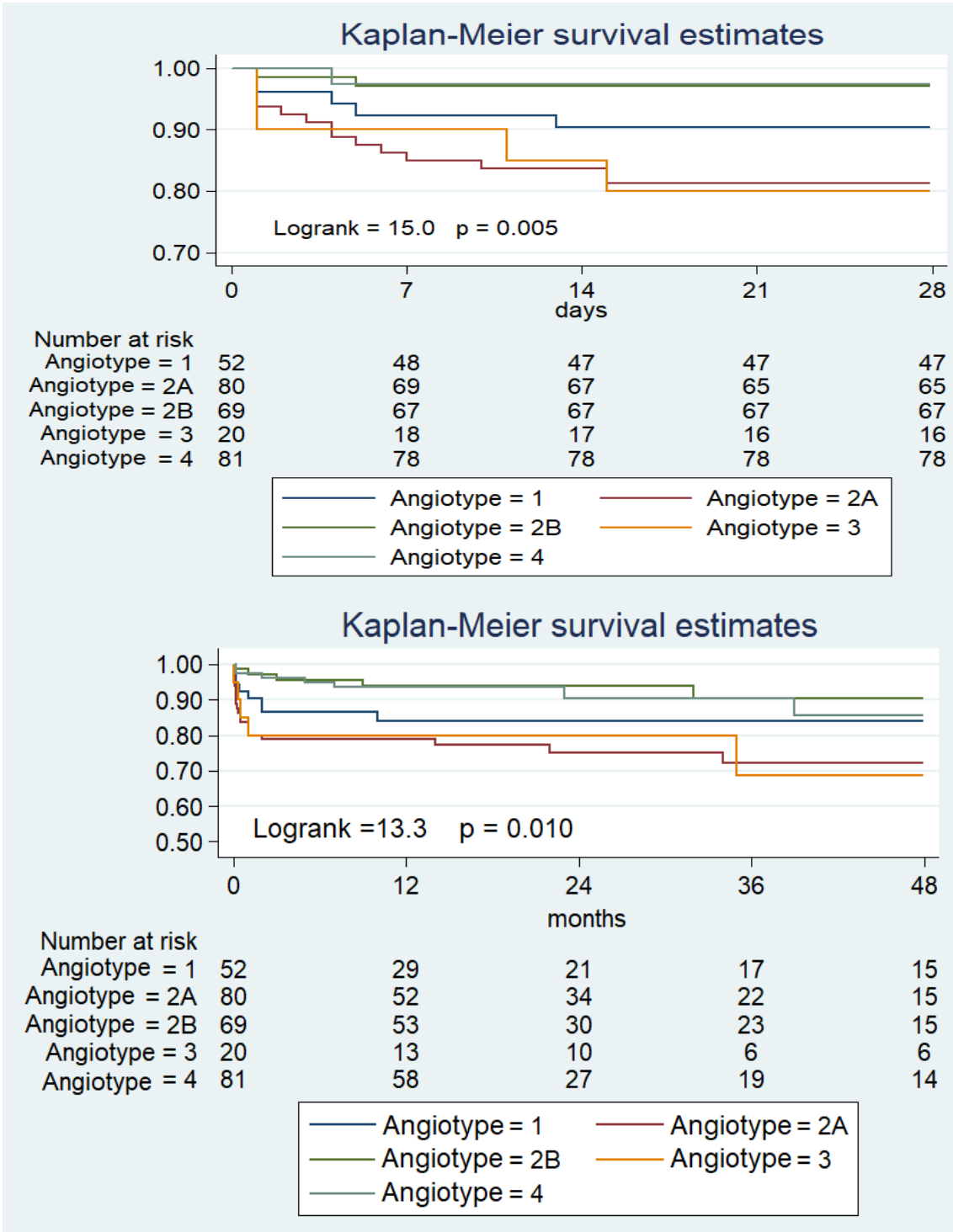
All coronary angiograms were sent to the coordinating centre and reviewed by two experienced interventional cardiologists (G. Quadri, C. Rolfo) for diagnostic confirmation. In case of disagreement, consensus was achieved after discussion with a third interventional cardiologist (F. Tomassini). Diagnostic criteria were based on angiography and intracoronary imaging data (whenever available) as previously described [1,2]. For the classification of SCAD, we followed the one proposed by Adlam et al [2] in the ESC-ACCA position paper on SCAD using five categories (**Supplementary Figure 1**).

After diagnosis corroboration of SCAD at the coordinating centre, the angiographic classification was performed in a second stage by both the registry coordinating centre (G. Quadri, C. Rolfo, E. Cerrato) and the study leading centre (R. Mori, F. Macaya, J. Escaned) with a previous consensus agreement on the specific criteria to be used, as well as subsequent online meetings to discuss unclear cases. The angiographic classification criteria used were as follows: angiotype 1 is the classic angiographic radiolucent flap or linear double lumen, often associated with contrast hold-up. Angiotype 2 is characterised by a long diffuse (≥ 20 mm by quantitative coronary angiography) and smooth stenosis, corresponding to an angiographically contained intramural haematoma (small fenestrations of the intimomedial lamina cannot be excluded solely on the grounds of angiography). This angiotype is further divided into angiotype 2A, in which there is recrudescence of normal distal vessel calibre, and angiotype 2B, where the stenosis (haematoma) involves angiographically the entire distal segment. Angiotype 3 consists of ambiguous stenoses shorter than 20 mm (by quantitative coronary angiography), angiographically indistinguishable from a focal atherosclerotic stenosis, that require diagnostic confirmation by means of intracoronary imaging or a scheduled surveillance angiogram confirming vessel healing. This angiotype also corresponds to an angiographically contained intramural haematoma. Finally, angiotype 4 SCAD corresponds to a total occlusion of the main dissected vessel or large branches with TIMI 0 flow. For diagnosing angiotype 4, the presence of other typical angiographic characteristics (angiotypes 1 and 2), visible at the time of the baseline injections, during PCI or in surveillance angiograms, was necessary to establish the diagnosis of SCAD when intracoronary imaging was not used. A sixth category, the angiotype 1/2 (comprising features of both angiotypes 1 and 2 in the same lesion), was dismissed for the sake of simplicity and classified as angiotype 1.

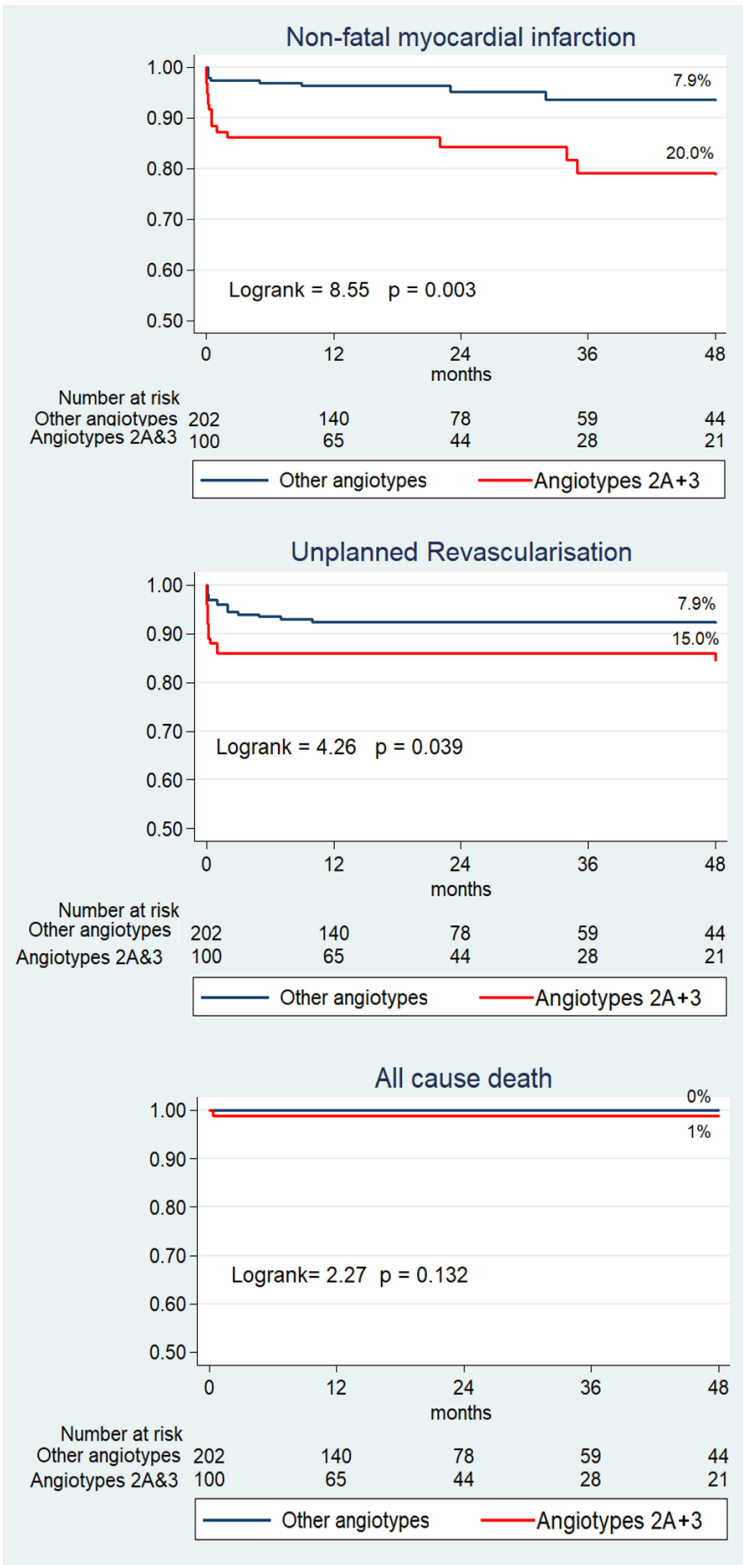
Supplementary Appendix 3. Statistical analysis

Angiographic type was the grouping variable (five groups). Non-categorical variables are summarised using means and were compared using ANOVA or Kruskal-Wallis tests according

to normality of distributions. Categorical variables are expressed as percentages and were compared using the chi-square or Fisher's exact tests if required. Kaplan-Meier curves were plotted for the time to occurrence of MACE by each angiographic type and were compared using the log-rank test, as it is the recommended test for infrequent events where the compared curves do not intersect. Multivariate adjustment was conducted using Cox regression including covariables with a significance level below 0.20 in the univariate analysis. Statistical significance was established at $p \leq 0.05$ (two-tailed) for all tests. All statistical analyses were conducted using Stata IC 14.1 (StataCorp, College Station, TX, USA).



Supplementary Figure 1. Kaplan-Meier curves for MACE in all angiotypes (Adlam's classification) during the first 28 days and long-term follow-up.



Supplementary Figure 2. Breakdown of the components of the composite major adverse cardiovascular events (MACE) in angiotypes 2A and 3 versus other angiotypes.

Supplementary Table 1. Pharmacologic treatment in the studied population according to the initial therapeutic strategy.

Medical treatment	Total (n=302)	Conservative strategy (n=198)	Revascularisation strategy (n=104)	<i>p</i>-value
Single antiplatelet therapy	74 (24.5)	67 (33.8)	7 (6.7)	<0.001
Dual antiplatelet therapy	228 (75.5)	131 (66.1)	97 (93.3)	<0.001
At least 12-month DAPT length	141 (46.7)	77 (38.9)	64 (61.5)	0.001
Beta-blockers	246 (81.3)	159 (80.3)	87 (83.7)	0.118
ACE inhibitors/ARBs	171 (56.6)	111 (56.1)	60 (57.7)	0.671
Statins	213 (70.5)	140 (70.7)	73 (70.2)	0.589
Calcium channel blockers	29 (9.6)	21 (10.6)	8 (7.7)	0.752

ACE: angiotensin-converting enzyme; ARBs: angiotensin receptor blockers; DAPT: dual antiplatelet therapy

Supplementary Table 2. MACE predictor analysis.

Predictor	Univariate analysis		Multivariate analysis	
	HR	p-value	HR	p-value
Age, years	0.97 (0.94-0.99)	0.043	0.98 (0.95-1.02)	0.527
Men	1.16 (0.49-2.73)	0.732		
Arterial hypertension	0.67 (0.36-1.25)	0.215		
Diabetes mellitus	0.71 (0.09-5.20)	0.742		
Smoking	1.42 (0.80-2.54)	0.227		
Recent pregnancy	1.75 (0.24-13.04)	0.583		
Post-menopausal	0.66 (0.32-1.37)	0.265		
Hormonal therapy	1.64 (0.79-3.40)	0.178	1.08 (0.32-3.66)	0.901
Hypothyroidism	0.58 (0.18-1.87)	0.365		
STEMI	0.98 (0.55-1.72)	0.937		
Cardiac arrest	1.80 (0.56-5.81)	0.323		
Initial TIMI flow 0	0.49 (0.21-1.17)	0.110	0.57 (0.20-1.65)	0.303
Proximal segment affected	0.52 (0.10-2.53)	0.418		
LAD as culprit vessel	1.12 (0.64-1.97)	0.671		
Adlam type 2A & 3	2.34 (1.34-4.08)	0.003	2.44 (1.24-4.80)	0.010
PCI as first treatment	1.45 (0.79-2.66)	0.229		
OCT use	0.68 (0.24-1.94)	0.480		
Beta-blocker treatment	0.83 (0.40-1.72)	0.616		
SAP	0.38 (0.16-0.91)	0.029	0.31 (0.11-0.87)	0.027
Anticoagulation	1.51 (0.59-3.84)	0.383		
New P2Y ₁₂ inhibitor	1.94 (1.03-3.68)	0.040	2.07 (0.98-4.36)	0.056

LAD: left anterior descending artery; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; SAP: single antiplatelet therapy; STEMI: ST-elevation myocardial infarction; TIMI: Thrombolysis In Myocardial Infarction

Supplementary Table 3. MACE during 48 months of follow-up according to the initial therapeutic strategy in each angiotype.

Adlam`s classification	Total	Conservative strategy		Total	Revascularisation strategy		p-value *
		MACE -	MACE+		MACE -	MACE +	
Type 1, n=52	27 (51.9)	19 (70.4)	8 (29.6)	25 (48.1)	22 (88)	3 (12.0)	0.177
Type 2A, n=80	61 (76.2)	48 (78.7)	13 (21.3)	19 (23.8)	12 (63.2)	7 (36.8)	0.226
Type 2B, n=69	59 (85.5)	54 (91.5)	5 (8.5)	10 (14.5)	9 (90)	1 (10.0)	1
Type 3, n=20	13 (65)	10 (76.9)	3 (23.1)	7 (35)	5 (71.5)	2 (28.5)	1
Type 4, n=81	38 (46.9)	38 (100)	0 (0)	43 (53.1)	37 (86.1)	6 (13.9)	0.027
Total, n=302	198 (65.6)	168 (85.4)	29 (14.6)	104 (34.4)	85 (81.7)	19 (18.3)	0.426

* p-value (for MACE+) comparing conservative strategy versus revascularisation strategy.