



Evolving management and improving outcomes of pregnancy-associated spontaneous coronary artery dissection (P-SCAD): a systematic review

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ABSTRACT

Background: Pregnancy-associated spontaneous coronary artery dissection (P-SCAD) is defined as SCAD occurring during pregnancy or within 3 months post-partum. Earlier systematic reviews have suggested a high maternal and foetal mortality rate. We undertook a structured systematic review of P-SCAD demographics, management and maternal and foetal outcomes.

Methods: Case study identification was conducted according to PRISMA guidelines, with screening of all published P-SCAD cases not meeting pre-defined exclusion criteria. Of two hundred and seventy-three publications screened, one hundred and thirty-eight cases met inclusion criteria. Cases were allocated to one of three time periods; 1960–85 (twenty cases) reflecting early management of P-SCAD, 1986–2005 (forty-two cases) reflecting recent management, and 2006–16 (seventy-six cases), reflecting contemporary management.

Results: The only significant demographic change in women experiencing P-SCAD over the last 50 years was an increasing proportion of primigravidas ($p = 0.02$). Management and outcomes, however, have altered significantly. Emergent angiography ($p < 0.0001$), reduced thrombolysis ($p = 0.006$) and increasingly conservative or percutaneous management ($p < 0.0001$) are associated with dramatic reductions in maternal mortality (85% in earliest reports to 4% in the last decade, $p < 0.0001$) and foetal mortality (50% in earliest reports to 0.0% in the last decade, $p = 0.023$).

Conclusion: This systematic review of temporal changes in presentation, management and outcomes of P-SCAD represents the widest range of variables analysed in the largest cohort of P-SCAD patients to date. In the setting of earlier coronary angiography and increasingly conservative management, maternal and foetal survival rates continue to improve.

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1. Case study

A 35-year-old G2P0 woman presented with chest pain and anterior ST elevation at \pm 34 weeks and 3 days gestation of an in vitro fertilisation (IVF) pregnancy. She had undergone two cycles of IVF therapy prior to pregnancy, and received a standard regime of hormonal stimulation. After discussion with the treating obstetrician, the cardiac catheterization laboratory was activated, with midwives and an obstetrics registrar on standby for urgent delivery in case of foetal distress or maternal arrest.

Radial coronary angiography performed with minimal contrast (70 mL), minimal radiation (skin dose 88 mGy), and abdominal shielding. A spontaneous dissection of our patient's distal left anterior descending artery was found. Due to her haemodynamic stability, the decision was made to treat her conservatively with optimal medical therapy.

Our patient commenced aspirin, clopidogrel, metoprolol and a heparin infusion (subsequently changed over to enoxaparin). Her electrocardiogram evolved to show anterior Q waves, and troponin peaked

at 40,494 ng/L (normal < 16 ng/L). Echocardiography showed anterior hypokinesis with an ejection fraction (LVEF) of 40%, and spontaneous echocontrast in the left ventricle. Screening for an underlying connective tissue disease, including a full vasculitic screen and imaging of cerebral and renal vasculature, was negative. She remained on cardiac monitoring, and daily foetal cardiotocography remained within normal limits.

At 38 weeks exactly gestation, our patient underwent elective lower uterine segment caesarean section under spinal anaesthesia, with clopidogrel cessation one week prior and enoxaparin cessation 48 h prior. Delivery was uncomplicated, with birth of a healthy female singleton. Post-partum, our patient commenced ramipril and warfarin, with agreement not to breastfeed. Seven days later, our patient returned home with her daughter, stable with New York Heart Association class I symptoms.

2. Methods

We conducted a systematic review according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [1], examining all case studies and case series published on pregnancy-

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associated spontaneous coronary artery dissection (P-SCAD) at any time up to December 2016. Two authors (EP and CK) searched on PubMed and EMBASE using the search term 'pregnancy AND spontaneous coronary artery dissection'. Prior published case reviews were identified, and cases cross-referenced with our search results. Citation tracking and searches of major journal databases were also performed to maximise case identification.

In line with accepted clinical definitions, P-SCAD was defined as spontaneous coronary artery dissection occurring during pregnancy or within 3 months post-partum [2]. The definition of pregnancy did not include patients undergoing IVF therapy not yet confirmed to be pregnant or receiving b-HCG injections for weight-loss purposes [3,4]. The diagnosis of P-SCAD was required to be confirmed either by invasive coronary angiography or at autopsy. Combined exclusion criteria included articles not in English, narrative reviews, healthcare system linkage studies without individual case details, cases not meeting pre-defined P-SCAD criteria, diagnosis made by cardiac imaging (i.e., CT coronary angiography only performed), full article not able to be accessed, or histopathology articles reporting autopsy findings of P-SCAD with minimal clinical history.

Our search strategy returned 273 results. Exclusion of duplicate results and articles not meeting specified a priori criteria (162 articles) resulted in 111 articles describing 138 cases of P-SCAD [5–92].

Demographic case details extracted from all case reports were maternal age, cardiac risk factors (defined as both number of cardiac risk factors and a binary variable), presence of an autoimmune or connective tissue disorder, gravidity/parity status, gestational time or days post-partum at onset of P-SCAD, and whether the pregnancy was a result of in vitro fertilisation (IVF) or a multiple pregnancy.

Parameters assessed with regards to cardiac presentation and outcome included mode of cardiac presentation (defined as ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, unstable angina or out of hospital cardiac arrest), culprit coronary artery and whether multivessel dissection was present, whether thrombolysis was used, whether the patient was taken emergently for coronary angiography, whether mechanical cardiac support such as an intra-aortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) was employed, treatment strategy (defined as conservative medical management, percutaneous coronary intervention, coronary artery bypass surgery or death prior to definitive coronary intervention), whether the patient subsequently underwent cardiac transplant, and mean left ventricular ejection fraction at follow-up.

With regards to obstetric management and outcome, we assessed whether emergency delivery was required if pregnant at time of P-SCAD, mode of delivery chosen (defined as normal vaginal birth or lower uterine segment caesarean section), and maternal and foetal survival rates.

2.1. Statistical analysis

Cases were grouped into three cohorts according to year of publication. The three categories reflected early management of P-SCAD in the years 1960–85 (twenty cases), management over the interval twenty years from 1986 to 2005 (forty-two cases) and contemporary management in the last decade (2006–16, seventy-six cases published).

A Shapiro-Wilk test was used to assess normality of distribution of continuous variables. Continuous variables that were normally distributed were assessed with a one-way ANOVA test with post-hoc Tukey testing, and are presented as mean \pm standard deviation. Continuous variables that were not normally distributed were assessed with Kruskal-Wallis testing and are presented as median values with inter-quartile ranges. Categorical variables are reported as proportions, and were assessed with chi-squared testing. All statistical calculations were performed using STATA software (StataCorp 2015, Texas).

3. Results

Mean maternal age did not differ across time cohorts; however, there were significant differences regarding gravidity/parity status at each time point (Table 1). In all time cohorts, the majority of patients were post-partum, with a median post-partum status of approximately two weeks. Patients in all cohorts had a mean age in the mid-thirties, however patients in the 1960–85 cohort had a median of three children at this age, compared to a median of 1 child for women in the 1986–2005 cohort, and 2 children in the 2006–16 cohort ($p = 0.001$). This was also reflected in a difference in the proportion of primigravidas across groups: the proportion of primigravidas peaked in the time period 1986–2005, representing over half of women experiencing P-SCAD ($p = 0.03$). As reported in earlier studies, P-SCAD most commonly occurred in the third trimester or postpartum period (105). Amongst women experiencing post-partum P-SCAD, dissection occurred progressively closer to the time of delivery in recent cohorts (11.5 days PP in 2006–16 vs 13.0 (1986–2005) vs 20.5 days (1960–1985), $p = 0.046$).

IVF-assisted pregnancies complicated by P-SCAD were only reported for the first time in the most recent decade 2006–16. However, due to small overall numbers, the difference between groups with regards to IVF therapy did not reach statistical significance. Likewise, multiple pregnancies were increasingly common in the most recent cohort, however the difference did not reach statistical significance. Due to the small numbers, assessment of statistical interaction between IVF status and multiple pregnancies was not feasible.

Multiple therapeutic strategies differed significantly between groups over time (Table 2). Women experiencing P-SCAD in the last decade have been significantly less likely to present with out of hospital cardiac arrest or receive thrombolysis ($p < 0.0001$ and $p = 0.006$ respectively). They were significantly more likely to receive urgent coronary angiography ($p < 0.0001$), and conservative management or percutaneous coronary intervention than coronary artery bypass surgery ($p < 0.0001$).

With regards to outcome measures, maternal and foetal survival have both increased dramatically from earliest reports to the current decade (15 to 96%, $p < 0.0001$ and 50 to 100%, $p = 0.023$ respectively), and women are less likely to require cardiac transplantation for cardiomyopathy ($p = 0.008$). However, there have been no significant changes in mean ejection fraction at follow-up. Follow-up time period were very inconsistently documented amongst studies, or not reported at all. Consequently, length of follow-up has not been included in our data-set.

4. Discussion

P-SCAD is a high-risk condition, with the potential for dual mortality [87]. It occurs in approximately 1.81 per 100,000 pregnancies [88].

Table 1
Baseline demographics of women experiencing P-SCAD.

	2006–16	1986–2005	1960–85	Significance
Number of case reports	76	42	20	–
Maternal age (years)	34.1 \pm 4.9	32.9 \pm 5.0	34.8 \pm 5.1	$P = NS$
Primigravida status (%)	32.3	54.8	14.3	$P = 0.02$
Median gravidity	2 [2–3]	2 [1–3]	3 [2–4]	$P = NS$
Median parity	2 [1–2]	1 [1–2]	3 [2–4]	$P = 0.001$
IVF pregnancy (%)	5.3	0.0	0.0	$P = NS$
Multiple pregnancy (%)	9.2	2.4	5.0	$P = NS$
Cardiac risk factors present (%)	45.1	31.0	30.0	$P = NS$
Median number of cardiac risk factors	0 [0–1]	0 [0–1]	0 [0–1]	$P = NS$
Autoimmune disease (%)	7.0	4.9	5.0	$P = NS$
Pregnant (%)	23.7	33.3	10.0	$P = NS$
Median gestational week ^a	34 [32–36]	33.5 [23–37]	40 [40–40]	$P = NS$
Postpartum (%)	76.3	66.7	90.0	$P = NS$
Median postpartum days ^b	11.5 [7–21]	13 [5–42]	20.5 [14–42]	$P = 0.046$

IVF = in vitro fertilisation.

^a If pregnant.

^b If postpartum.

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