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Pregnancy and Cardiovascular Disease (N Scott, Section Editor)

Spontaneous Coronary Artery Dissection and Pregnancy

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Opinion statement

Spontaneous coronary artery dissection (SCAD) is a non-atherosclerotic, non-traumatic cause of coronary artery dissection. SCAD is the most common cause of myocardial infarction in pregnancy or the postpartum period and results in significant cardiovascular morbidity and mortality in the pregnant population. It is important to consider pregnancy-associated spontaneous coronary artery dissection (PASCAD) high on the differential for a pregnant woman who presents with symptoms consistent with acute coronary syndrome. Management of these patients requires a thoughtful, multidisciplinary approach, with consideration of conservative management if possible. Counseling regarding future pregnancies is also critical and requires compassionate care. Given our limited understanding of SCAD, including PASCAD, more data and research are needed to help guide diagnosis, management, and determination of prognosis.

Introduction

Spontaneous coronary artery dissection (SCAD) is a non-atherosclerotic, non-traumatic cause of coronary artery dissection. Findings from both intracoronary imaging and autopsy suggest that compression of the true lumen of the affected coronary artery by intramural hematoma results in impaired coronary flow and myocardial infarction [1–3]. The vast majority of these patients present with acute coronary syndrome (ACS) and, in some cases, sudden cardiac death [4]. Based on our contemporary registries, SCAD is a condition that disproportionately affects younger women, with greater than 90% of cases in females at an average age of 45–53 years [4, 5]. While it is still considered rare, it is a common cause of ACS in women under the age of 50, accounting for 35% of cases in one series [6]. The underlying cause of SCAD is currently not understood, although a substantial portion of patients also carry a diagnosis of fibromuscular dysplasia (FMD), a non-atherosclerotic and non-inflammatory disorder that leads to arterial stenosis, dissection, and aneurysm [7–9]. This suggests that the pathophysiology of SCAD may be explained by FMD in a portion of these patients.

SCAD was first described by Harold Pretty in 1930 [10] in a case of a 42-year-old woman who suddenly died after "partaking in a good meal of fried fish and chip potatoes" which resulted in "severe retching and vomiting" throughout the night. Upon autopsy, she was found to have "marked atheroma with dissecting

aneurysm" of her right coronary artery. Since this initial description, case reports had largely described SCAD in the setting of pregnancy, leading to the assumption that this was a disease of pregnancy. However, contemporary series suggest pregnancy-associated spontaneous coronary artery dissection (PASCAD) actually accounts for a relative minority of cases [11]. That being said, SCAD is the most common cause of myocardial infarction in pregnancy or the postpartum period and results in significant cardiovascular morbidity and mortality in the pregnant population [12]. Here, we will review the literature to date regarding PASCAD, defined as SCAD in the antepartum, peripartum, or postpartum period. We will also discuss the current issues surrounding reproductive health after SCAD.

Pregnancy-associated spontaneous coronary artery dissection

In the largest series to date, Havakuk et al. performed a recent analysis of 120 cases of PASCAD identified through literature searches [13]. In this series, the mean age was 34 years, with 40% of women over the age of 35. The vast majority of cases (72.5%) presented in the postpartum period, with 17% presenting in the 3rd trimester. There were no cases identified in the first trimester and only a small percentage in the 2nd trimester or peripartum period. This is consistent with other studies which suggest the postpartum period is the highest risk period for PASCAD [14], an important point given the misconception that cardiovascular complications are limited to the antepartum and peripartum period. There is an observed association with breastfeeding, and cases of late postpartum SCAD have been described in women who have been breastfeeding up to 16 months [15]. As seen with SCAD patients as a whole, a small percentage of patients have traditional risk factors such as family history of coronary artery disease, smoking, hypertension, diabetes, and hyperlipidemia. Twelve percent of patients in the series were noted to have pre-eclampsia, and while this was a minority of patients, this is a substantially higher incidence of pre-eclampsia than in pregnant patients overall [16]. There are also data suggesting multiparity as a risk factor [15]. It has been proposed that progressive progesterone and estrogen mediated weakening of the vessel wall with repeated pregnancies may at least in part explain this finding [17]. In the Elkayam series, the overwhelming majority of patients presented with chest pain (94%), with 75.5% presenting with an ST elevation myocardial infarction (STEMI) of which 62% were anterior STEMIs. Of the 90 patients in which LV function was reported, the average ejection fraction was 40%. Sixty percent of cases showed a lesion in 1 artery, 22.5% in 2 arteries, and 17.5% in 3 or more arteries. The left main was affected in 36% of cases and the left anterior descending (LAD) in 72% of cases. The high incidence of LAD involvement is consistent with other reviews of the literature [14, 17, 18]. The lower ejection fraction and the higher percentage of left-main and LAD-artery dissections in PASCAD as compared to SCAD patients overall suggest a more severe form of SCAD in pregnancy. Why this may be the case is yet to be elucidated, although the hemodynamic and hormonal changes of pregnancy are thought to play a substantial role.

At the current time, we believe that most cases of SCAD should be managed by conservative means when possible. This is based on data that suggest an increased risk of dissection propagation with percutaneous intervention as well

as evidence that the vast majority of dissections heal with time [4]. In cases of coronary artery bypass grafting (CABG), the graft will often fail due to competitive flow from the native artery once it heals. Therefore, at the current time, we do not recommend attempt at revascularization via PCI or CABG unless there is evidence of symptoms refractory to medical management, hemodynamic instability, or left-main (and perhaps proximal LAD) dissection. In the Havakuk series, 44 of the patients underwent PCI, with difficulty in catheter engagement or passing of the wire reported in 9 cases and propagation of dissection in 11 cases. This reflects the technical difficulties and iatrogenic risks of attempted intervention. Forty-four women underwent CABG due to hemodynamic instability, failed PCI, complex anatomy, or ongoing ischemia despite conservative management. Fifty-four patients were managed conservatively. Of these, 18 eventually went on to CABG or PCI due to ongoing symptoms. It should be noted that 6 cases with left-main involvement and 21 cases with LAD involvement were medically managed, which suggests that conservative management may still be preferred even with high-risk lesions.

In terms of conservative therapy, there is large variation in practice for SCAD patients overall, with no standard approach to management. As a general rule, much of the management guidelines for atherosclerotic causes of ACS are used when treating SCAD. In the case of PASCAD, teratogenicity as well as drug effects on a breastfeeding infant must be kept in mind. LactMed, a mobile-phone application by the National Institutes of Health, is a helpful resource as is the Food and Drug Administration pregnancy drug safety profile. Given the paucity of data, particularly for medical management in PASCAD, suggestions and considerations for medical management in pregnancy and lactation are outlined below:

Aspirin 81 mg: Given its use in pre-eclampsia prevention, aspirin 81 mg can be used during pregnancy after weighing risks/benefits. At the 81-mg dose, it is also safe during lactation. It is recommended that breastfeeding is avoided 1–2 h after a dose to minimize the risks of antiplatelet effects on the infant.

Clopidogrel: Can be given during pregnancy but should only be considered for those with PASCAD who have received PCI. Avoid using drug during lactation or discontinuing breastfeeding. Importantly, the American Society of Regional Anesthesia does recommend holding clopidogrel 7 days before regional anesthesia [19].

Beta blockers: Can be used during pregnancy after careful discussion of risks and benefits given reports of intrauterine growth retardation. Beta blockers are generally deemed safe during breastfeeding. There is a preference for metoprolol given some reports of significant bradycardia with atenolol.

Calcium channel blockers: Can be used during pregnancy after discussion of risks and benefits. There is inadequate human data on use of amlodipine or diltiazem, and nifedipine is the preferred agent. There is some suggestion that higher doses of amlodipine are excreted during lactation. Diltiazem or nifedipine would be preferred.

Anticoagulation: As a general rule, heparin therapy is stopped at the time of diagnosis of SCAD given concern for propagation of intramural hematoma. However, heparin products are deemed safe during pregnancy and lactation.

Statins: Not recommended in SCAD given some evidence of increased recurrence in those using statins [5]. Regardless, statins are contraindicated during pregnancy and lactation.

While conservative management is recommended in stable patients, it appears the population of women with PASCAD present with high rates of complications that may necessitate invasive means of stabilization. In the Havakuk series, there were 29 cases of cardiogenic shock and 19 cases of ventricular arrhythmias. Urgent PCI was required in 34 cases, urgent CABG in 33 cases, and mechanical circulatory support (i.e., intra-aortic balloon pump, ventricular assist device, extracorporeal membrane oxygenation) in 34 cases. Of the five deaths reported, all had involvement of the left system. Three cases were a result of cardiogenic shock, one due to uncontrolled bleeding, and one during cardiac catheterization. When PASCAD in the Havakuk series was compared to SCAD not associated with pregnancy in series by Tweet et al. and Saw et al., the data supported greater morbidity and mortality with PASCAD. Sixty-nine percent of patients with PASCAD presented with STEMI as opposed to 26 and 37% in the Saw et al. and Tweet et al. studies, respectively. There was also substantially greater left-main involvement and LAD involvement. Multivessel disease and ventricular arrhythmias were also substantially more common in PASCAD as was systolic dysfunction, cardiogenic shock, need for mechanical circulatory support, and mortality. This again points to PASCAD as a higher risk form of SCAD. It also highlights the importance of a multidisciplinary approach to these patients with collaboration between maternal–fetal medicine, cardiology, cardiothoracic surgery, and pediatrics. If at all possible, patients with PASCAD should be cared for at a center with expertise in these areas as well as in SCAD.

The exact mechanism by which PASCAD results in a more severe form of SCAD is unclear. Estrogen receptors are present in the coronary arteries and may mediate changes during pregnancy which weaken the vessel wall. Hormone-mediated focal fragmentation of elastic fibers and loss of acid mucopolysaccharide substance leads to cystic medial necrosis and lack of vasa vasorum structural support [12, 20]. It is likely that this underlying abnormality of the vessel wall in combination with the hormonal and hemodynamic changes of pregnancy may predispose these women to PASCAD. It is also important to screen these women for FMD, given its known association with SCAD. Renal FMD can result in hypertension which may become unmasked during pregnancy [21]. It is therefore particularly important to have heightened suspicion for FMD in the women with both pre-eclampsia and SCAD. While connective-tissue diseases such as Marfan syndrome are diagnosed in only a minority of SCAD patients, women with PASCAD should be screened for connective-tissue disease, preferably in conjunction with a specialist familiar with these conditions. Genetic testing should be done in those whom there is suspicion for a connective-tissue process.

Reproductive health after spontaneous coronary artery dissection

Given SCAD is a condition that tends to affect younger women, a sizeable portion are still of reproductive age at the time of their event. Its known

association with pregnancy as well as emerging evidence suggesting high morbidity and mortality of PASCAD make pregnancy after SCAD high risk. Furthermore, there is no clear consensus in terms of management of PASCAD, given significant morbidity and mortality with both conservative and aggressive (i.e., PCI and CABG) strategies. Therefore, in general, we do not recommend pregnancy in patients with a history of SCAD. We suggest contraception with a progestin-based intrauterine device (IUD) such as the Mirena, given its local delivery of progestin. Estrogen-based contraception is avoided due to its hypercoagulable effects and possible adverse effects of the vessel wall. Systemic progesterone is also discouraged, as it is felt to be a main contributor to the weakening of the vessel wall. Discussion of contraception with the obstetrician or gynecologist is an important part of management after SCAD.

Discussions of abstaining from pregnancy after SCAD are often extremely difficult, particularly for women who have not yet had children and/or were planning future pregnancies. The recurrence risk of SCAD overall is approximately 10–20% [4, 5]. In terms of recurrence of SCAD during pregnancy, the only published data to date are from Tweet et al. in a series of eight patients from Mayo Clinic followed for a median of 36 months [22]. One patient had a recurrence in the postpartum period and ultimately required CABG. It should be noted that the patient's prior event was not during pregnancy. This suggests that those with SCAD not associated with pregnancy are not necessarily at lower risk of PASCAD. Given the paucity of data, it is difficult to deem SCAD an absolute contraindication for future pregnancy. That being said, we will often categorize it as a relative contraindication with significant risk for both mother and fetus. Unlike other cardiovascular diseases during pregnancy (i.e., aortopathy, valvular heart disease, etc.), there is no way to monitor for an impending event. If the patient has the means to consider it, surrogacy is often a viable alternative. If the woman does wish to plan future pregnancies, despite the heightened risk, we recommend waiting at least 1 year from the SCAD event to allow for healing of the vessel. Consideration can also be made for evaluation via a coronary CT angiogram in order to confirm healing prior to pregnancy, although this form of imaging is predominantly useful in proximal dissections as distal dissections are often difficult to visualize by CT. Prior to conceiving, the patient should establish care with a cardiologist that is familiar with SCAD as well as a maternal–fetal-medicine specialist. A multidisciplinary approach should be taken in managing these patients throughout pregnancy, and a plan for delivery should be delineated ahead of time. While there are no data for mode of delivery, our institution and others opt for vaginal delivery with an assisted second-stage delivery so as to limit valsalva by the mother. This is consistent with our practices for pregnant patients with other cardiovascular conditions [23]. While cesarian section is an option, it is felt that the risks of hemorrhage, infection, complications from anesthesia, and thrombotic complications likely outweigh any presumed benefit of avoiding the strain of a vaginal delivery. It should be noted that this continues to be a point of debate, and future research is needed to better determine the safest mode of delivery.

Compliance with Ethical Standards

Conflict of Interest
The author declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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