Cardiac operations for mitral valve disease during pregnancy

Hamilelikte mitral kapağa yönelik kardiyak girişimler

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Background: The frequency of open heart operations during
pregnancy has increased as cardiac operations became com-
mon.

Methods: We evaluated 12 cases (mean age 28.1±5.4 years;
range 19 to 37 years) who required cardiac surgery for mitral
valve pathology during pregnancy and assessed preoperative
status, maternal and fetal mortality and morbidity. Nine
patients with rheumatic mitral stenosis presented with cardiac
decompensation refractory to medical treatment. Three
patients presented with pulmonary edema due to valve
obstruction of mitral prosthesis and underwent emergent re-
replacement. Closed mitral commisurotomy (CMC) was per-
formed in seven patients. Two patients with severe mitral
valve calcification and concomitant mitral regurgitation
required mitral valve replacement. In one of three patients
who underwent emergent mitral valve re-replacement for
obstructed mitral prosthesis, a bioprosthetic mitral valve was
replaced whereas a mechanical valve was replaced in two.

Results: There were neither operative mortality nor cardiac
morbidity. All patients who underwent elective CMC gave
birth spontaneously at term without any cardiac complications
and none of the babies had any problem. Two patients with
elective mitral valve replacement delivered healthy babies 10
and 6 weeks after operation. Among the three patients under-
going emergent mitral re-replacement, cesarean section before
cardiac operation was performed in one who delivered a
healthy baby, and spontaneous abortion occurred in the other
two patients on the second postoperative day. Fetal mortality
rate was 16.7%. None of patients who underwent closed mitral
commisurotomy required reoperation during a mean follow-
up of 37.4 months. One case undergoing mitral re-replacement
with a bioprosthesis expired from stroke 11 months after the
operation. No other late mortality was observed.

Conclusion: Cardiac operations for mitral valve disease can
be performed in pregnant patients with low fetal mortality
and without any maternal mortality and morbidity. In patients
with eligible mitral valve pathologies, CMC may be an
option.

Key words: Cardiopulmonary bypass/adverse effects; mitral
valve/surgery; pregnancy.

Amaç: Kalp cerrahisinin yaygınlaşmasına paralel olarak, ge-
belik sırasında uygulanan açık kalp cerrahisi ameliyatları da
artmaktadır.

Çalışma planı: Mitral kapak hastalığı nedeniyle ameliyat
edilen 12 hasta (ort. yaş 28.1±5.4; dağılım 19-37) incelene-
rek, ameliyat öncesi durumları, maternal ve fetal mortalite ve
morbidite oranları değerlendirildi. Hastaların dokuzu roma-
tizmal mitral darlığı ve medikal tedaviye yanıt vermeyen
kardiyak dekompansasyon nedeniyle başvururken, üç has-
ta mitral protez kapak obstrüksiyonuna bağlı akciğer öde-
mi tablosuyla acil olarak ameliyata alındı. Çalışmaya alı-
nan yedi hastada kapalı mitral komissürotomi (KMK) uy-
gulandı. İki hastada mitral kapakta ileri derecede kalsifi-
kasyon saptandı. Bu iki hastaya mitral kapak replasmanı
uygulandı. Acil olarak ameliyat edilen üç hastaya ise ye-
niden mitral kapak replasmanı yapıldı. Bir hastaya biyop-
rotez kapak, diğer iki hastaya tekrar mekanik kapak uygu-
laması yapıldı.

Bulgular: Ameliyata bağlı mortalite ve kardiyak morbidite
gözlenmedi. Elektif olarak KMK uygulanan hastaların tümün-
de, kardiyak herhangi bir sorun gelişmeden zamanında normal
vajinal doğum gerçekleşti. Bebeklerin hiçbirinde sorun görül-
medi. Elektif mitral kapak replasmanı uygulanan iki hastada
ameliyattan altı ve on hafta sonra sorunsuz olarak doğum ger-
çekleşti. Acil mitral kapak re-replasmanı uygulanan üç hasta-
nın birinde kalp ameliyatından hemen önce sezaryen uygulana-
rak sağlıklı olan bebek alınırken, diğer ikisinde ameliyat sonra-
sı ikinci günlerinde spontan abortus gelişti. Fetal mortalite ora-
nı %16.7 olarak gerçekleşti. Kapalı mitral komissürotomi uy-
gulanan hastaların ortalama 37.4 aylık takibinde hiçbir hastada
tekrar ameliyat gerekli olmadı. Biyoprotez ile mitral re-replas-
manı yapılan hasta ameliyattan 11 ay sonra serebrovasküler
olay nedeniyle kaybedilirken başka mortalite gözlenmedi.

Sonuç: Gebelik sırasında, mitral kapak hastalığı nedeniyle,
kardiyopulmoner bypass ile açık kalp ameliyatları uygulana-
bilir. Bu girişimler maternal mortalite ve morbidite gözlen-
meden, düşük fetal mortalite oranlarıyla yapılabilir. Mitral
kapak patolojisi uygun olan hastalarda KMK tercih edilebilir.

Anahtar sözcükler: Kardiyopulmoner bypass/yan etki; mitral ka-
pak/cerrahi; gebelik.

Although the coincidence of cardiovascular diseases and pregnancy decreased over the last decades, the incidence of heart disease in pregnant women has been reported to range from 1% to 4% and mitral disease is the responsible pathology in most of these cases.[1,2] Patients with mild or moderate degrees of mitral regurgitation usually tolerate pregnancy well, because systemic vascular resistance falls markedly during pregnancy. But the increased heart rate and cardiac output associated with pregnancy compromise patients with mitral valvular stenosis. Mitral valve stenosis is the most common, most important cardiac valvular problem during pregnancy. Atrial fibrillation aggravated by altered hemodynamics in such patients may be associated with the onset of acute pulmonary edema. Pulmonary edema has been shown to be the leading cause of maternal death.[4,5] Physiological changes during pregnancy include a gradual increase in cardiac output, in blood volume, in heart rate and myocardial oxygen consumption all of which may cause decompensation in women with underlying cardiac disease. In such cases, medical therapy may not be sufficient and surgical intervention may become necessary to save patient's life.

In addition to native mitral valve disease, women with previous mitral valve replacement are under increased risk of complications. During pregnancy, platelet number and activation of coagulation cascades increase, in contrast fibrinolytic activity decreases. These changes increase the risk of valvular thrombotic complications in patients with previous mitral valve replacement[3] which may necessitate emergent surgical reintervention with high maternal and fetal mortality.

In this study we evaluated patients who required cardiac surgery for mitral valve pathology during pregnancy and assessed preoperative status, maternal and fetal mortality and morbidity.

PATIENTS AND METHODS

Between 1991 and 2004, 12 pregnant patients (mean age 28.1±5.4 years; range 19 to 37 years) underwent cardiac operation for mitral valve disease. All patients were in New York Heart Association (NYHA) functional class III or IV at presentation. Preoperative demographic data of the cases are summarized in Table 1. Most of the patients were in the 2nd or 3rd trimester of pregnancy, only two being in 1st trimester.

Nine patients diagnosed as rheumatic mitral stenosis, with a mean mitral valve area of 1.1 ± 0.1 cm^2 presented with cardiac decompensation refractory to medical treatment. Two of them had additional calcification of mitral valve leaflets and mitral insufficiency. Three patients presented with cardiac failure and pulmonary edema due to valve obstruction of mitral prosthesis and underwent emergent re-replacement. In all of these patients mobility of mitral prostheses were severely limited by obstructive thrombi. Two of them were under medical follow-up and were receiving heparin whereas the other patient, had ceased her medications including anticoagulants without medical consultation.

Table 1. Preoperative demographic and echocardiographic data of patients

Characteristic	Mean±SD	n	%
Mean age (range)	28.1±5.4 (19-37) years		
Gestational week			
8-10 wk		3	25
24-30 wk		8	66.7
35th wk		1	8.3
Gravida			
Primi		6	50
Multi		6	50
NYHA class			
III		7	58.3
IV		5	41.7
Rhythm			
Atrial fibrillation		3	25
Sinus rhythm		9	75
Echocardiographic data			
Mitral valve area (cm^2)	1.1±0.1 (0.8-1.2)		
Ejection fraction (%)	55.4±5.5 (50-65)		
Mitral insufficiency >2nd degree		2	16.7
Mitral valve calcification		2	16.7
Pulmonary arterial pressure >60 mmHg		3	25

All patients were evaluated by clinical, hemotological, electrocardiographical and echocardiographical examination preoperatively. Chest-X-ray examination was not performed in order to prevent the fetus from exposure to radiation. On echocardiographic examination of patients with mitral stenosis, valve leaflets and subvalvular apparatus were assessed for mobility, chordal shortening, thickening and papillary muscle involvement. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were performed by VINGMED CFM 800 multiplan 5 mHz probe. The echocardiographic evaluation data are given in Table 1.

In all patients, the development of the fetus was evaluated by ultrasonography during the obstetric consultation before the operation.

Anesthetic management. Basic principles of perioperative anesthetic management include providing maternal safety first, avoidance from teratogenic drugs and intrauterine asphyxia and prevention of premature birth if possible. In patients with gestational age above 20 weeks, operations were performed with patients in slightly left lateral position to prevent caval compression by the uterus. Choice of premedication depends on the specific cardiac pathology, clinical state of the patient, teratogenicity of the drug and urgency of the operation. In our patients we did not use any sedative premedications. We used H_2 receptor antagonists and metoclopramide for prevention of gastroesophageal reflux and cefazoline for antibiotic prophylaxis. Maternal monitorization included electrocardiogram, invasive arterial pressure, pulmonary arterial catheterization for patients with pulmonary hypertension, urinary catheterization and pulse oximeter. Uterine contractions and fetal heart beats were monitored by a cardiotachometer in patients with a gestational age above 26 weeks. Anesthesia was provided by fentanyl and pancuronium and volatile anesthetics with inhalation of 50%:50% oxygen and nitrous oxide. In cases that inotropic support was needed, combined alpha and beta adrenergic drugs were used since alpha-aderenergic drugs may cause excessive vasoconstriction and may decrease umbilical flow thereby stimulating uterine contractions. For prevention of uterine contractions indomethacin suppository was administered per rectally the day before and on the day of surgery and continued 3 to 5 days postoperatively. In case of uterine contractions, 2 grams magnesium was administered by intravenous infusion within 5 minutes and 4 grams/hour infusion was continued postoperatively.

Surgical technique. Closed mitral commisurotomy (CMC) was performed in seven patients. They were in the second trimester of pregnancy with gestational ages between 25-27 weeks. Before the CMC procedure, left atrial and appendicial thrombus, left atrial spontaneous echo-contrast, mitral valve excursion, regurgitation were determined for each patient. All of these patients were in sinus rhythm with pliable valve leaflets without any mitral calcification, mitral regurgitation, left atrial thrombus. CMC was performed through the 4th or 5th left intercostal space while the patient was in right lateral decubitus position. During CMC procedure, Tubbs dilator, set on opening span 3.5 cm, was introduced from the left ventricular apex through the cordae. The Tubbs dilator was advanced to proper position into the mitral leaflets with the guidance of TEE and the index finger extended through left atrial appendage. Tubb's dilator was positioned in the mitral valve to achieve optimum dilatation without causing mitral regurgitation and checked by four chamber and transgastric TEE images. Transesophageal echocardiography confirmed the adequacy of valvulotomy and the presence of no or minimal mitral regurgitation intraoperatively.

Two patients with mitral valve calcification and concomitant mitral regurgitation required mitral valve replacement with bileaflet mechanical valve prosthesis. One of these patients was at the 10th week of gestation and other was in the 24th week and obstetric consultation revealed both fetuses being immature. Three patients with previous mitral valve replacement underwent emergent mitral valve re-replacement for obstructed mitral prosthesis. The mean interval between the first operation and reintervention was 4±2.7 (range; 1.5-7) years. One of these patients was in the 35th of gestation and a cesarean section was performed before cardiac intervention. All five patients underwent cardiac operation under conventional cardiopulmonary bypass with mild hypothermia (34 °C) and with a mean arterial pressure of about 70 mmHg and flow rate above 3 L/minutes/m². Hematocrite levels were kept between 22-25% and cardiac arrest was provided with retrograde isothermic hyperkalemic blood cardioplegia. Activated clotting time was kept above 400 seconds. Operative variables of all patients are summarized in Table 2.

Patients were followed in the intensive care unit and fetal monitorization continued postoperatively. Hematocrite level was kept around 35%, a value higher than that in non-pregnant patients. Obstetric consultation assessed fetal viability by ultrasonography immediately after the operation and then repeated within 24 hours. All patients receiving a prosthetic valve were anticoagulated with heparin or low molecular weight heparin during early postoperative period. In two of these patients, anticoagulant therapy was continued with Warfarin only until the last week of their gestation.

RESULTS

There was neither operative mortality nor cardiac morbidity. Three patients required inotropic support during

Table 2. Operative and postoperative variables

	Closed mitral commisurotomy	Elective mitral valve replacement	Emergency mitral valve re-replacement
n	7	2	3
Mean aortic cross clamp time (min)	–	44±19.7 (30-58)	55.3±4.9 (52-61)
Mean cardiopulmonary bypass time (min)	–	63.5±19 (50-77)	75.6±6 (70-82)
Temperature (°C)	Normothermia	35	34
Mean perfusion pressure (mmHg)	–	72.5±2.5 (70-75)	73.7±1.2 (70-75)
Mean perfusion flow rate (mL/minutes)	–	3900±141.4 (3800-4000)	3766.6±208.1 (3600-4000)
Activated clotting time (sec)	200	>400	>400
Mean intubation time (hour)	4.6±1.9 (2-6)	9.5±4.9 (6-13)	8.0±2.0 (6-10)
Mean intensive care unit stay (day)	2±0.7 (1-3)	3±1.4 (2-4)	2.6±1.1 (2-4)
Mean hospital stay (day)	6.6±2.4 (4-10)	10.5±4.9 (7-14)	17±5.1 (14-23)
Maternal mortality	None	None	None
Fetal mortality	None	0	2
Spontaneous birth at term	7	2	0
Cesarean section before cardiac operation	0	0	1
Medical abortus	0	0	0
Spontan abortus	0	0	2

weaning from cardiopulmonary bypass and early postoperative period. All three of these patients were in atrial fibrillation rhythm before and after the operation and all underwent mitral valve replacement, two of them underwent emergent reoperation. All patients were extubated after the mean intubation duration of 6.6±3.1 hours (range; 2-13 hours) and stayed in the intensive care for 2.4±0.9 days (range; 1-4 days). Patients who underwent closed mitral commisurotomy had shorter duration of intubation and stay in the intensive care unit. Postoperative variables according to the operation strategy are summarized in Table 2.

All patients who underwent elective closed mitral commisurotomy gave birth spontaneously at term without any cardiac complications and none of the babies had any complication. Two of the patients who underwent elective mitral valve replacement in the 26th and 32nd weeks of gestation, delivered healthy babies 10 and 6 weeks after operation, respectively. Uterine contractions were observed during rewarming phase of cardiopulmonary bypass and early after the operation in the second patient undergoing mitral valve replacement. Tocolysis with indomethacin, rectal suppository and intravenous magnesium infusion was performed. In this patient, acalculous cholecystitis developed at the 5th day after the operation and resolved with medical therapy which was arranged according to the gastroenterologic and surgical consultations.

One of the three patients who underwent emergent mitral re-replacement was in the 35th week of gestation and had cesarean section before cardiac operation. This patient was 19-years-old and since she expected anoth-

er baby, a bioprosthetic mitral valve was replaced. One patient was at the 26th week of gestation and obstetric consultation revealed loss of fetal heart beats and movements before the onset of operation. Firstly, cardiac operation was performed and dead fetus was spontaneously expelled from the uterus on the second day after the operation. Other patient was on the 8th week of gestation and spontaneous abortion occurred on the second postoperative day.

Patients were followed up for a total period of 455.5 months. None of patients who underwent closed mitral commisurotomy required reoperation during a mean follow-up of 37.4 months. The 19-year-old case who underwent reoperation for mitral mechanical valve obstruction and received a bioprosthetic mitral valve replacement died from stroke 11 months after the operation. This patient was in sinus rhythm and was not receiving any anticoagulant treatment. No other late mortality was observed.

DISCUSSION

Organic heart disease has an incidence of 1% to 4% in pregnant women and physiological changes during pregnancy may cause heart failure in women with underlying cardiac disease. Mitral stenosis is the most frequently encountered valvular pathology and may require surgical intervention when the lesion is severe enough to cause heart failure in spite of medical therapy. In addition to native mitral valve disease, women with previous mitral valve replacement are under high risk of complications and may require emergent surgical reintervention with high maternal and fetal mortality rates.[6]

The choice of optimum operative strategy and timing of operation are very important for both maternal and fetal outcome. Many investigators reported the maternal mortality between 1.5% and 5% and fetal mortality between 16% and 33%.[7] Although we didn't observe any maternal mortality we observed a fetal mortality rate of 16.7% (two fetuses). In one patient, the miscarriage was not a consequence of operation but a consequence of medical status of the patient since fetal movements and heart beat were lost prior to the operation. From the fetal point of view, delivery before surgery is the best choice if postnatal viability is expected. If this is not possible, the ideal age of gestation for fetal outcome has been reported to be between 13th and 28th weeks.[8] There is higher risk of fetal malformations in the first trimester and preterm delivery in the third.[9] Supporting this view, the only fetal loss in our patient group, was at the 8th week of gestation. Some authors reported that, surgical complications, not the duration of gestation at the time of surgery influence maternal outcome[10] whereas others stated that maternal hemodynamic alterations and mortality increased in the third trimester[9] and surgery performed immediately after delivery led to a significant deterioration of the maternal outcome.[11] Previous studies have shown that hemodynamic burdens in the healthy gravid women do increase with increasing duration of pregnancy and peak during delivery and the early postpartum period and that cardiovascular recovery to the preconception level may last up to 12 weeks.[12] In most patients, unless there is an emergency, we preferred to perform the operation in second trimester. When the fetal viability after delivery was of question, it was planned to deliver the baby after the operation when the maternal cardiac stability and fetal maturity were provided.

The choice of operative technique is also very important. Three alternative methods, open mitral comissurotomy (OMC), closed mitral comissurotomy (CMC) and percutaneous balloon mitral valvotomy (PBMV), have been presented in the treatment of pure mitral stenosis during pregnancy. Although OMC provides the best conditions for surgical treatment of pure mitral stenosis, it has disadvantages, such as the necessity of cardiopulmonary bypass. Closed mitral commissurotomy was the first effective intervention in valvular heart disease. The possibility of opening a stenotic mitral valve by digital splitting of the fused commissures was apparently suggested by Samways as early as 1898. Recently, CMC has been reexplored due to the concepts of less invasive valvular surgery. In patients with stenotic mitral valves with pliable and uncalcified leaflets and no thrombus in left atrium, CMC is a safe and cost-effective procedure as stated previously.[5,13]

Meanwhile, more efforts have been made to introduce new techniques in minimal invasive valve surgery.

Percutaneous balloon mitral valvotomy (PBMV) is associated with lower trauma than cardiac operations, however early restenosis and risk of radiation hazard limits its use during pregnancy and there is a risk of emergency surgical intervention in case of the failure of the procedure.[14] As the least invasive method, PBMV has many complications such as cardiac perforation, left to-right shunting at the atrial level due to dilatation of atrial septal puncture. Rarely the defect is large enough to cause right heart failure. Systemic arterial hypotension may occur due to transient occlusion of left ventricular inflow during balloon inflation. In addition all patients are exposed to radiation during the procedure.[15,16]

Avoidance from cardiopulmonary bypass and short duration of operation is a very important advantage of the closed mitral commisurotomy procedure for pregnant patient. Transesophageal echocardiography (TEE) during pregnancy has been reported to be safe[17] and can be used to assess mitral valvular structure and left atrial thrombus preoperatively. The possibility of performing TEE intraoperatively, increased the safety and applicability of this procedure in the recent years. In our patients who underwent CMC, we didn't observe any maternal and fetal mortality and morbidity. All patients reached to term and gave birth to healthy babies without any complications.

Cardiac operations in pregnant women can be performed under cardiopulmonary bypass with a risk for mother similar to that for nonpregnant female patients but fetal mortality is still high. Use of high flow rate, high-pressure, normothermic cardiopulmonary bypass for the shortest period possible is thought to decrease fetal risk. The fetal response to cardiopulmonary bypass is bradycardia, thought to be due to hypoperfusion secondary to malperfusion of fetoplacental unit and uterine contractions and this problem can be overcome by increasing perfusion rate. It has been stated that nonpulsatile perfusion leads to a vasoconstrictive response of the fetoplacental circulation mediated by prostaglandins and/or inhibition of endothelium-derived relaxation factor nitric oxide (NO).[18] Also it was shown that pulsatile perfusion reduces endogenous cathecholamine production and peripheral vascular resistance during bypass, thereby increasing placental perfusion.[19] But these theoretical advantages of pulsatile perfusion are unproven. Uterine contractions occur frequently during cardiopulmonary bypass and are considered to be one of the most important predictors of fetal death. Cardiopulmonary bypass is a strong stimulus for uterine contractions and extensive contractions especially during the rewarming phase after moderate or profound hypothermia can be observed. Although the reason for these contractions is not known, their frequency increases with increasing gestational age. Avoiding hypothermia during cardiopulmonary bypass in pregnant patients can prevent development of uterine

contractions although hypothermia is believed to protect the fetus by reducing fetal oxygen requirement. In our practice, we performed elective operations with normothermic cardiopulmonary bypass but in urgent cases, with apparent symptoms of low cardiac output, we preferred to use mild hypothermic cardiopulmonary bypass for better myocardial and organ protection.

Fetal monitoring during cardiac operations is very important and has been reported to reduce fetal mortality rate to 9.5% as a result of earlier recognition of potential problems.[7] Continuous cardiotocographic monitorization throughout the procedure is mandatory since early constitution of tocolytic treatment can save the fetus. Magnesium, beta agonists such as ritodrine and terbutalin, calcium channel blockers, progesteron and prostaglandin inhibitors can be used for tocolysis. We preferred indomethacin rectal suppository for prophylaxis and used magnesium in the presence of uterine contractions. Continuous monitorization in the early postoperative days is highly recommended because of the high risk of premature labor in this period. Assessment of fetal viability and heart rate by ultrasonographic evaluation of the fetus early after surgery is also important especially in patients with small gestational age since this is the easiest way for assessment of embryonic sac and placenta.

In conclusion, cardiac operations for mitral valve disease can be performed in pregnant patients with acceptable fetal mortality and low maternal mortality and morbidity rates. If the mitral valve is not calcified, with preserved subvalvular apparatus and no thrombus in left atrium, CMC should be performed because of the main advantage of avoidance from cardiopulmonary bypass and with excellent maternal and fetal outcome. It is preferable to perform this intervention during the second trimester of gestation. If it is obligatory to perform an open cardiac surgery due to rapidly deteriorating clinical status with unsuitable valvular structure for CMC or due to the need for emergency intervention; *i)* if the postnatal fetal viability is expected, cesarean section just before commencing of cardiopulmonary bypass is the best choice for fetal outcome, *ii)* if postnatal viability is not possible, cardiac intervention followed by close monitorization of both maternal and fetal vital signs is the best strategy, *iii)* if intrauterine death of fetus is detected before the operation cardiac intervention should be performed first. If the fetus is not expelled from the uterus spontaneously, medical abortion should be performed after two days, *iv)* and whatever the type of surgery, selection of appropriate and nonteratogenic anesthetic and supportive agents, maintenance of acid-base balance during surgery, maintenance of hemodynamic stability at best and continuous monitorization of fetal and maternal status is mandatory.

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