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# Spontaneous Coronary Artery Dissection Associated With Pregnancy

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## ABSTRACT

**BACKGROUND** Spontaneous coronary artery dissection (SCAD) is the most common cause of pregnancy-associated myocardial infarction and remains poorly characterized.

**OBJECTIVES** This study sought to assess presentation, clinical factors, and outcomes of pregnancy-associated spontaneous coronary artery dissection (P-SCAD) compared with spontaneous coronary artery dissection not associated with pregnancy (NP-SCAD).

**METHODS** A Mayo Clinic registry was established in 2010 to include comprehensive retrospective and prospective SCAD data. Records were reviewed to identify women who were pregnant or ≤12 weeks postpartum at time of SCAD. Complete records were available for 323 women; 54 women met criteria for P-SCAD (4 during pregnancy) and they were compared with 269 women with NP-SCAD.

**RESULTS** Most events occurred within the first month postpartum (35 of 50). Compared with NP-SCAD, P-SCAD patients more frequently presented with ST-segment elevation myocardial infarction (57% vs. 36%; $p = 0.009$), left main or multivessel SCAD (24% vs. 5%; $p < 0.0001$; and 33% vs. 14%; $p = 0.0027$, respectively), and left ventricular function ≤35% (26% vs. 10%; $p = 0.0071$). Among women with imaging of other vascular territories, P-SCAD was less likely with a diagnosis of fibromuscular dysplasia and extracoronary vascular abnormalities (42% vs. 64%; $p = 0.047$; and 46% vs. 77%; $p = 0.0032$, respectively). Compared with U.S. birth data, women with P-SCAD were more often multiparous ($p = 0.0167$), had a history of infertility therapies ($p = 0.0004$), and had pre-eclampsia ($p = 0.001$). On long-term follow-up (median 2.3 years) recurrent SCAD occurred in 51 patients, with no difference in the Kaplan Meier 5-year recurrence rates (10% vs. 23%; $p = 0.18$).

**CONCLUSIONS** P-SCAD patients had more acute presentations and high-risk features than women with NP-SCAD did. The highest frequency of P-SCAD occurred during the first postpartum month and P-SCAD patients less often had extracoronary vascular abnormalities. Hormonal, hemodynamic variations, and yet-undefined mechanisms might be significant contributors to P-SCAD. (The "Virtual" Multicenter Spontaneous Coronary Artery Dissection [SCAD] Registry [SCAD]; NCT01429727; Genetic Investigations in Spontaneous Coronary Artery Dissection [SCAD]; NCT01427179)
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Spontaneous coronary artery dissection (SCAD) represents the most common etiology of pregnancy-associated myocardial infarction (MI) and is an important cause of acute coronary syndrome in young patients without atherosclerotic coronary artery disease (1,2). In a pregnant or postpartum woman, MI is a dramatic and potentially fatal presentation of SCAD, which remains poorly characterized. The purpose of this study was to comprehensively describe clinical features and outcomes of women who experienced SCAD during or shortly following pregnancy (P-SCAD) and compare them with women with SCAD not associated with pregnancy (NP-SCAD).

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The ongoing Mayo Clinic SCAD Registry, a "virtual" multicenter registry, includes both retrospective and prospective data on patients with SCAD (3). It was established in 2010 in response to the efforts of an online community of SCAD patients seeking further research on their condition. We used the online group to identify patients diagnosed as having at least 1 episode of SCAD and recruited them to participate in a clinical investigation of their condition, creating the "virtual" multicenter registry. A pilot study demonstrated the feasibility of conducting research via this novel, international "virtual" registry (3).

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The diagnosis of SCAD is confirmed on coronary angiography review by experienced interventional cardiologists with subsequent acquisition of patient medical records, images, narratives, extensive patient surveys, and mental health assessments. Additionally, participants and their family members have contributed specimens to the Mayo Clinic SCAD DNA Biorepository. The Mayo Clinic SCAD Registry rapidly grew and currently includes hundreds of participants. Participants learned about the study through social media and online networks, the Internet, patient self-referral, and referring clinicians. We sought to assess presentation, clinical factors, and outcomes of P-SCAD compared with other women with NP-SCAD.

## METHODS

The Mayo Clinic Institutional Review Board approved this study, with written informed consent obtained for participation in the Mayo Clinic SCAD Registry (3). We reviewed 323 patients enrolled in the registry between July 2011 and February 2016 with complete medical records and surveys. Although participation in the Mayo Clinic SCAD Registry and DNA Biorepository do not require a clinical visit, many patients are also evaluated in the dedicated Mayo Clinic SCAD Clinic (54% of the patients included in the present study).

Of the 323 patients, 54 were pregnant, postmiscarriage, or postpartum at time of their SCAD. For this study, the postpartum period was empirically defined as 12 weeks following delivery, consistent with methodologies of prior studies (2,4-6). Patient data, including medical and reproductive history, clinical characteristics, and current medical status, were evaluated via review of available medical records, patient narratives, and a series of questionnaires including the following: Mayo Clinic Women's Heart Clinic Cardiovascular Risk Assessment; the Survey for Women with Heart Disease; and the Mayo Clinic SCAD Questionnaire and Supplemental Survey. Duration of follow-up was determined by last clinical visit or study correspondence. Angiographic diagnosis of SCAD was confirmed by experienced interventional cardiologists (R.G., P.J.M.B.). In those patients with percutaneous coronary intervention, the procedure was considered successful as previously defined (1). The majority of patients with imaging for fibromuscular dysplasia (FMD) underwent 1 of 2 dedicated Mayo Clinic computed tomography angiography (CTA) protocols as described previously (7), which were interpreted by dedicated vascular radiologists: 1) first version with CTA imaging of the neck, chest, abdomen, and pelvis; or 2) second version with CTA imaging of the head, neck, abdomen, and pelvis (modified due to the finding that intracerebral abnormalities are present whereas intrathoracic abnormalities are uncommon) (8). Images of studies to detect extracoronary vascular abnormalities, such as FMD, performed outside of Mayo Clinic were formally reviewed by Mayo Clinic vascular radiologists and included in the analyses. Diagnostic criteria for extracoronary vascular abnormalities and FMD are described elsewhere (8). Follow-up data included patient contact as part of their clinical care (e.g., medication refill, questions), self-motivated patient updates, periodic prospective assessments, and a follow-up survey.

Statistical analysis was performed with JMP version 10.0 (SAS Institute, Inc., Cary, North Carolina). Continuous data were summarized as a mean ± SD and comparisons were performed with a Student *t* test and Cochran-Armitage trend test for ordinal variables. Discrete variables were expressed as frequencies or percentages, and comparisons were performed with a Fisher exact probability test. Kaplan-Meier methods and log-rank tests were used to estimate survival curves for follow-up recurrence.

The U.S. comparator data were derived from National Vital Statistics Reports 2013 birth data including women between 20 and 44 years of age (9), the 2012 Fertility Clinic Success Rates Reports (10), and the 1980 to 2010 U.S. pre-eclampsia rates (11), and were compared using a 2-sided chi-square 1-sample proportion test. A 2-sided value of $p < 0.05$ was considered significant for all statistical analyses.

## RESULTS

Of the 54 women identified as P-SCAD, 4 were pregnant at the time of SCAD (**Figure 1**). Of the remaining

### ABBREVIATIONS AND ACRONYMS

**CABG** = coronary artery bypass graft

**CTA** = computed tomography angiography

**FMD** = fibromuscular dysplasia

**LVEF** = left ventricular ejection fraction

**MI** = myocardial infarction

**NP-SCAD** = spontaneous coronary artery dissection not associated with pregnancy

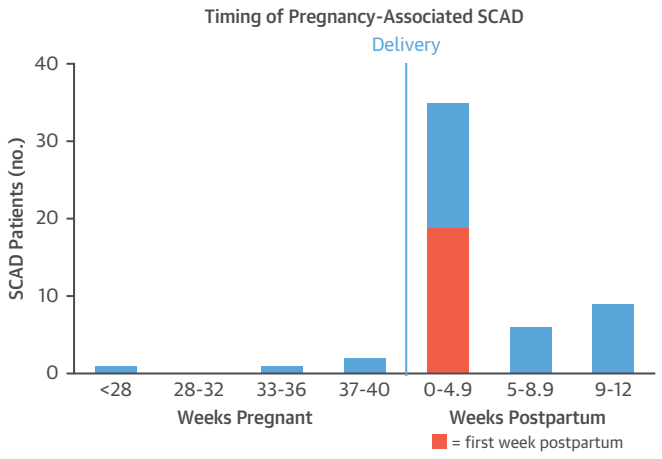
**P-SCAD** = spontaneous coronary artery dissection during or shortly following pregnancy

**PPCM** = peripartum cardiomyopathy

**SCAD** = spontaneous coronary artery dissection

**STEMI** = ST-segment elevation myocardial infarction

**FIGURE 1 SCAD Timeframe**




Most pregnancy-associated spontaneous coronary artery dissection (SCAD) events occurred during early postpartum.

**TABLE 1 Clinical Characteristics**

| | P-SCAD (n = 54) | NP-SCAD (n = 269) | p Value |
|---|---|---|---|
| Age at event, yrs | 35 (26–42) | 47 (20–71) | <0.0001 |
| Body mass index, kg/m$^2$ | 26 ± 5 | 25 ± 5 | 0.34 |
| Caucasian | 48 (89) | 260 (97) | 0.025 |
| Imaged for fibromuscular dysplasia | 26 (48) | 135 (50) | 0.88 |
| Diagnosis of fibromuscular dysplasia | 11 (42)* | 87 (64)† | 0.047 |
| Diagnosis of extracoronary vascular abnormality | 12 (46)* | 104 (77)† | 0.0032 |
| Reports extreme exertion before SCAD | 0 | 40 (15) | 0.0005 |
| Reports extreme emotion before SCAD | 6 (11) | 37 (14) | 0.83 |
| Marfan syndrome | 0 | 3 (1) | >0.99 |
| Ehlers-Danlos syndrome | 0 | 3 (1) | >0.99 |
| Rheumatoid arthritis | 0 | 2 (0.7) | >0.99 |
| Polycystic kidney disease | 1 (2) | 1 (0.4) | 0.31 |
| Polycystic ovarian syndrome | 4 (7) | 5 (2) | 0.046 |
| Chronic hypertension | 15 (28) | 71 (26) | 0.86 |
| Hyperlipidemia | 14 (26) | 99 (37) | 0.16 |
| Diabetes mellitus | 2 (4) | 1 (0.4) | 0.07 |
| Migraine headaches | 17 (31) | 80 (30) | 0.87 |
| Thyroid disease | | | |
| Hyperthyroidism | 2 (4) | 4 (1.4) | 0.26 |
| Hypothyroidism | 5 (9) | 39 (15) | 0.39 |
| Active tobacco use | 0 | 2 (0.7) | >0.99 |
| Prior tobacco use | 12 (22) | 72 (27) | 0.61 |
| Tobacco within 2–3 days of SCAD | 0 | 15 (6) | 0.14 |
| Prior cocaine use | 3 (6) | 15 (6) | 0.99 |
| Cocaine within 2–3 days of SCAD | 0 | 0 | NA |
| History of prior chest trauma | 0 | 5 (2) | 0.59 |
| Fen-Phen/Redux weight loss drug | 4 (7) | 13 (5) | 0.50 |

Values are mean (range), mean ± SD, or n (%). *n = 26. †n = 135.

NP-SCAD = spontaneous coronary artery dissection not associated with pregnancy; P-SCAD = pregnancy-associated spontaneous coronary artery dissection; SCAD = spontaneous coronary artery dissection.

50 women, 48 had P-SCAD within 12 weeks following delivery of viable infants (89%); 1 had P-SCAD following a first trimester miscarriage (2%); and 1 had P-SCAD following a stillbirth at 36 weeks (2%). Of the 48 women who delivered viable infants before SCAD, 22 had normal spontaneous vaginal delivery, 7 had induced vaginal delivery, 7 delivered by caesarean section, 3 delivered by caesarean section following failure to progress with induction attempt, and 9 did not have childbirth details available. Most P-SCAD events occurred during the first month following delivery or miscarriage (35 of 50; 70%), mostly within the first week following delivery (19 of 35; 54%) at a median of 5 days (range 2 to 7 days). Mean age at time of SCAD was 35 ± 4 years (range 26 to 42 days) (Table 1). The majority of women were Caucasian with a nonpregnant mean body mass index of 26 ± 5 kg/m$^2$. Similar to other SCAD patients in the Mayo Clinic Registry and prior series, typical risk factors for atherosclerotic disease were uncommon. Only 10 patients (19%) had hypertension during pregnancy, 6 (11%) were diagnosed with pre-eclampsia, and 4 (7%) had gestational diabetes mellitus (Table 2). One patient carried a diagnosis of autoimmune mixed connective tissue disease and another had a fibrillin gene variant of uncertain significance. No patient reported known family history of arterial dissections or SCAD.

Among those who underwent comprehensive extracoronary vascular imaging, 11 of 26 patients with P-SCAD (42%) had evidence for FMD compared with 87 of 135 (64%) patients with NP-SCAD (p = 0.047). Extracoronary vascular abnormalities were also less common among patients with P-SCAD compared with patients with NP-SCAD (46% [12 of 26] vs. 77% [104 of 135]; p = 0.0032). Patients with P-SCAD trended toward more often having prior history of single or combination infertility treatment (28% vs. 16%; p = 0.055) including selective estrogen receptor modulators (8 of 15), gonadotropin therapy (5 of 15), and aromatase inhibitors (2 of 15). Five of the 15 patients also had history of in vitro fertilization. Compared with patients with NP-SCAD, patients with P-SCAD were older at time of first childbirth (p = 0.016) and more frequently had multiple pregnancies (91% vs. 76%; p = 0.018) with no difference in number of live childbirths (80% vs. 70%; p = 0.19).

Compared with other women of childbearing age in the U.S. population (9), patients with P-SCAD were more frequently multiparous (80% vs. 64%; p = 0.0167), and the SCAD population was more frequently treated for infertility (28% vs. 12%; p = 0.0004) (Table 3) (10). Six (11%) patients had a diagnosis of pre-eclampsia as compared with the estimated 3.4% of the U.S. population (p = 0.001) (11).

**ACUTE PRESENTATION.** Compared with patients with NP-SCAD, patients with P-SCAD more often presented with ST-segment elevation myocardial infarction (STEMI) (57% vs. 36%; p = 0.009) (Table 4). One patient's postpartum SCAD was a recurrence, occurring 14 months after an initial SCAD, which was not associated with pregnancy. All but 1 patient reported chest pain or pressure at the time of SCAD, although other described symptoms included upper extremity pain or numbness, mandibular pain, back pain, diaphoresis, nausea, vomiting, and a "popping" or "clicking" sensation in the chest. The patient who did not present with chest pain described right arm pain and nausea. Six (11%) patients reported the onset of SCAD symptoms during or shortly after lactation.

Patients with P-SCAD had a lower mean left ventricular ejection fraction (LVEF) at SCAD diagnosis (46 ± 17% vs. 53 ± 7%; p = 0.0003) with more frequent findings of LVEF ≤35% (26% vs. 10%; p = 0.0071). Those with P-SCAD were more likely to experience SCAD affecting the left main or multiple vessels (24% vs. 5%, p < 0.0001; and 33% vs. 14%; p = 0.0027, respectively). As to the location of the most frequently dissected arteries, 38 (70%) involved the left anterior descending coronary artery (Figure 2), 11 (20%) involved the right coronary artery, and 8 (15%) involved the left circumflex artery. Twenty-two (41%) patients with P-SCAD were managed conservatively and were more likely than were those with NP-SCAD to experience progression requiring revascularization (3 of 22 vs. 3 of 139; p = 0.03). Unsuccessful percutaneous coronary intervention was common in both groups (35% vs. 20%; p = 0.17). Compared with those patients with NP-SCAD, patients with P-SCAD more frequently had coronary artery bypass graft (CABG) surgery (26% [14] vs. 7% [19]; p = 0.0002). Three patients had CABG surgery because of unsuccessful percutaneous coronary intervention, and 1 had CABG surgery because of SCAD progression despite conservative management. There were no in-hospital deaths in either group.

Of the 4 women who were pregnant at the time of SCAD, 1 patient underwent elective pregnancy termination shortly thereafter. The 3 others had emergency cesarean sections, 2 of which occurred before emergency CABG.

**FOLLOW-UP.** There were no deaths at a median follow-up of 2.3 (interquartile range: 1.0 to 5.1) years. Eight patients with P-SCAD (15%) had SCAD recurrence, 4 of which were within 3 months following delivery. All P-SCAD recurrences occurred in different coronary territories (Figure 3); only 1 patient presented initially with multivessel recurrent SCAD. Overall, Kaplan-Meier estimated 5-year rates of recurrence were no different between P-SCAD versus NP-SCAD (10% vs. 23%; p = 0.18) (Figure 4).

On follow-up, the mean LVEF was lower among patients with P-SCAD (52 ± 11% vs. 57 ± 10%;

**TABLE 2 Clinical Characteristics Relevant to Gynecologic or Obstetric History**

| | P-SCAD (n = 54) | NP-SCAD (n = 269) | p Value |
|---|---|---|---|
| Nulliparous | NA | 34 (13) | NA |
| Total pregnancies | 3.2 (1–10) | 2.6 (0–8) | 0.0118 |
| Total deliveries | 2.5 (1–6) | 2.0 (0–7) | 0.0065 |
| Multiple pregnancies (>1) | 49 (91) | 202 (76) | 0.018 |
| Multiple childbirths (>1) | 43 (80) | 186 (70) | 0.19 |
| Hypertension during pregnancy | 10 (19) | 27 (10) | 0.10 |
| Pre-eclampsia | 6 (11) | 15 (6) | 0.12 |
| Eclampsia | 0 | 1 (0.4) | >0.99 |
| HELLP syndrome | 0 | 0 | NA |
| Gestational diabetes mellitus | 4 (7) | 13 (5) | 0.50 |
| Breastfed children | 40 (74) | 184 (68) | 0.52 |
| History of fertility-related therapies | 15 (28) | 44 (16) | 0.055 |
| Selective estrogen receptor modulator | 8 (15) | 25 (9) | 0.22 |
| Gonadotropin therapy | 5 (9) | 10 (4) | 0.15 |
| Aromatase inhibitor | 2 (4) | 2 (1) | 0.13 |
| Dopamine agonist | 0 | 1 (0.4) | >0.99 |
| Leuprolide | 1 (2) | 0 | 0.17 |
| Progesterone | 3 (6) | 3 (1) | 0.06 |
| Do not recall | 0 | 2 (1) | >0.99 |
| In vitro fertilization | 5 (9) | 10 (4) | 0.15 |
| Age at first childbirth | | | 0.016 |
| <19 yrs | 0 (0) | 12 (4) | |
| 20–24 yrs | 6 (11) | 58 (22) | |
| 25–29 yrs | 19 (35) | 75 (28) | |
| >30 yrs | 25 (46) | 75 (28) | |
| Hormone replacement therapy | | | |
| Used to take | 0 | 49 (18) | <0.0001 |
| Currently taking | 0 | 20 (7) | 0.032 |
| History of hormonal birth control | | | |
| Used to take | 42 (78) | 237 (88) | 0.051 |
| Currently taking | 0 | 2 (1) | >0.99 |

Values are mean (range) or n (%).

HELLP = hemolysis, elevated liver enzymes, and low platelet count; NA = not applicable; other abbreviations as in Table 1.

**TABLE 3 Clinical Characteristics of Patients With P-SCAD Compared With U.S. Data**

| | P-SCAD (n = 54) | Reported U.S. Data* | p Value |
|---|---|---|---|
| Age >30 yrs at time of first delivery | 46 | 41 | 0.43 |
| Multiple childbirths | 80 | 64 | 0.0167 |
| Treated for infertility | 28 | 12 | 0.0004 |
| Pre-eclampsia | 11 | 3.4 | 0.001 |

Values are %. *Data reported in Martin et al. (9), National Center for Chronic Disease Prevention and Health Promotion, Division of Reproductive Health (10), and Ananth et al. (11).

P-SCAD = pregnancy-associated spontaneous coronary artery dissection.

**TABLE 4 Clinical Presentation and Management**

| | P-SCAD (n = 54) | NP-SCAD (n = 269) | p Value |
|---|---|---|---|
| Presentation | | | |
| Chest pain | 50 (93) | 265 (99) | 0.03 |
| Unstable angina* | 0 (0) | 8 (3) | 0.36 |
| ST-segment elevation myocardial infarction* | 30 (57) | 98 (36) | 0.009 |
| Non-ST-segment elevation myocardial infarction* | 23 (43) | 163 (61) | 0.02 |
| Cardiac arrest | 5 (9) | 28 (10) | >0.99 |
| Left ventricular ejection fraction, %† | 46 ± 17 | 53 ± 7 | 0.0003 |
| Left ventricular ejection fraction ≤35%† | 12 (26) | 25 (10) | 0.0071 |
| Coronary artery distribution | | | |
| Left main | 13 (24) | 13 (5) | <0.0001 |
| Left anterior descending | 38 (70) | 161 (60) | 0.17 |
| Right | 11 (20) | 35 (13) | 0.20 |
| Left circumflex | 8 (15) | 39 (14) | >0.99 |
| Multivessel | 18 (33) | 39 (14) | 0.0027 |
| Acute management | | | |
| Medical management only | 22 (41) | 139 (52) | 0.18 |
| Progressed and revascularization | 3 (14)‡ | 3 (2)§ | 0.03 |
| PCI | 23 (43) | 123 (46) | 0.76 |
| Unsuccessful PCI | 8 (35)‖ | 25 (20)¶ | 0.17 |
| Coronary artery bypass grafting | 14 (26) | 19 (7) | 0.0002 |
| Follow-up | | | |
| Follow-up, yrs | 4.3 (2.0–7.6) | 2.0 (0.94–4.50) | 0.0008 |
| Death | 0 | 0 | NA |
| Recurrent SCAD, Kaplan Meier 5-yr estimate | 10 | 23 | 0.18 |
| Recurrent chest pain | 29 (54) | 144 (54) | >0.99 |
| Left ventricular ejection fraction, %# | 52 ± 11 | 57 ± 10 | 0.005 |
| Left ventricular ejection fraction ≤35%# | 5 (12)** | 11 (6)†† | 0.20 |
| Implantable defibrillator | 6 (11) | 14 (5) | 0.16 |

Values are n (%), mean ± SD, or median (interquartile range), or %. *1 patient did not have electrocardiogram data available to discern subtype of myocardial infarction. †47 and 247 patients had initial echocardiograms among the P-SCAD and NP-SCAD groups, respectively. ‡n = 22. §n = 139. ‖n = 23. ¶n = 123. #Forty-three and 183 patients had follow-up echocardiograms of the P-SCAD and NP-SCAD groups, respectively. **n = 43. ††n = 183.

PCI = percutaneous coronary intervention; other abbreviations as in Tables 1 and 2.

p = 0.005). Of the 25 patients with P-SCAD presenting with an LVEF <50%, 20 had follow-up echocardiography available, with recovery of function in 11 patients (55%). This rate of recovery trended less than the NP-SCAD group did; of the 71 patients with NP-SCAD presenting with an LVEF <50%, 56 had follow-up echocardiography available with recovery of function in 41 patients (73%) (p = 0.16). Those patients with P-SCAD with history of left main coronary dissection and follow-up echocardiography data available were less likely to have left ventricular function recovery (2 of 9 vs. 9 of 11; p = 0.02). Four patients received an implantable defibrillator because of persistent left ventricular dysfunction. More than one-half of both SCAD groups (54% vs. 54%; p > 0.99) reported recurrent or persistent chest pain in follow-up questionnaires.

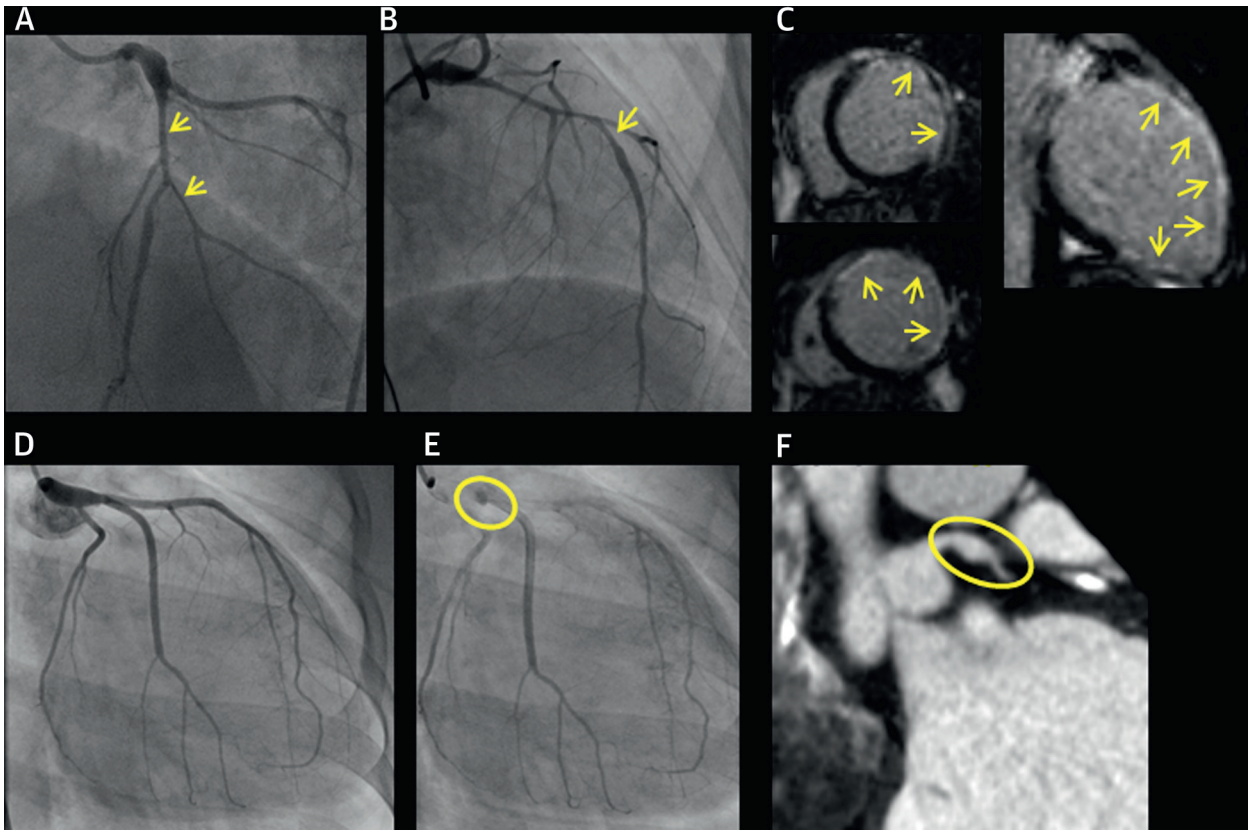
## DISCUSSION

The study's primary findings were: 1) patients with P-SCAD had a more severe clinical presentation than did those patients with NP-SCAD, often with multivessel dissections and acute heart failure; 2) although SCAD may occur any time during pregnancy or postpartum, the highest frequency of SCAD was during the first postpartum month and in particular the first postpartum week; 3) women with P-SCAD frequently are multiparous with a history of fertility treatments or pre-eclampsia; and 4) the prevalence of extracoronary vascular abnormalities in patients with P-SCAD who underwent vascular imaging was less than in women with NP-SCAD (**Central Illustration**).

Pregnancy-associated hormonal and hemodynamic changes and coronary shear stress have been hypothesized as contributing to P-SCAD (12). Within the first 6 weeks of pregnancy, notable hemodynamic changes begin to occur, including expansion of blood volume, increase in red cell mass, reduction of systemic vascular resistance, and increased cardiac output (13). By the end of pregnancy, plasma volume increases by 30% to 50% for a total of 4.7 to 5.2 l (14,15). Cardiac output increases from 4 to 5 l/min at baseline to 6 to 7 l/min during the second trimester and peaks as high as 10 to 11 l/min during labor. In conjunction with active Valsalva efforts ("pushing") in the second stage of labor, these physiological adaptations may hypothetically contribute to regional demands on the coronary arteries and precipitate SCAD. Although it is possible for SCAD patients to develop subclinical coronary intramural hematomas intrapartum, leading to a SCAD MI, the highest frequency of P-SCAD did not occur during labor or delivery. Rather, peak timing of P-SCAD events was during the first postpartum month, particularly the first postpartum week, strikingly similar to that of those with pregnancy-associated MI from any cause (5), in P-SCAD case reports (4), and in patients with peripartum cardiomyopathy (PPCM) (16). This timing might correlate in part with the cardiac stress due to the rapid post-delivery uterine contraction and return of massive blood volume to the systemic circulation (17). However, hemodynamic changes alone might not account for the entire pathogenesis of SCAD.

The pregnant state induces elevated levels of progesterone and estrogen, which peak at term and then fall rapidly postpartum. The vascular endothelium, which has estrogen and progesterone receptors (18), is likely affected by these dramatic shifts. Estrogen can up-regulate vascular smooth muscle relaxation

**FIGURE 2** **Postpartum Spontaneous Coronary Artery Dissection: 10-Day Myocardial Infarction**



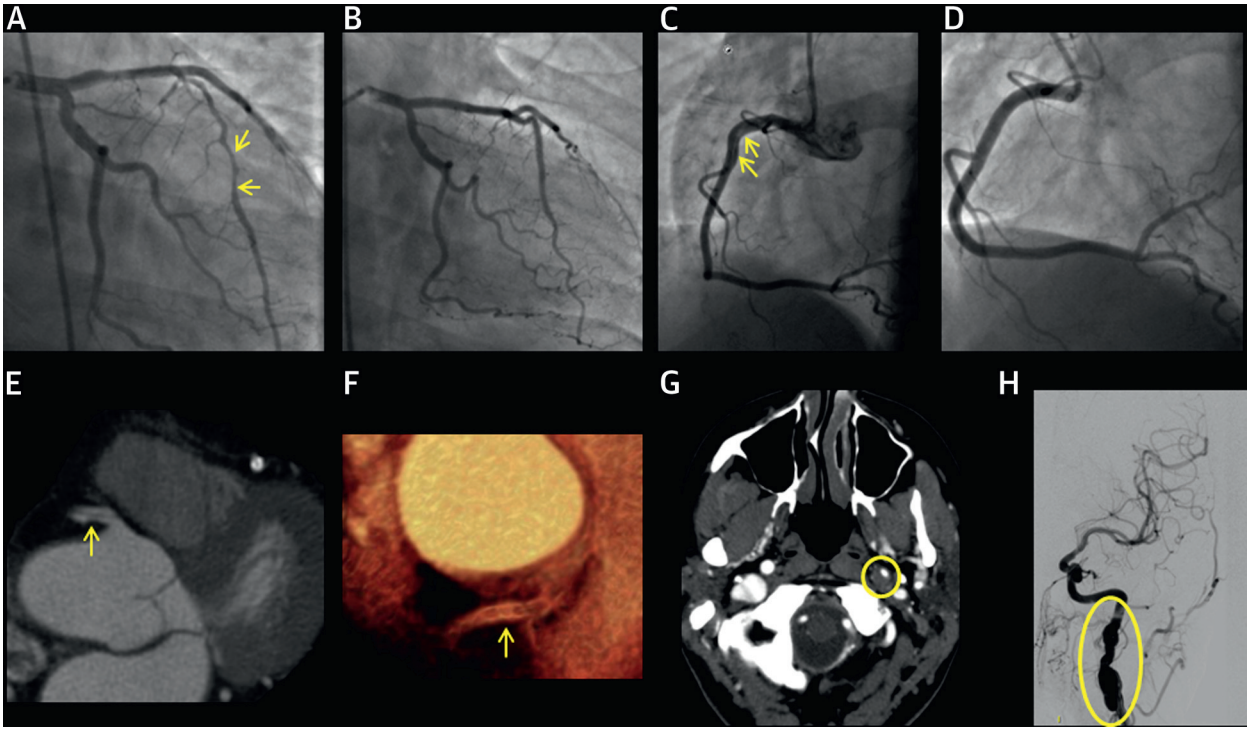

This coronary angiography comes from a 31-year-old woman with myocardial infarction 10 days postpartum with a history significant for peripartum cardiomyopathy (left ventricular ejection fraction 30% to 40% after the third pregnancy, recovering to 60% before the fourth pregnancy). **(A, B)** There was spontaneous coronary artery dissection of the left main coronary artery extending into the left anterior descending and diagonal coronary arteries **(arrows)**. **(C)** Cardiac magnetic resonance imaging showed extensive myocardial delayed enhancement **(arrows)** consistent with infarction of the anterior wall and septum (left ventricular ejection fraction 27%). **(D)** Follow-up angiography showed improved coronary caliber. Region of persistent contrast **(E)** correlated with distal left main aneurysmal changes on **(F)** computed tomography (**ovals** indicate corresponding regions).

via release of nitric oxide (19) and has been considered potentially cardioprotective (20-23); however, estrogen may also release matrix metalloproteinase, thereby degrading exovascular structural support (24,25). The pregnant state has been considered a histological contributor to arterial degeneration including reticular fiber fragmentation, elastic fiber disorganization, hypertrophy, and hyperplasia of smooth muscle cells (26,27). These changes as well as the increased fragility of the coronary artery vasa vasora coupled with the extracellular fluid volume shifts of late pregnancy, labor, and delivery, and the early postpartum state may predispose vulnerable patients to SCAD.

Interestingly, 6 patients explicitly described the onset of the SCAD MI symptoms during lactation. Oxytocin is an important neuromodulator that also peaks toward the end of pregnancy and persists as the responsible trigger for milk letdown during breastfeeding, the vascular effects of which remain subject to investigation. Additionally, dysfunctional cleavage of the hormone prolactin, which increases during pregnancy and regulates milk production, into a bioactive and possibly cardiotoxic fragment has been associated with the myocardial dysfunction of PPCM (28-31). The implications of this observation for counseling SCAD patients regarding advisability of lactation remain uncertain at this time.

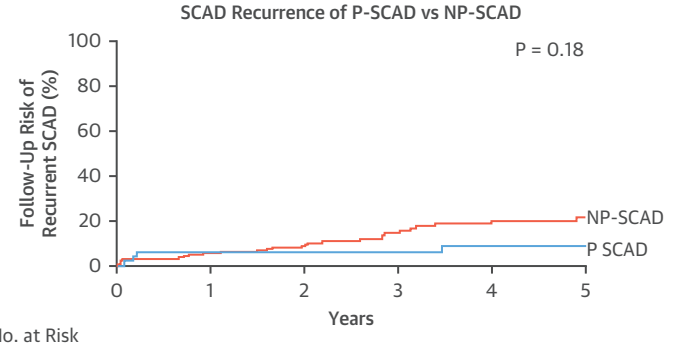
The overlap of P-SCAD with pre-eclampsia and similar pattern of presentation with PPCM observed in our study is hypothesis generating, particularly because pre-eclampsia and PPCM are speculated as

**FIGURE 3 Postpartum SCAD: 1-Week ST-Segment Elevation Myocardial Infarction**




This coronary angiography is of a 37-year-old woman presenting with ST-segment elevation myocardial infarction at 1 week postpartum with spontaneous coronary artery dissection (SCAD) of the **(A)** left anterior descending coronary artery **(arrows)**, which was treated with 3 stents. **(B)** The left anterior descending coronary artery caliber was normal on coronary angiography 6 years later, when she presented with **(C)** recurrent SCAD of the right coronary artery (RCA) **(arrows)** that **(D)** previously had been normal. After a period of observation, she was treated with single bypass grafting to the RCA due to persistent chest pain and SCAD progression on coronary angiography. **(E, F)** Follow-up cardiac computed tomography imaging showed persistent RCA dissection **(arrows)**. **(G, H)** Her history was complicated by severe headache with left carotid dissection and pseudoaneurysm (**circle** and **oval**) requiring stenting 2 weeks before her second event.

**FIGURE 4 5-Year Rates of Recurrence**

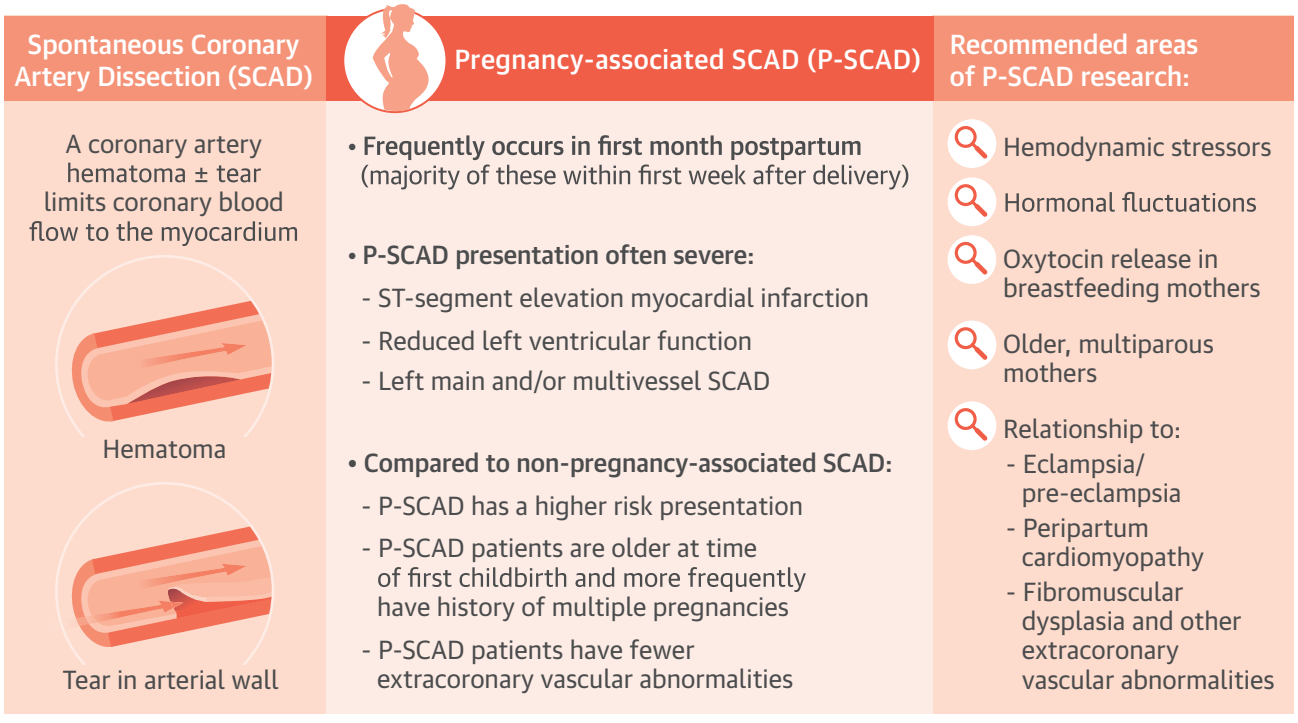



| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| All SCAD | 323 | 229 | 157 | 125 | 86 | 68 |
| NP SCAD | 269 | 184 | 120 | 91 | 60 | 47 |
| P SCAD | 54 | 45 | 37 | 34 | 26 | 21 |

Kaplan-Meier estimated 5-year rates of recurrence were no different between spontaneous coronary artery dissection (SCAD) during or shortly following pregnancy (P-SCAD) and SCAD not associated with pregnancy (NP-SCAD) (10% vs. 23%; p = 0.18).

possibly sharing mechanisms of pathogenesis (32). Small studies have demonstrated increased levels of vascular endothelial growth factor inhibitors such as soluble fms-like tyrosine kinase 1 and placental growth factor levels in hypertensive diseases of pregnancy (33,34) and relatively increased levels of soluble fms-like tyrosine kinase 1 in PPCM (29). Although the cardiomyopathy of SCAD is thought to be primarily ischemic from decreased epicardial coronary blood flow, there is at present no knowledge regarding the role of microvascular disease and angiogenic signaling pathways. One may hypothesize that the mechanisms of PPCM, hypertensive heart diseases of pregnancy, and P-SCAD represent a singular underlying disease process, with patients exhibiting clinical manifestations contingent on individual susceptibilities, particularly in those patients with cardiomyopathy out of proportion to the SCAD coronary territory or those patients with both pre-eclampsia and SCAD.

**CENTRAL ILLUSTRATION** **Features of Pregnancy-Associated Spontaneous Coronary Artery Dissection**




**Tweet, M.S. et al. J Am Coll Cardiol. 2017;70(4):426-35.**

In this study, pregnancy-associated spontaneous coronary artery dissection (P-SCAD) was found to occur most frequently in the first month postpartum, and patients often presented with ST-segment elevation myocardial infarction or reduced left ventricular function. The underlying mechanisms are likely multifactorial and not well understood. P-SCAD = spontaneous coronary artery dissection during or shortly following pregnancy; SCAD = spontaneous coronary artery dissection.

A unique observation of the present study was the lower prevalence of extracoronary vascular abnormalities among the P-SCAD population. FMD and other extracoronary vascular abnormalities, such as dilation or dissection, are common in SCAD patients, with prevalence ranging from 25% to 86% (1,35-37). Similarly, no patients had concurrent diagnoses of connective tissue dysplasias, such as Marfan syndrome, Loeys-Dietz syndrome, or Ehlers-Danlos syndrome type IV, which also have been observed in SCAD (37). Although limitations in systematic imaging could affect prevalence and comparison between the 2 groups (e.g., only about one-half of the patients in each group underwent imaging), this unexpected observation is hypothesis generating, highlighting the potential importance of other contributing factors in P-SCAD.

Although multiparity was more common in the P-SCAD group, given the increased frequency of associated assisted reproductive technologies, infertility or the treatments for infertility may constitute a risk factor. Other studies regarding pregnancy-associated MI and small postpartum SCAD series have observed advanced maternal age, multiparity, and concurrent conditions such as eclampsia or pre-eclampsia (2,5,38-43). The reason for these associations is uncertain, although histological studies suggested that the association of pregnancy and arterial degeneration might be permanent and additive with multiple pregnancies (26,27).

The more severe clinical presentation observed among patients with P-SCAD is consistent with the recent, comprehensive review of 120 cases of P-SCAD, which included women up to 210 days following delivery (44). Of these, 113 were published cases, which subjects the data to notable publication bias, as severe presentations intrinsically are more likely to be considered for documentation and publication; furthermore, the SCAD cohorts to which the cases were compared included postpartum patients. The present study overcame these limitations and provided additional insight regarding P-SCAD.

**STUDY LIMITATIONS.** Inherent limitations of this study included the small sample size as well as selection, referral, and attrition biases due to the unavoidable nature of a registry. For instance, the current cohort, by default, did not incorporate patients who did not survive their initial SCAD. Patients who were enrolled for <5 years or who had not yet returned the follow-up survey were included. Extracoronary vascular arteriopathy status was evaluated in about one-half of all patients, which could affect prevalence between both groups. Further, if the images of outside studies were not available they were not included in the analyses. Finally, specific data regarding intrapartum obstetrical management or anesthetic types were not available. The information collected in the Mayo Clinic SCAD Registry is critical for gaining insight regarding P-SCAD.

## CONCLUSIONS

This study demonstrated that patients with P-SCAD have a more severe clinical MI presentation, most often within the first postpartum month. Variations in hemodynamic and hormonal factors might contribute to SCAD events in susceptible women. Although some patients with P-SCAD had a diagnosis of extracoronary vascular arteriopathy, including FMD, the prevalence was lower when compared with patients with NP-SCAD, prompting consideration of yet-undefined pathophysiological mechanisms intrinsic to pregnancy.

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## PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** MI due to P-SCAD carries more severe clinical implications, including ST-segment elevation, left ventricular dysfunction, and left main or multivessel involvement than do other causes of MI in pregnant women.

**COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS:** P-SCAD can occur during or after pregnancy, but occurs most commonly during the first month postpartum.

**TRANSLATIONAL OUTLOOK:** The mechanisms responsible for SCAD and its association with advanced maternal age, multiparity, eclampsia or pre-eclampsia and PPCM warrant further investigation.

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**KEY WORDS** **cardiac computed tomography, fibromuscular dysplasia, myocardial infarction, optical coherence tomography, women**