Pregnancy and the Risk of Spontaneous Coronary Artery Dissection

An Analysis of 120 Contemporary Cases

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Background—Because of the rarity of this condition, information on pregnancy-associated spontaneous coronary artery dissection is limited. We reviewed a large number of contemporary pregnancy-associated spontaneous coronary artery dissection cases in an attempt to define the clinical characteristics and provide management recommendations.

Methods and Results—A literature search for cases of pregnancy-associated spontaneous coronary artery dissection reported between 2000 and 2015 included 120 cases; 75% presented with ST-segment–elevation myocardial infarction, and 80% had anterior myocardial infarction. Left anterior descending coronary artery was involved in 72% of cases, left main segment in 36%, and 40% had multivessel spontaneous coronary artery dissection. Ejection fraction was reduced to <40% in 44% of cases. Percutaneous coronary intervention was successful in only 50% of cases. Coronary artery bypass surgery was performed in 44 cases because of complex anatomy, hemodynamic instability, or failed percutaneous coronary intervention. Maternal complications included cardiogenic shock (24%), mechanical support (28%), urgent percutaneous coronary intervention (28%), urgent coronary artery bypass surgery (27.5%), maternal mortality (4%), and fetal mortality (2.5%). During follow-up for 305±111 days, there was a high incidence of symptoms because of persistent or new spontaneous coronary artery dissections, and 5 women needed heart transplantation or ventricular assist device implantation.

Conclusions—Pregnancy-associated spontaneous coronary artery dissection is commonly associated with left anterior descending, left main, and multivessel involvement, which leads to a high incidence of reduced ejection fraction, and life-threatening maternal and fetal complications. Percutaneous coronary intervention is associated with low success rate and high likelihood of complications, and coronary artery bypass surgery is often required. Recurrent ischemic events because of persistent or new spontaneous coronary artery dissection are common during long-term follow-up. **(*Circ Cardiovasc Interv*. 2017;10:e004941. DOI: 10.1161/CIRCINTERVENTIONS.117.004941.)**

Key Words: acute coronary syndrome ■ angiography ■ myocardial infarction ■ percutaneous coronary intervention ■ preeclampsia ■ pregnancy

Spontaneous coronary artery dissection (SCAD) is an uncommon cause of acute coronary syndrome and has been found in 0.2% to 4% of patients with acute coronary syndrome undergoing invasive angiography.[1–3] In contrast to the general population, including young women[4] in whom atherosclerotic disease is the main cause of myocardial infarction (MI), SCAD is the most common mechanism of pregnancy-associated MI and has been documented in >40% of cases.[5] Because of the rarity of this condition, most available information on pregnancy-associated spontaneous coronary artery dissection (PASCAD) is limited. The aim of this study was, therefore, to review and analyze data from a large number of contemporary cases of PASCAD in an attempt to further define the clinical characteristics of this condition and its effect on maternal and fetal outcome and to provide management recommendations.

See Editorial by Saw

Methods

Study Population

Literature searches for cases of PASCAD reported between the years 2000 and 2015 were performed using Google scholar, PubMed, and Medline. We used the terms myocardial infarction and coronary dissection in conjunction with the terms pregnancy and partum. In addition, references from identified publications were crosschecked to find additional cases that may have remained uncovered by the initial search. All original articles were obtained from the University of Southern California library or interlibrary communications. Medical translators were used to translate articles written in languages other than English. A total of 113 cases published between 2000 and 2015 were identified.[6–102] In addition, 4 cases presented in the 2010, 2012, and 2016 international congresses on cardiac problems in pregnancy and 3 patients

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WHAT IS KNOWN

- Pregnancy is associated with an ≈3-fold increased risk of acute myocardial infarction compared with the risk in nonpregnant women of similar age.
- In contrast to the general population, in whom atherosclerotic disease is the main cause of myocardial infarction, spontaneous coronary artery dissection is the most common mechanism of pregnancy-associated myocardial infarction and has been documented in >40% of cases.

WHAT THE STUDY ADDS

- The majority of pregnancy-associated spontaneous coronary artery dissection (PASCAD) present during the postpartum period or the third trimester of pregnancy.
- Compared with nonpregnant women with spontaneous coronary artery dissection, PASCAD is associated with a higher incidence of left main and multivessel dissections resulting in a larger myocardial injury.
- PASCAD is associated with an increased incidence of cardiogenic shock, life-threatening arrhythmias, emergent coronary artery bypass surgery, use of mechanical support and cardiac transplantation, and a high maternal and fetal mortality.
- Percutanous coronary intervention in PASCAD is associated with a low success rate and high incidence of complications including iatrogenic dissections and propagation of existing dissections.
- These findings suggest that conservative management strategies should be considered in stable women with PASCAD.

treated or consulted on by the authors were also included. Data were presented as mean values±SD and proportions of patients characteristics. Conclusions and recommendations were established based on the analyzed information with the understanding that the cases identified do not represent all patients with PASCAD that occurred during the study period and that information available may be incomplete.

Data Collected

The following data were collected: age, coronary artery disease (CAD) risk factors, use of hormonal therapy, obstetric history, time of presentation during pregnancy, peripartum (defined as the 24 hours before or after the delivery) or the postpartum periods, mode of delivery, clinical presentation, type and location of MI, types of imaging modalities used, timing of coronary angiography, coronary arteries involved and location of SCAD within the involved coronary arteries, left ventricular (LV) ejection fraction at presentation and during follow-up, treatment modalities including medical therapy, percutaneous coronary intervention (PCI), and coronary artery bypass (CABG) surgery. In addition, we collected information on PCI and CABG complications and other complications including mortality, heart transplantation or ventricular assist device implantation, cardiogenic shock, need for mechanical support, arrhythmias, recurrent ischemia or MI, need for urgent angiography, and the resulting PCI or CABG surgery. We also analyzed patient outcomes according to conservative (without interventions) versus interventional approach. For further clarity of the data collected, we specified in parenthesis the number of patients for whom information was available for each part of the results.

Results

Baseline Characteristics

The study analyzed information obtained in 120 women (Table 1). Age (n=116) ranged between 22 and 52 years with a mean of 34±4 years. Ninety-four of the women (81%) were >30 years and 47 (40.5%) were >35 years. Traditional risk factors for atherosclerotic CAD were reported as follows: family history (n=95) in 14 cases (15%), history of cigarette smoking (n=96) in 12 cases (12.5%), dyslipidemia (n=94) in 9 cases (10%), hypertension (n=95) in 5 cases (5%), and diabetes mellitus (n=95) in 4 cases (4%). In addition, preeclampsia or eclampsia (n=65) were reported in 8 cases (12%), hypercoagulability disorders (n=42) in 4 patients (9.5%), connective tissue disorder (n=44) in 2 patients (4.5%), and illicit drug abuse (n=49) in 1 patient (2%). Use of hormonal therapy before pregnancy (n=38) was reported in 7 women (18.5%), 4 used oral contraceptives and 3 were hormonally treated for infertility.

In the 87 women who developed SCAD postpartum, mode of delivery was reported in 52 cases, 27 of them had vaginal delivery, 23 underwent cesarean section (CS), and 2 of the cases were post abortion. Of the 28 patients who presented antepartum, 21 (75%) were delivered by CS.

Presentation

Timing was reported in 119 patients; 21 patients (17.5%) presented with SCAD during the third trimester of pregnancy, 7 (6%) during the second trimester, and none of the patients presented during the first trimester (1 patient, however, experienced SCAD 10 days after an abortion at sixth week). Four cases (3%) presented during the peripartum period; the first presented 1 day after a CS, the second during induction of spinal anesthesia for CS, the third occurred in a woman treated with ritodrine for preterm delivery, and in the fourth case, data on circumstances were not reported. Eighty-seven patients (72.5%) presented in the postpartum period between day 3 and day 210 after the delivery (Figure 1).

The main symptomatic presentation (n=104) was chest pain in 98 patients (94%; with typical symptoms of acute myocardial infarction [AMI] in 92 of them) and shortness of breath in 32.

Type of MI

One hundred and fifteen patients had MI: 87 patients (75.5%) presented with ST-segment–elevation myocardial infarction (STEMI) and 28 patients (24.5%) with non-STEMI. The location of STEMI was reported in 76 patients and was anterior in 47 cases (62%), anterolateral in 14 cases (18%), and inferior in 15 cases (20%).

Ten patients developed ventricular fibrillation requiring emergency defibrillation, 9 of these events were reported in patients with STEMI.

LV Function

Data on LV function at initial assessment were available in 90 patients (Figure 2). Mean group LV ejection fraction was 40±9%; 40 of the patients had ejection fraction<40%, 28 had ejection fraction ≤30%, and 7 had ejection fraction ≤20%.

Table 1. Baseline Characteristics of 120 Patients With PASCAD

Variable*	Patients, n (%)
Age, y, mean±SD (n=116)	34±4
Age >30 y	94 (81)
Age >35 y	47 (40.5)
Family history of CAD (n=95)	14 (15)
Smoking (n=96)	12 (12.5)
Dyslipidemia (n=94)	9 (10)
Hypertension (n=95)	5 (5)
Diabetes mellitus (n=95)	4 (4)
Preeclampsia/eclampsia (n=65)	8 (12)
Hypercoagulability disorders (n=42)	4 (9.5)
Connective tissue disorders (n=44)	2 (4.5)
Illicit drug abuse (n=49)	1 (2)
Use of hormonal therapy (n=38)	7 (18.5)

CAD indicates coronary artery disease; and PASCAD, pregnancy-associated spontaneous coronary artery dissection.

*Numbers in parenthesis represent the number of patients for whom information was reported.

Coronary Anatomy

Sixty-eight of the patients, 58 with STEMI and 10 with non-STEMI, underwent a coronary angiography urgently and the rest later during the hospitalization. SCAD was shown in a total of 191 coronary arteries, with involvement of 1 coronary artery in 72 cases (60%), 2 arteries in 27 cases (22.5%), and ≥3 arteries in 21 cases (17.5%). The left main (LM) segment was involved in 43 cases (36%), left anterior descending (LAD) artery in 86 cases (72%), left circumflex artery in 28 cases, and the right coronary artery in 18 cases. Dissection was located at the ostial or proximal segments of the arteries in 75 cases (62.5%), in the mid segment in 19 cases, and in the distal segment in 8 cases. During initial angiography, complete occlusion of coronary arteries was shown in 31 patients (26%), of which, 5 presented with non-STEMI. Optical coherence tomography was used in 3 of the cases during the initial angiography and intravascular ultrasound in 11 cases. Use of intravascular ultrasound provided additional information in 8 of the patients: uncovering the presence of SCAD in 3 cases, assisting in the assessment of its extension in 4 cases, and demonstrating malposition of the guidewire in 1 case.

Noncoronary Arteries Dissection

Involvement of a vertebral artery was reported in 4 cases, with a concomitant involvement of the left internal thoracic artery in 1 case. The diagnosis of the noncoronary dissection preceded the diagnosis of SCAD in 1 case, was made simultaneously in 2 cases, and after the diagnosis of SCAD in another case. The clinical presentation of these patients involved visual disturbances and neck pain. All noncoronary dissections were medically treated with antithrombotic therapy.

Percutaneous Coronary Intervention

PCI was performed during the index admission in 44 patients (Figure 3). Thirty-three of the procedures were done immediately after the coronary angiography, because of the presence of completely occluded arteries in 18 cases and ongoing angina in another 6 cases. The reason for early PCI was not described in the other 9 cases. In 7 cases, PCI was done later during the course of hospitalization (because of the development of cardiogenic shock in 2, heart failure in 1, STEMI in 2, and continued angina in 2). In the other 4 cases, the timing of PCI was not reported. Difficulty with catheter engagement or wire passing was reported in 9 cases (all of them with totally occluded arteries), and propagation of the dissection was reported in 11 cases (7 of them had occluded arteries). Overall, complete success was reported in 22 patients (50%), including 3 patients who had dissection propagation, but in none of those reported to have difficulty with catheter engagement or wire passing. Stenting was performed in 37 patients; bare metal stents were used in 14 cases and drug-eluting stents in 11 cases; the type of stent was not reported in the rest of the patients.

CABG Surgery

Forty-four patients underwent CABG surgery during their index admission (Figure 3). Thirty-three cases were referred to surgery directly after the coronary angiography: 9 because of hemodynamic instability, 6 after a failed PCI, and 18 because of complex coronary anatomy (involving the LM segment in 13 cases and 3-vessel disease in 9 cases [both LM and 3-vessel disease

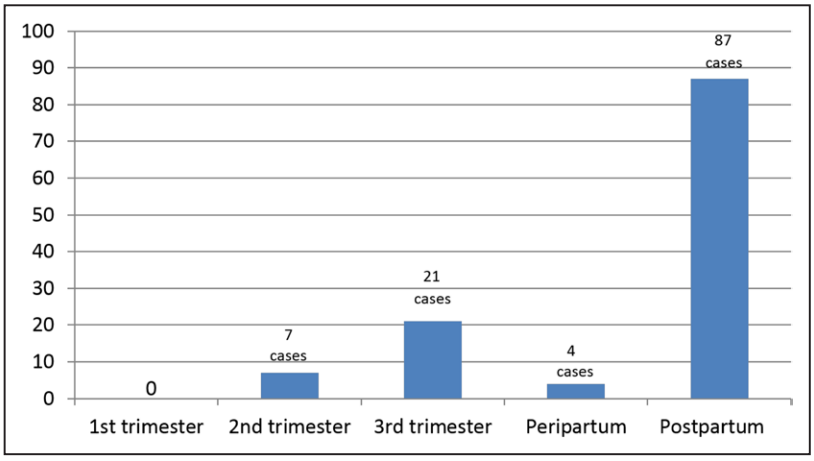

Figure 1. Timing of presentation of 119 patients with pregnancy-associated spontaneous coronary artery dissection.

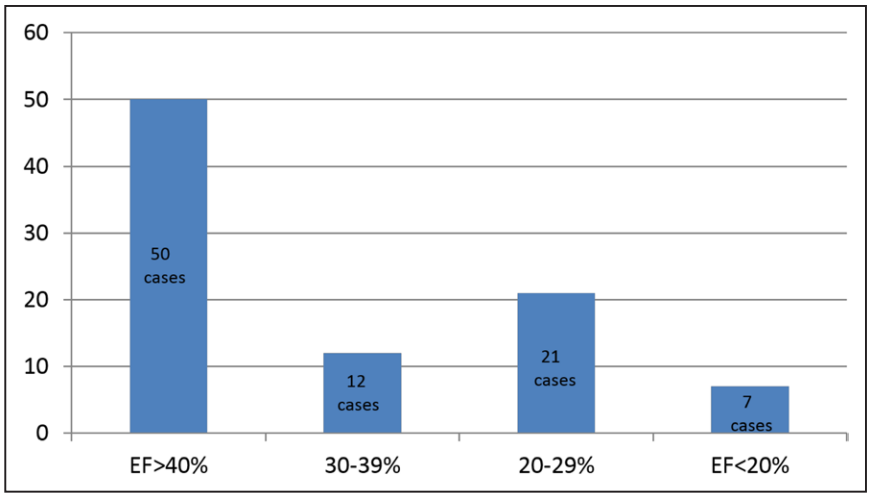

Figure 2. Left ventricular ejection fraction (EF) during initial assessment, n=90.

involvement in 4 cases]). The other 11 cases were initially treated conservatively and later referred for surgery because of continued ischemic symptoms in 3 cases, development of STEMI in 1 case, cardiogenic shock in 3 cases, and SCAD extension, found on a second scheduled angiography after 48 hours, in 1 case. The indications for surgery were not specified in 3 cases.

CABG surgery was done immediately after emergent CS in 6 cases; one newborn experienced brief cardiac arrest and another required mechanical ventilation. Surgery was performed during pregnancy in 4 women; in 1 case, it was immediately followed by CS because of fetal distress (required intubation), in 2 cases it resulted in fetal loss, and in the fourth case, the baby was born prematurely at 35 weeks (4 weeks after the surgery).

Conservative Therapy

Fifty-four patients were initially managed conservatively (Figure 3). However, 18 of them eventually underwent a coronary intervention during the index admission, 11 patients were referred to CABG surgery, and 7 patients underwent PCI (as described above), leaving a total of 36 patients who were managed only conservatively. Of these 36 patients, 25 presented with STEMI, 29 had a single vessel dissection; LM stem was involved in 6 cases and the LAD in 21 cases. Completely occluded arteries were demonstrated in only 3 patients in this group (LAD in 1 case and marginal arteries in the other 2 cases). None of these patients experienced ventricular tachyarrhythmia but 2 presented with cardiogenic shock: one was stabilized initially with intra-aortic balloon pump (IABP) and inotropes and underwent CABG surgery 3 weeks later, and the second was stabilized on medications after a failed attempt of PCI.

Drug Therapy

Drug therapy included aspirin in 71 patients, a second antiplatelet drug in 37 cases (clopidogrel in 33 and prasugrel in 4), anticoagulation in 65 cases (unfractionated heparin in 45, low-molecular-weight heparin in 19, and bivalirudin in 1), β-blockers in 34 cases, and nitrates in 34 cases. Thrombolytic

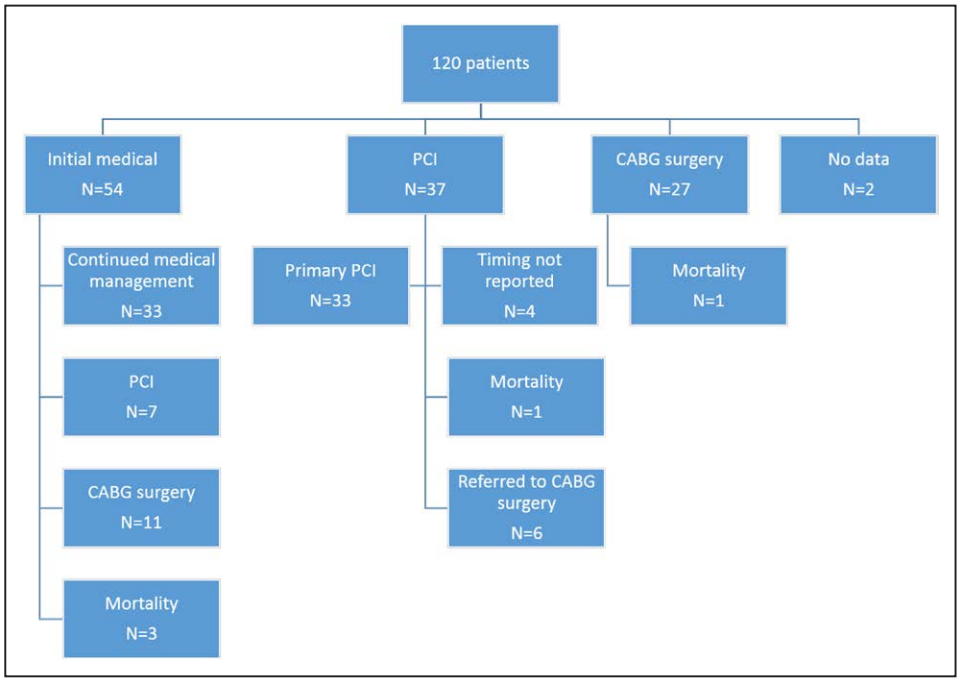

Figure 3. Chart demonstrating the initial management and outcome of all patients during the index hospitalization. CABG indicates coronary artery bypass; and PCI, percutaneous coronary intervention.

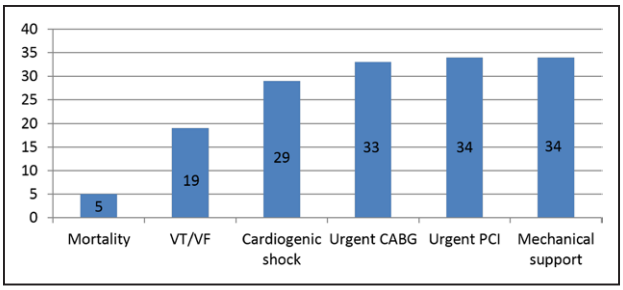

Figure 4. Maternal complications. CABG indicates coronary artery bypass; PCI, percutaneous coronary intervention; VF, ventricular fibrillation; and VT, ventricular tachycardia.

agents were used in 10 patients; in 8 of them, it was followed by either PCI (3 cases) or CABG surgery (5 cases). The indication for CABG surgery in those cases was usually complex coronary anatomy.

Maternal Complications

High incidence of life-threatening maternal complications was reported (Figure 4), including cardiogenic shock in 29 cases (on presentation in 18 cases and later during the course of the hospitalization in another 11 cases) and ventricular arrhythmias requiring defibrillation in 19 cases (on presentation in 10 cases and later during the hospitalization in 9 additional patients). Urgent PCI was required in 34 cases, and urgent CABG surgery was required in 33 cases. Mechanical support was required in 34 cases (IABP in 29, left ventricular assist device in 1, extracorporeal membrane oxygenation in 2, IABP+extracorporeal membrane oxygenation in 1, and IABP+left ventricular assist device in 1); 30 of them presented with STEMI (20 had LM and 20 had multivessel involvement). The indications for mechanical support were cardiogenic shock in 24 cases and high-risk coronary interventions in 10 cases.

Maternal Mortality

Maternal mortality occurred in 5 patients (Table 2). None of the cases had a history of conventional cardiovascular disease risk factors, although one woman was diagnosed with Ehler–Danlos syndrome. Four cases presented postpartum and 1 antepartum. Three cases presented with STEMI. The left coronary system was involved in all cases (LAD and circumflex alone in 1 patient each, both in 2, and both plus LM in 1), and 3 of the cases had completely occluded arteries. The cause of death was cardiac arrest during cardiac catheterization in 1 patient, uncontrolled bleeding in another, and cardiogenic shock in 3.

Fetal and Newborn Complications

Fetal mortality was reported in 3 of the cases, all of them in women with LM dissection. Two were related to CABG surgery (see above), and one occurred in a woman who survived a STEMI. Newborn complications were reported in 8 cases and included 2 cases of resuscitated cardiac arrest, 2 cases of mechanical ventilation, and 4 cases of premature delivery (range, 30–35 weeks).

Follow-Up

Follow-up information was reported in 96 patients. The mean duration of follow-up was 305±111 days. Repeat coronary angiography was performed in 39 patients after a mean period of 84±57 days. The procedure was done as part of scheduled surveillance in 23 women and showed SCAD persistence in 5 and involvement of new vessels in 3 cases. The indication for repeat angiography in the other 16 women (Figure 5) was ischemic symptoms with ECG changes in 9 (all were found to have SCAD; in the same vessel in 3 and in new vessels in 6) and chest pain alone in 6 cases (5 showed persistence of SCAD). In one case, the reason for repeat angiography was not reported, and SCAD persistence was shown.

PCI was performed during the follow-up period in 14 patients, of which, 9 had a previous PCI and 5 were treated conservatively during the index hospitalization. The reasons for the repeat angiography and PCI were clinical deterioration in 5 of the 9 patients who were post-PCI and in 4 of the 5 patients who were initially treated medically.

CABG surgery was performed during the follow-up in 4 patients; in one, 18 hours after the first surgery because of graft failure and hemodynamic collapse and in the other 3 because of SCAD extension to LM stem, which was asymptomatic in 2.

Of the 36 patients who were medically treated during their initial admission, 17 patients underwent repeated angiography, and 8 were found to have SCAD. Thirteen of these cases underwent elective angiography as part of a scheduled elective follow-up, 2 showed persistence of SCAD in the same artery and 2 an involvement of a new artery. The remaining cases underwent repeated coronary angiography because of chest pain with ECG changes in 2, both had de novo SCAD; 1 case with persistent chest pain showed SCAD healing in one vessel but persistence in another vessel. Reason for repeat angiography was not elaborated in 1 case who was found to have SCAD persistence.

LV Function

LV ejection fraction was reported in 90 patients and showed mean value of 48±12%. Of the 28 women with baseline

Table 2. Mortality Cases

Study	Age, y	Presentation Timing	Vessel Involved	Cause of Death
Nakamura et al[47]	33	120 d postpartum	LCX	Uncontrolled bleeding
Pabla et al[57]	35	56 d postpartum	LAD, LCX	Cardiac arrest during coronary angiography
Petrou et al[85]	39	4 d postpartum	LM, LAD, LCX	Multiorgan failure
Sultan et al[95]	NA	Postpartum (timing NA)	LAD	Cardiogenic shock
D'Ovidio et al[99]	35	Prepartum—35 wk	LAD, LCX	Cardiogenic shock

LAD indicates left anterior descending; LCX, left circumflex artery; LM, left main; and NA, not available.

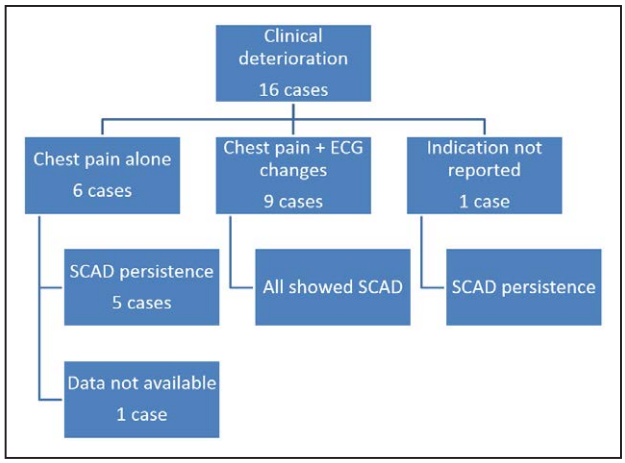

Figure 5. Findings of coronary angiography in 16 symptomatic patients during follow-up. SCAD indicates spontaneous coronary artery dissection.

ejection fraction ≤30%, 5 underwent heart transplantation or ventricular assist device implantation. Of the remaining 23 cases, LV function during follow-up was reported in 17 cases and showed improvement to ejection fraction ≥35% in 15 cases. Of these 15 cases, 14 underwent an intervention during their index SCAD admission, either by PCI (5 cases) or by CABG surgery (9 cases).

Table 3. Comparison Between Patient Women With PASCAD and Nonpregnant Patients With SCAD

Parameters	Saw et al[104]	Tweet et al[103]	PASCAD
No. of patients	168	189	120
Diabetes mellitus, n (%)	8 (5)	4 (2)	5 (4)
Hypertension, n (%)	66 (39)	42 (22)	6 (5)
Smoking, n (%)	21 (12.5)	13 (15)	15 (12.5)
Family history of coronary artery disease, n (%)	49 (29)	NA	18 (15)
Dyslipidemia, n (%)	52 (31)	45 (24)	12 (10)
Age, y	52±9	43±10	33±5
STEMI, n (%)	43 (26)	70 (37)	83 (69)
LM, n (%)	2 (1.2)	8 (4)	43 (36)
LAD, n (%)	108 (64)	115 (61)	86 (72)
LCX, n (%)	57 (34)	47 (25)	28 (23)
>1 vessel involvement, n (%)	32 (19)	28 (15)	42 (35)
VT/VF, n (%)	8 (5)	0 (0)	19 (16)
CABG surgery, n (%)	5 (3)	20 (11	44 (37)
Shock, n (%)	0 (0)	1 (0.5)	29 (24)
Mechanical support, n (%)	2 (1.2)	0 (0)	34 (28)
Mortality, n (%)	0 (0)	1 (0.5)	5 (4)

CABG indicates coronary artery bypass; LAD, left anterior descending; LCX, left circumflex artery; LM, left main; NA, not available; PASCAD, pregnancy-associated spontaneous coronary dissection; SCAD, spontaneous coronary artery dissection; STEMI, ST-segment–elevation myocardial infarction; VF, ventricular fibrillation; and VT, ventricular tachycardia.

Differences Between PASCAD and SCAD Not Associated With Pregnancy

Table 3 provides a comparison between PASCAD as found in this study and 2 large groups of patients (92% women) with SCAD not associated with pregnancy.[103,104] Women with PASCAD were younger, had lower incidence of risk factors for CAD, had higher incidence of STEMI, multiple folds higher rate of LM dissection, and ≈2-fold higher rate of >1 vessel involvement. In addition, women with PASCAD had a substantially higher rate of complications including ventricular arrhythmias, cardiogenic shock, need for mechanical support and CABG surgery, and mortality.

Discussion

The results of this study demonstrate the unique characteristics of pregnancy-associated MI caused by SCAD that need to be taken into account in the management of this condition.

Risk Factors

In comparison with a nonpregnant women at a similar age with AMI, including those with SCAD, the incidence of traditional risk factors in this study was either similar or lower (Table 3).[4,105,106] The incidence of preeclampsia was higher compared with pregnant women in the United States without PASCAD.[107] Similar association was found between preeclampsia and pregnancy-associated myocardial infarction in previous studies.[108,109] Hormonal therapy has been suggested as a potential cause for SCAD in nonpregnant women. History of hormonal therapy before pregnancy was reported in 37 patients and was positive in 10 who received either oral contraceptives or infertility treatment.

Similar to previous studies of pregnancy-associated myocardial infarction of any cause,[5,108–110] older age was the strongest risk factor for PASCAD with 78% of the patients being >30 years of age and almost half >35 years of age.

Timing of Presentation and Potential Mechanisms

Most of the patients presented during the postpartum period or the third trimester and none during the first trimester. Timing of presentation should, therefore, be helpful in predicting SCAD in women with pregnancy-associated myocardial infarction.

The exact mechanism of PASCAD is not completely clear and may be related to the hemodynamic changes of pregnancy[110] and the hormonally mediated alterations of vascular walls.[111–113] Normal hemodynamic changes in pregnancy include an increase in stroke volume and heart rate and, in addition, a significant compression of the aorta and the iliac arteries by the enlarged uterus, which increases outflow resistance and tension on the aortic wall and coronary arteries. In the presence of pregnancy-induced pathological changes in the arterial wall, which include fragmentation of the reticulin fibers, diminished amount of mucopolysaccharides, and loss of the normal corrugation of elastic fibers,[114] dissection may occur.

Type and Location of AMI and Coronary Anatomy

The great majority of the patients in this study presented with STEMI and the rest with non-STEMI. Location of the MI was anterior or anterolateral in 80% of the cases. These findings are significantly different from those recently described

by Saw et al[104] and Tweet et al,[106] who reported a STEMI in only one third of cases, in a large population of mostly (>90%) nonpregnant women with SCAD (Table 3). Although the preponderance of LAD dissection found in this study was similar to that reported in the nonpregnant populations, rate of LM involvement was strikingly higher (33% compared with 1.2% and 4%, respectively).

Similarly, the rate of multivessel involvement was >2-folds higher compared with the nonpregnant patients. The high incidence of multivessel coronary involvement reported in this and previous studies[5,115,116] strongly support the heightened vulnerability of blood vessels during pregnancy. This assumption is further supported by a concomitant dissection of the vertebral artery in 4 of the patients in this study and the reported increased incidence of extracoronary vascular dissections and ruptured aneurysms during pregnancy.[117]

LV Function and Complications

Almost half of the patients were found to have a marked reduction of LV systolic function, a rate significantly higher than that reported in nonpregnant women with SCAD.[106,117] This finding is most likely a result of a higher rate of LM and multivessel SCAD, resulting in larger MIs leading to a strikingly high incidence of complications. Cardiogenic shock was reported in almost a quarter of the patients, a need for mechanical assist device in a similar number of patients, and ventricular tachyarrhythmias in 16% of the patients. This high rate of life-threatening complications is in a sharp contrast to the report by Saw et al[104] of no cardiogenic shock in any of their 168 cases, ventricular assist device in only 1%, and ventricular arrhythmias in 5% of nonpregnant SCAD patients. The incidence of maternal mortality in our cohort was 4% and caused by cardiogenic shock in more than half of the patients. The rate of maternal mortality in this study was 2-fold higher than that reported in nonpregnant women of comparable age with MI[105] and is also significantly higher compared with nonpregnant women with MI because of SCAD (Table 3).[104,106]

Percutaneous Intervention

The use of catheter-based reperfusion therapy in SCAD has been controversial.[118] Shamloo et al[119] in a retrospective review of 440 cases of SCAD published between 1931 and 2008 reported improved outcome in those treated with an early aggressive strategy including CABG or stent placement. A retrospective study of 189 patients presenting with the first SCAD episode by the Mayo clinic group reported procedural failure in 53% of patients managed with PCI resulting in an emergency CABG surgery in 13% of the patients. In addition, 90% of the patients treated conservatively had a favorable in-hospital course, and the 5-year rate of target vessel revascularization and recurrent SCAD were similar in patients receiving revascularization versus conservative therapy.[103] Saw et al[104] reported on a prospective evaluation of 168 patients with SCAD, the majority of them treated conservatively on initial presentation. Thirty-three patients had PCI during the index hospitalization, 36% were unsuccessful and 27% were only partially successful. Among the successful and partially successful cases, 57% had procedural extension of a dissection including 14% into the LM requiring additional stenting, repeat PCI, or CABG surgery. The present study provides further support to the challenge of PCI in pregnant patients with SCAD; PCI was performed in 44 patients with only partial success and a relatively high rate of complications. Successful procedure was reported in only half of the patients, and there was a high incidence of propagation of the dissection, often leading to CABG surgery or repeat PCI during follow-up for recurrent ischemic symptoms. The risk of coronary interventions during pregnancy or the postpartum period is further emphasized by previous reports by our group and others[5,87,115] of iatrogenic coronary dissection as a result of intracoronary contrast injection or guidewire manipulations leading to severe complications including urgent CABG surgery, severe heart failure with ventricular assist device implantation, and mortality.

Stenting in this study was limited to the use of bare metal or drug-eluting stents. A successful use of bioabsorbable vascular scaffolds (BVS) has been recently reported in several patients with non–pregnancy-related SCAD.[120–122] There is a potential advantage for the use of BVS for the treatment of PASCAD over stents, which may allow sealing and healing with scaffold resorption over time, avoiding lifetime commitment to metallic stents in young patients and possible return of vasoreactivity.[123] This aspect is especially important because PCI in women with SCAD is often associated with extension of coronary dissections requiring implantation of several stents. At the same time, the inferior deliverability, mandatory predilation, and the often-required intracoronary imaging for positioning of the BVS[123] may result in increased radiation time and risk of iatrogenic dissection in PASCAD.[124] In addition, tensile strength of BVS has been reported to be low compared with that of the metal stents, which may not provide enough scaffold and increase risk of stent thrombosis.[125] Such risk may be accentuated in women with PASCAD because of the frequent need for multiple stents and hypercoagulable state of pregnancy and the postpartum period. For all these reasons and until new-generation BVS with long-term clinical outcome will be available, it does not seem advisable to recommend BVS for the treatment of PASCAD.

CABG Surgery

The incidence of CABG surgery in this study population was striking, representing >20-fold increased rate compared with nonpregnant women with MI at the child-bearing age[105] and >10 times compared with nonpregnant women with SCAD.[103] The explanation for the marked increase in the need for CABG surgery was a higher incidence of complex coronary anatomy (LM and multivessel involvement) and failed PCI and hemodynamic instability.

CABG surgery was performed during pregnancy in 4 women and resulted in fetal death in 2 cases and other fetal complication in the other 2. This information substantiates a previously published evidence for high fetal risk associated with cardiac surgery during pregnancy.[126]

Conservative Management

Almost one third of the patients were treated conservatively in their index admission. During a follow-up of ≈1 year and mostly within the first 3 months, almost half of these patients

underwent a repeat angiography because of recurrent symptoms, and approximately one third of these patients required revascularization procedures. In addition, one third of asymptomatic patients who underwent repeat elective coronary angiogram were found to have a persistent or new SCAD.

Follow-Up

Forty percent of 96 patients who were followed up for an average of 1 year had repeat coronary angiography, which showed persistence of SCAD in approximately one third and involvement of new vessels in another third of patients. These findings are at variance with previous reports of spontaneous healing in most nonpregnant patients with SCAD[103,117,127,128] and emphasize the difference in the natural history of this disease when associated with pregnancy.

Drug Therapy

Only half of the patients in this study received aspirin and anticoagulants, and only one third received other antiplatelet therapy, β-blockers, and nitrates. This low use of standard medications probably reflects the concern on fetal safety and the uncertainty related to the risk versus benefit ratio of antiplatelet and anticoagulants in MI secondary to SCAD.[129] The role of thrombolytic therapy (TT) is also controversial because of the risk of dissection extension. Buys et al[130] published a case of LAD SCAD who presented with MI and demonstrated clinical and electrocardiographic deterioration during TT. Shamloo et al[119] reported on 87 patients with SCAD who received TT with clinical deterioration in 60%. Thrombolytic agents were used in 10 patients in the present study and were followed by either PCI or CABG surgery in most of them. Similar findings were reported by Saw et al[104] and Tweet et al,[106] respectively, in SCAD patients receiving TT. These data, therefore, seem to support a potential unfavorable effect of TT in patients with SCAD-associated MI.

Intracoronary Imaging

SCAD was diagnosed by angiography in the majority of cases. The angiographic diagnosis is based on the presence of arterial wall contrast staining with multiple radiolucent lumens and diffuse or tubular stenosis that can mimic atherosclerosis. Intracoronary imaging including intravascular ultrasound and intracoronary coherence tomography that image the arterial wall layers can improve the diagnosis.[129] Intracoronary coherence tomography and intravascular ultrasound were used in 14 of our patients during the initial angiography and were reported to be helpful in establishing the diagnosis of SCAD, assisting in the assessment of its extension, or demonstrating malposition of the guidewire during PCI. However, because of the documented vulnerability of the coronary arteries in women with PASCAD, use of intracoronary devices should be limited to cases in which the potential benefits clearly outweigh the risks.

Subsequent Pregnancy

This study did not provide information on risk of subsequent pregnancy in women with a history of PASCAD. The results of this investigation, however, demonstrate an important pregnancy-related vulnerability of the coronary arteries and the potential dire consequences of PASCAD and a continuous instability of the coronary arteries during the follow-up. Published information is limited to 8 women with report of recurrent SCAD and STEMI 9 weeks after the delivery in 1 patient.[131]

Study Limitations

The study is limited by its retrospective design and data collected mostly from case reports and small case series. The data may, therefore, be incomplete and could reflect a selection and ascertainment bias and preferential submission and publication of more complicated cases. These limitations may be offset by the relatively large number of contemporary patients treated by a large number of clinicians at different medical centers. In addition, the results of this study are in part consistent with data presented in previous surveys[115,116] and in large population studies of pregnancy-related AMI.[5,108,109] There is also only limited information on extra coronary manifestation of vascular disease, primarily fibromuscular dysplasia commonly described in patients with SCAD.[125]

Summary and Conclusions

The results of this study highlight the unique and important characteristics of PASCAD that should be taken into account by clinicians treating such patients. PASCAD occurs in

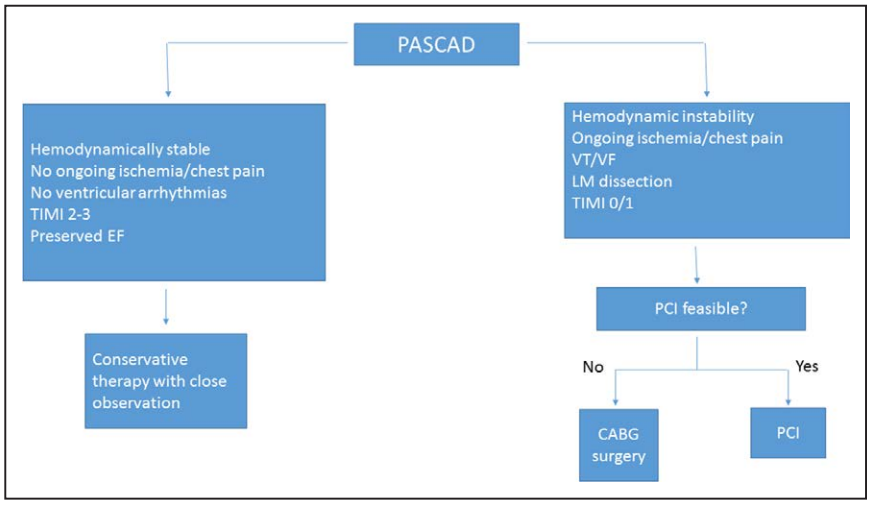

Figure 6. Suggested management algorithms for women with PASCAD. Because of high risk for iatrogenic coronary dissection, coronary angiography should be reserved for women with unstable features. In patients with spontaneous coronary artery dissection (SCAD), revascularization should be preserved to unstable women or those with left main dissection or high-risk proximal left anterior descending (LAD) SCAD. CABG indicates coronary artery bypass; EF, ejection fraction; LM, left main; PASCAD, pregnancy-associated spontaneous coronary artery dissection; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction; VF, ventricular fibrillation; and VT, ventricular tachycardia.

otherwise healthy women, mostly >30 years of age with low incidence of traditional risk factors for atherosclerotic CAD. The majority of cases presented during the postpartum period or the third trimester of pregnancy. Compared with nonpregnant women with SCAD, PASCAD is associated with more extensive involvement of the coronary arteries manifested by a significantly higher rate of LM and multivessel dissections. In addition, there is a markedly higher incidence of STEMI and involvement of LV anterior wall, and as a result, a mark decrease in LV ejection fraction compared with nonpregnant patients. This large myocardial insult leads to worse outcome with an increased incidence of cardiogenic shock, life-threatening arrhythmias, a need for emergent CABG surgery, use of mechanical support and cardiac transplantation, and a high rate of maternal and fetal mortality. PCIs are associated with a low success rate and high incidence of complications including iatrogenic dissections and propagation of existing dissections requiring emergency CABG surgery. These findings in addition to previous reports of iatrogenic coronary dissection after contrast injection leading to catastrophic complications[5,24] suggest that a noninvasive approach to diagnosis and a conservative management strategies are preferred in the stable, low-risk women with PASCAD (Figure 6). Coronary angiography should be done with caution and intra coronary manipulations should only be done when benefits clearly outsight the risk. CABG surgery is often used because of involvement of LAD and LM, multiple coronary arteries dissection, high incidence of PCI-related complications, and hemodynamic instability. Surgery seems to be associated with a favorable maternal outcome but can result in a high rate of fetal complications when performed antepartum. For this reason, a CS before surgery should be considered in every case of a viable fetus.

Most guideline-recommended drugs for patients with MI are either unsafe or have only paucity of information related to fetal safety. There does not seem to be a good rational for antiplatelet or anticoagulant therapy in women with SCAD. In addition, the use of antiplatelet and anticoagulants, as well as TT, may lead to an unfavorable effect because of possible extension of the dissection. For this reason, it is advisable to transfer a patient with pregnancy-associated STEMI, who is diagnosed in a secondary hospital without a cardiac catheterization laboratory, to a tertiary care hospital if possible, rather than provide thrombolytic therapy. Rate of healing of PASCAD is lower than that reported in the nonpregnant SCAD patients, and recurrence of ischemic symptoms is common both in patients treated aggressively and conservatively because of persistence of SCAD or involvement of new vessels and should be anticipated. Because of high rate of recurrent symptoms, a close and long-term follow-up is recommended in women with PASCAD. Little information is available on the risk of subsequent pregnancy in women with a history of PASCAD. However, because of the high incidence of recurrent SCAD and pregnancy-related vulnerability of the coronary arteries, subsequent pregnancy does not seem advisable.

Disclosures

None.

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