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Pregnancy-associated myocardial infarction: Prevalence, causes and interventional management

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Abstract

Pregnancy-associated myocardial infarction (PAMI) is a primary contributor to maternal cardiovascular morbidity and mortality. Specific attention to the etiology of myocardial infarction (MI), diagnostic evaluation, treatment strategies, and post-event care is necessary when treating women with PAMI. This review summarizes the current knowledge, consensus statements, and essential nuances.

Keywords

acute coronary syndrome; myocardial infarction; pregnancy; spontaneous coronary artery dissection

Introduction and Definition of Pregnancy-Associated Myocardial Infarction (PAMI)

In contrast to the overall global decline of maternal mortality, the United States rates continue to rise.[1, 2] PAMI accounts for over 20% of maternal cardiac deaths.[1] PAMI is defined as MI[3] during pregnancy or the postpartum period. Formal postpartum definitions vary in the literature, typically ranging from 6 to 12 weeks with some authors suggesting a period of ≥12 months.[4]

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Nearly half of maternal deaths occur within the first day of delivery, and 66% of deaths occur within the first week.[5] Many of the dramatic hemodynamic and physiologic changes of pregnancy(Figure 1[6-8]) and early postpartum period return to normal by 6-12 weeks postpartum.[6, 7] Pregnancy-associated hypercoagulability decreases by 6 weeks and normalizes around 12 weeks.[9] Generally, the time period after miscarriage, termination, or stillbirth is considered postpartum, although the associated changes may be of a different magnitude and duration than those following a full-term pregnancy.

Incidence and Prevalence of PAMI

PAMI occurs in 2.8-8.1 per 100,000 deliveries[10-12] which is 4-fold higher than the MI occurrence among non-pregnant, reproductive-aged women.[10] The incidence of PAMI is increasing and may relate to improved case detection and greater numbers of older women with underlying cardiovascular risk factors becoming pregnant. The case fatality rate in contemporary studies is estimated at 5%[12] and is higher than MI fatality rates among non-pregnant women of reproductive age.[13]

One of the most consistently reported risk factors for PAMI is age >35 years.[10, 11, 14] Other risk factors include cigarette smoking, hypertension, diabetes, and hyperlipidemia but are less common in women with PAMI compared to MI not associated with pregnancy.[10, 11, 14, 15] This observation is consistent with the high prevalence of non-atherosclerotic etiologies of PAMI, such as spontaneous coronary artery dissection (SCAD). Less common risk factors include preeclampsia,[11] multiple gestation,[16] thrombophilia, blood transfusions, and postpartum infections.[10] Black women have higher rates of PAMI, likely mediated by a higher prevalence of other coexistent risk factors.[10, 11]

A meta-analysis of population-based, international studies found that the incidence of PAMI is highest in the antepartum period,[13] whereas a US PAMI population-based study observed most cases occurring postpartum.[12] In 150 case reports of women with PAMI, 24% were diagnosed in the 3rd trimester and 47% were postpartum.[14] The majority(75%) presented with ST-segment elevation MI(STEMI) and 24% had severely reduced left ventricular ejection fraction(LVEF) ≤30%, with complications of cardiogenic shock(38%) and ventricular arrhythmias(12%).[14] In a registry study of 54 women with PAMI due to SCAD, 54% occurred within the first week postpartum. Women with pregnancy-associated SCAD were more likely to present with STEMI, left main and/or multivessel SCAD, and reduced LVEF compared to women with SCAD not associated with pregnancy.[17]

Presentation and Diagnosis of PAMI

PAMI should be suspected in pregnant or postpartum women presenting with cardiac arrest, acute onset of angina or dyspnea, ischemic changes on electrocardiogram(ECG), and/or elevated cardiac biomarkers.[18, 19,20] Changes in symptoms, physical exam, ECG, and biomarkers may occur during normal pregnancies and are important to distinguish from those indicative of PAMI(Figure 2[18, 21-25]). For instance, dyspnea is common in late pregnancy, but associated orthopnea or chest discomfort should prompt a cardiovascular evaluation. Normal pregnancies are associated with ECG abnormalities including left axis

deviation, inferior Q-waves, and T-wave inversions. Transient ST-depression can occur in healthy women during cesarean section delivery under regional anesthesia.[18, 21]

After uncomplicated labor and delivery, creatine kinase and creatine kinase-MB can exceed the upper limit of normal.[22] Cardiac troponin I(cTnI) and troponin T(cTnT) levels usually remain within normal limits after delivery, although high sensitivity cTnT may be elevated immediately postpartum in up to 4% of asymptomatic women.[22, 23] Preeclampsia and gestational hypertension are associated with abnormal cTnT and cTnI levels after delivery.[24] Therefore, clinical suspicion should be based on presentation and symptoms, interval changes in biomarkers, and regional wall motion abnormalities on echocardiography.

Etiologies of PAMI

PAMI may be caused by either obstructive or nonobstructive lesions in the coronary arteries. Patients with MI with normal or non-obstructive (<50% stenosis) coronary arteries are considered as having MI with nonobstructive coronary arteries(MINOCA).[26] Etiologies of MINOCA overlap with etiologies of obstructive MI as discussed below and include coronary plaque disruption with thrombosis and spontaneous thrombolysis; coronary vasospasm with resolution prior to angiography; coronary embolism; SCAD; and microvascular dysfunction.[3, 26] The algorithm for work-up of MINOCA[26] can be applied to patients with PAMI; however, studies such as cardiac magnetic resonance imaging and coronary function assessment should be considered after delivery.

Plaque rupture and/or erosion with atherothrombosis:

Obstructive, unstable atherosclerotic coronary artery disease represents the underlying mechanism in roughly one-third of PAMI.[14, 27] This occurs due to rupture of the thin fibrous cap of a lipoprotein-rich plaque with exposure of the necrotic core and coronary thrombosis formation.[28, 29] Coronary thrombus may also form in response to plaque erosion in which disrupted endothelium exposes plaque predominantly composed of smooth muscle cells and proteoglycans.[29, 30]

SCAD:

Although the exact prevalence is uncertain,[31] SCAD is increasingly recognized as likely causing at least one-third of PAMI.[14, 17] SCAD is due to a hematoma ±an intimal tear of the coronary arteries associated with an obstruction of flow that is not attributed to atherosclerotic, iatrogenic or traumatic causes.[32, 33] Intracoronary thrombus is typically absent.[34] Patients with SCAD commonly have fibromuscular dysplasia(FMD) or other arteriopathies such as dilatation, dissection, and aneurysms.[32, 33]

In-situ thrombosis or embolus:

Pregnancy is a physiologic, hypercoagulable state that may lead to in-situ intracoronary thrombus or embolism to the coronary arteries.[8, 16, 35] Predisposing conditions include Kawasaki's disease,[18] systemic inflammatory conditions, autoimmune disorders such as antiphospholipid antibody syndrome, tumors, malignancy, atrial fibrillation, cardiomyopathy, and valvular heart disease.[36] Since half of patients with thrombosis during

pregnancy have an underlying thrombophilia and thrombophilia is a risk factor for PAMI, testing for thrombophilia if there is no other predisposition for thrombosis beyond pregnancy is advisable.[10, 37]

Coronary vasospasm:

Coronary vasospasm is challenging to diagnose as the etiology of PAMI, but it has been observed to cause STEMI during pregnancy[14, 38] and was noted in 2% of a PAMI series.[14] Prolonged vasospasm may contribute to intracoronary thrombus formation.[38]

Differential Diagnosis:

A number of serious conditions may have a similar clinical presentation as PAMI occasionally with abnormal ECG and biomarker elevation(Figure 3[13, 18, 39-46]).

Initial Management of PAMI

Expeditious diagnosis and treatment of an acute PAMI is of utmost importance due to the high maternal and fetal mortality. Appropriate therapy focused on maternal outcomes will also increase fetal survival, and thus, the maternal condition should dictate clinical management. A multidisciplinary “Pregnancy Heart Team” consisting of expertise from cardiology, obstetrics and/or maternal fetal medicine, anesthesiology and, depending on the clinical situation, cardiothoracic surgery, neonatology, and critical care may facilitate collective decision-making.[18]

Importantly, standard of care for the nonpregnant woman with MI should be standard of care for the pregnant woman[47-50] with modifications as indicated. This includes using aspirin, heparin, clopidogrel, and nitrates(Figure 4[51-53]). Full dose aspirin(325 mg) may be used until 32 weeks gestation, and 81 mg may be used any time during gestation. Heparin is the preferred anticoagulant since it does not cross the placenta and safety during pregnancy is established.[51] Clopidogrel is the preferred P2Y12 inhibitor in pregnancy, and the more potent options should be avoided or used with caution.[51] Due to the absence of safety data, glycoprotein IIb/IIIa inhibitors generally should be avoided or used with caution. Dual antiplatelet therapy(DAPT) is reasonable if a percutaneous coronary intervention(PCI) with intracoronary stenting is planned. Single agent aspirin may be considered such as in PAMI due to SCAD[32], although this is based on expert consensus,[32] and data demonstrating benefit versus harm is lacking. Beta-blockers are generally considered safe in pregnancy, but use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers must be delayed until after delivery due to risks to the fetus.[51] Nitrates can alleviate discomfort or resolve/diagnose coronary vasospasm but should be used prudently to avoid maternal hypotension and placental hypoperfusion.[14] As with any MI, primary PCI is preferred to fibrinolytic therapy if it can be performed in a timely fashion. This may be particularly true in the pregnant women, given the multiple etiologies of MI, the increased bleeding risks, and the relative contraindication to fibrinolytic therapy.[27] Nonetheless, successful utilization of thrombolytics in pregnancy, particularly for treatment of pulmonary embolism, has been reported.[54]

Diagnostic Coronary Angiography in PAMI

Ionizing radiation from coronary angiography (and PCI) is considered an acceptable risk in pregnancy when the procedure is otherwise indicated (Figure 5[55-57]). Fetal radiation effects are unlikely to occur for dose levels below 50 millisieverts(mSv). Given that the fetal radiation dose associated with coronary angiography is expected to be less than 1mSv, the risk of radiation injury to the fetus is likely negligible in comparison with the natural incidence of congenital abnormalities.[55-57] Standard practice methods to minimize patient (and fetal) radiation dose include short fluoroscopy time, decreased frame rates, and minimization of cineangiography.

Interventionalists should be prepared for procedural complications. In one review, 5/129(3.8%) women with PAMI had coronary dissection during angiography.[14] It is unclear if these were all iatrogenic dissections, if some were exacerbations of unidentified SCAD, or if this risk would be similar in a population-based study. It is also possible for patients to decompensate or arrest due to evolving ischemia during coronary angiography. If coronary angiography is being performed at a viable gestational age(≥23 weeks), administration of antenatal corticosteroids and notification of a “standby” obstetrical team able to perform emergent resuscitative cesarean delivery in the event of maternal decompensation should be considered. Continuous fetal heart rate monitoring during the procedure should be performed only if immediate cesarean delivery for refractory non-reassuring fetal heart rate pattern is feasible.

In the non-ST-elevation-acute coronary syndrome (NSTE-ACS) guidelines, an ischemia-guided management strategy without routine diagnostic coronary angiography has been suggested for patients with low risk (assessed by risk scores such as the TIMI and GRACE scores)[47]; this recommendation is based on data from non-pregnant patients with MI. The most recent European Society of Cardiology consensus suggests consideration for management without invasive angiography of low-risk NSTE-ACS patients with PAMI(Figure 6).[18, 48] However, the risk scores do not incorporate the excess risk associated with the pregnant/postpartum state nor have they been validated in a PAMI population. Coronary CTA is a noninvasive, alternative diagnostic modality to consider in those who are low-risk, although limitations include the possibility of inconclusive findings due to limited resolution or motion artifact.[58] Identifying the etiology of MI informs the future care of a PAMI patient, even if revascularization is not performed. Therefore, invasive diagnostic coronary angiography should be considered unless the anticipated risks outweigh the perceived benefits in a low-risk patient, such as someone with resolved symptoms and negative or mildly elevated cardiac biomarkers.

Coronary Revascularization in PAMI

Coronary revascularization should be reserved for women with the greatest likelihood to derive benefit, which varies considerably based on the timing of MI with respect to labor and delivery, clinical status, coronary anatomy, and the mechanism of infarction. Consequently, management must be individualized. PCI is recommended for STEMI[59] or NSTEMI with favorable coronary anatomy and high-risk features, including refractory angina despite

medical therapy, hemodynamic instability, sustained ventricular arrhythmias, clinical signs of heart failure, or ischemic mitral regurgitation.

The mechanism of PAMI is a key determinant of the benefit of PCI. When obstructive, unstable atherosclerotic coronary artery disease is present, PCI with stent implantation is ideal. In patients with flow-limiting coronary thromboembolism in the absence of atherosclerotic stenosis, aspiration thrombectomy ± balloon angioplasty with antithrombotic therapy may be sufficient to achieve coronary revascularization, and stent implantation may be deferred.[60] Among patients with MINOCA, PCI is not indicated and treatment is determined by the underlying etiology.[26]

PCI for SCAD is associated with reduced rates of technical success and significant risk of procedural complications.[32, 34, 61] Deep guide catheter engagement during coronary cannulation and high-pressure contrast injections can propagate dissections and expand infarction. Coronary guidewires may be unintentionally positioned in a false lumen or dissection plane where stent deployment would be a potentially devastating complication. Therefore, in cases of SCAD where the patient is hemodynamically stable with satisfactory coronary flow, conservative management is generally preferred.[32] The coronaries often heal, although initial inpatient monitoring is recommended due to risk of interval worsening of SCAD requiring revascularization.[62] Unfortunately, most SCAD PAMI patients have severe clinical presentations including STEMI, left main or multi-vessel SCAD, reduced LVEF, and hemodynamic instability.[17, 19, 63] In these patients, emergent PCI or CABG may be necessary.

Novel PCI techniques may reduce the risks of coronary intervention for SCAD. When there is uncertainty regarding coronary guidewire position, intracoronary imaging may prevent balloon angioplasty or stent deployment within the false lumen. One group reported successful antegrade dissection re-entry to treat a SCAD occlusion when the wire was subintimal on intracoronary images.[64] Stenting segments of healthy vessel proximal and distal to the dissection has been a suggested strategy to reduce propagation. Some have suggested cutting balloon angioplasty to achieve vessel fenestration and decompression of intramural hematoma prior to stent implantation or as a stand-alone therapy.[65] Since there are no prospective studies comparing PCI techniques in SCAD, procedural considerations are based on expert opinion and institutional experience.

Evidence supporting the safety of PCI in pregnancy consists of case series of bare metal coronary stent(BMS) implantation.[14, 27] Although drug-eluting stents(DES) have been used in pregnancy without apparent harm to the fetus,[14, 57, 66] there are no large series to support the safety of this approach. Nonetheless, DES confer reduced risks of MI and repeat revascularization in non-pregnant adults compared with BMS,[67] and in the absence of any evidence of fetal harm, DES use would be preferred. Due to the usual requirement of >3months of DAPT after DES implantation, stent selection may depend on the timing of MI with respect to anticipated delivery and the associated bleeding risks. In general, DES are preferred in the first two trimesters, while BMS or DES may be reasonable in the third trimester.

Current recommendations indicate that DAPT should be continued for a year following MI.[47, 49] However, pregnant patients may need to interrupt DAPT with cessation of Plavix at about 7 days prior to neuraxial anesthesia. If such interruption is necessary earlier than 3 months after DES placement, short-acting intravenous glycoprotein IIb/IIIa inhibitors such as epitifibatide have been suggested as a bridge.[68,66, 69] However, the safety of epitifibatide or intravenous P2Y12 inhibitors such as cangrelor is unknown in pregnancy; therefore, these should avoided when possible and only cautiously considered when weighing options in unique situations. Alternatives to be discussed by the multidisciplinary Pregnancy Heart Team include a shortened timeframe for DAPT interruption prior to neuraxial anesthesia or an elective cesarean section under general anesthesia despite DAPT. Such decisions depend on the nuances of each patient and should be individualized.

CABG may be considered in patients with an indication for coronary revascularization who are poor candidates for PCI based on guidelines for non-pregnant adults.[70] In patients with SCAD, CABG should be considered when PCI is considered to confer excess risk, such as left main or two-vessel SCAD, or as bailout therapy in cases of PCI failure.[32] Arterial grafts optimize durability of revascularization and are often preferred for those with atherosclerotic MI.[71] In those with SCAD, venous or arterial grafts may occlude or become atretic after native vessel healing and restoration of competitive flow.[34] While uncommon, FMD may affect the left internal mammillary artery(LIMA).[72] Therefore, decision-making regarding grafts among those with SCAD require a case-by-case assessment and may depend on factors such as timeliness of graft harvesting.

Cardiogenic Shock, Congestive Heart Failure, and Cardiac Arrest

In a report of 150 women with PAMI, 38% developed shock or congestive heart failure.[14] In these high risk patients with hemodynamic instability, mechanical circulatory support with intra-aortic balloon pumps, percutaneous ventricular assist devices and extracorporeal membrane oxygenators have been used during pregnancy[73-75] and are considered life-saving measures.

Women with PAMI may also present with or decompensate to cardiac arrest. If cardiac arrest occurs, prompt, high-quality cardiopulmonary resuscitation(CPR) is of most benefit to the mother and fetus.[20] Patients should be supine on a firm backboard with CPR performed according to the standard protocol. No medication substitutions or dose modifications are required. Recommendations specific to pregnancy include continuous manual left uterine displacement to offload aortocaval compression during CPR, intravenous access in a vein above the diaphragm to ensure that therapy is not obstructed by the gravid uterus, and full preparation to conduct an immediate resuscitative cesarean delivery if return of spontaneous circulation is not achieved after 4 minutes of resuscitation. Maternal CPR should be continued with minimal interruptions during the preparation and performance of a cesarean delivery. Cesarean delivery should be performed at the site of arrest if possible to best optimize the mother’s condition.[20]

Delivery after PAMI

Presuming hemodynamic stability, timing of delivery may be predicated by gestational age at initial event, current maternal cardiac status and anticipated degree of interim recovery, availability of key personnel and resources, and future anticoagulation requirements. Practice guidelines recommend postponing delivery for at least 2 weeks after PAMI, but this recommendation is based on expert opinion[18] due to literature suggesting a high rate of maternal mortality with early delivery.[27] Time and circumstance permitting, a multidisciplinary Pregnancy Heart Team should devise a detailed plan with contingencies for management of pregnancy and delivery.[18]

In the absence of specific antepartum maternal or fetal complications, delivery is undertaken for standard obstetric indications: either a gestational age of 39-40 weeks is elected or spontaneous labor is awaited. Existing data in the congenital heart disease population suggests that elective cesarean delivery does not appear to confer either obstetrical or cardiovascular benefit,[76] and vaginal delivery is preferred.[12, 18, 77]

Certain obstetric medications should be avoided in women with PAMI(Figure 7[78]). With regard to intrapartum analgesia, a neuraxial anesthetic can be used if the patient is on baby aspirin alone but not on DAPT. The P2Y12 inhibitor should be stopped 7 days prior if safe. An intrapartum “cardiac protocol” may include 1)early administration of neuraxial anesthesia; 2)arterial catheter placement for direct blood pressure monitoring; 3)meticulous recording of fluid status; 4)continuous telemetry monitoring (as applicable); 5)delayed Valsalva maneuvers in the second stage of labor to optimize cardiac output and continuous cardiac venous return, with operative vaginal delivery (forceps, vacuum, other assistive devices) reserved exclusively for standard indications; 6)avoidance of excessive blood loss.

For patients who are not candidates for or decline regional anesthesia, intravenous opioid analgesics (fentanyl, meperidine, morphine) represent a “second-line” option, recognizing none confer similar hemodynamic benefits to neuraxial anesthesia. Minimal data currently exists regarding safety of inhaled nitrous oxide, which has mixed efficacy for pain reduction.[79] Nitrous oxide is associated with myocardial depression and transient pulmonary hypertension, although a higher risk of postoperative cardiac events was not observed in the non-pregnant surgical population.[79, 80] In anticipation of significant physiologic intravascular-extravascular fluid redistribution, patients with PAMI are usually monitored in an intensive care unit for the initial 24-48 hours postpartum.

Acute Management of Post-Partum MI

Acute management of MI in the postpartum period is more straightforward than antepartum MI as fetal risks are no longer pertinent. Maternal bleeding risks may persist early after delivery but are expected to decline with time. Considerations for coronary revascularization for postpartum MI are similar to those in non-pregnant women.[81, 82]

Breastfeeding after PAMI

General recommendations regarding lactation should be tailored to individual patient, although most medications cross into breast milk(Figure 4). If further radiographic studies utilizing iodinated contrast are planned, lactation does not need to be interrupted, since less than 1% is excreted into breast milk.[55] Other post-PAMI management strategies are outlined in Figure 8[30, 32, 33, 49, 50, 83].

Future Pregnancies

Advisability of pregnancy following PAMI is contingent on the primary etiology and degree of left ventricular dysfunction. Two small series from the 1990s describe maternal complication rates of 71-100% with fetal growth restriction a common sequelae.[84, 85] A more contemporary series found 10% recurrence rate of significant cardiac complications with mortality rate up to 23% and increased frequencies of postpartum hemorrhage and fetal/neonatal demise.[86] None of the major cardiac risk stratification strategies(CARPREG I/II, ZAHARA, modified WHO) index PAMI specifically, although severe systemic ventricular dysfunction(LVEF<30%) is listed as a contraindication to pregnancy in the modified WHO classification. The European Society of Cardiology consensus indicates that pregnancy may be considered without clinical evidence of persistent left ventricular dysfunction or ischemia, with a recommendation to delay conception for 12 months following MI.[18] If the previous MI was due to SCAD, the consensus has been to recommend against future pregnancy, cognizant there may be a role for individualized counseling.[32]

Conclusion

PAMI represents a unique patient population for which careful consideration of etiologies, thoughtful and expedient decision-making for treatment, and attentive outpatient care is necessary. These measures, along with the input from a multidisciplinary Pregnancy Heart Team, are pertinent for individualizing care with guidance from published series, consensus documents, and prior experience.

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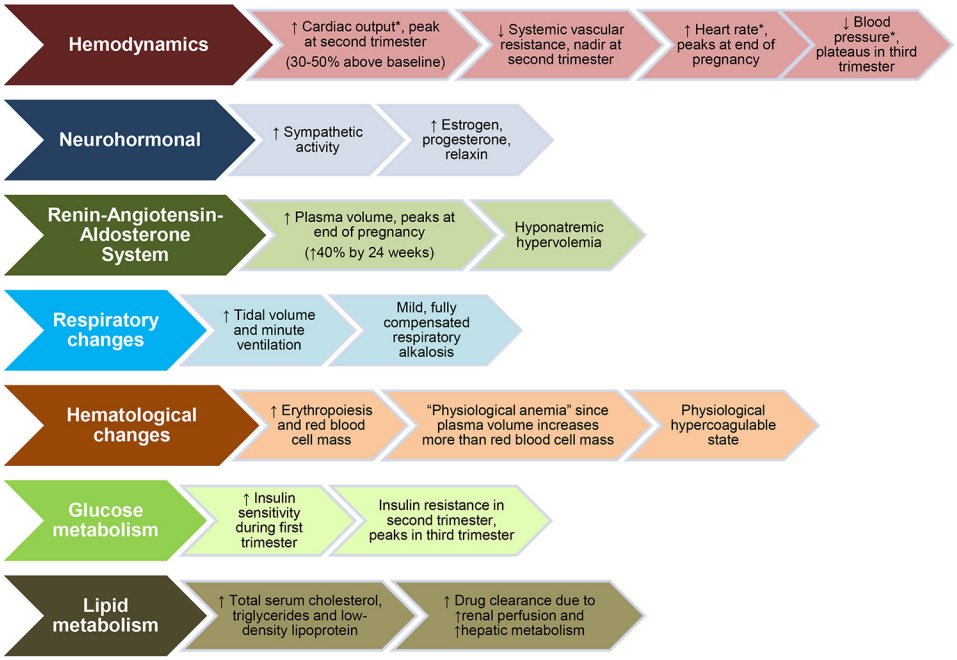

Figure 1.

Hemodynamic, physiologic and metabolic changes of pregnancy.

*Cardiac output, heart rate, and blood pressure all increase substantially during labor and delivery

	Normal Changes in Cardiac Exam and Testing during Pregnancy and Delivery	Abnormal Cardiac Exam and Testing during Pregnancy and Delivery
Symptoms	• Dyspnea is reported in up to 76% by 3rd trimester • Reduction in exercise tolerance, palpitations, and light-headedness are commonly reported	• Chest pain, pressure, or discomfort • Dyspnea out of proportion to pregnancy, especially if occurs or worsens suddenly • Associated pain radiating to arms, shoulder, or jaw, diaphoresis, nausea, or vomiting
Physical exam	• Normal or mild jugular venous distension • Soft, mid-systolic flow murmur • Widely split S1, loud S3 • Cervical venous hum	• Prominent jugular venous distension • Holosystolic murmur at apex • Diastolic murmur • Fixed split S2, S4 • Pulmonary rales
Electrocardiogram	• Q waves in leads III and aVF • T wave inversions in leads III, V1 – V3 • Transient ST depressions with cesarean delivery	• ST elevations • ST depressions that are persistent or occur in the setting of chest pain • T wave inversions, especially if deep and/or present in leads other than V1 – V3
Cardiac Biomarkers	• Levels generally peak at 24 hours after delivery • CK and CKMB can double after delivery and may exceed ULN • High sensitivity TnT can be elevated after uncomplicated deliveries in a minority of women • Preeclampsia and gestational HTN can be associated with increases in TnI and TnT	• Elevated biomarkers in the setting of new symptoms, especially if not occurring immediately after delivery, if elevation is more than mild, or if the levels increase on serial measurements

Figure 2.

Normal and abnormal symptoms, exam, and testing in pregnancy and delivery.

CK=creatine kinase; ULN=upper limit of normal; TnT=troponin T; TnI=troponin I

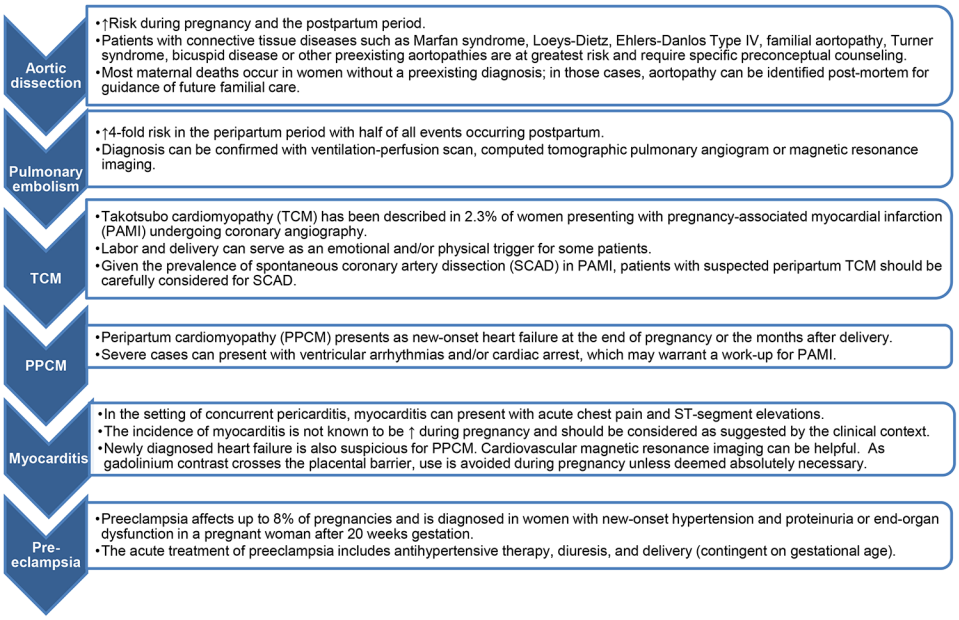

Figure 3.
The differential diagnosis of pregnancy-associated myocardial infarction.

Medication	Use during pregnancy?	Pregnancy Notes	Use during lactation?
Aldosterone antagonists	No.	Crosses the placenta, feminization of the male fetus.	Yes
ACEI/ARBs	No.	Contraindicated in pregnancy due to intrauterine growth restriction, decreased fetal renal function, lung hypoplasia, skeletal malformations, and oligohydramnios (Class X).	Enalapril or captopril are preferred, would NOT use ARBs.
Aspirin	Yes.	The 325 mg daily may be utilized until 32 weeks gestation due to concern for premature closure of the fetal ductus arteriosus. However, the 81mg formulation may be used at any time during gestation and does not require discontinuation prior to delivery. Higher doses (>180 mg) are associated with increased bleeding, birth defects, premature closure of patent ductus arteriosus, intrauterine growth restriction, birth defects, and fetal mortality.	Yes (81mg/day).
Beta-blockers	Yes.	Beta blockers such as metoprolol, labetalol, carvedilol are variably associated with fetal growth restriction (Class C). Nonselective beta-blockers can increase uterine activity. Atenolol crosses the placental and can cause fetal bradycardia, hypoglycemia, intrauterine growth restriction, birth defects, apnea (Class D).	Yes.
Bivalrudin	If needed.	Limited data and may cause maternal and fetal adverse effects.	Unknown.
Calcium Channel Blockers (CCB)	If needed.	All but diltiazem cross the placenta, but diltiazem is associated with adverse fetal effects in animal studies. Associated with pre-maturity, intrauterine growth restriction, fetal bradycardia. Useful for hypertension, ischemic symptoms (amlodipine) and atrial fibrillation when there are contraindications to beta-blockers but important to avoid hypotension.	Nifedipine considered safe, otherwise unknown as CCB transfer to milk.
Clopidogrel	Yes.	Clopidogrel (Class B) may be used during pregnancy but must be discontinued 5-7 days prior to delivery if neuraxial anesthesia is planned. Case reports and post marking surveillance demonstrates increased bleeding risk at delivery without other noted risks.	Unknown.
Fibrinolytics	If needed.	Limited data. Unknown if it crosses the placenta with isolated case reports of use.	Unknown.
Glycoprotein IIb/IIIa inhibitors	If needed.	Limited information in pregnancy with isolated case reports of use.	Unknown.
Heparin/low-molecular weight heparin	Yes.	Does not cross the placenta. Well studied without significant risks, Class C for unfractionated heparin, Class B for enoxaparin.	Yes.
Isosorbide dinitrate	Yes.	Limited information in pregnancy with isolated case reports of safety (Class B).	Unknown.
Nitroglycerin	Yes.	Risk of hypotension and uterine and placental hypoperfusion (Class C).	Yes.
Direct-acting oral anticoagulants	No.	Crosses the placenta with potential for placental and fetal bleeding.	Unknown.
Statins	No.	Risk of congenital anomalies (Class X).	Unknown.
Warfarin	Yes.	Risk of embryopathy is reduced at doses ≤5 mg/day. If requiring higher doses, use heparin for first 12 weeks.	Yes.

Figure 4.

Cardiac medications and safety during pregnancy and lactation.

ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin II receptor blocker

Note that the prior FDA Classification System is used in the above table, although it has now been transitioned to a different classification system.

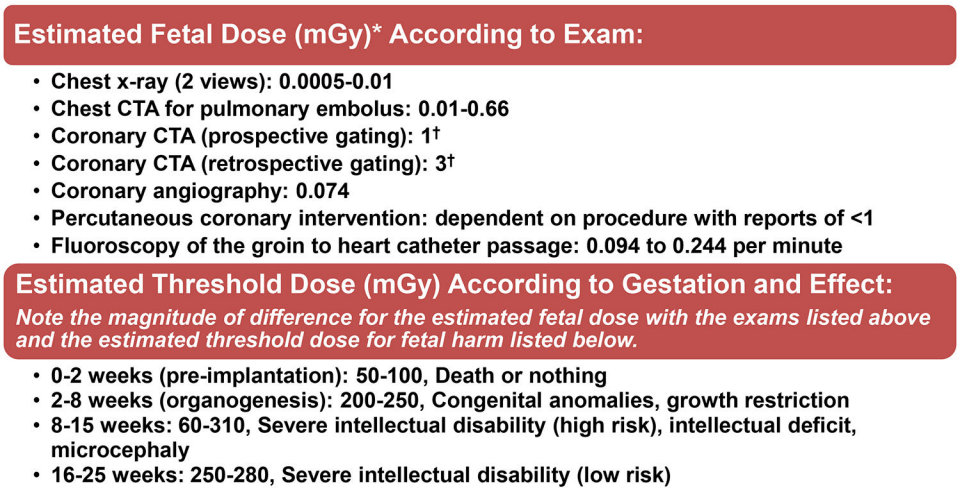

Figure 5.

Radiation safety: estimated fetal dose according to exam and threshold dose according to gestation.

CTA=computed tomography angiography; mGy=milligray.

*The amount of energy deposited per kilogram of tissue is measured in mGy as reported above whereas the amount of energy deposited per kilogram of tissue normalized for biological effectiveness is measured in milliSieverts. Annual average background radiation is 1.1-2.5 mGy.

†These coronary CTA estimates likely represent the high end of fetal radiation exposure. Since the fetus is outside of the primary beam, scatter is the primary contributor of radiation and therefore expected to be low. Fetal exposure for chest imaging increases with gestation due to the fetus being closer to the primary beam. Larger patients require higher peak kilovoltage and tube current thereby increasing radiation exposure. Variation in the imaging techniques such as scan mode and pulsing window (e.g., the narrowest pulsing window leads to the lowest dose) can be optimized to reduce the total radiation exposure.

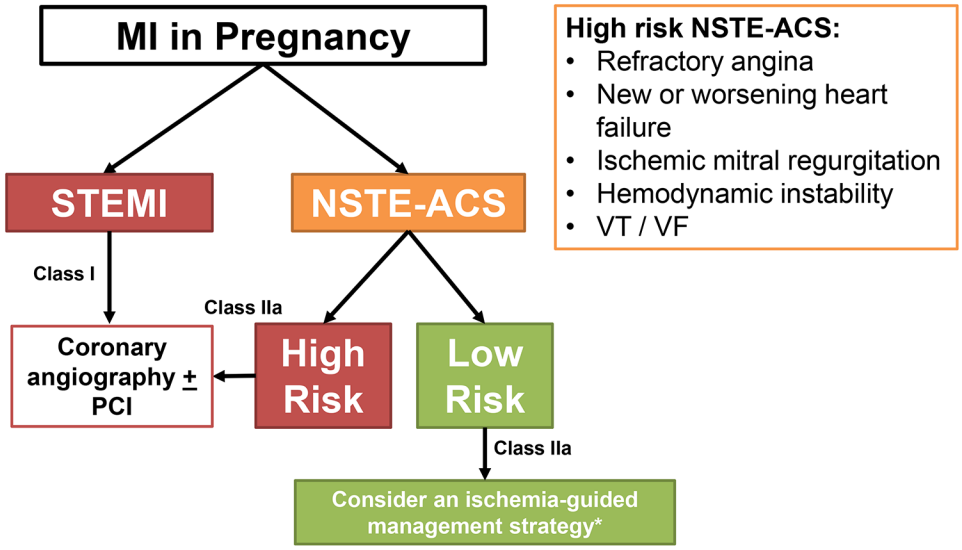

Figure 6.

Management strategy for pregnancy-associated myocardial infarction.

* An ischemia-guided management strategy without routine invasive coronary angiography may be appropriate in select, low-risk patients with NSTE-ACS, such as a patient with resolved symptoms or negative/mildly elevated cardiac biomarkers. Recommend caution with use of the NSTE-ACS risk scores as they do not incorporate the risk of pregnancy and have not been validated in a PAMI population.

MI=myocardial infarction; NSTE-ACS=non-ST-elevation acute coronary syndrome; PCI=percutaneous coronary intervention; STEMI=ST-elevation myocardial infarction; VF=ventricular fibrillation; VT=ventricular tachycardia

Medication	Use during pregnancy?	Indications	Caveats
Antenatal corticosteroids (either betamethasone or dexamethasone)	Yes.	Should be administered if delivery is expected within the next 7 days; a course consists of either betamethasone (12mg IM every 24 hours x2 doses) or dexamethasone (6mg IM every 12 hours x4 doses) and may be repeated once prior to 34 weeks gestation if preterm delivery has not occurred but is again considered imminent.	Although either drug may exert mineralocorticoid activity to a small degree, fluid retention and pulmonary edema have only been described with other contributing factors (tocolytic medications, multiple gestation, and intra-amniotic infection). A transient interval of hyperglycemia is common in diabetic patients.
Carboprost tromethamine	With Caution.	Uterotonic agent to treat postpartum hemorrhage.	May cause secondary hypertension.
Magnesium sulfate	Yes.	Administered intravenously for fetal neuroprotection prior to 32 weeks gestation, to effect seizure prophylaxis in patients with preeclampsia or eclampsia, and infrequently as a tocolytic medication.	Cardiovascular side-effects include hypotension (with bolus administration) and bradycardia.
Methylergonovine	No.	Uterotonic agent to treat postpartum hemorrhage.	Can cause coronary arterial spasm, so this should be avoided.
Oxytocin	With Caution.	Typically given to augment uterine contractility, either during labor or immediately postpartum.	Associated with hypotension and ventricular arrhythmias.
Terbutaline	No.	A beta-mimetic compound utilized intrapartum to treat uterine tachysystole (excessive contraction frequency).	It should be avoided as tachycardia and arrhythmias are common side-effects.
Tranexamic acid	No.	An antifibrinolytic agent utilized to augment hemostasis in postpartum hemorrhage.	Use is contraindicated with active thrombosis.

Figure 7.

Obstetric medication considerations in women with pregnancy-associated myocardial infarction.

Recommendation after PAMI	Rationale
Screen and treat for anxiety, depression and post-traumatic stress disorder.	Postpartum depression prevalence is 13% and associated with morbidity and mortality.
Refer to cardiac rehabilitation.	Cardiac rehabilitation improves anxiety and depressive symptoms, quality of life, and survival while reducing risk of recurrent MI.
Modify risk factors: BP<130/80 mmHg, tobacco cessation, lipid management, healthy diet and exercise.	Known recommended strategies to improve overall health and reduce cardiovascular risk.
Beta blockers and angiotensin converting enzyme inhibitors should be prescribed, especially in patients with additional indications such as ventricular dysfunction.	Reduce workload and promote recovery post MI.
Additional Considerations	
Etiology of Atherosclerosis: Dual antiplatelet therapy (DAPT) regardless of stent implantation for 12 months and aspirin for life. High intensity statin if not breastfeeding.	
Etiology of direct or paradoxical coronary embolism: Oral anticoagulation (time frame dependent on etiology and stent implantation may affect decision-making regarding triple therapy versus dual agent). Depending on clinical suspicion, evaluate for etiologies such as thrombus or atrial shunt with echocardiography, atrial fibrillation, and causes of thrombophilia.	
Etiology of SCAD: DAPT if stent implantation for 12 months. For SCAD patients without stent implantation, consensus is that DAPT cessation may be considered prior to 12 months with daily baby aspirin thereafter (data to guide this decision-making is lacking). Statin if not breastfeeding and if indicated for hyperlipidemia. Assess for fibromuscular dysplasia, arteriopathy, and inherited connective tissue disease (investigations can be conducted after delivery).	

Figure 8.
Outpatient management considerations after pregnancy-associated myocardial infarction.