Review Article

Role of Echocardiography in Assessing Pregnant Women With and Without Heart Disease

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Abstract

The cardiocirculatory changes during pregnancy and delivery are marked. In some diseases and conditions, the maternal and fetal risks are high. Echocardiography plays a very important role to diagnose and to follow up in pregnant women with heart diseases, because it is noninvasive and does not expose the patients to radiation. We reviewed the value of echocardiography to determine the conditions under which women with heart disease can tolerate pregnancy, and the fetomaternal prognosis for major heart diseases.

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Key words: pregnancy, heart disease, echocardiography, fetomaternal prognosis

Introduction

With recent advances in cardiovascular and neonatal medicine, the number of patients with heart disease who reach childbearing age has increased, and the range and severity of heart diseases with which pregnancy and delivery are possible is expanding. Subsequently, guidelines have been prepared in various countries[1, 2]. In Japan, the Japanese Circulation Society (JCS) joint working group issued guidelines for the management of pregnancy and delivery in women with heart diseases in 2005 (JCS 2005 guidelines)[3]. The cardiocirculatory changes associated with pregnancy and delivery are marked, and in some diseases and conditions, the maternal and fetal risks are high. In this review article, we emphasized the value of echocardiography to (1) examine healthy

pregnant women, (2) determine the conditions under which women with heart disease can tolerate pregnancy, and (3) determine the fetomaternal prognosis for major heart diseases.

1. Echocardiographic findings and hemodynamic changes during pregnancy in healthy pregnant women

Echocardiography can assess the hemodynamic changes noninvasively, thus it is widely used to measure cardiocirculatory indexes during pregnancy and after delivery.

From the sixth week of gestation to the second trimester during pregnancy, through the mechanisms such as water and sodium retention mediated by the renin-aldosterone system stimulated by the estrogen increase, the volume of circulating plasma is increased by an average of 1.5 fold. Cardiac output measured by Doppler echocardiography also increases by approximately 50 percent. From weeks 20 to 24, stroke volume increases reaching its peak, and then heart rate increases by 10 to 20 beats/min (Figure 1)[4]. On the other hand, arterial pressure and systemic vascular resistance decrease[5].

During labor and delivery, oxygen consumption increases about three fold, and uterine contraction

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Fig. 1. Percent changes in heart rate, stroke volume, and cardiac output measured by echocardiography in the lateral position throughout pregnancy[4] (modified by and taken from the textbook "Braunwald's heart disease 7th edition, p1966")

accompanying labor increases the amount of circulating blood by 300-500 ml. At the same time, cardiac output increases by 15-25%, exceeding 8-10 L/min. Immediately after delivery, uterus-induced compression of the inferior vena cava is relieved, thereby rapidly elevating venous return. Cardiac output decreases by 10-20% within one hour of delivery. As the amount of circulating blood increases during pregnancy, transient overload persists for 4 to 6 weeks after delivery[6].

With regard to the changes in echocardiographic parameters, left ventricular (LV) end-diastolic and end-systolic dimensions and wall thickness increase, and contractile function enhances. Functional pulmonary, tricuspid and mitral regurgitation, and mild pericardial effusion are occasionally seen in normal pregnancy. About diastolic performance, findings such as significant increases in transmitral peak E velocity in the first trimester and peak A velocity in the third trimester of pregnancy have been reported[7]. Tissue Doppler echocardiography determined mitral annular early diastolic velocity (E') decreases, and late diastolic velocity (A') remains unaltered [8].

2. Required conditions for pregnancy based on echocardiographic findings

We have experienced about 70 deliveries of heart disease women over one year. Figure 2 shows the annual number of deliveries by women with heart disease in our hospital. While the number of patients

with arrhythmia is almost constant, those with congenital heart disease or other heart diseases tend to increase.

In the past, medical decisions as to whether heart disease patients could become pregnant and deliver were based on the heart function classification system developed by the New York Heart Association (NYHA), and it has been generally accepted that class I or II women can become pregnant. Studies have shown that the maternal mortality for NYHA class I/II was <1% and for NYHA class III/IV was 5-15%[9], and the rate of maternal cardiovascular events such as heart failure, arrhythmia and cerebral infarction for NYHA class I was about 10% and for II/III/IV was about 30%. The rate of live-born infants for NYHA class I was about 80% and for II/III/IV was about 70%[10].

Recently, echocardiographic parameters have been widely used to determine the risk of pregnancy. A study of 562 pregnant women with heart diseases identified the following factors for poor maternal prognosis: prior cardiac event (heart failure, transient ischemic attack, or stroke before pregnancy) or arrhythmia, NYHA functional class > II or cyanosis, left heart obstruction (mitral valve area < 2 cm², aortic valve area < 1.5 cm², or peak left ventricular outflow tract gradient > 30mmHg by echocardiography) and systemic ventricular dysfunction (ejection fraction < 40%). When assigning one point for each condition, the incidence of maternal cardiovascular events during pregnancy was

Fig. 2. The annual number of deliveries by women with heart disease at National Cardiovascular Center

Table 1. Multivariate analyses of maternal and neonatal risk predictors

Complications	Predictor	Odds Ratio (95% CI)	P
Cardiac	Prior cardiac event or arrhythmia	6 (3-14)	< 0.001
	NYHA functional class > II or cyanosis	6 (2-22)	0.009
	Left heart obstruction	6 (3-14)	< 0.001
	Systemic ventricular dysfunction	11 (4-34)	< 0.001
	NYHA functional class > II or cyanosis	3 (1.1-6.1)	0.035
Neonatal	Heparin/warfarin during pregnancy	3 (1.4-8.2)	0.0093
	Smoking	2 (1.3-3.9)	0.0045
	Multiple gestation	22 (6-85)	< 0.001
	Left heart obstruction	2 (1.01-2.9)	0.044
	Peripartum heparin or warfarin	7 (2-22)	0.001
Postpartum hemorrhage	Cyanosis	27 (4-177)	< 0.001

CI : Confidence Interval, NYHA : New York Heart Association

(Modified by and taken from Siu : Circulation, 104 (5) [11])

5% for a score of 0 point, 27% for a score of 1 point and 75% for a score of 2 or higher. In addition, the incidence of fetal complications such as premature delivery and low birth weight reached 20%, and severe complications such as respiratory distress syndrome, intracranial bleeding and death were confirmed in 5%. The factors that exacerbated fetal prognosis were NYHA class > II or cyanotic heart disease, anticoagulant therapy, smoking, multiple pregnancy and left ventricular obstruction (Table 1) [11]. In addition to the

above factors, a recent study documented other risk factors; severe pulmonary regurgitation and right ventricular dysfunction with an odds ratio of 9.0 and 27.2, respectively [12].

Based on these results, the JCS 2005 guidelines list heart diseases that require close monitoring during pregnancy or should avoid pregnancy (Table 2) [3]. Echocardiography plays a pivotal role in assessing these conditions.

Table 2. Heart diseases that require careful monitoring during pregnancy and diseases with which pregnancy should be avoided [3]

1. Pulmonary hypertension (Eisenmenger syndrome)
2. Outflow tract obstruction (severe aortic valve stenosis : >40-50 mmHg)
3. Heart failure (NYHA class: $\geq$ III, LVEF : <35-40%)
4. Marfan's syndrome (Diastolic aortic diameter : >40 mm)
5. Prosthetic valve
6. Cyanotic disease (oxygen saturation : <85%)

NYHA : New York Heart Association

3. Echocardiographic findings during pregnancy in cardiovascular diseases

Here, we describe major cardiovascular diseases in pregnancy with some case presentations.

3-1. Congenital heart disease

3-1-1. Non-cyanotic heart disease

Left-to-right shunts, such as atrial septal defect (ASD), ventricular septal defect (VSD), patent foramen ovale (PFO), and patent ductus arteriosus (PDA) are sometimes diagnosed during pregnancy due to loud heart murmur from increased shunt volume caused by increased circulating blood volume (Figure 3). In patients with large shunt volume, decreases in peripheral vascular resistance balances out the increased blood volume, and in most cases, pregnancy and delivery are completed without any complications. However, caution must be exercised in the event of rapid bleeding, as peripheral vasoconstriction may increase shunt blood flow, decrease cardiac output and cause congestive heart failure, shock and ventricular fibrillation.

Masuda et al. reported changes in pulmonary output (Qp) and systemic output (Qs) measured by Doppler echocardiography in 17 pregnant women (10 with VSD and 7 with ASD) in our hospital. During pregnancy, both Qp and Qs increased in all patients, resulting in an insignificant change in Qp/Qs (Table 3)[13].

(1) ASD: When compared to normal pregnancy, the risks for miscarriage and premature birth are higher, and these conditions can accompany supraventricular arrhythmia or paradoxical emboli. One study found that when compared to pregnancy after ASD-closure surgery, pregnancy before surgery has higher risks for

miscarriage and maternal cardiovascular events[14]. Hence, if surgery is indicated, it should be performed before pregnancy. Recently, non-invasive procedure to close ASD was developed as an alternative treatment. There is a case report of percutaneous closure of ASD during pregnancy[15].

(2) VSD: In patients with untreated VSD without heart failure which is discovered during pregnancy, there are few problems, except when there is marked aortic regurgitation (AR) due to right coronary cusp herniation. As shunt volume of VSD is exaggerated by marked AR during pregnancy, surgery is recommended before pregnancy.

In a study of 309 pregnancies in 126 pregnant women with congenital heart diseases including ASD and VSD, the incidence of miscarriage was 17%, average duration of pregnancy was 34 weeks, maternal mortality was 0%, and fetal heart disease was 2.5%[16].

3-1-2. Non-cyanotic heart disease after surgical correction

In general, if patients keep good cardiac function, pregnancy and delivery are tolerable. Echocardiography often shows cardiac constrictive signs (such as septal bounce and increased respiratory changes in transmitral/transtricuspid flow) in pregnant patients who had open heart surgery. We think that increased blood volume can cause such a condition, and some should be carefully observed.

3-1-3. Cyanotic heart disease after surgical correction

In patients with good functional class (NYHA class I or II) and sinus rhythm, pregnancy and delivery are possible, but the incidence of miscarriage is high.

Repaired tetralogy of Fallot (TOF): In patients who underwent corrective surgery, pregnancy and delivery are possible. In one study of 112 pregnancies in 43

Fig. 3. Echocardiograms from a 29-year-old woman who was diagnosed with a small ventricular septal defect during her first pregnancy. Shunt flow increased in third trimester of her pregnancy (a) compared with 1 year after her delivery (b). Her left atrial dimension was 44mm during pregnancy. In contrast, it was 38mm after delivery.

Table 3. Changes in Qp/Qs measured by Doppler echocardiogram in 17 pregnant women with VSD or ASD

	Early phase of pregnancy (mean 13.8 th week of gestation)	Early phase of pregnancy (mean 32.1 th week of gestation)	Postpartum (mean 7.6 weeks after delivery)
Qp/Qs ratio in all patients (n=17)	1.78 ± 0.99	1.80 ± 0.76	1.56 ± 0.54
Qp/Qs ratio in VSD patients (n=10)	1.27 ± 0.17	1.52 ± 0.44	1.38 ± 0.38
Qp/Qs ratio in ASD patients (n=7)	2.50 ± 1.23	2.20 ± 0.96	1.88 ± 0.70

Qp; pulmonary output, Qs; systemic output, VSD; ventricular septal defect, ASD; atrial septal defect

patients of repaired TOF, delivery rate was 73%, and six women (14%) had cardiac events[17]. Pregnancy risk factors included: residual VSD, moderate to severe pulmonary valve stenosis and insufficiency, aortic insufficiency, pulmonary hypertension, dilated aorta (≥ 40 mm), ventricular dysfunction, and past history of tachyarrhythmia.

We experienced 14 deliveries in 13 patients of repaired TOF from 1998 to 2006. Three patients (23.1%) needed diuretics or bed rest because of pulmonary hypertension assessed by Doppler echocardiography.

3-1-4. Cyanotic heart disease without pulmonary hypertension

During pregnancy, systemic vascular resistance decreases to elevate right-to-left shunt, thus exacerbating cyanosis. While the incidence of complications is high in pregnant women with cyanotic heart diseases, cyanosis is treatable and mortality risk is low. However, fetal prognosis is poor, and in severe cyanosis,

fetal development is hindered (the rate of live births is 12% at $\leq 85\%$ oxygen saturation). In one study of 96 pregnancies in 44 patients with cyanotic heart diseases, maternal cardiac complications were seen in 32%, and the rate of live births was 43%. Hemoglobin ≤ 16 g/dL and oxygen saturation $\leq 85\%$ were found to be prognosticators[18].

3-2. Pulmonary hypertension

In patients with primary pulmonary hypertension, maternal mortality exceeds 50%, and pregnancy is contraindicated. In patients with Eisenmenger syndrome, maternal mortality ranges from 30 to 70%, and fetal mortality is as high as 50%[19, 20]. Hence, if patients with these diseases wish to continue their pregnancies, they must be admitted to a specialized hospital after week 20 of gestation to be treated with resting, oxygen administration and anticoagulation[21]. In our hospital, we experienced 2 (15.4%) maternal deaths among 13 patients with pulmonary hypertension[22].

Table 4. Maternal and fetal risk for patients with valvular disorders

	Low risk for mother and child	High risk for mother and child
Aortic stenosis	<ul style="list-style-type: none"> Asymptomatic Normal LV function Mild to moderate stenosis : Systolic pressure gradient $< 40 \sim 50$ mmHg 	<ul style="list-style-type: none"> Severe stenosis: systolic pressure gradient $> 40 \sim 50$ mmHg LV dysfunction
Aortic insufficiency	<ul style="list-style-type: none"> NYHA class I/II Normal LV function 	<ul style="list-style-type: none"> NYHA class III/IV LV dysfunction
Mitral insufficiency	<ul style="list-style-type: none"> NYHA class I/II Normal LV function 	<ul style="list-style-type: none"> NYHA class III/IV LV dysfunction
Mitral stenosis	<ul style="list-style-type: none"> NYHA class I/II Mild to moderate stenosis Valvular area: > 1.5 cm² Pressure gradient: < 5 mmHg Without pulmonary hypertension 	<ul style="list-style-type: none"> NYHA class III/IV Severe stenosis Valvular area: < 1.5 cm² Pressure gradient: > 5 mmHg With pulmonary hypertension ($\geq 75\%$ systemic blood pressure)
High risks for mothers Left ventricular dysfunction (LVEF: $< 40\%$) Past history of heart failure Anticoagulation therapy during pregnancy (prosthetic valve patients) Past history of cerebral embolism or transient cerebral ischemia Aortic regurgitation accompanying Marfan's syndrome		
High risks for children Mother's age: < 20 years or > 35 years Anticoagulation therapy during pregnancy (prosthetic valve patients) Exposure to smoking, drinking or other environmental factors during pregnancy		

LV: left ventricular, NYHA: New York Heart Association, EF: ejection fraction
(Modified US ACC/AHA guidelines[25])

Fig. 4. Doppler echocardiograms from a woman with severe mitral stenosis
A thirty-one year-old woman with severe mitral stenosis (estimated mitral valve area= 0.6 cm²) showed increased tricuspid regurgitation in her 26-week gestation (a) and decreased after cesarean section (c). The RA-RV pressure gradients derived by tricuspid regurgitant velocity (TRPG) also changed from 111 mmHg in her 26-week gestation (b) to 40 mmHg after cesarean section (d).

3-3. Patients with valvular disorders or prosthetic valves

During pregnancy, increased circulating blood volume often reduces cardiac function in patients with valvular heart diseases. The incidence of congestive heart failure and arrhythmia is about 40 and 15%, respectively, although maternal mortality is low[23]. Table 4 shows the JCS 2005 pregnancy guidelines for patients with valvular disorders established based on ACC/AHA guidelines[3, 24, 25].

Generally, patients with stenosis are less tolerable for volume overload than patients with regurgitation. We recommend patients with severe mitral or aortic stenosis to be treated by percutaneous transvenous mitral commissurotomy or operation before pregnancy. Figure 4 shows a 31 year-old woman with severe mitral stenosis who showed worsening pulmonary hypertension during her pregnancy and needed medical treatment and a cesarean section.

In patients with mechanical valves, because warfarin is teratogenic, heparin is used from weeks 6 to 12 of gestation, and then they are followed by subcutaneous low-molecular-weight heparin or oral warfarin with another switch to heparin at weeks 34 to 36. The risk for bleeding and embolization is high for both mothers and children. We reported pregnancy outcome in women with prosthetic mechanical valve replacement[26]. Among 16 pregnancies in 12 women with mechanical heart valve, 8 women (50%) had cesarean live births. Two babies died during the neonatal period. Four cases ended in early miscarriage, and one case ended in intrauterine fetal death. Therapeutic abortion was performed in 3 cases. Three mothers developed valve thrombosis, and one died from heart failure.

3-4. Marfan's syndrome

During pregnancy, estrogen and other hormones make vessels more fragile, and as a result, in pregnant

women with Marfan's syndrome, the risk for aortic dissection is higher than in non-pregnant women. In patients with annuloaortic ectasia (≥ 44 mm), pregnancy without replacement surgery is contraindicated. At 40-44 mm, while the risks are high, pregnancy and delivery are possible with conservative therapy although weekly echocardiographic observation is desirable. At <40 mm, normal delivery is possible. Under general anesthesia, cesarean section is performed, and blood pressure and pain management are very important.

We reviewed 8 pregnant patients with Marfan's syndrome experienced in our hospital[27]. Aortic dissection occurred in 3 patients (37.5%), one of whom developed rapid dilatation of the ascending aorta during her pregnancy and needed Bentall operation. Luckily, however, all patients tolerated the pregnancy well, with favorable maternal and fetal outcomes. Follow-up echocardiography showed no apparent worsening of cardiovascular status attributable to pregnancy except for one patient. In conclusion, dilatation of the ascending aorta during pregnancy is an important predictor for aortic dissection, and echocardiography must be performed weekly or biweekly.

3-5. Cardiomyopathy

Among pregnant women with hypertrophic cardiomyopathy, maternal mortality is around 1%, and most patients can go through pregnancy. However, in about half of the patients who had symptoms before pregnancy, the NYHA functional class was exacerbated (NYHA class III/IV) during pregnancy[28]. We often recognize elevated intraventricular pressure gradient and pulmonary hypertension in obstructive patients. Figure 5 shows a clinical course of a pregnant woman with hypertrophic obstructive cardiomyopathy. In patients at high risk for sudden death, such as those with ≥ 30 mm maximum wall thickness, past history of cardiac arrest or ventricular tachycardia and family history of sudden death, it is essential to carefully monitor pregnancy and delivery.

In dilated cardiomyopathy, because prognosis is poor, especially for young patients, and most patients take medication such as an ACE inhibitor, very few patients become pregnant. In general, maternal prognosis is also poor, and as a result, caution must be exercised, even in patients with mild cardiac dysfunction. In our hospital, in fact, we experienced 4 maternal deaths (death within 2 years after delivery) out of 8 patients with cardiomyopathy[22]. Figure 6 shows

Fig. 5. The clinical course of a 30 year-old pregnant woman with hypertrophic obstructive cardiomyopathy

The patient was admitted during her 13th week of gestation. After she started to take cibenzoline, left ventricular outflow (LVOT) pressure gradient decreased from 109 mmHg to 28 mmHg and RA-RV pressure gradient derived by tricuspid regurgitant velocity (TRPG) also decreased. Then, the velocity gradually increased again, and additional medications were not effective to decrease it. At her 27th week of gestation, she started to complain of dyspnea on mild effort, and echocardiography showed increased left atrial (LA) dimension from 48 mm to 52 mm and increased mitral regurgitation from 2/4 to 3/4. She was taken for a cesarean section (CS) 3 days later. After delivery, LVOT pressure gradient decreased to around 30 mmHg.

Fig. 6. M-mode echocardiographic changes in a woman with dilated cardiomyopathy (DCM) during her pregnancy and after delivery

The patient was a 26 year-old woman with slightly dilated left ventricle and history of ventricular tachyarrhythmia. At 16th week of gestation, left ventricular end-diastolic/end-systolic dimensions (LVDd/Ds) were 53/33 mm with fractional shortening (FS) of 37.7% (a) and at 36th week of gestation, LVDd/Ds were 54/39 mm (FS, 27.8%) (b). At 8 weeks after delivery, LVDd/Ds were 54/38 mm (FS, 29.6%) (c). Even in a mild DCM patient, peripartum left ventricular function is decreased.

changes in cardiac function during pregnancy and after delivery in a patient with dilated cardiomyopathy.

In peripartum cardiomyopathy, cardiac function recovers in about half of patients, but in this relatively rare disease, 20% of patients die or require a heart transplant. In patients with a past history of peripartum cardiomyopathy, multiple deliveries would worsen cardiac function, and as a result, caution must be exercised if a patient becomes pregnant again. The risk for cardiac events during first or subsequent pregnancy is dependent on the severity of left ventricular dysfunction[29], and assessment of left ventricular function by echocardiography is important.

4. Conclusions

In pregnant women with heart diseases, echocardiography plays a very important role because it is noninvasive and does not expose the patients to radiation. Long-term maternal prognosis has not been fully clarified, and there have been few studies investigating the relationship between echocardiographic findings and prognosis. Moreover, there are no reports about changes of cardiac function during pregnancy mea-

sured by new echocardiographic techniques such as tissue Doppler imaging and three-dimensional echocardiography[30, 31]. Further investigations are thus warranted.

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