Coronary artery disease and myocardial infarction in pregnancy: A review of epidemiology, diagnosis, and medical and surgical management

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Ischemic heart disease is uncommon during pregnancy, occurring in approximately one in 10,000 live births. With the increasing age and fertility of mothers, the incidence of coronary artery disease in pregnancy is likely to increase. Atherosclerosis appears to be the most common cause of acute myocardial infarction, although coronary spasm, coronary dissection and thrombus have been reported, among others. The diagnosis of ischemic heart disease in the pregnant population can be challenging and not without risk to the fetus. Although there have been many reports of acute myocardial infarction and cardiopulmonary bypass surgery during pregnancy, most knowledge is based on anecdotal reports. Even less is known about the use of thrombolytics, percutaneous coronary intervention and the optimal medical management of ischemic heart disease during pregnancy. The epidemiology, diagnosis, medical and surgical treatment, and prognosis of ischemic heart disease in pregnancy are the subject of the present review.

Key Words: CAD; Coronary artery disease; Ischemic heart disease; Myocardial infarction; Pregnancy

La coronaropathie et l'infarctus du myocarde pendant la grossesse : Une analyse de l'épidémiologie, du diagnostic et de la prise en charge médicale et chirurgicale

La cardiopathie ischémique est peu courante pendant la grossesse, puisqu'elle se produit dans environ un cas pour 100 000 naissances vivantes. Puisque les mères sont fertiles plus longtemps et ont des enfants plus tard, l'incidence de coronaropathie pendant la grossesse est toutefois susceptible d'augmenter. L'athérosclérose semble être la principale cause d'infarctus aigu du myocarde, bien que des spasmes coronariens, des dissections coronaires et des thrombus aient été déclarés, entre autres. Le diagnostic de cardiopathie ischémique chez les femmes enceintes peut être difficile à poser et comporter des risques pour le fœtus. Même s'il existe de nombreux comptes rendus d'infarctus aigus du myocarde et de pontages aortocoronariens pendant la grossesse, la plupart des connaissances se fondent sur des rapports isolés. On en sait encore moins sur le recours aux thrombolytiques, aux interventions coronaires percutanées et à la prise en charge médicale optimale de la cardiopathie ischémique pendant la grossesse. L'épidémiologie, le diagnostic, le traitement médical et chirurgical et le pronostic de la cardiopathie ischémique pendant la grossesse font l'objet de la présente analyse.

METHODS

A literature search was performed using the MEDLINE bibliographical database from 1966 to January 2009, to identify all English-language literature included under the following headings: myocardial infarction, acute coronary syndrome, coronary artery disease, myocardial ischemia, coronary artery bypass grafting, percutaneous coronary intervention, percutaneous intraluminal balloon angioplasty, thrombolysis, human, and pregnancy. All original articles were obtained from the University of Calgary (Calgary, Alberta) library or interlibrary communications. In addition, a manual search was performed using the references from all retrieved reports, review articles and chapters from textbooks.

EPIDEMIOLOGY

Cardiovascular disease complicates approximately 0.4% to 4% of all pregnancies (1). Although rare, the incidence of acute myocardial infarction is estimated at 0.6 to one per 10,000 pregnancies (2,3), with a case fatality rate of 5.1% to 37% (2-4). Most maternal deaths occur at the time of infarction or within two weeks of infarction, usually in association with labour and delivery. Fetal death occurs in 12% to 34% of cases, most of which are associated with maternal death (2,4). Maternal survival is generally associated with a good fetal outcome.

The risk of acute myocardial infarction appears to be approximately three to four times higher in pregnancy compared with non-pregnant women of reproductive age (3). The risk of myocardial infarction increases significantly with age (8.8, 19.0 and 30.2 per 100,000 deliveries among women aged 30 to 34 years, 35 to 39 years,

and 40 years or older, respectively [3]) and occurs most commonly in multigravidas (2). The risk of myocardial infarction also differs by race or ethnicity, with black women having the highest risk (11.4 per 100,000) compared with white and Hispanic women (7.6 and 4.2 per 100,000, respectively [3]). Although myocardial infarction has been reported in pregnant women at all stages of pregnancy and postpartum, it occurs more commonly in the third trimester and most commonly involves the anterior wall (2).

With the increasing age and fertility of mothers, and the ongoing risks of cigarette smoking, cocaine use and diabetes, the incidence of coronary artery disease in pregnancy is likely to increase.

RISK FACTORS

Risk factors for coronary artery disease in pregnancy are similar to those traditional risk factors observed in the general population. More common cardiac risk factors in young women include a family history of atherosclerotic disease, dyslipidemia, diabetes mellitus, cigarette smoking and previous use of oral contraceptives. Dyslipidemia may be worsened during pregnancy because high-density lipoprotein cholesterol is significantly decreased during gestation. There is no significant change in low-density lipoprotein cholesterol or triglyceride levels during pregnancy (5).

Although underlying atherosclerotic disease appears to be the primary cause of myocardial infarction during pregnancy, other potential causes include thrombosis, coronary artery spasm (spontaneous or induced), coronary artery dissection, vasculitis such as Kawasaki disease, collagen vascular disease, amniotic fluid embolism, pheochromocytoma

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TABLE 1
Medical conditions and the risk of pregnancy-related acute myocardial infarction

Medical condition	OR (95% CI)	P
Hypertension	11.7 (6.9–21.2)	<0.01
Thrombophilia (including history of thrombosis and antiphospholipid syndrome)	22.3 (8.2–61.1)	<0.01
Anemia	2.0 (1.3–3.2)	<0.01
Diabetes mellitus	3.2 (1.5–6.9)	<0.01
Migraine headaches	4.2 (1.0–17.1)	0.05
Smoking	6.2 (4.1–9.5)	<0.01

Data from reference 3

and cocaine use (2,6-9). In a review of 125 reported cases of pregnancy-related acute myocardial infarction, coronary artery morphology was reported in 68 cases. Atherosclerosis with or without intracoronary thrombus was found in 43% of patients, definite or probable coronary thrombus without evidence of atherosclerotic disease in 21%, dissection in 16%, spasm in 1% and normal anatomy in 29% of cases (2). Possible explanations for the finding of normal anatomy include the late performance of angiography or autopsy, healed coronary dissection, clot lysis and unrecognized coronary vasospasm. Methylergonovine has been used diagnostically to provoke coronary vasospasm, and several cases of acute myocardial infarction following postpartum methylergonovine administration have been reported (10-13).

Medical conditions that are strongly associated with acute myocardial infarction include thrombophilia, hypertension and smoking (Table 1). Pre-eclampsia is associated with endothelial dysfunction, and has been identified as a risk factor for myocardial infarction and mortality from cardiovascular disease later in life (3). A significant increase in myocardial contraction band necrosis is seen in patients who die of eclampsia compared with controls, suggesting coronary artery spasm may also be common in this condition (14). Alterations in the coagulation and fibrinolytic system, including decreased tissue plasminogen activator activity and a reduction in functional protein S level, can also increase the risk of thrombosis during pregnancy.

The normal physiology of pregnancy can also exacerbate underlying coronary artery disease. The marked increases in blood volume, stroke volume and heart rate seen in pregnancy increase myocardial oxygen demand, while physiological anemia and decreased diastolic blood pressure reduce myocardial oxygen supply.

Patients at high risk for coronary artery disease should be screened noninvasively before becoming pregnant. Adequate control of vascular risk factors, including hypertension and diabetes, must be achieved before conception.

DIAGNOSIS

The diagnosis of coronary artery disease during pregnancy is challenging and not without risk to the fetus. If at all possible, noninvasive methods that pose the least risk to the fetus should be employed first.

The accuracy of exercise electrocardiography in diagnosing coronary artery disease is lower in women than in men, and fetal bradycardia has been reported during maximal exercise in healthy women (15). As such, a submaximal exercise protocol with fetal monitoring is recommended for the evaluation of ischemic myocardial disease during pregnancy (16,17). Nuclear imaging should be avoided, especially during organogenesis (10 to 50 days) due to the risk of teratogenesis. In the second and third trimesters, nuclear imaging may still pose a risk of intrauterine growth retardation, central nervous system abnormalities and, perhaps, an increased risk of malignancy. Stress echocardiography is a reasonable option for assessing ischemia and left ventricular function during pregnancy, and can be used in patients with known or suspected coronary disease.

Cardiac catheterization also carries risks, but can be performed safely in pregnancy. Appropriate abdominal shielding, use of a brachial

or radial approach, and lower fluoroscopy times are important to minimize fetal exposure to radiation. Exposure to less than 10 rad is considered to be low risk, but exposure of greater than 15 rad carries a high risk of fetal harm (17). Cardiac catheterization should only be used during pregnancy in urgent circumstances, or when other diagnostic modalities are not adequate or appropriate.

It is likely that the diagnosis of acute myocardial infarction is not suspected as often as it should be in the pregnant population. In general, there is a low level of suspicion for myocardial infarction, and its signs and symptoms can be mistaken for normal manifestations of pregnancy. There is also a reluctance to intervene. In a study of 859 cases of acute myocardial infarction in pregnancy and postpartum, only 45% were reported to have undergone cardiac catheterization (3). Of those, 81% underwent angioplasty, stent placement or cardiopulmonary bypass.

As in nonpregnant patients, the diagnosis of acute myocardial infarction in pregnant patients is confirmed primarily by electrocardiography and changes in cardiac enzyme levels. Left- or right-axis deviation, a small Q wave in lead III, T wave inversion, or an increased R/S ratio in leads V1 and V2 can be seen in normal pregnancy, which can make the electrocardiographic diagnosis of ischemia more challenging. ST segment depression mimicking myocardial ischemia but not associated with wall motion abnormalities has also been reported during caesarean section (16). Measurement of cardiac troponin level is preferred over other cardiac markers. Troponin level is not increased by uterine contraction or the cell breakdown that occurs during labour and delivery, which can lead to a significant increase in myoglobin, creatine kinase and creatine kinase MB (18). Echocardiography is also useful in evaluating wall motion, although it is not a definitive test for ischemia.

TREATMENT

Although the management of acute myocardial infarction and its complications should follow the usual principles of care, fetal considerations may affect the choice of therapy (2). Management of the patient requires a multidisciplinary approach involving the attending obstetrician, internist or cardiologist, and anesthetist. Ideally, the patient should be treated in an intensive care unit that is capable of providing maternal and fetal monitoring as well as a comprehensive obstetric service. A plan for emergency delivery of a potentially viable fetus in the case of sudden maternal deterioration should also be established.

MEDICAL MANAGEMENT

The most appropriate medication regimen for pregnant patients with ischemic heart disease or acute myocardial infarction is unknown. There is a significant amount of anecdotal evidence supporting the use of salicylates, beta-blockers, nitroglycerin, calcium antagonists and heparin during pregnancy (Table 2), but little is known about the optimal combination of these medications.

Salicylates cross the placenta and enter fetal circulation. High doses of acetylsalicylic acid have been associated with fetal complications including mortality, intrauterine growth retardation, salicylate intoxication, bleeding abnormalities, neonatal acidosis and premature closure of the ductus arteriosus (19). Adverse effects reported in the mother include anemia, hemorrhage, prolonged gestation and prolonged labour. In general, low doses of acetylsalicylic acid (40 mg/day to 150 mg/day) during pregnancy do not cause fetal harm and should be used in patients with known coronary artery disease.

Due to its large molecular size, heparin does not cross the placenta and is not teratogenic. It is, therefore, the anticoagulant of choice during pregnancy. Chronic use of high-dose subcutaneous heparin requires monitoring of factor Xa levels. Heparin should be discontinued 24 h before elective delivery; in the case of spontaneous labour, protamine sulphate may be required to reduce the risk of bleeding, and to allow safe local and epidural anesthesia (2). Heparin can be resumed following delivery once adequate homeostasis has been achieved.

TABLE 2
Ischemic heart disease medications in pregnancy

Drug	Placental transfer	Pregnancy risk factor*	Potential fetal effects	Breastfeeding
ACEI	Yes	C	Renal failure, oligohydramnios, neonatal anuria, IUGR, premature labour, neonatal hypotension, anemia, bony malformations, limb contracture, persistent patent ductus arteriosus, pulmonary hypoplasia, respiratory distress and fetal wasting	Compatible
Acetylsalicylic acid	Yes	C (low dose); D (full dose, third trimester)	Increased hemorrhage, increased perinatal mortality, growth retardation and premature closure of ductus arteriosus	Compatible
Amlodipine	Yes	C	Embryotoxic effects have been demonstrated in small animals. There have been no adequate human studies	Not recommended
Beta-blockers				
Acebutolol	Yes	B	Fetal bradycardia, IUGR, prematurity, hypoglycemia and respiratory depression	Compatible; monitoring of infant's heart rate recommended
Labetolol	Yes	C		
Metoprolol	Yes	C		
Propranolol	Yes	C		
Atenolol	Yes	D		
Clopidogrel	Unknown	B	No adequate human studies. No fetal toxicity in rabbits or rats	Not recommended
Diltiazem	Yes	C	Limited data. Increased incidence of major birth defects	Compatible
Hydralazine	Yes	C	One report of fetal arrhythmia; transient neonatal thrombocytopenia and fetal distress reported following late third trimester use. Available evidence suggests safe use during pregnancy	Compatible
Nifedipine	Yes	C	Hypotension and IUGR reported	Compatible
Nitroglycerin	Unknown	C	Limited data. Use is generally safe; few cases of fetal heart rate deceleration and bradycardia have been reported	No data
Statins	Unknown	X	Teratogenic in rats, but not rabbits. Increased skeletal and central nervous system abnormalities reported in humans	Not recommended
Unfractionated heparin	No	C	Not teratogenic	Compatible
Verapamil	Yes	C	No adequate human studies	Compatible

*Pregnancy risk factor: A – controlled studies show no risk to fetus; B – no evidence of risk in humans; C – risk cannot be ruled out; D – positive evidence of risk; X – contraindicated in pregnancy. ACEI Angiotensin-converting enzyme inhibitor; IUGR Intrauterine growth retardation. Data from references 2, 9, 16, 17, 19 and 44

Little is known about the safety of other antiplatelet agents in pregnancy including clopidogrel, ticlopidine and the platelet glycoprotein IIb/IIIa inhibitors. The limited published information consists of case reports describing the use of clopidogrel at as early as 18 weeks' gestation (20-22). Maternal hemorrhage requiring transfusion was required in one case; a positive fetal outcome was described in all three. The use of ticlopidine has also been described at 38 weeks (23,24), with no adverse maternal or fetal consequences.

Substantial anecdotal experience suggests that many of the beta-adrenergic blocking agents, including propranolol, atenolol, labetalol and metoprolol, are safe during pregnancy, although various fetal side effects have been reported (Table 2). There are no adequate studies of carvedilol in pregnancy. Increasing experience with the use of nifedipine during pregnancy has shown the safety of this drug (2). Little information is available regarding the use of verapamil and diltiazem, although teratogenic and embryotoxic effects have been demonstrated in small animals exposed to diltiazem.

Although cholesterol-lowering therapy reduces both recurrent coronary events and mortality, the use of statins during pregnancy is contraindicated. Angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers and direct renin inhibitors are also contraindicated due to the increased risk of teratogenicity and fetal death.

REVASCULARIZATION

No studies have compared percutaneous coronary intervention with thrombolysis in pregnant women suffering acute myocardial infarction. Each case must be evaluated individually to determine whether revascularization should be pursued and, if so, which method is most appropriate. Survival is the primary concern and revascularization should not be withheld because the patient is pregnant.

Although the incidence of thromboembolic disease is increased during pregnancy, clinical experience with thrombolytic therapy in

this population is limited. The majority of pregnant patients exposed to thrombolytics have been treated for pulmonary embolus, deep vein thrombosis or thrombosed prosthetic heart valves (25,26). There have been only a handful of reports of thrombolysis in the treatment of acute ST elevation myocardial infarction during pregnancy (27-30). Pregnancy is considered to be a relative contraindication to thrombolytic therapy, although evidence for this is based on case reports and case series. Complications including maternal hemorrhage (8.1%), maternal death not related to lytic therapy (1.2% to 7%), preterm delivery (2.9%) and fetal loss (5.8% to 8%) have been reported (2,25,27). The risk for hemorrhagic complications seems to increase when thrombolytic therapy is given at the time of delivery. No congenital abnormalities have been reported when thrombolytic therapy has been given at as early as nine weeks' gestation. In most cases, maternal and fetal outcomes are favourable, and permanent sequelae have not been observed in the surviving children.

Although pregnant patients should first be treated with the most conservative therapy to minimize the risk to the mother and fetus, it is not justified to withhold thrombolytic therapy from pregnant patients if effective alternatives are lacking. Thrombolysis is not recommended if coronary dissection has been diagnosed on coronary angiography because it may cause propagation of the dissection and expansion of the intramural hematoma (31). Thrombolysis is also not recommended in patients with placenta previa or abnormal placental insertion, or in those who are close to term.

Percutaneous coronary intervention has been well documented during pregnancy, and is considered to be safe for maternal and fetal survival (20,22-24,32). In most cases, percutaneous coronary intervention is preferred over thrombolysis due to the decreased risk of hemorrhage and the increased incidence of coronary dissection as a cause of myocardial infarction in the pregnant population. The risks of angioplasty in pregnancy are similar to those in the nonpregnant patient.

The risk of radiation to the fetus is highest in the first trimester. As with diagnostic angiography, appropriate abdominal shielding, use of a brachial or radial approach, and lower fluoroscopy times are important to minimize fetal exposure to radiation. The safety of drug-eluting stents in pregnant patients is not known, nor is the safety of combination antiplatelet therapy to reduce stent thrombosis. Bare-metal stents may be the preferred option because insertion of drug-eluting stents may mandate a longer period of combination antiplatelet therapy and, thus, increase the risk of bleeding (9,22). The use of an intra-aortic balloon pump to improve left ventricular output and coronary perfusion is also considered safe (33), although the patient should be positioned in the left lateral recumbent position to reduce compression of the inferior vena cava.

Outside of acute myocardial infarction, invasive treatments should only be used if medical therapy is failing or if the mother's health is believed to be seriously compromised without revascularization (19).

CORONARY ARTERY BYPASS GRAFTING

Hundreds of cases of cardiopulmonary bypass have been reported in the literature since it was first used during pregnancy in 1959. Over time, there have been significant improvements in maternal and fetal outcomes. Currently, the maternal mortality is similar to that of the general population at 1.7% to 3%, with a fetal mortality rate of 9.5% to 19% (34-38). Fetal survival is most closely related to maternal stabilization and survival. In a systematic review of cardiovascular surgery cases published between 1984 and 1996, Weiss et al (39) reported a higher mortality (6%) in pregnant compared with nonpregnant patients; however, the majority of deaths occurred in patients with aortic-arterial dissection or pulmonary embolism, and there were no deaths in women undergoing coronary artery bypass surgery.

Timing of surgery does have an impact on fetal outcome. No relationship has been found between the gestational age and fetal mortality (35); however, congenital malformations do occur more commonly when cardiopulmonary bypass is performed during the first trimester (37). Surgery during the early second trimester after the period of organogenesis is preferred. Surgery during the late second trimester or early third trimester should be avoided when possible to minimize the risk of preterm labour and delivery (9,34,35). If the fetus is at more than 28 weeks' gestation, consideration must be given to deliver the child immediately before, and during the same operation as, the cardiac operation (37).

There are several technical considerations that can optimize fetal outcome. First, if gestational age is more than 20 weeks, the patient should be positioned in the left lateral recumbent position during surgery to prevent aortic and caval compression. Second, high-flow extracorporeal circuits (2.5 L/m²/min to 2.7 L/m²/min) and normothermic or mildly hypothermic conditions should be used because these techniques have been shown to improve fetoplacental perfusion (34,35). Third, continuous fetal monitoring should be used throughout surgery as an indirect means of assessing fetoplacental perfusion. Fetal bradycardia and loss of beat-to-beat variability suggest poor fetoplacental perfusion, and can be corrected by increasing the flow rate (5 L/min or greater) and maternal temperature. Placental hypothermia also causes poor oxygenation in terms of hematic gases, transplacental flow and flow to the fetal organs, and fetal mortality is higher if the temperature is below 35°C (38). Fourth, an adequate mean arterial pressure must be maintained throughout surgery. Placental perfusion is dependent on mean arterial pressures of 70 mmHg or greater in the relaxed uterus, and higher pressures in the contracting uterus (37). Uterine activity should also be monitored because cardiopulmonary bypass and rewarming can place the patient at risk for early contractions (34). Controlling contractions is crucial in avoiding placental insufficiency and secondary fetal hypoxia. Finally, hemodilution must be kept to a minimum to maximize oxygen-carrying capacity to the fetus, and the time necessary for cardiopulmonary bypass should be kept to a minimum.

LABOUR AND DELIVERY

In the case of acute myocardial infarction, delivery should be postponed, if possible, for at least two weeks from the time of infarction (2,4). Maternal mortality is significantly higher during this time, possibly due to the increased hemodynamic requirements during labour that increase myocardial demand and the risk of myocardial ischemia.

The most important consideration in deciding on the route of delivery is to determine which will provide the least hemodynamic burden. In most cases, caesarean delivery is only performed for obstetrical indications because a vaginal delivery minimizes stress. Most patients with coronary artery disease can tolerate vaginal delivery. In older reviews, maternal mortality in the setting of recent myocardial infarction was reported at 14% for vaginal deliveries and 23% for caesarean sections (4). In more recent reviews, no convincing support for one method of delivery over the other has been found (2). In cases of vaginal delivery, assistance during the second stage of delivery is recommended (40). The team must also be prepared to perform a caesarean section if maternal or fetal decompensation occurs, or if the labour is failing to progress adequately and the hemodynamic demands on the mother are becoming excessive (4).

During labour, our practice is to provide the patient with supplemental oxygen. The mother should be placed in the semisitting or left lateral decubitus position to reduce aortocaval compression and to maximize cardiac output. Monitoring devices should include an electrocardiogram, a pulse oximeter and a fetal heart monitor. An arterial catheter and pulmonary artery catheter should be considered if there has been a recent cardiac event or if left ventricular function is significantly impaired. This recommendation is based on anecdotal evidence (2,4,41-43) and management should be individualized. Early, continuous epidural anesthesia is important to minimize pain, which can increase maternal heart rate and myocardial oxygen demand. Tachycardia and hypertension should be promptly corrected. Ephedrine is usually the vasopressor agent of choice for hypotension associated with regional anesthesia because it helps maintain placental perfusion (41). Ergot alkaloids immediately after delivery should be avoided because of the risk of coronary artery spasm. After initial recovery, the patient should be monitored for 48 h postpartum in a coronary intensive care or general intensive care unit due to the significant hemodynamic changes that occur during this time.

SUBSEQUENT PREGNANCY

Previous myocardial infarction is not an absolute contraindication to pregnancy. The associated risks probably depend on a number of factors including residual left ventricular function, coronary anatomy, ongoing myocardial ischemia, and the time between myocardial infarction and previous pregnancy (1,41). A full cardiac evaluation including electrocardiogram, stress test, echocardiography and assessment of the coronary arteries should be pursued preconception. A new cardiac evaluation may also be required when a patient is taken off medications that are contraindicated during pregnancy.

Patients with previous revascularization or infarction should also be advised to delay pregnancy until the risks of recurrent ischemia and restenosis have reduced significantly, generally one year after revascularization or after infarction (9). Preconception counselling is required to advise the patient of the cardiac risks associated with pregnancy, labour and delivery. Once pregnancy is diagnosed, patients should undergo a review of their physical activity and cardiac symptoms, and be placed on restricted activities if necessary. Pregnant mothers should be followed closely by specialists in high-risk obstetrics and cardiology, preferably in a tertiary care centre with experience in cardiac disorders in pregnancy. Patients are at continued risk of ischemia and all of its associated complications as pregnancy progresses due to the progressive increase in myocardial demand.

CONCLUSION

Although rare, ischemic heart disease in pregnancy can have a significant impact on maternal and fetal outcome. The diagnosis of ischemic heart disease and acute myocardial infarction can be challenging in this population, and requires a high index of suspicion. Heparin, salicylates,

beta-blockers, nitrates and some calcium channel blockers can be used safely during pregnancy. If emergency revascularization is required, percutaneous coronary intervention is preferred, although thrombolysis can be used if angioplasty is not available. If necessary, coronary artery bypass grafting can be performed safely during pregnancy. Fetal outcome can be optimized by using high-flow, normothermic conditions. Survival is the primary concern and treatment should not be withheld because the

patient is pregnant. Most patients with coronary artery disease can tolerate a vaginal delivery; adequate pain control and assistance with the second stage of delivery are recommended. Although previous myocardial infarction is not an absolute contraindication to pregnancy, patients are potentially at risk for further ischemia and left ventricular dysfunction. Patients with known coronary artery disease should be carefully evaluated before conception and must be followed closely during pregnancy.

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