JACC: CARDIOVASCULAR INTERVENTIONS
PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN
COLLEGE OF CARDIOLOGY FOUNDATION

VOL. 11, NO. 1, 2018
ISSN 1936-8798/$36.00
https://doi.org/10.1016/j.jcin.2017.09.029

EDITORIAL COMMENT

Spontaneous Coronary Artery Dissection

Reflections on an Uncommon Etiology of Acute Myocardial Infarction*

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Spontaneous coronary artery dissection (SCAD) is an infrequent, but potentially lethal, condition that can be easily missed in patients presenting with acute myocardial infarction (AMI). It has a different pathophysiology and prognosis than most AMI events, and requires a distinct treatment approach (**Table 1**) (1-3). The 2012 Third Universal Definition of Myocardial Infarction acknowledged dissection complicating coronary atherosclerotic plaque as a potential mechanism of type 1 myocardial infarction, but did not recognize or expand on SCAD as a distinct entity (4). In addition, most of the information on the clinical presentation and management of SCAD originates from case reports and registry data. These data are derived from small, retrospective studies subject to bias, and are fraught with issues related to diagnosis ascertainment and the inability to establish treatment appropriateness. A recent meta-analysis comparing upfront conservative versus revascularization strategies in SCAD patients encompassed 11 nonrandomized studies, and yet, included only a total of 631 patients (5). This underscores the paucity of existing data and the need to examine SCAD using larger and comprehensive datasets. It is in this context that the excellent study by Mahmoud et al. (6) in this issue of *JACC: Cardiovascular Interventions* should be viewed.

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The investigators queried the National Inpatient Sample (NIS) database for women hospitalized with AMI and concomitant SCAD between 2009 and 2014 (6). They found an overall prevalence of SCAD of ~1% with decreasing incidence over time. Compared with AMI patients without SCAD, women with SCAD were younger, had fewer comorbidities, including lower rates of prior revascularization and ischemic events, and were more likely to present with ventricular arrhythmias and cardiogenic shock (6). SCAD patients had higher in-hospital mortality compared with other AMI patients. Notably, both in-hospital mortality and percutaneous coronary intervention (PCI) rates in SCAD patients appear to be declining over time (6). In addition, women presenting with non-ST-segment elevation myocardial infarction (NSTEMI) and SCAD who underwent PCI had higher in-hospital mortality compared with those who did not undergo PCI, a finding that was not evident in their ST-segment elevation myocardial infarction (STEMI) counterparts (6).

The authors' remarkable work boasts many strengths and merits (6). The investigators used a very large and relatively contemporary dataset to shed light on this uncommon etiology of AMI, and their report currently stands as the largest among all published studies on SCAD. They provided a detailed description of SCAD patients and highlighted their increased in-hospital mortality and the potential role of PCI, all of which are clinically very important. They also conducted robust analyses inclusive of propensity score matching and multivariable regression analyses, and corroborated their findings in subgroup analyses showing concordant results in 12 examined patient subpopulations.

On the other hand, their study has several controversies and limitations. The increasing incidence of SCAD over time is interesting. It is unclear,

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

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TABLE 1 What Should Interventional Cardiologists Know About SCAD

Clinical attributes:
- Prevalence ~1%*
- Affects predominantly younger women (men in ~5% to 10% of cases)
- Associated or predisposing etiologies include: pregnancy, fibromuscular dysplasia, chronic systemic inflammatory diseases, hormonal therapy, connective tissues disorders (e.g., Marfan and Ehler-Danlos type 4 syndromes), familial inheritance (~1% of cases), and so on.
- Possible precipitating factors: extreme emotional stress or physical activity, sympathomimetic drugs, high-dose hormonal therapy exposure, activities with intense Valsalva-like maneuvers (e.g., vomiting, coughing, childbirth)
- Clinical presentation: usually AMI (less commonly: ventricular arrhythmias, cardiogenic shock, sudden cardiac death)
- SCAD patients have usually preserved LV ejection fraction and/or near full-recovery after their initial presentation
- Inpatient monitoring for at least 5 days is recommended among conservatively managed SCAD patients (given risk of early progression of the dissection)
- Recurrence: SCAD can recur in the same or different artery (~27% at 4 to 5 yrs after the initial event); future pregnancy should likely be avoided; CTA utility is uncertain (likely not helpful for diagnosis, but possibly helpful to document coronary healing)

Angiographic characteristics:
- Angiographic types of SCAD:
  - Type I: extraluminal contrast staining, multiple radiolucent lumen, spiral dissection (~29% of cases)
  - Type II: diffuse stenosis of varying severity/length—usually >20 mm in length—with abrupt changes in arterial caliber, from normal caliber to diffuse narrowing (~68% of cases)
  - Type III: focal/tubular stenosis mimicking atherosclerosis—usually < 20 mm in length (~3% of cases)
- Usually (>90%) affects the middle and distal coronary segments
- Coronary artery involvement:
  - LAD and branches: ~45% to 60% of cases (most affected)
  - Left circumflex and branches: ~15% to 45% of cases
  - RCA and branches: ~10% to 40% of cases
  - LM: ~0% to 4% of cases
  - Multiple arteries dissected: ~9% to 19% of cases
- TIMI flow grade 3: ~19% to 55% of cases on presentation

Medical therapies:†
- Dual-antiplatelet therapy (aspirin + $P2Y_{12}$ receptor inhibitor): likely useful, theoretically may reduce false lumen thrombosis and consequent true lumen compression
- Beta-blocker: reduces arterial shear stress, and possibly useful in the short-term and in the long-term to prevent recurrence
- Anticoagulation: controversial, risk of extending the dissection vs. helping resolve the lumen thrombus and improve true lumen patency
- Fibrinolytic therapy: likely harmful and should be avoided (possible extension of the dissection and intramural hematoma)
- Angiotensin-converting enzyme or angiotensin receptor inhibitor: beneficial in SCAD patients with LV dysfunction; no proven benefits otherwise‡
- HMG CoA-reductase inhibitor (statin): no proven benefit in the absence of concomitant atherosclerotic disease‡
- Cardiac rehabilitation program: evidence shows that a dedicated program is beneficial in SCAD patients

Revascularization vs. conservative management:
- SCAD arteries usually heal spontaneously (100% healing ≥26 days post-dissection)
- PCI is associated with low success rates (range 47% to 73%)
- The optimal therapeutic strategy (revascularization versus conservative) should be tailored to patient's clinical scenario. Conservative management may be reasonable in many instances. However, revascularization, preferably with PCI (or CABG if needed), should be undertaken in patients with ongoing ischemia and/or electrical and hemodynamic instability.

PCI technical challenges and tips:
- The femoral artery approach is preferred (more iatrogenic dissections observed with radial artery catheterization)
- Long stents are preferred to adequately cover both edges of the intramural hematoma
- For very long lesions, multistep and multistenting approach is reasonable (i.e., stenting the distal then the proximal edge, to prevent propagation of the intramural hematoma, followed by stenting of the middle coronary segment)
- The distal coronary segments—usually affected by SCAD—may be too small and not amenable to PCI with stenting
- Intravascular imaging—OCT or IVUS—should be used cautiously. Intravascular imaging is possibly helpful (e.g., helps visualize intimal tears, false lumen, and intramural hematoma and thrombi; also ascertains the extent of dissection and adequate stent coverage and apposition), but carries potential hazards (see the following text)
- Operators should beware of the:
  - Risk of iatrogenic catheter-induced dissection
  - Potential difficulty to enter the true lumen with the wire or balloon/stent
  - Risk of propagation of the dissection (by the wire/imaging catheter/balloon/stent or through contrast-induced hydraulic extension)
  - Risk of coronary rupture
  - Risk of stent malapposition following the resorption of the intramural hematoma

Table compiled from multiple studies and reviews (1–3,6,8–10). *Likely an underestimate. †Only SCAD-specific benefits are summarized in this section. Evidence-based recommendations for medical therapies are lacking, and the summarized therapies herein are theoretical and extrapolated from the known benefits of these treatments in AMI patients. ‡The SAFER-SCAD (Statin and Angiotensin-Converting Enzyme Inhibitors on Symptoms in Patients With SCAD) trial is ongoing, and should shed light on the utility of statins and angiotensin-converting enzyme inhibitors in SCAD patients.

AMI = acute myocardial infarction; CABG = coronary artery bypass graft; CTA = computed tomography angiography; IVUS = intravascular ultrasound; LAD = left anterior descending coronary artery; LM = left main coronary artery; LV = left ventricular; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; RCA = right coronary artery; SCAD = spontaneous coronary artery dissection; TIMI = Thrombolysis In Myocardial Infarction.

however, whether this is a true or a spurious finding related to miscoding/misdiagnosis, increased use of angiography and/or heightened awareness of this entity over time. Even if true, the changes over time—while statistically significant—do not appear to be clinically significant. Most importantly, the current report highlights the fact that SCAD is not as rare as previously believed, especially among older women.

Around 77% of women with SCAD in this study were >50 years of age (6). The current study also likely underestimates the incidence of SCAD, given the investigators included only AMI patients who underwent an invasive strategy (thus missing other SCAD presentations, such as sudden cardiac death) and given the lack of data on invasive intracoronary imaging (the likely underuse of intracoronary imaging might have resulted in missed diagnoses of types 2 and 3 SCAD).

Another major limitation of the study is its use of administrative data that utilize billing codes for research. Although the NIS dataset has been extensively validated (crosschecked annually by the Agency for Healthcare Research and Quality, and compared with other databases), its accuracy for the identification of SCAD in particular remains unknown. In general, administrative data that rely on International Classification of Disease codes are entered by individuals with minimal medical expertise, have no mechanisms to verify the accuracy of data at entry, usually lack in granularity, and are subject to miscoding and medical inaccuracies. As an example, the current report lacks data on medical therapies, imaging and angiographic variables (e.g., left main coronary artery, multivessel involvement, Thrombolysis In Myocardial Infarction flow grade, left ventricular function), and on PCI success (6).

Furthermore, in their attempt to assess the utility of PCI in SCAD patients, the investigators ended up overstating their findings (6). They concluded that conservative management should be the preferred initial strategy for management of women with AMI presenting with SCAD. They based their conclusions on 2 premises: the observed reduction in mortality among SCAD patients, which was concordant with reduction in PCI rates; and the higher hospital mortality among NSTEMI SCAD patients who underwent PCI compared with those who did not (6). Given the observational nature of their study, the relationship between PCI and mortality is at best an association and does not prove causality. Given also the lack of data on procedural variables and adjunctive therapies, all of which can confound the mortality finding in NSTEMI patients, the authors' conclusions about the role of PCI are controversial. Clinicians may argue that an upfront invasive angiography strategy (coupled with intracoronary imaging, when needed), can help delineate the coronary anatomy and dictate the need for PCI, and is indeed the preferred modality. In the case of STEMI with compromised coronary flow (nearly 45% of SCAD patients in the current report presented with STEMI [6]) or in patients with hemodynamic or electrical instability, it is difficult to justify anything short of attempted revascularization, preferably with PCI. Therefore, clinicians should account for the heterogeneity in the clinical presentation of SCAD and ascribe a tailored approach to these patients. Notably, the meta-analysis by Martins et al. (5) showed no significant differences in SCAD patients between revascularization and conservative management with respect to mortality, MI, target vessel revascularization, or SCAD recurrence.

Despite the aforementioned shortcomings, the authors are to be congratulated on their laudable efforts. They provided a comprehensive characterization of SCAD patients presenting with AMI as well as insights into SCAD outcomes and the impact of PCI (6). Although we have come a long way since the publication of the original SCAD report in 1931, the current report highlights the need for more research in this field. Registry-based randomized studies, as stated by the authors, may shed more light into this field and should be conducted. Such trials may be particularly useful to explore long-term therapeutic strategies among SCAD patients including, but not limited to, the role of dual-antiplatelet therapy, the impact of beta-blockers on preventing SCAD recurrence, and the role of computed tomography versus invasive angiography to document coronary healing. In addition, clinically relevant questions can still be addressed by the existing NIS database. In future investigations, the authors can potentially examine SCAD presentation and outcomes among men, who account for ~5% to 10% of all SCAD events. Moreover, predictors of increased mortality in SCAD patients undergoing PCI can be explored and may provide guidance to interventional cardiologists on which patients to likely benefit from PCI. Overall, given SCAD's infrequent nature, developing expertise in SCAD is a daunting task for clinicians. Therefore, prospective and standardized clinical registries dedicated to SCAD are absolutely needed. The social networking community-initiated multicenter SCAD registry (7), which also includes a biorepository of blood samples, is just one example of such a registry and should be strongly supported and expanded.

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KEY WORDS angiography, coronary, dissection, infarction