Introduction

Women in the reproductive age group are considered low risk for the development of coronary artery disease (CAD) and myocardial infarction (MI). Pregnancy increases the risk of MI by 3–4 times. ***(1)***. Incidence of Pregnancy with CAD even lowers, and has been estimated to occur at a frequency of approximately 3–10 per 100,000 deliveries. ***(2)***. The incidence of CAD and MI is increasing among pregnant women, most probably as a result of the increased incidence of smoking among females ***(3).***

While MI is rare in pregnancy, when it occurs it is associated with a disproportionately high maternal mortality rate which was reported to be 5–37%. ***(2)***. The mortality rate in 68 cases was 35%, Among these cases only 13% of the patients were known to have had CAD prior to the pregnancy, and the remaining cases occurred among patients in whom there was no clinical suspicion of CAD.

Two-thirds of the women suffered their infarction in the third trimester; the mortality for these women was 45% as compared to 23% in patients who had an infarct in the first or second trimester. Therefore treatment needs to be prompt and urgent due to the high mortality rate and the grave outcome associated with some cases. ***(4).***

Pregnancy in ischemic heart disease

Ischemic heart disease (IHD) in pregnancy particularly myocardial infarction (MI) is a rare yet potentially fatal condition for the mother and the fetus, with delays in the age of conception, the changes in some social habits among females including cigarette and shisha smoking in addition to an increased prevalence of diabetes mellitus, IHD may represent a real hazard among pregnant women in the near future.

The difficulty in the diagnosis emerges from the similarity of the signs and symptoms of ischemia and infarct to some of the physiological adaptations that occur in a normal pregnancy.

The physiological changes that are normal in pregnancy may aggravate pre-existing disease and may unmask some underlying unrecognized coronary vascular changes; therefore, the diagnosis requires a high index of suspicion and careful assessment of the underlying risk factors.

The management of IHD always requires a multidisciplinary team approach. The management of each patient should be individualized according to the clinical condition, the risk factors, and the availability of the necessary support. Pregnancy after MI may be an acceptable and reasonably safe option provided the cited criteria are met.

Classification of IHD

In general IHD are classified into angina pectoris (transient myocardial ischemia) and MI (fixed myocardial ischemia/necrosis).

Angina pectoris: In its various manifestations angina pectoris is relatively rare in pregnancy with only a few reported cases, Most women who have MI in pregnancy present with sudden infarction that is not preceded by angina pectoris. Despite the rarity of angina pectoris in pregnancy, patients with angina pectoris in pregnancy should be considered at high risk of developing subsequent MI, and should be managed accordingly.

Myocardial infarction: MI presents in pregnancy with a variety of symptoms. Classically the patient will complain of central chest pain, usually severe in nature, radiating to the jaw and left arm. The pain may be associated with faintness or even collapse, the patient will be extremely anxious, sweating and may have some nausea and vomiting.

Epidemiology of myocardial infarction in pregnancy

The first case of MI in pregnancy was reported by Katz. ***(5)***. between 1922 and 1985, 70 cases of MI in pregnancy were reported. ***(4)***. with an average of 1.1 case reports per year. Between 1986 and 1989 an additional 38 cases were reported bringing the total number of cases to 108 ***(3).***

And giving an incidence of approximately 7.6 cases per year. Between 1990 and 1994 an additional 32 cases have been reported with an average of 8 case reports per year. From 1995 until 2005, 103 cases were reported with an average of 9.4 cases per year.

In total until 2005 there have been 251 cases of MI reported in pregnancy. It is unclear from the literature whether the incidence of MI is increasing or more of these cases are being reported.

In recent years the changes in the obstetrics practice may have altered or even increased the incidence of MI. Thus, for example, illicit drug use (cocaine), the use of tocolytics (Ritodrine), prostaglandins (PGE2) and the increase of multiple pregnancies in the population as a consequence of assisted reproductive technology may all have contributed to the apparent increased incidence of MI. It is important to realize that information related to ischemic heart disease in pregnancy is derived from case reports and small series, therefore, is subject to considerable reporting bias.***(6)***.

Prevalence

The prevalence of myocardial ischemia is low overall in pregnant women, with a variable presentation from asymptomatic to cardiogenic shock or sudden cardiac arrest. The incidence and prevalence of myocardial infarction and ischemia related to pregnancy is expected to increase more women are delaying child-bearing to later years, with a technical definition of an age >35 years as advanced maternal age (AMA). ***(5-9).***

Although obstructive atherosclerotic heart disease occurs in reproductive age women, the pathophysiology of ischemic heart disease (IHD) in women also includes a greater proportion of non-obstructive coronary disease than found in men. ***(9).***

However, patients with stable angina and normal coronary arteries or non-obstructive plaque burden have been shown to have increased risks

for major adverse cardiovascular events (MACE). ***(10,11)*** Pregnant patients may present with a medical attention with a clinical context of acute coronary syndrome (ACS) with chest discomfort, dyspnea, or other more atypical symptoms such as referred pain, nausea, or profound fatigue.

Electrocardiography (ECG) and assessment of cardiac biomarkers are essential to diagnosis, per practice guidelines. The absence of ST-elevation on an ECG would likely suggest non-ST-elevation ACS (NSTEACS). NSTEACS can by further subdivided as a non-ST-elevation myocardial infarction (NSTEMI) with elevated myocardial injury biomarkers, or unstable angina (UA). ***(12)***

The CVD complication rate during pregnancy is 0.2–4.0 % in Western societies, with hypertension occurring in 6–8 % of all pregnancies. Management of these complications is not standardized and is largely guided by Level of Evidence (LOE) C data, that is, consensus opinions of experts, case reports, and adaptations of care standards. ***(13, 14)***. Of those with CVD during pregnancy, adult congenital heart disease comprises 75–80 % in Europe and North America, while rheumatic valvular heart disease comprises the 56–89 % of pregnancy-associated CVD in non-Western countries. ***(15,16***).

The occurrence of an acute MI has a rate of one in 35,700 pregnancies with a high mortality rate of 7.3 %.***(17***).Pregnancy increases the risk for MI three to four times over the non-pregnancy state, which could be due in part to the physiologic “stress test” of increased cardiac output. ***(18***).

The presentation of a contemporary cohort of pregnant patients with IHD was predominantly in the third trimester or postpartum period and 95 %

had chest pain. Etiologies of IHD are variable between different retrospective cohorts, but the major etiologies are primarily coronary dissection (35–56 %), atherosclerosis (35 %), thrombus (22–35 %), and "normal" coronary anatomy (11 %).***(19,20).***

Maternal mortality

The maternal mortality related to MI in pregnancy is a significant and devastating event; in the early reports the mortality rate was as high as 50% in the peripartum period ***(4)***. Reports in the last decade have revealed a reduction in the maternal mortality rate probably related to early detection and the advance in the medical care, particularly invasive cardiology, intensive care units, anaesthesia and high-risk obstetric practice. The maternal mortality reported by Roth and Elkayam. ***(21)***. had declined from 21% in their 1996 review to 11% in their second review of all MI cases reported in the last decade ***(3)***.

Others had reported a lower mortality rate including 7.3% . ***(6).*** and 5.1% ***(1)***. The risk of death from MI increases as pregnancy advances: mortality rate in the first and second trimester is approximately 25%, in the third trimester 40%, and if the infarction occurs in the peripartum period, the mortality rate increases to 50% ***(4)***. Data from the last decade showed that the mortality rate almost doubled if the infarction occurred in the peripartum period compared to antepartum and post-partum period ***(3,6)***.

Foetal loss

The foetal loss rate is primarily the result of the maternal outcome. Overall the foetal loss rate with MI in pregnancy was 37% in the early reports ***(16)***.which decreased to 9% in more recent reviews ***(3)***.

Predisposing factors

Risk factors that predispose to MI are smoking, maternal age, familial hyperlipidemia, hypertension, diabetes mellitus. Multiparty, and prior cardiac events. Pregnancy is known to be associated with an increased probability of developing hypertension (preeclampsia, eclampsia) or for the worsening of pre-existing essential or secondary hypertension. In one-third of the cases of MI in pregnancy that have been reported, there was a history of elevated blood pressure ***(4)***.

In a review of MI associated with pregnancy in the last decade Roth and Elkayam. BI reported that among the 103 studied cases 45% of the patients were smokers, 24% had hyperlipidemia, 22% had family history of MI, 15% had hypertension and 11% had diabetes mellitus. They also reported that 72% of the patients were older than 30 years and 38% were older than 35 years. James. ***(1)***. Added to the list thrombophilia, transfusion and post-partum infection as significant risk factors.

Myocardial infarction etiological classification

Based on autopsy findings, MI in pregnancy may be due to a variety of causes. Arterial sclerotic vascular disease is the most common pathological finding in pregnant women who have died from MI ***(15)***. Embolic complications secondary to cardiac arrhythmia are an unusual but recognized cause of MI. Coronary artery spasm which may be spontaneous, familial, or ergot-induced is a rare but recognized cause of MI in pregnancy ***(22)***.

Aneurysm, hematoma, and/or spontaneous dissection of the coronary artery vessels have been reported ***(23)***. Collagen vascular disease ***(24)*** and congenital malformations such as aortic valvular stenosis or anomalous

origin in the coronary arteries vessels are among the rare causes of MI in pregnancy. ***(25)***. Other rarer causes include cocaine abuse, ***(26)***. Pheochromocytoma, ***(27)***. Sickle cell anaemia, ***(28).*** and Kawasaki disease, ***(29).*** With the development and introduction of some pharmacological agents in obstetrical practice, some reported cases of MI were linked to those agents including prostaglandin E. ***(30).*** And clomiphene citrate prescribed for ovulation induction. 29 % of the 123 cases reviewed by Roth and Elkayam ***(21).***by defining the coronary artery anatomy were found to have normal coronary arteries and it was hypothesized that the cause of the infarction may have occurred because of transient coronary arteries spasm.

The diagnosis of myocardial infarction in pregnancy

The diagnosis of MI in pregnancy may be difficult and is challenging for the following reasons: the disease is rare in pregnancy and therefore is rarely considered in a young apparently healthy population and the physiological adaptations of pregnancy may mimic the signs and symptoms of cardiac disease in non-pregnant patients. Such symptoms and signs include dyspnoea, palpitation, decreased exercise tolerance, nausea and heart burn, epigastric or chest pain (gastro-esophageal reflux), Peripheral oedema, distended neck veins, lateral displacement of the cardiac apex, and the presence of a third heart sound and ejection systolic murmur.

In the non-pregnant patient these symptoms and signs are commonly observed in patients with IHD with associated myocardial damage. In pregnant patients these findings may be normal. Therefore caution should be taken to avoid confusing the epigastric and chest pain of gastro-esophageal reflux with angina pectoris.

The occurrence of sweating and faintness with chest pain is not a feature of gastro-oesophageal reflux and strongly suggests IHD. Physiological ECG changes such as left axis deviation, T-wave inversion and non-specific ST changes have been reported in as high as 37% in women having elective caesarean section. ***(31)***.

In the non-pregnant patient these findings are of the patient experiencing CAD or MI. The interpretation of the ECG in the pregnant women will depend on the index of suspicion and on the severity of patient's complaint.

Pregnancy-associated plasma protein-A

Pregnancy-associated plasma protein-A (PAPP-A) is one of the circulating proteins in the maternal plasma and is present in unstable plaques. Elevated levels of PAPP-A in pregnancy may reflect instability of atherosclerotic plaques. PAPP-A is a new candidate marker of unstable angina and acute MI and may have diagnostic value in unstable angina or acute MI during pregnancy ***(32)***.

The early reports on the utilization of PAPP-A in coronary artery disease in pregnancy was further supported by several investigations. You ***(33)***. measured the plasma level of PAPP-A in 70 patients with acute coronary syndrome, comprised of 18 with unstable angina, 37 with acute MI and 15 with stable angina; Levels of PAPP-A were significantly higher in the unstable angina and acute MI groups than in the stable angina and control groups.

Furthermore an elevation of PAPP-A level in patients with negative troponin testing was detected and the researchers concluded that PAPP-A seems to be associated with inflammation and might be used to detect

plaque instability and rupture before an increase in cardiac troponin is detectable. Investigating whether pregnancy-associated plasma protein-A (PAPP-A) is a prognostic marker in patients admitted with high-risk acute coronary syndrome.

Iversen ***(34)***.Examined two populations of patients admitted with a high-risk of non-ST-segment elevation acute coronary syndrome (NSTE-ACS), (123 patients) and ST-segment elevation myocardial infarction (STEMI) (314 patients). These patients were evaluated with serial measurements of PAPP-A. The incidence of mortality and nonfatal MI was reported for 2.66 to 3.47 years and it was concluded that PAPP-A seems to be valuable in predicting the outcomes of patients admitted with high-risk NSTE-ACS or STEMI. Addressing the prognostic value of serum PAPP-A in unselected stable CAD patients,

Iversen ***(35)***. Followed 4243 patients prospectively and reported the causes of mortality and concluded that in patients with stable CAD elevated serum PAPP-A seems promising as aid in identifying patients at high risk for death.

Clinical presentation

The typical presenting symptom of MI is excruciating retrosternal chest pain that radiates to the left shoulder. The critical point to differentiate the pain related to MI from other causes of chest pain related to pregnancy is the intensity of the pain and diaphoresis (sweating) which is usually associated with myocardial ischemia/infarction. In the patient with acute MI the physical examination is non-revealing. Occasionally cardiac murmurs may be heard but this is not diagnostic and generally not useful.

The observation of pulmonary edema and heart failure are hallmark features of severe MI and portend a worse prognosis.

Laboratory investigation

The **troponin I** level in serum appears to be the marker of choice of myocardial injury in the pregnant patient because levels are not altered by normal pregnancy and delivery or influenced by obstetric anaesthesia. Cardiac enzymes are useful in the diagnosis of MI. An **elevated creatine kinas CK-MB** fraction is a characteristic feature of MI. It is important to note that CK-MB may be elevated in labour. ***(36)***. A rising level of CK-MB (>5% of total CK) in the presence of signs and symptoms of MI is diagnostic. Elevated LDH is less reliable in the diagnosis of MI and needs to be interpreted within the overall enzyme profile.

Diagnostic imaging

Electrocardiogram (ECG): The EKG changes of MI or ischemia are well described. Sustained T-wave inversion, ST-segment depression, and q-wave formation are diagnostic features of MI. ***(37)***.

Exercise testing should be performed in patients with known heart disease who plan pregnancy. This Task Force recommends submaximal exercise testing (80% of predicted maximal heart rate) in asymptomatic patients with suspected heart disease if already pregnant. There is no evidence that it increases the risk of spontaneous miscarriage. Stress echocardiography using bicycle ergometry may improve diagnostic specificity. Dobutamine stress is rarely indicated during pregnancy and, because pregnancy in itself is a stress test, its use should be avoided when other options are available. ***(38).***

Echocardiography determination of ventricular ejection fraction are useful in assessing the severity of myocardial damage but are of limited value in making a diagnosis. Transoesophageal echocardiography is relatively safe; however, the risk of vomiting/aspiration and sudden increases in intra-abdominal pressure should be considered, and foetal monitoring performed. ***(38)***.

Radio-nucleotide imaging is a useful technique to assess coronary artery patency. This technique requires the use of radioactive thallium or Sestamibi and as such presents a theoretical risk of radiation exposure to the foetus. The estimated total dose of radiation exposure with thallium nucleotide heart scan is estimated to be less than 1 rad. In symptomatic patients or in patients in whom coronary artery disease is strongly suspected this minor foetal radiation exposure is an acceptable risk. ***(39)***.

Chest radiography and computed tomography

Although the foetal dose from chest radiography is <0.01 mGy, it should only be performed if other methods fail to clarify the cause of symptoms. Lung ultrasound is a promising alternative imaging modality, although its use in pregnancy has yet to be clarified. CT is usually not necessary for cardiac disease during pregnancy and is not recommended, except for the diagnosis or exclusion of pulmonary embolism (PE) or aortic pathology where other diagnostic tools are insufficient (section 10), and where low radiation CT with 0.01–0.66 mGy can be used ***(38)***.

Magnetic resonance imaging (MRI)

Cardiac MRI does not involve ionizing radiation, there are few indications for use in the acute setting. MRI has not been shown to have a harmful effect on the fetus, with teratogenesis, miscarriage, or acoustic

damage, however, a strong magnetic field and substantial noise of greater than 100 dB, although attenuated by the mother's body, are of potential concern. ***(40, 41)***.

Gadolinium-based contrast has been shown to induce teratogenic effects in animal models in doses above any clinical indication, however, case series studies have not shown an association between gadolinium contrast and adverse fetal outcomes ***(42,43)***

The American College of Radiology (ACR) recommends that a risk benefit analysis be performed before MRI, and that gadolinium-based agents may be given to a patient under a consensus agreement by the referring physician and radiologist when no other imaging modalities are favorable, and when the imaging cannot be performed after delivery. ***(44,45).***

Invasive testing

Cardiac catheterization: was reported in 386 patients by James ***(1)***; however, no information was provided regarding the outcome of these procedures.

In the review by Roth and Elkayam. (***3).*** Cardiac catheterization was performed in 92 (89%) of the 103 patients reviewed with equal distribution among patients presented antepartum, peripartum, or post-partum. The procedure resulted in fatal coronary dissection in one patient, and coronary dissection leading to bypass surgery in another. Since this procedure has been associated with maternal death coronary artery angiography and catheterization is an option that should be reserved for selected patients only ***(22)***.

Complications

The complications that occur with MI do not differ between pregnant and non-pregnant patients. A summary of the common complications of myocardial infarction, arrhythmia, heart failure, hypotension, cardiogenic shock, valvular insufficiency, myocardial rupture, ventricular aneurysm, pericarditis, post MI syndrome, emotional instability, and sudden death

Management

The management of ischemic heart disease in pregnancy should be a multidisciplinary team approach, including an obstetrician, cardiologist, anaesthesiologist, dietician and a social worker. This team should work together to advise the patient on how to eliminate and avoid risk factors for subsequent ischemia and infarction, to recognize the progression of ischemia to infarction, to institute the appropriate monitoring systems and to prepare the patient for the potential complications of the condition. In early pregnancy the issue of abortion for the treatment of the patient with IHD is controversial ***(46)***.

The evidence that pregnancy termination diminishes the risk in the patient with myocardial ischemic infarction is unclear. However for the patient with evidence of worsening ventricular failure pregnancy termination may be a preferable option.

General measures:

In the symptomatic patient bed rest to reduce oxygen demand may be beneficial. **Oxygen** supplementation should be initiated in patients during acute attacks.

In patients with infarction pain control is an important aspect of their care. **Analgesia** should be given intravenously, and should be adequate to reduce or eliminate the pain. The benefit of pain reduction is a decrease in anxiety and stress. **Morphine** (risk category C) is the agent of choice. In addition to its powerful analgesic effect, morphine causes a reduction in pre-load by increasing venous pooling. Morphine should be administered intravenously since this route produces immediate effect and avoids release of muscle enzymes at the injection site which may lead to confusion in the interpretation of cardiac enzyme profiles.

Decreasing anxiety by providing emotional and psychological support to the patient may reduce the incidence of MI or prevent the extension of the existing one.

In the patient with acute MI in late pregnancy delivery should be delayed. Ideally the patient with an acute infarct should remain undelivered for at least two weeks after the onset of the infarct. Prolonging the interval between infarct and delivery has been shown to reduce the mortality rate by at least 15%, from 50% to 35% or less ***(47,48)***. This is an important clinical point because in some instances the occurrence of infarct creates an anxiety among the obstetric team to deliver the patient.

The ideal delivery **position** is the lateral recumbent position. This position will avoid vena caval compression and its subsequent reduction in venous return, stabilization of venous return may be reflected in improved cardiac contractility, sustained coronary blood flow and diminished myocardial oxygen demand.

The patient in labour with acute MI should be managed in the Coronary Intensive Care Unit. Since these patients are at risk for acute extension of the myocardial infarct and acute lethal dysrhythmias, their care should be in an area where immediate and appropriate response is available. Since in most instances the foetus is unaffected by the maternal MI, the focus should be to the mother and less so to the foetus.

In patients with MI continuing pregnancy monitoring in hospital is recommended. Careful and frequent assessment for signs and symptoms of HF and/or ventricular dysrhythmias should be part of the post-infarction care.

The role of prophylactic **antiarrhythmic** drugs is controversial. In general, in the patient with uncomplicated MI who is not exhibiting serious dysrhythmia there is no role for prophylaxis. In patients who have transient dysrhythmias or sustained dysrhythmias, intravenous prophylaxis is indicated. Antiarrhythmic treatment should be initiated by the cardiologist and in consultation with the obstetrician. Intravenous Lidocaine (risk category B) is usually the drug of choice for controlling acute dysrhythmias in the setting of an MI.

The occurrence of heart failure (HF), manifested by worsening peripheral and pulmonary edema is a medical emergency in the patient with acute MI. The use of **furosemide** to reduce intravascular volume is recommended.

Patients with MI are predisposed to developing thromboembolic disease. This risk is probably increased in pregnancy because of the hypercoagulable state known to exist in pregnancy. Accordingly,

prophylactic heparin should be initiated. The usual dose is 5000–10,000 SC bid for unfractionated Heparin,

Low molecular weight Heparin (LMWH) such as Enoxaparin 40 mg bid (risk category C) can be used despite the fact it has a longer half- life with theoretical risk of bleeding if the patient started laboring within few hours of the administration. In patients with a suspected or proven intramural thrombus full heparinization is mandatory. ***(49)***.

Specific measures

Specific measures for the treatment of patients with acute MI include both surgical and medical interventions.

Nitro-glycerine (risk category B) given either orally, sublingually, intravenously or by dermal patch, can be used in the treatment of the patient with acute MI. In the presence of nitro-glycerin the coronary vessels are dilated leading to improved myocardial perfusion. Nitro-glycerin has no known teratogenic effects; however, careful adjustment of the dose is needed to avoid maternal hypotension leading to foetal distress.

The use of nitro-glycerine has not been shown to reduce infarct size or mortality in the thrombolytic era. Special care is needed in patients with inferior MI and right ventricular involvement with the use of nitro-glycerin as it can cause severe hypotension.

Due to the low frequency of MI in pregnancy, **anti-platelet,** and anticoagulation therapies are managed similarly to non-pregnant patients, as pregnancy has never been evaluated in clinical trials of these agents.

Aspirin is given a class D designation, mostly due to animal models exposed to high-doses resulting in premature fetal ductus arteriosus closing. ***(50).*** Aspirin at a low dose (75–100 mg) is safe to use in pregnancy with no increased maternal or fetal bleeding risks or effects on the ductus arteriosus on meta-analysis. Additionally, aspirin was not found to increase the risk for bleeding from neuraxial anesthesia when continued through delivery. ***(51).***

The platelet P2Y12 receptor blockers of clopidogrel and prasugrel are considered pregnancy class B agents, while ticagrelor is a class C agent with limited literature comprising one case report. ***(52,53).***

Regarding **anticoagulation**, unfractionated heparin does not cross the placenta, but is a pregnancy class C agent. Due to the neurologic effects on the neonate of benzyl alcohol, which is present in some formulations of heparin as a preservative, some practices have limited the administration of heparin to pregnant patients to preservative-free heparin, if possible. ***(54,55).***

Enoxaparin is a class B agent, does not cross the placenta, and is well tolerated in pregnancy from a bleeding perspective when stopped before a planned delivery. The direct thrombin inhibitors of bivalirudin and argatrobran are class B agents due to animal studies, and their use is limited to case reports of pregnant patients with heparin-induced thrombocytopenia. ***(56,57).***

European guidelines on the management of pregnancy and heart disease recommend the use of clopidogrel and avoidance of glycoprotein IIb/IIIa inhibitors, prasugrel, ticagrelor, and bivalirudin. ***(58).***

In a pregnant patient who had recently received a bare metal stent, clopidogrel was stopped 7 days prior to delivery. Eptifibatide was used as a bridging agent and discontinued 12 hours prior to neuraxial analgesia, with clopidogrel resumed within 24 hours. ***(59).***

The use of **beta blockers and calcium channel blockers** (risk category C) in the treatment of acute MI is controversial. Despite published reports on their safety in pregnancy ***(60-21).*** The decision to use these medications should rest with the cardiologist managing the case, in consultation with the obstetrician.

Thrombolytic agents are used as acute therapy for occlusion of the coronary vessels and prevention or limitation of MI. Tissue plasminogen activators (t-PA) such as tenecteplase (TNKase) and Reteplase are the agents of choice. The complications of these agents include bleeding, premature labour and incoordinate uterine contractions; the risk/benefit ratio of thrombolytic agents is controversial ***(63,64)***. The decision to utilize thrombolytic agents should be made by consensus between the cardiologist and the obstetrician.

In cases of MI that do not respond to thrombolytic agents, **rescue PCI** (percutaneous coronary intervention) of the infarct related artery can be performed with acceptable results.

Percutaneous coronary intervention

PCI for the treatment of coronary artery occlusive disease is a well-established treatment modality in patients with angina pectoris and acute MI. James ***(13)***. Reported PCI in 135 pregnant patients with stent

placement in 127 of them. No information was provided on the timing of these procedures or their outcome.

The best time is after the 4th month in the second trimester. By this time, organogenesis is complete, the foetal thyroid is still inactive, and the uterine volume is still small, so there is a greater distance between the foetus and the chest than in later months. ST-elevation MI (STEMI) management in pregnancy mainly relies on primary percutaneous coronary intervention (PCI) ***(38)***.

In a review by Roth and Elkayam. Coronary angiography was performed in 92 of 103 patients included in their review; 49 of these procedures were done antepartum and 43 post-partum. PCI was performed in 38 of 92 (41%) subjects (23 antepartum, 6 peripartum, and 9 post-partum) with stent placement in 55% of these patients. Duration of pregnancy in 23 patients who underwent the procedure in the antepartum period (mostly in the third trimester) ranged from 6 to 38 weeks.

All reported stenting during the acute phase of MI during pregnancy were performed with bare metal stents; the safety of drug-eluting stents in pregnant woman is therefore still unknown. Because drug-eluting stents require prolonged antiplatelet therapy and the incidence of caesarean section deliveries in patients with heart disease is relatively high, the use of drug-eluting stent during pregnancy may be problematic and should be avoided if possible.***(3).***

PCI with stents remain the treatment of choice in an acute STEMI, although this does not take into account the high-prevalence of SCAD in pregnant patients. Consultation with a high-risk obstetrician regarding the feasibility and duration of dual anti-platelet therapy should ideally occur

before angiography. Additional precautions due to the high incidence of coronary dissection are to perform careful guide engagement of the coronary arteries and to minimize injections, using low-pressure. Treatment for SCAD has been a controversial topic, with no randomized controlled data on management. Retrospective studies of SCAD reveal that half of these patients with ACS present with a STEMI, and likely from guidelines advocating early and invasive management for STEMI and NSTEACs, many of these patients have been treated with PCI. ***(65).***

Some studies report favorable outcomes for PCI management of SCAD, and others report a high failure rate of PCI and a better prognosis of conservative management. The largest single-center study of 189 patients with SCAD reported a PCI procedural failure rate of 53 %, and more vessel occlusion with revascularization than conservative management (44/95 versus 18/94, respectively). The conclusion from this study was that a conservative strategy with observation may be preferable in those clinically stable patients with TIMI grade 2–3 flow. ***(66)***.

There are no data with respect to outcomes on bare-metal versus drug-eluting stents in the pregnant patient. Bare-metal stents have been used more frequently than drug-eluting devices in pregnant patients, to reduce the length of dual anti-platelet therapy and potential bleeding complications surrounding delivery, ***(67,68)***.

A high rate of iatrogenic coronary dissection with angiography and stenting in one study suggests that a conservative and noninvasive approach be maintained for most pregnant patients, and that revascularization attempts remain for those with severe and proximal obstruction or hemodynamic compromise. ***(18)***.

Coronary artery bypass graft (CABG)

in pregnancy has been associated with a maternal mortality rate of 1–2% and a foetal loss rate of approximately 33%; the mortality figure with coronary by-pass in the pregnant population does not differ from that observed in the non-pregnant population in one limited report ***(69)***. however, the limited available information precludes reaching definite conclusions regarding the safety of coronary artery bypass graft surgery during pregnancy.

Labour and delivery

Timing of delivery

The occurrence of an MI in pregnancy is an indication to delay delivery after the infarct. The maternal mortality is inversely related to the interval between the infarct and delivery. Every effort should be taken to stabilize the patient after the infarct and defer delivery. It is assumed that during the period of infarct the maternal cardiovascular system is unstable, and the superimposition of the stresses of labour can lead to acute deterioration. Within approximately 5–7 days after acute myocardial infarct a degree of stability returns to the maternal ventricular function and the risk of added stress of labour diminish.

Analgesia in labour

Epidural analgesia is the method of choice in the patient with a previous MI. The advantages of epidural analgesia are: marked decrease in the pain, stress, and anxiety, decrease in the afterload reduces the amount of cardiac work required. Preload reduction is a recognized potential disadvantage of epidural anaesthesia. This complication can be prevented

by ensuring that the patient is adequately hydrated at the time of induction of the epidural. Vasopressure agents are contraindicated in the treatment of epidural induced hypotension in the patient with a previous MI.

Mode of delivery

Pregnant women who have experienced an MI or ACS prior to or during their pregnancy should be delivered in a tertiary care center if possible, with a coordinated team consisting of a high-risk obstetrician, cardiologist, and obstetric anesthesiologist. In patients with an MI vaginal delivery is the method of choice. Caesarean section should be reserved only for those patients with obstetrical indications and should be approached very cautiously. The reported maternal mortality with vaginal birth after MI is 14% whereas the mortality in patients delivered by caesarean section is 23% ***(70,71)***.

The **advantages** of vaginal birth are the elimination of the surgical stress, the lack of a general anaesthetic, lower incidence of post-partum infection, and diminished blood loss. Patients delivered vaginally are more likely to ambulate early, thereby reducing the risk of thromboembolic disease. There is usually minimal need for analgesics after vaginal delivery. The **disadvantages** of vaginal delivery are the prolongation of the delivery process and the unpredictable mode and time of delivery.

The **advantages** to caesarean section are that delivery can take place under controlled circumstances, with the personnel and equipment required for care of the mother and the foetus immediately available. Caesarean section is associated with shorter duration of the hemodynamic

changes associated with the delivery process. The **disadvantages** of caesarean section include increased blood loss which may be associated with hypotension, which in turn may either precipitate a second infarct episode or lead to extension of the existing infarct. Caesarean section is also associated with an increased risk of infection, pulmonary morbidity and metabolic demands associated with a surgical procedure and the healing process. In the patient with acute heart failure as a consequence of MI, caesarean section is the method of choice for delivery, ***(72)***.

In patients in whom the decision has been made to attempt a vaginal delivery it is usually recommended that the second stage be foreshortened by the use of outlet forceps or vacuum extractor ***(73)***.

Management of the third stage of labour

In the patient with an uncomplicated vaginal delivery, no active intervention is required in the management of the third stage.

In patients who have experienced complicated third stage of labour aggressive treatment is always indicated. In particular, patients with post-partum haemorrhage should be treated early. Oxytocin is the drug of choice for controlling post-partum hemorrhage in a patient with previous MI.

Ergot compounds are contraindicated. The use and safety of prostaglandin F2α in patients with MI has not been demonstrated to date.

Indication for invasive monitoring

The use of Swan-Ganz catheters and arterial lines to monitor blood pressure, central venous pressure, pulmonary artery and pulmonary

wedge pressure is indicated only in patients in whom there is evidence of or a strong suspicion of heart failure.

Preconception counseling and recommendations

A critical question raised by the patient is, “What are the risks of recurrence of MI and death with a subsequent pregnancy?”

Frenkel ***(74)***. Reviewed the literature and reported 20 cases of pregnancy following MI. In this report they added an additional four cases from their own experience. No maternal deaths occurred in subsequent pregnancies. Two foetal losses were reported. They suggested that subsequent pregnancy in a patient with an MI is associated with a small but definitely increased risk of perinatal loss.

Vinatier ***(75)***. Reported 30 cases in the literature and added one case of their own where they concluded that pregnancy after MI is possible provided that certain precautions are taken including a pre-pregnancy cardiac examination to evaluate the cardiac function and to screen for etiology for coronary disease. While these series are small, the results are encouraging. Patients should be advised that there is some increased probability of increased MI, but in the majority of instances the pregnancy proceeds without complication.

It may also be added to ensure an optimal outcome in those cases that the patient should be symptom-free without medication, the period between infarct and pregnancy should be more than one year and the patient should have had a recent negative coronary angiogram and have no residual left ventricular dysfunction on echocardiography.

Long-term Management

All women with known heart disease or those who experience an MI or ACS and desiring pregnancy should be referred to a cardiologist ideally before stopping birth control. Pregnant women with known heart disease should be managed by a high-risk obstetrician, preferably at a tertiary care center, with a consultant cardiologist. Women with PAMI should be followed by a cardiologist closely before and after delivery.

Counseling with respect to future pregnancies after an ischemic event must be tailored with the severity of the ischemic event, coronary anatomy and the severity of atherosclerosis, the status of her right and left ventricular function, and the need for dual antiplatelet or anticoagulation therapy.

Contraindicated medications during pregnancy include angiotensin converting enzyme inhibitors(ACEIs), angiotensin II receptor blockers (ARBs), and statins due to teratogenic effects. ***(76)***.

Breast-feeding An open dialogue about intentions for **breast-feeding** needs to begin before hospital discharge and continue in the postpartum appointments between the cardiologist, obstetrician, and patient to discuss the risk to benefit ratio of cardiovascular medications to both the infant and mother.

Unfortunately, ACE inhibitors, ARBs, and statins as a class are likely to be avoided with respect to breast-feeding, as the data are inadequate and controversial. Metoprolol is a Category C drug for pregnancy, but is likely safe during breast-feeding. Atenolol should be avoided in all pregnant and breast-feeding patients. ***(77)***.

Risk in Future Pregnancies

Due to the paucity of data regarding MI in pregnancy, not much is known about the risk for future cardiovascular events in subsequent pregnancies. A case series of pregnancy after a diagnosis of SCAD was examined in a single institution. 8 women with prior SCAD became pregnant, and 7 had no CV complications. However, one woman had recurrent SCAD of the left main coronary artery and underwent emergent CABG and subsequently developed posttraumatic stress disorder. ***(78)***.

As such, future pregnancy is not advised after SCAD, even if the prior SCAD was not associated with pregnancy. Pregnant women with pre-existing CAD or a history of MI/ACS are at increased risk for angina, MI, ventricular arrhythmias, or cardiac arrest during their pregnancies, comprising 10 % from one retrospective review.

The highest rates of cardiac complications are seen in women with atherosclerotic disease. Interestingly, the risk for neonatal adverse events, such as preterm labor, intrauterine growth restriction, or low birth weight, is greater for women with known CAD (30 %) than with known valvular or congenital heart disease (18 %), and is substantially higher than the risk in women without heart disease (7 %).***(20)***.

The Cardiac Disease in Pregnancy (CARPREG) investigators reported that predictors of complications in pregnancy are: an impaired systolic function, any prior cardiovascular event including stroke, left-heart obstruction (mitral or aortic stenosis), or New York Heart Association (NYHA) function class II or above. ***(15)***.The ZAHARA (in Dutch, Zwangerschap bij vrouwen met een Aangeboren HARtAfwijking) investigators limited their risk score to pregnant women specifically with

congenital heart disease. ***(79)***.Neither of these risk scores evaluated women with histories of MI or ACS, likely due to the low prevalence of pregnant women with known CAD.

Conditions in pregnancy that predispose the mother to future CV events after pregnancy are similar to other risk factors in the general population. Women with hypertensive disorders of pregnancy became diagnosed with hypertension 7.7 years earlier than women without pregnancy complications and were at a significantly increased risk for CVD with a hazard ratio of 1.21 (95 % CI [1.10– 1.32]).

Maternal obesity and preeclampsia predispose the mother to CV events later in life. Women with prior MI or known CAD should undergo CV evaluation as part of preconception planning. While there are no specific guidelines for this evaluation, it is reasonable to perform physical examination, ECG, echocardiography, and functional testing for inducible ischemia in most women. In addition to those with prior SCAD, women with significantly reduced left ventricular (LV) function or HF or ischemic symptoms should be advised against pregnancy. ***(78,79)***.

Conclusion

Although IHD is rare in pregnancy, the maternal mortality from heart disease is several folds above the non-pregnant population. The strongest risk factors for IHD in pregnancy are age, smoking, multiparity, and a history of MI or ACS. In this rare population, SCAD should remain high on the differential for PAMI, followed by atherosclerosis. Critical to the management of pregnant patients with IHD is a multidisciplinary and involved team of at least an obstetrician, noninvasive and interventional cardiologists, and obstetric anesthesiologists at a tertiary center.

Additional cardiovascular follow-up, mitigation of risk factors, and counseling regarding plans for future pregnancy are imperative toward best possible outcomes.

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