# Epidemiology and Pathophysiology of Spontaneous Coronary Artery Dissection

Subjects: Cardiac & Cardiovascular Systems

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Spontaneous Coronary Artery Dissection (SCAD) refers to the spontaneous separation of the layers of the vessel wall caused by intramural hemorrhage, with or without an intimal tear. This condition is not associated with trauma, atherosclerosis or iatrogenic causes and may be an expression of an underlying systemic arterial disease, namely, fibromuscular dysplasia.

spontaneous coronary artery dissection | multimodality imaging | coronary imaging

## 1. Epidemiology

### 1.1. Sex, Age, Ethnicity

The real incidence of spontaneous coronary artery dissection (SCAD) is difficult to define as it is often underestimated. Although SCAD is an uncommon cause of all heart attacks (<1% of all acute myocardial infarctions are caused by spontaneous dissections) [1], its incidence in acute myocardial infarctions in women remains considerable. It is estimated that about 1/3 of acute myocardial infarctions in women <50 years are caused by spontaneous dissections [2][3]. The "typical" SCAD patient is a middle-aged woman with few traditional cardiovascular risk factors, albeit acute coronary syndrome (ACS) due to SCAD has been observed from the late teens to the ninth decade of life [3]. SCAD is likely influenced by a combination of factors that include sex; hormonal fluctuations; underlying arteriopathies; genetics; and environmental, physical, and emotional precipitants. Women comprise 87% to 95% of SCAD with a mean age of presentation between 44 and 53 years [4][5][6]. Data on SCAD in men are limited because the prevalence of this condition among men is low. SCAD in men is more frequently associated with excessive physical exertion (e.g., exercise or heavy lifting) and tends to have a lower prevalence of fibromuscular dysplasia than in women with SCAD [1].

White Caucasian ethnicity predominates in most observational series; however, cases have been described in many racial groups [3]. SCAD fatalities are uncommon; however, their incidence remains unknown, due to challenges with accurate post-mortem diagnosis [7].

### 1.2. Pregnancy-Associated SCAD

The strong female sex predominance of SCAD and the association with pregnancy and perhaps multiparity strongly suggest some association between female sex hormones and the pathophysiology of SCAD. However, the precise relationship remains unknown, and SCAD has been described in men, post-menopausal and nulliparous women. SCAD has been described in patients taking hormonal contraception and hormone replacement therapy. However, it has never been demonstrated that exogenous hormone use is more prevalent in SCAD or that continuing to take hormones after SCAD increases the risk of recurrence [3]. Pregnancy-associated SCAD (P-SCAD; usually defined as SCAD occurring during gestation or within 12 months of delivery) accounts for approximately 5–10% of cases of SCAD. Reportedly accounts for 10–22% of ACS events in pregnancy and 23–67% of postpartum ACS [2][3][8]. There is growing evidence that P-SCAD is associated with a more severe phenotype with proximal and extensive dissections and larger infarcts. SCAD has also been observed in association with multi-parity and pre-eclampsia in some studies [9][10][11][12].

### 1.3. Inflammatory Conditions

Even if SCAD is not frequently related to systemic inflammatory disorders, laboratory testing to rule out autoimmune diseases may be taken into consideration in the post-acute setting of patients symptomatic of rheumatologic conditions [2].

### 1.4. Inheritance and Genetics

SCAD occurs rarely in patients with known hereditary conditions.

Familial SCAD is rare [13], and pathogenic variants were identified in only 3.5% of unselected patients in a genome sequencing study, suggesting that most cases are sporadic; therefore, at present, testing genetic is not recommended in all cases of SCAD [14].

### 1.5. Risk Factors for Ischemic Heart Disease

Although the prevalence of classic risk factors for ischemic disease is low, coronary dissection is more frequently associated with arterial hypertension and less frequently with diabetes mellitus [15][16][17]. Indeed, whilst risk factors are less common in SCAD patients than in atherosclerotic patients, SCAD should not be excluded from diagnostic consideration when risk factors are present.

The left anterior descending coronary artery is involved in about 40% of SCAD [18][19], mainly in its mid-to-distal segments. Other vessels or multivessel SCADs are less common [2][20].

## 2. Pathophysiology

SCAD is an acute coronary event linked to the formation and expansion of an intramural hematoma that determines the separation of the intima or intima-media complex from the underlying vessel lumen creating a false lumen that compresses the true light. This process determines, depending on the degree of compression of the

true lumen, ischemia, or myocardial infarction. Two mechanisms have been hypothesized to explain the entry of blood into the vessel wall [21][22]:

Inside-out mechanism: Rupture of the endothelium with the passage of blood from the true lumen to the subintimal space.

Outside-in mechanism: Formation of “de novo” hematoma at the level of the middle tunic due to rupture of the vasa vasorum or by dissection of the medium tunic with a consequent false lumen. Several pieces of evidence, acquired with the IVUS (intravascular ultrasound)/ OCT (optical coherence tomography) method, support this hypothesis.

Frequently, there is no communication between the true and false lumen and when fenestrations are created, these derive from the breaking of the false lumen into the true lumen and not vice versa; in addition, serial angiography performed during SCAD have shown that the intramural hematoma precedes the intimal dissection [21][22][23][24]. More rarely, the occlusion of the true lumen may be due to thrombosis generated by the exposure of the pro-thrombogenic subendothelium following injury to the intima.

To explain the pathogenesis, predisposing conditions have been identified that cause the weakening of the vascular wall and precipitating conditions that, by increasing the wall stress, favor its rupture. There is a complex relationship between a vulnerable subject and potential triggers that initiate a spontaneous arterial tear or intramural hematoma

Among the predisposing conditions, the most frequent is fibromuscular dysplasia (FMD), a non-atherosclerotic segmental idiopathic disease of the medial tunic of the arterial walls manifested by stenosis, aneurysms, tortuosity, or spontaneous dissections of small and medium arteries caliber. FMD is linked to the proliferation of smooth muscle cells and fibrous tissue [25]. The association of SCAD with multifocal FMD in arteries has been the most frequently found and coronary dissection could be the first manifestation of FMD [20]. Multifocal FMD is defined from an angiographic point of view as areas of alternating stenosis and dilatation. There is a high prevalence of concomitant extra coronary arterial anomalies in registries of SCAD patients. In patients without diagnostic features of FMD, other arterial abnormalities have been reported, such as dissections, aneurysms, or arterial tortuosity (78%) [26][27][28].

About 80–90% of patients with FMD are female (prevalence about 4% of the population). The presence of any extracoronary vascular abnormalities (EVA) in patients with SCAD is high and includes aneurysms and noncoronary dissections. The cerebral aneurysm has been detected in 7 to 14% of patients with SCAD who have undergone screening [29][30][31].

Whether or not SCAD is a coronary manifestation of fibromuscular dysplasia or a unique but related entity with a considerable number of arterial features in common, SCAD may be a *forme fruste* of an underlying systemic arteriopathy that leaves the affected patient vulnerable to dissection when exposed to arterial shear stress related to an inciting trigger [1].

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