


Different patients, different outcomes: A case-control study of spontaneous coronary artery dissection versus acute coronary syndrome

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Introduction: There is progressive interest worldwide in spontaneous coronary artery dissection (SCAD). To identify a SCAD cohort and compare risk factors, presentation, and management outcomes compared to acute coronary syndrome (ACS) matched controls.

Methods: Retrospective analysis was performed from 2000 to 2015. Clinical data included a neuropsychiatric history, with management and clinical outcomes assessed at 12 months. Patients were matched on a 1:3 case-control basis according to type of ACS. Twenty-two SCAD patients were matched to 66 controls by ACS type (ST-elevation myocardial infarction 45%, Non-ST-elevation myocardial infarction 41%, unstable angina 14%).

Results: The SCAD group were more likely female (77.3% vs 19.7%, $P < 0.0001$), of younger age (48.7 ± 10.7 years vs 61.3 ± 10.6 years, $P < 0.0001$) with no cases of diabetes (0% vs 33.3%, $P = 0.002$), compared to controls. SCAD patients had a high prevalence of anxiety, depression or previous neuropsychiatric history (52.4% SCAD vs 1.5% ACS, $P < 0.0001$). A conservative revascularization strategy with stenting was performed in a minority of SCAD patients (13.6% SCAD vs 83.3% ACS, $P < 0.0001$), with no significant difference in cumulative major adverse cardiac or cerebrovascular events (MACCE) of death, stroke, re-admission, or repeat angiography rates between both groups (13.6% SCAD vs 27.3% ACS $P = \text{NS}$).

Conclusion: SCAD affects young females with a paucity of cardiovascular risk factors. The major risk factor for SCAD was a history of anxiety, depression, or neuropsychiatric illness. A conservative approach to SCAD revascularization led to similar MACCE when compared to ACS controls undergoing guideline revascularization at 12 months.

KEYWORDS

acute coronary syndrome, percutaneous coronary intervention, revascularization, spontaneous coronary artery dissection

Abbreviations: ACEi, angiotensin converting enzyme inhibitors; ACS, acute coronary syndrome; ARB, angiotensin receptor blockers; BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass grafting; DBP, diastolic blood pressure; FMD, fibromuscular dysplasia; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; MACCE, major adverse cardiovascular and cerebrovascular events; NSTEMI, non-ST elevation myocardial infarction; OAC, oral anticoagulant; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; RCA, right coronary artery; SBP, systolic blood pressure; SCAD, spontaneous coronary artery dissection; STEMI, ST elevation myocardial infarction; UA, unstable angina.

1 | INTRODUCTION

There is progressive interest worldwide in spontaneous coronary artery dissection (SCAD), a rare and unique cause of chest pain, with estimated prevalence of 0.1-1.1% within large acute coronary syndrome (ACS) registries.¹⁻³ Patients may present with an ACS, ventricular fibrillation, or sudden cardiac death.^{4,5} The pathophysiology differs from atherosclerotic plaque rupture, and although not well defined, the most plausible theory includes tunica media hemorrhage or intimal tear within the coronary vessel causing a true and false lumen.^{1,2,6} The tear can occur between the intima and media, or the media and adventitia.⁷ Hemorrhage and thrombus propagation within the false lumen leads to compression of the coronary artery, causing downstream myocardial ischemia and infarction.

SCAD occurs predominantly in females and often in the absence of traditional cardiovascular risk factors.⁸ One third of women are peri or postpartum, or on the oral contraceptive pill. Further risk factors include connective tissue disorders and fibromuscular dysplasia (FMD), however, a proportion of cases are idiopathic.⁵ In males, the major risk factor is extreme exertion,^{8,9} or sympathomimetic agents such as cocaine or methamphetamines.^{5,10,11} Coronary angiography is the gold standard for diagnosis of SCAD with the classic finding of an intimal flap often accompanied by multiple radiolucent lumens (see Figure 1).¹²

The goal of treatment in SCAD is providing flow to the affected ischemic tissue, however, the optimal strategy for revascularization and medical therapy is unknown. In comparison to atherosclerotic ACS, minimal data exists comparing risk factors, optimal treatment methods, and outcomes of SCAD. This case control study's aim was to retrospectively identify a SCAD cohort and compare demographic characteristics, risk factors, presentation, and management outcomes compared to matched controls experiencing ACS due to atherosclerotic plaque rupture.

2 | METHODS

Identification was obtained for patients admitted to St Vincent's Hospital, Melbourne, Australia, a large referral hospital with SCAD over the period 1/1/2000-12/31/2015. Patients were either admitted directly from the emergency department or transferred to the center from smaller regional and rural hospitals across Victoria and southern New South Wales.

Cases of SCAD were identified through discharge coding on medical records. To maximize case capture, cross-checking was performed of angiographic diagnoses entered into hemodynamic monitoring databases at coronary angiography (Sensis software, Siemens 2015). Full case histories were then accessed via electronic medical records, paper files, or microfilm. The St Vincent's human research ethics committee approved the study as a low risk research application (LRR 200/15). As the study was retrospective in nature, a consent form was not required.



FIGURE 1 Coronary angiogram demonstrating a multi-vessel spiral spontaneous coronary artery dissection of the left anterior descending, first diagonal, and proximal left circumflex arteries with multiple radiolucent lumens

We identified 22 patients admitted with SCAD from the time period. These patients were matched on a 1:3 basis with 66 ACS patients admitted during the same timeframe. Matching was performed according to type of ACS, with three groups identified: ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), or unstable angina (UA). Controls were randomly selected from the local database of coronary angiograms performed at our institution over the same years. Random selection was acquired using an Excel-based random selection algorithm (MS Excel, Microsoft Office 2015).

Baseline characteristics assessed included age, gender, body mass index (BMI), heart rate and systolic, and diastolic blood pressure (BP) on admission. Risk factors assessed included hypertension, smoking status (defined as ever-smoker or never-smoker), diabetes, family history, or dyslipidaemia. The presence of anxiety, depression, or any other formally diagnosed psychiatric disorder (assessed as a composite variable of any psychiatric history) was quantified through medical records and detailed medical interview. Further risk factors of SCAD including pregnancy, post-partum status, or oral contraceptive pill use (assessed as a composite variable reflecting heightened oestrogen exposure), menopausal status, use of illicit drugs, and extreme exertion preceding the event were assessed. Clinical baseline characteristics included culprit vessel responsible for SCAD or ACS, presence of multi-vessel disease on coronary angiography, mean left ventricular ejection fraction (LVEF), assessed via either Simpson's biplane method at echocardiography or calculated assessment at echocardiography or left ventriculogram, requirement for inotropic support, and if thrombolysis was administered.

Further baseline characteristics included ACS medical therapy commenced, including dual antiplatelet therapy (DAPT) with aspirin or thienopyridine, HMG CoA-reductase inhibitors, beta-blockers, angiotensin converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB), and anticoagulation (Tables 1-4).

2.1 | Outcomes

Outcomes assessed included the management strategy: medical (conservative) therapy, or revascularization techniques of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). A composite endpoint of major adverse cardiovascular or cerebrovascular endpoints (MACCE) was compared between groups; this endpoint included death, stroke, recurrent ACS within 12 months or need for repeat revascularization within 12 months. Individual endpoints of stroke, death, requirement for repeat coronary angiography, repeat

TABLE 1 Baseline characteristics of spontaneous coronary artery dissection versus acute coronary syndrome controls

	SCAD (n = 22)	ACS (n = 66)	P-value
Age (years)	48.7 ± 10.7	61.3 ± 10.6	<0.0001
Male gender (%)	22.7	80.3	<0.0001
BMI (kg/m ²)	24.9 (22.3-30.1)	28.8 (26.4-33.2)	0.009
Heart rate on admission (bpm)	80 (74-92)	70 (64-80)	0.003
Median SBP (mmHg)	123.5 (112-140)	140.5 (116-150)	NS
Mean DBP (mmHg)	77 (66-82)	75.5 (70-89)	NS
HTN (%)	40.9	63.6	NS
Ever-smoker (%)	54.5	62.1	NS
Diabetes (%)	0	33.3	0.02
Hypercholesterolemia (%)	27.3	60.6	0.007
Family history premature coronary disease (%)	31.8	45.4	NS
Anxiety/depression/other neuropsychiatric illness (%)	52.4	1.5	0.0001
Peri-partum, post-partum <6 weeks or on oral contraceptive (% of women)	16.7	0	NS
Post-menopausal (% of women)	22.2	53.8	NS
Illicit drug or sympathomimetic use (%)	0	3	NS
Extreme exertion prior to presentation	13.6	0	0.002

BMI, body mass index; bpm, beats per minute; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Normally distributed continuous data are presented as mean ± standard deviation. Non-normally distributed continuous data are presented as median (interquartile range). Categorical data is presented as percentage values.

TABLE 2 Angiographic and clinical characteristics spontaneous coronary artery dissection versus acute coronary syndrome controls

Parameter	SCAD (n = 22)	ACS (n = 66)	P-value
Culprit vessel (%)	Left Main 8%	Left Main 5%	NS
	LAD 48%	LAD 45%	
	LCX 15%	LCX 18%	
	RCA 29%	RCA 32%	
Multi-vessel disease (%)	13.6	59.0	<0.0001
Median LVEF (%)	60 (50-65)	55 (45-60)	NS
Inotropic support	9.1	4.5	NS
Thrombolysis administered from rural/regional transfer	18.2	25.7	NS

LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; LVEF, left ventricular ejection fraction.

Normally distributed continuous data are presented as mean ± standard deviation. Non-normally distributed continuous data are presented as median (interquartile range). Categorical data is presented as percentage values.

SCAD, length of stay, and readmission to the cardiology unit within 12 months were also separately calculated.

2.2 | Statistical analysis

Patients were matched on a 1:3 case-control basis with matching according to type of ACS. For comparison of categorical variables, a chi-squared test was used with values reported in proportions as a percentage (%). Continuous variables were assessed for normality of distribution utilizing a Shapiro-Wilk test. For normally distributed continuous variables, a two-tailed t-test was used, with results reported as mean values ± standard deviations. Non-normally distributed continuous variables were assessed with Mann-Whitney test, with results reported as median (interquartile range). A P-value of <0.05 was considered statistically significant, with a value >0.05 considered non-significant (NS). All statistical analysis was performed with STATA 2015 (STATA Corp Software, TX, USA).

3 | RESULTS

Twenty-two SCAD patients were identified during the study period matched on a 1:3 basis to 66 ACS controls. In the cohort 45% presented with STEMI, 41% with NSTEMI and 14% with unstable angina.

The majority of SCAD patients were female (77.3% vs 19.7%, $P < 0.0001$), younger in age (48.7 ± 10.7 years vs 61.3 ± 10.6 years, $P < 0.0001$), with a lower median body mass index (24.9 vs 28.8 kg/m², $P = 0.009$), compared to the ACS group. Traditional cardiovascular risk factors were less common in the SCAD group with an absence of diabetes mellitus (0% vs 33.3% $P = 0.02$), and lower rate of hypercholesterolemia (27.3% vs 60.6% $P = 0.007$).

TABLE 3 Management strategies of spontaneous coronary artery dissection versus acute coronary syndrome controls

Outcome	SCAD (n = 22)	ACS (n = 66)	P-value
PCI (%)	13.6	83.3	0.0001
IVUS/OCT (%)	13.6	1.5	0.02
CABG (%)	9.0	1.5	NS
No revascularization-medical therapy	77.3	16.7	0.0001
DAPT	81.8	91.0	NS
Aspirin	100.0	97.0	NS
Clopidogrel	59.1	69.7	NS
Ticagrelor	22.7	24.2	NS
HMG CoA reductase inhibitors	68.2	97.0	0.0001
Warfarin or OAC	9.1	1.5	NS
ACEi/ARB	72.7	86.4	NS
Beta blocker	72.7	84.8	NS

ACEi/ARB, angiotensin converting enzyme inhibitor/angiotensin receptor blocker; CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; IVUS/OCT, intravascular ultrasound/optical coherence tomography; OAC, oral anticoagulant; PCI, percutaneous coronary intervention. Normally distributed continuous data are presented as mean \pm standard deviation. Non-normally distributed continuous data are presented as median (interquartile range). Categorical data is presented as percentage values.

SCAD patients had a higher median heart rate at presentation (80 vs 70 bpm, $P = 0.003$); reasons for this may include a higher rate of reported extreme exertion (13.6% vs 0.0%, $P = 0.02$) or the elevated presence of anxiety, depression, or other neuropsychiatric illness amongst SCAD patients (52.4% vs 1.5%, $P < 0.0001$).

A minority of the patients were peri-partum, post-partum (<6 weeks post delivery), or on the oral contraceptive pill, compared to none of the ACS patients (16.7% vs 0%, $P = NS$). Similarly a minority of SCAD patients were post-menopausal compared to ACS controls (22.2% vs 53.8%, $P = NS$).

At coronary angiography, culprit vessel anatomy did not differ between the two groups, however, multi-vessel disease was more common in the ACS group (59.0% vs 13.6%, $P < 0.001$). Clinical characteristics of left ventricular function including inotropic support (9.1% vs 4.5%, $P = NS$) and median ejection fraction (60% vs 55%, $P = NS$) was similar.

Revascularization strategies differed significantly between the two groups with four patients (13.6%) in the SCAD group undergoing PCI versus 55 patients (83.3%) in the ACS group ($P < 0.0001$). Rates of CABG, however, did not differ significantly. "Conservative therapy" (no revascularization with medical treatment alone) occurred in 17 patients (77.3%) with SCAD versus 11 patients (16.7%) in the ACS group ($P < 0.0001$).

The use of DAPT (aspirin and one of clopidogrel or ticagrelor) was high in both groups (81% SCAD vs 91% non-SCAD $P = NS$), with

TABLE 4 Twelve-month outcomes of spontaneous coronary artery dissection patients versus acute coronary syndrome controls

Outcome	SCAD	ACS	Significance
MACCE (%)	13.6	27.3	NS
Death (%)	4.5	6.1	NS
Stroke (%)	0	0	NS
Readmission with cardiovascular diagnosis (%)	9.1	21.2	NS
Need for repeat coronary angiography (%)	9.1	16.7	NS
Length of index hospital admission (days)	5 (3-9)	3 (2-4)	NS
Recurrent SCAD (%)	0	N/A	N/A

MACCE, major adverse cardiovascular or cerebrovascular event; SCAD, spontaneous coronary artery dissection.

Normally distributed continuous data are presented as mean \pm standard deviation. Non-normally distributed continuous data are presented as median (interquartile range). Categorical data is presented as percentage values.

ticagrelor used Australia from 2013 with similar uptake between both SCAD and ACS patients (22.7% vs 24.2% $P = NS$). There was no statistically significant difference in the use of ACEi/ARB or beta-blockers.

Twelve-month outcomes were assessed in both groups. Major adverse cardiovascular or cerebrovascular events (MACCE) were a composite of death, stroke, readmission with cardiovascular diagnosis, or need for repeat coronary angiography. There was a numerical difference in composite MACCE with SCAD patients having a rate of 13.6% versus 27.35% in ACS controls however this was not statistically significant ($P = NS$). Stroke was not observed in either group at 12 months, with death rates similar in both groups (4.5% SCAD vs 6.1% ACS $P = NS$). Length of index hospital admission was longer in patients with SCAD at 5 days compared to ACS controls 3 days however this was not statistically significant ($P = NS$). One SCAD patient required a heart transplant after presenting with a recurrent SCAD 8 years after the initial event, with multi-vessel involvement leading to refractory heart failure despite revascularization.

4 | DISCUSSION

This study demonstrates that a history of anxiety, depression, or previous neuropsychiatric diagnosis is the major risk factor for developing SCAD when compared to ACS (52.4% vs 1.5%, $P < 0.0001$). With previous research suggesting up to one third of patients suffer from anxiety or depression,¹³ this is at a higher rate than other large cohorts.^{5,8} Further weight is added to this finding as the neuropsychiatric history was undertaken in all patients prior to the coronary angiogram, thus eliminating a possible recall bias once the

diagnosis of SCAD was known. Contrasting to ACS, which affects predominantly post-menopausal women, our SCAD group was numerically pre-menopausal (77.8% vs 46.3%, $P = \text{NS}$). In comparison to diseases such as Takotsubo cardiomyopathy that predominantly affects post-menopausal women and involves a neuro-cardiac action,^{14–16} a similar mechanism in the pathophysiology of SCAD has not been analyzed. Screening reports of SCAD patients have shown depression and anxiety may be under-reported¹³ and emotional stress prior to the event is common.¹⁰ One theory is increased release of catecholamines leads to coronary artery vasospastic activity with subsequent increases in arterial wall stress leading to intimal rupture or disturbance within the vaso-vasorum.¹⁰

SCAD patients often find it hard to comprehend why they have suffered an ACS in the absence of a traditional cardiac risk factor profile. Cardiac rehabilitation is useful in education, risk factor control, and assisting adherence to medical therapy in both SCAD and ACS patients and was offered to all patients in both groups prior to discharge.^{13,17} Moreover, dedicated SCAD cardiac rehabilitation services have been trialled with favorable improvements in chest pain and long term cardiac, psychosocial, and exercise benefits when compared to ACS controls.¹⁸ Regardless of the absence of recurrent SCAD in our study, review with a cardiologist is mandatory to ensure improved outcomes, as recurrent SCAD has been reported with variable rates between 10 and 50% of patients during follow up.^{5,8,19}

The SCAD patients were more likely to be female (77.3% vs 19.7%, $P < 0.0001$) and of a younger median age (48.7 ± 10.7 years vs 61.3 ± 10.6 years, $P < 0.0001$) compared to ACS patients. This is consistent with previous research suggesting the majority of SCAD patients are less than 50 years of age.^{1,20} Despite the statistically significant difference of traditional cardiovascular risk factors such as diabetes (0% vs 33.3%, $P = 0.02$) and hypercholesterolemia (27.3% vs 60.6%, $P = 0.007$) in the SCAD compared to the ACS group, there was no difference in the risk factors of hypertension (40.9% and 63.6% $P = \text{NS}$) or smoking (54.5% and 62.1% $P = \text{NS}$). This finding is supported by previous work suggesting patients with idiopathic SCAD have higher rates of smoking and hypertension.⁶

There are no guidelines on the optimal treatment strategy for SCAD. Management should be individualized to each patient and is balanced on presence of symptoms, amount of myocardium at risk and hemodynamic stability. The medical management of SCAD is similar to that of an ACS, however, the evidence is limited to retrospective and case series data.²¹ With regards to antiplatelet activity, the hypothesized benefit of DAPT prevents thrombus formation at the site of dissection within the true lumen.^{7,9} However, others authors suggest the failure of thrombus to form in the false lumen may continue axial progression and extension of the disease.²¹ In the absence of convincing randomized evidence, 81.8% of patients in our SCAD cohort received DAPT with clopidogrel or ticagrelor, in the absence of major bleeding risk for 12 months despite the role of extending therapy to prevent recurrent MACCE being unknown.

Thrombolytic therapy is also controversial for patients presenting with STEMI with a subsequent diagnosis of SCAD. One paper found 60% of SCAD patients who received thrombolysis had a clinical

deterioration necessitating the need for revascularization with PCI or CABG.²⁰ Other authors have described successful pharmacological revascularization with thrombolysis.²² As 45% of our patients in both groups presented with STEMI, thrombolysis was not withheld and administered in patients presenting to rural, regional and non-PCI centers. Although the results were not pre-specified, there was no overall difference in MACCE outcomes between the two groups. Thrombolysis should not be withheld however in a patient with STEMI without cardiovascular risk factors as the risk of thrombotic occlusion is much higher than a pathophysiology of SCAD.⁷

The role of beta blockade in SCAD is hypothesized to be the mainstay of therapy by negative chronotropic and inotropic effects leading to decreased shear stress and risk of dissection propagation.⁷ There were no differences in uptake in either group (72.7% SCAD vs 84.8% ACS controls, $P = \text{NS}$). ACE-i/ARB agents were administered in similar numbers for both groups in patients with myocardial necrosis or left ventricular dysfunction (72.4% SCAD vs 86.4% ACS, $P = \text{NS}$). Two patients in the SCAD group sustained a left ventricular thrombus extensive infarction requiring warfarin or anticoagulant therapy for a minimum of 3 months with appropriate resolution compared to none in the ACS control group. One of these patients developed an ischemic cardiomyopathy with refractory heart failure admissions necessitating successful orthotopic heart transplantation. The other presented with an mid LAD SCAD in the third trimester of pregnancy, managed with aspirin, clopidogrel, and enoxaparin subcutaneous injections.

HMG CoA reductase inhibitors with statin therapy was prescribed less frequently in SCAD patients compared to the non-SCAD group (68.2% vs 97% $P < 0.0001$), with the decision of therapy at the discretion of the treating cardiologist, despite the evidence an increase in recurrent SCAD for the those patients prescribed statin therapy at discharge.⁸ Interestingly, we reported no recurrent SCAD events in our study population. The current approach hypothesized for SCAD is not to prescribe statins unless there is evidence of hypercholesterolemia or further atherosclerotic disease in other coronary vessels.²¹

Revascularization of SCAD with PCI or CABG has mixed results. PCI should be undertaken with care, as there is risk of dissection propagation with wire engagement in the false lumen. Repeated coronary contrast injection can induce a further hydraulic dissection and extend the intramural hematoma. Careful attention must be taken with co-axial placement of diagnostic and guide catheters to avoid pressure damping and deep intubation. In one large series of 87 patients with SCAD, 43 underwent primary PCI with technical success achieved in 65%.⁸ Intravascular ultrasound (IVUS) or optical coherence tomography (OCT) can be utilized in the diagnosis of SCAD.^{11,23} When undertaking PCI IVUS and OCT are useful in assessing the true lumen and ensuring adequate stent deployment.²⁴ In our SCAD group, IVUS or OCT was performed in all patients undergoing revascularization with PCI compared to a minority of ACS controls (13.6% vs 1.5% $P = 0.02$), in order to ensure correct coronary guide-wire position in the true lumen and stents were well apposed. PCI was commonly reserved in our study for a small number of SCAD patients (13.6%) who had ongoing evidence of hemodynamic instability or active ischemia at

coronary angiography in proximal large caliber coronary vessels supplying a large territory of myocardium. The ACS control group underwent significant rates of guideline driven routine PCI guided revascularization when compared to SCAD (83.3% vs 13.6% $P < 0.0001$), with a “medical-therapy” approach adopted in 77.3% of SCAD versus 16.7%, $P < 0.0001$ in the ACS group. None of the patients who were treated conservatively with medical therapy required repeat coronary angiography or revascularization during the index hospital admission. A “watchful-waiting” conservative strategy of ischemia driven PCI in SCAD is supported by Alfonso et al showing both acute and long-term favorable clinical outcomes.^{3,21} The numerical increase in length of stay in the SCAD group (5 vs 3 days in ACS control, $P = NS$) is likely explained by the increased coronary care unit observation post initial presentation for patients treated with medical therapy alone.

Similar to patients presenting with an ACS, repeat coronary angiography was not performed in our cohort as a routine, unless the patient presented with repeated chest pain or an acute coronary syndrome (two patients 9.1% SCAD vs 11 non-SCAD ACS patients 6.7%, $P = NS$). Of the two patients in the SCAD group, one presented with troponin negative chest pain and was found to have complete resolution of the previous SCAD. The other patient had a repeat study as a workup for heart transplantation. The findings are consistent with research demonstrating routine repeat coronary angiography reveals a healed dissection at 9 months in up to 50% of patients.³

Two patients (9.0%) underwent CABG in the SCAD group where PCI was deemed inappropriate or technically challenging for patients with ongoing active ischemia. One patient presented with residual dynamic ST-elevation in both the anterior and inferior leads post thrombolysis from a peripheral center, and was found to have multi-vessel spiral dissection involving the ostial to apical LAD, involving the first diagonal artery and a dominant LCX (see Figure 1), and survived without MACCE or left ventricular impairment. CABG is considered for patients with left main or multi-vessel involvement but may be challenging for the surgeon when navigating the true lumen of grafts and dealing with friable and fragile vessels. Routine coronary angiography post SCAD has demonstrated a proportion of grafts may fail post revascularization.⁸

Twelve-month death rates were low with one patient in the SCAD group compared to 4 in the ACS group (4.5 vs 6.1, $P = NS$). This finding is consistent with a favorable short-term prognosis from SCAD with a 95% 2-year survival.^{3,25} There was a numerical difference with reduction in 12 month MACCE between the two groups (13.6% vs 27.35%) suggesting SCAD patients are at lower risk of recurrent events and death than the ACS population however this was not statistically significant ($P = NS$), likely due to the relative small number of patients observed. Long-term prognosis has been observed however with relatively high rates of cumulative 10-year major adverse cardiac events (death, heart failure, myocardial infarction, or recurrent SCAD) at 47%.⁸ This high rate implores the need to involve SCAD patients in cardiac rehabilitation, neuropsychiatric counseling, secondary prevention, and risk factor modification in what may be incorrectly viewed as a low risk group.

4.1 | Limitations

As our study is a single center case control in design, the major limitation is of a selection bias and the results on exposure to SCAD are subject to an observation bias. Furthermore, the small sample size and relatively short period of follow up may lead to a referral bias.

There have been multiple studies demonstrating FMD as a significant risk factor for the development of SCAD.⁵ Our work did not involve imaging studies in either the ACS or SCAD group to specifically screen for the characteristic femoral or renal artery “string of beads” sign of FMD on angiography.^{5,21} A further limitation of this study is the absence of plasma catecholamine measurement at presentation in both groups, which may provide insight into the pathophysiology mechanism and interplay within the neurological and cardiac axis. This hypothesis has grounds for future study.

The inability to observe resolution or healing of SCAD may be seen as a limitation to our findings, however, we do not feel repeat coronary angiography was likely to change management for the majority of our patients, provided they remained asymptomatic. Therefore, it may be seen as unethical to subject patients to the risks (albeit low) of repeat coronary angiography. There may be a role for computed tomography derived coronary angiography has been postulated as a possible tool to assess resolution of SCAD,⁷ however, this was not performed in this analysis.

5 | CONCLUSION

When compared to ACS, SCAD affects younger, more typically female patients with a paucity of traditional cardiovascular risk factors. The major risk factor for SCAD compared to ACS is a history of anxiety, depression, or neuropsychiatric illness. An ischemia driven conservative approach to revascularization in the SCAD group led to similar MACCE when compared to ACS controls undergoing guideline revascularization techniques at 12 months.

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CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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