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# CORONARY ARTERY DISEASE

# Background

Coronary artery disease (CAD) is the leading cause of death worldwide in women. It has already been noted that rates are increasing with the rising prevalence of diabetes, obesity, and metabolic syndrome. Acute myocardial infarction (AMI) in pregnancy is rare, but when it occurs is still most commonly due to obstruction of coronary arteries due to rupture of an atherosclerotic plaque. However in women of childbearing age, other nonatherosclerotic etiologies should always be considered, as these are relatively more common in such women than would be seen in older males with similar symptoms. The differential diagnosis includes: spontaneous coronary artery dissection, vasculitis such as Kawasaki disease, in situ coronary thrombosis, coronary embolism and coronary spasm.

The prevalence of coronary artery disease in pregnancy is low, with an estimated risk of an AMI of 1 per 16000 women during pregnancy. (1) However, pregnancy has been shown to increase the risk of AMI 3- to 4-fold. (2) Along with traditional coronary heart disease risk factors, age is one of the major determinants of pregnancy-related myocardial infarction. As women delay childbearing until an older age, perhaps assisted by advances in reproductive technology, AMI during pregnancy will be encountered more frequently.

# Effects of pregnancy-related hemodynamic and hormonal changes

Pregnancy is associated with significant hemodynamic changes including an increase in cardiac output (see Cardiovascular Changes During Pregnancy), which results in increased myocardial oxygen demand. In addition, the physiological anemia and decreased afterload during gestation may reduce myocardial oxygen supply and contribute to the development of myocardial ischemia in women with underlying CAD.

At the time of labour and delivery, uterine contraction results in a further increase in systolic blood pressure and cardiac output.

In the peripartum period, the combination of reabsorption of extracellular fluid and decompression of the inferior vena cava results in an increased hemodynamic load. The hemodynamic changes that normally occur during late pregnancy and during delivery may explain, at least in part, the poor outcome reported in women who suffer an AMI in the peripartum period.

As well, there are alterations in the coagulation and fibinolytic pathways during pregnancy and the post partum period, which increases the risk for formation of

thrombus. These include a decrease in tissue plasminogen activator (3), change in the level of circulating coagulation factors, and reduction in protein S levels, all of which potentially contribute to acute myocardial infarction during pregnancy.(4) Cigarette smoking during pregnancy further increases the risk of thrombosis due to enhanced platelet aggregability.

### Maternal cardiac complications

Acute myocardial infarction can occur at all stages of pregnancy. Previous studies have shown AMI most commonly occurs in multigravidas and in women over the age of 30. (5) A high incidence of coronary risk factors is noted in women with AMI. Maternal mortality in AMI is found to be considerably higher during the peripartum period compared with the antepartum or post-partum periods. (6) A recent literature review reported a maternal mortality rate of 11%, which is considerably lower than previously reported rates, and likely a result of improvement in AMI management. (6)

Spontaneous coronary artery dissection in pregnancy is a rare, life threatening condition that most commonly occurs in the peripartum period. It affects the left anterior descending coronary artery more often than other coronary arteries, although multiple vessels may be involved. The most common clinical presentation is an acute coronary syndrome, with severity ranging from unstable angina to cardiogenic shock. Pregnancy-related coronary dissections are thought to be due to high levels of progesterone that mediate weakening in the walls of the coronary arteries that predispose to coronary dissection. As well, the increased cardiac output in pregnancy may increase shear forces in the vessel resulting in a greater likelihood of dissection in the predisposed artery.

# **Fetal complications**

The incidence of fetal mortality in pregnancy-associated AMI has been reported to be 9%. Most of the fetal deaths are associated with maternal mortality. (6)

#### **Management strategies**

#### Preconception counseling/Contraceptive methods

A successful pregnancy can be achieved in some women with CAD; however, preconception risk stratification is important. The burden of ischemia and the severity of associated risk factors (i.e. diabetes) will determine the safety/risk of pregnancy.

#### Women with suspected CAD

In women with an intermediate or high pre-test likelihood of CAD, diagnostic studies are required prior to conception. These may include exercise myocardial perfusion imaging, stress echocardiography, or cardiac catheterization as appropriate. Ideally, a comprehensive cardiovascular examination should be undertaken before embarking on pregnancy. When necessary, stress echocardiography can be used during pregnancy to evaluate women with intermediate pre-test probability for CAD. Fetal bradycardia and absence of body movement have been reported during moderate to heavy maternal

exercise, thus a submaximal protocol is preferred. (7) Exercise myocardial perfusion imaging should be avoided because of the potential risk of radiation to the fetus.

In a woman presenting with an acute coronary syndrome during pregnancy a diagnosis is important. Non-atherosclerotic causes of the ACS are relatively more common. A strategy that includes early diagnostic coronary angiography may be the best strategy to pursue in the unstable patient. Cardiac catheterization may result in fetal exposure to radiation of as little as 0.02mSv, though longer procedures could yield a fetal exposure of up to 1mSv. The 8<sup>th</sup> to 15<sup>th</sup> week of gestation is the most radiation-sensitive period for the fetus. If cardiac catheterization is performed, appropriate shielding of the fetus from direct exposure to radiation is important, though shielding cannot prevent scatter radiation.

# Women with CAD

Women of childbearing age who are diagnosed with coronary artery disease should be advised about the potential complications than can occur. Modifiable cardiovascular risk factors should be identified and treated.

Women with a history of prior myocardial infarction, prior revascularization with percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG) should be counseled on their risk in the event of pregnancy. Counseling these women is based upon a thorough evaluation of their cardiac status, particularly their functional status, their left ventricular systolic function, any ongoing myocardial ischemia, and their underlying coronary anatomy. Impaired left ventricular systolic function is a major determinant of adverse maternal outcomes. Transthoracic echocardiography should be performed to determine left ventricular ejection fraction (LVEF). An LVEF> 40% and a good response to exercise testing likely portend a good outcome, although complications can still occur.

A discussion about contraceptive methods is appropriate in all women with CAD. The combined oral contraceptive pill (containing estrogen) is associated with an increased risk of thromboembolism and is contraindicated in women with CAD. Progesterone-only forms of contraception are not associated with thromboembolic risk and can be suitable alternatives. Other options are discussed in the section on contraception. (see Contraception)

Women with CAD are often treated with aspirin or beta blockers and both can be used during pregnancy when necessary. The safety profiles of other antiplatelet agents, such as clopidogrel, are not known. Statins, angiotensin receptor blockers, and angiotensin converting enzyme inhibitors are not safe during pregnancy. Medication use should be reviewed if a woman is contemplating pregnancy or is pregnant. The MOTHERISK website (<u>http://www.motherisk.org</u>) is an excellent resource.

# Ante-partum care

Coordinated care with a heart disease specialist and a high-risk obstetrician should be implemented. The frequency of assessments during pregnancy should be determined on an individual basis.

Frequent monitoring for symptoms is important, with specific attention to complaints of angina. Management should focus on optimizing therapy, treating other conditions that

may contribute to symptoms (i.e. anemia), and management of CAD risk factors (note: total cholesterol, LDL, and triglyceride levels can increase during pregnancy).

In women with reduced LVEF due to a previous MI, concurrent management of heart failure may be necessary. Particular attention should be focused on the recognition of ventricular arrhythmias.

In women who develop new/worsening angina or an acute coronary syndrome (ACS) during pregnancy, both maternal and fetal considerations should influence the therapeutic approach. In the setting of an ACS, close monitoring of the mother and fetus should take place in an intensive care unit. Criteria for the diagnosis of AMI are the same as the general population. In terms of biomarkers, troponins are preferred to CK for the diagnosis of AMI due to the physiological increase in CK levels during labour and delivery. (8)

The treatment of pregnant women with an ST-elevation MI (STEMI) and its potential complications should follow the usual standard of care, although both maternal and fetal considerations will affect therapy. Thrombolytic therapy is relatively contraindicated in pregnancy. Although teratogenicity has not been reported with thrombolytics, the reported risk of maternal hemorrhage is 8%. An invasive strategy for accurate diagnosis with a view to coronary revascularization with PCI in the event of atherosclerosis, management of dissection when found, and management of coronary thrombosis/embolism/spasm if found, is the preferred approach in women presenting with a STEMI.

### Labour and delivery

Labour and delivery should be planned carefully with a multidisciplinary team well in advance. It is important to communicate the delivery plan to the woman and to other physicians involved in her care. The best delivery plan is not useful if information is not readily available when needed.

Generally, vaginal deliveries are recommended unless there are obstetric indications for a cesarean delivery. Good pain management for labour and delivery is very important in order to minimize maternal cardiac stress. To decrease maternal expulsive efforts during the second stage of labour, forceps or vacuum delivery is often utilized. To decrease potential harmful complications from difficult mid cavity-assisted delivery, uterine contractions are often utilized to facilitate the initial descent of the presenting part.

Because of the increased hemodynamic stress associated with labour, it has been recommended that induction of labour or scheduled cesarean section be delayed, if possible, for at least two to three weeks after an acute MI. However, there are no clinical trials that have prospectively evaluated the optimal timing of surgical procedures or labor and delivery after an acute (one to seven days) or recent (7 to 30 days) MI, especially in the current era of cardiac therapies and modern anesthesia.

The need for maternal monitoring at the time of labour and delivery is dictated by the women's clinical status, the absence/presence of CAD symptoms, and the degree of ventricular dysfunction.

## Post-partum care

The immediate post partum period is associated with a large hemodynamic load on the heart because of enhanced venous return with relief of caval compression and additional blood into the systemic circulation from the contracting emptied uterus. Women with underlying CAD may be at higher risk for AMI during this period because of increased myocardial oxygen demand and the prothrombotic milieu.

The hemodynamic changes of pregnancy may take up to six months to normalize. Women should be seen early after pregnancy (usually within 6-8 weeks). The frequency of additional follow up visits should be dictated by the clinical status of the women.

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