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Original article

Pregnancy outcomes in women with dilated cardiomyopathy: Peripartum cardiovascular events predict post delivery prognosis

Tae Yokouchi-Konishi (MD)[a,b], Chizuko A. Kamiya (MD, PhD, FJCC)[a,*], Tadasu Shionoiri (MD)[a], Atsushi Nakanishi (MD)[a], Naoko Iwanaga (MD, PhD)[a], Chisato Izumi (MD, PhD, FJCC)[c], Satoshi Yasuda (MD, PhD, FJCC)[c], Jun Yoshimatsu (MD, PhD)[a]

[a] Department of Obstetrics and Gynecology, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan
[b] Advanced Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan
[c] Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan

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ABSTRACT

Background: The number of pregnant women with dilated cardiomyopathy (DCM) is relatively small, and therefore their prognosis after pregnancy is unknown. This study aims to elucidate pregnancy outcomes among women with DCM, as well as the long-term prognosis after pregnancy.
Methods: Thirty-five pregnancies and deliveries in 30 women, diagnosed with DCM before pregnancy, were retrospectively analyzed.
Results: All women had a left ventricular ejection fraction (LVEF) over 30% and belonged to the New York Heart Association (NYHA) class I or II before pregnancy. The mean gestational age at delivery was 36 weeks with 15 (43%) preterm deliveries. Eight pregnancies (23%) were complicated by peripartum cardiac events including 1 ventricular arrhythmia, 6 heart failures, and 1 significant deterioration in LVEF requiring termination of pregnancy. NYHA class II, pre-pregnancy use of angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker/diuretics, elevated brain natriuretic peptide (BNP), and advanced diastolic dysfunction assessed by Doppler echocardiography were defined as risk factors for cardiac events. Although the more severe cases took beta-blockers during pregnancy, the rates of cardiac events and decreasing LVEF did not differ significantly between those taking beta-blockers and those who were not. Values of LVEF decreased by almost 10% after the average 4-year post-delivery follow-up period. The long-term event-free survival was considerably worse among women with peripartum cardiac events than in those without ($p < 0.0001$).
Conclusions: DCM women with pre-pregnancy LVEF over 30% tolerated pregnancy, but the rate of preterm delivery was high. Peripartum cardiovascular events occurred more often in women with NYHA class II, as well as those who received medications before and during pregnancy and showed more elevated BNP and advanced diastolic dysfunction before pregnancy. Beta-blockers likely allowed similar outcomes for DCM patients with lower initial LVEFs. Close monitoring later in life is required, particularly among the women with peripartum cardiac events.

Introduction

Dilated cardiomyopathy (DCM) is characterized by an enlarged left ventricle and systolic dysfunction. Pregnant patients with DCM are rare as a result of the disease severity in the young. Plasma volume and cardiac output increase by 40–50% and 30–50%, respectively during pregnancy [1], and the ability to adjust to these dynamic changes is of great clinical importance, especially in pregnant women with decreased cardiac function. The Japanese Circulation Society 2018 guideline [2] therefore advises against pregnancy in women with a left ventricular ejection fraction (LVEF) less than 35–40% while the World Health Organization classification of maternal cardiovascular risk uses a cut-off of 30% [3,4].

* Corresponding author at: Department of Obstetrics and Gynecology, National Cerebral and Cardiovascular Center, 6-1 Kishibeshimmachi, Suita, Osaka 564-8565, Japan.
E-mail address: chiz@ncvc.go.jp (C.A. Kamiya).

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A few studies have assessed the outcomes of pregnancies complicated by DCM and the risk factors for cardiovascular events during pregnancy [5–7]. However, the influence of medical therapy on pregnancy outcomes and long-term prognosis after pregnancy remains unknown. Beta-blockers are a widely used first-line treatment in chronic heart failure conditions including DCM, but their effect on pregnant DCM patients is not clear. Therefore, the aims of this study were 1) to review the outcomes of pregnant patients with DCM and the risk factors for peripartum cardiac events, 2) to examine the influence of beta-blockers during pregnancy on both cardiac function and complications, and 3) to follow-up patient's prognosis after delivery and analyze the relationship between peripartum cardiac events and long-term outcomes.

Materials and methods

This retrospective study analyzed the medical charts of women who were diagnosed with DCM prior to pregnancy and who delivered between January 2000 and July 2019 at the National Cerebral and Cardiovascular Center in Japan. DCM was defined by the presence of left ventricular or biventricular reduced systolic contraction in the absence of any other cause for such myocardial changes as per the guidelines and consensus document [8–10]. Women, who had a previous history of LVEF <45% and who were diagnosed with DCM through detailed examinations prior to pregnancy, were included in the study. There are 2 types of morphological DCM associated with pregnancy, preexisting DCM and peripartum cardiomyopathy (PPCM). The incidences of peripartum heart failure and poor perinatal outcomes are higher for PPCM than for preexisting DCM [9]. Thus distinguishing between these different types is important. Women diagnosed with DCM-like cardiomyopathy during pregnancy were excluded in order to ensure that all patients included in the study had preexisting DCM and not PPCM. This study received ethical approval from the institutional review board at the National Cerebral and Cardiovascular Center (M28-101).

The following baseline data were collected: age at diagnosis of DCM; age at the time of pregnancy; duration between DCM diagnosis and pregnancy; family history of DCM and cardiac death; history of cardiac events (heart failure, arrhythmia, and thromboembolism) after diagnosis of DCM and prior to pregnancy; the status of device implantation such as pacemakers (PM) and implantable cardiac defibrillators (ICD); smoking status; body mass index before pregnancy, and New York Heart Association (NYHA) class. The following obstetric data were collected: gestational age at delivery; mode of delivery; spontaneous or induced delivery, and small for gestational age (SGA). Adverse peripartum cardiac events during pregnancy and within 1 month after delivery were defined as heart failure with the existence and worsening of pulmonary hypertension; significant decrease in LVEF which required termination of pregnancy; new onset arrhythmia requiring treatment; thromboembolism; cardiac arrest or death.

Medication status, blood pressure, heart rate, values of brain natriuretic peptide (BNP), and echocardiographic assessments, including left ventricular end-diastolic/end-systolic diameter (LVDd/LVDs), LVEF, early to late diastolic transmitral flow velocity (E/A), deceleration time (DcT), E to early diastolic mitral annular tissue velocity (E/e), and valvular function, prior to pregnancy or at the latest during the first trimester, the second, and the third trimesters during pregnancy, within 1 week, 1–3 months, and 6–12 months after delivery and at the final follow up were reviewed and analyzed. LVEF was routinely measured using a modified Simpson method, or exceptionally by using the Teichholz method.

Statistical analysis

Data are presented as means ± SD or number of patients and were evaluated using Student *t*-tests or Mann-Whitney *U*-tests to compare continuous variables and categorical variables were evaluated using Fisher exact tests. The Holm-Sidak test was used for multiple comparisons. Elapsed time from delivery to cardiovascular events was analyzed using the Kaplan-Meier method with log-rank tests. Values with $p < 0.05$ were considered to indicate a significant difference in all statistical analyses. All analyses were performed using GraphPad Prism (version 7.0; GraphPad Software, Inc., La Jolla, CA, USA).

Results

Thirty-five pregnancies in thirty women were reviewed. Table 1 shows the baseline characteristics of the study population. An average LVEF at DCM diagnosis was 39.0%. Five women had a history of a cardiovascular events prior to their pregnancy: heart failure and arrhythmias in each of 3 women (including one with both of them). Four women had a device implanted before pregnancy; PM in 2 (for sick sinus syndrome in 1 and for advanced atrioventricular block in 1), ICD in 2 women (for primary prevention use in 1 and for secondary prevention use in 1). The average length of time from DCM diagnosis to pregnancy was 9 years. Twenty-four women were nulliparous. All women belonged to NYHA class I or II. Their LVEF prior to pregnancy was 30–44% in 12 pregnancies, 45–54% in 18 pregnancies, and ≥55% in 5 pregnancies of 5 women who were diagnosed as having DCM with LVEF <45% previously and recovered cardiac contraction before pregnancy. However, 3 of the 5 with LVEF ≥55% showed reduced LVEF during or right after pregnancy. The other 2 had a family history of DCM and showed re-decreased LVEF later, after pregnancy.

Most medications, except for angiotensin-converting-enzyme inhibitors (ACE-I) and angiotensin II receptor blockers (ARB), were continued after conception. Medications were administered during pregnancy to 26 patients (74.2%), including beta-blockers in 23 [65.7%; comprising carvedilol (n = 19), propranolol (n = 2), metoprolol (n = 1), and bisoprolol (n = 1)].

Cardiac outcomes

Eight (22.8%) pregnancies in 8 women experienced peripartum cardiac events; heart failure in 6, significant deterioration of LVEF in 1 and arrhythmia in 1 (Table 2). All cardiac events occurred either during the third trimester or postpartum. Four patients needed preterm delivery due to the cardiac events. All complications were treatable.

The background characteristics between women with and without peripartum cardiac events are compared in Table 1. There was no significant difference in blood pressure and heart rate between the groups, through pregnancy and postpartum. It is important to note that women with NYHA class II and women who received ACE-I or ARB and/or diuretics before pregnancy, and women who received diuretics during pregnancy were more likely to develop peripartum cardiac events. BNP levels were increased more in women with cardiac events than in those without. There were only 2 women whose BNP values were >100 pg/ml pre-pregnancy, and both were complicated with cardiac events (cases 4 and 6 in Table 2). Moreover, women with peripartum cardiac events showed more advanced diastolic dysfunction before, or in the first trimester, than those without.

Table 1
Baseline characteristics of 35 pregnancies in 30 patients.

Variable	All ($n=35$)	Cardiac events ($n=8$)	No cardiac events ($n=27$)	p[a]
Age at diagnosis as DCM (years)	21.2 ± 11.4	20.3 ± 14.1	21.4 ± 10.8	0.81
Age at the time of pregnancy (years)	31.3 ± 5.4	32.3 ± 5.2	31.0 ± 5.5	0.55
Years between diagnosis to pregnancy (years)	9.2 ± 8.5	11.8 ± 9.7	8.5 ± 8.2	0.34
BMI before pregnancy	21.5 ± 3.8	22.4 ± 4.6	21.3 ± 3.3	0.45
Smoking history[b]	4 (13.3%)	2 (25.0%)	3 (13.6%)	0.56
History of cardiac events[b]	5 (16.6%)	2 (25.0%)	3 (13.6%)	0.56
PM/ICD implantation[b]	4 (13.3%)	2 (25.0%)	2 (7.4%)	0.21
Family history[b]	9 (30.0%)	2 (25.0%)	15 (55.5%)	0.22
NYHA class before pregnancy				0.03
Class I	28 (80.0%)	4 (50.0%)	24 (88.8%)	
≤II	7 (20.0%)	4 (50.0%)	3 (11.1%)	
≥III	0	0	0	
Systolic blood pressure at the first pregnancy visit (mmHg)	105 ± 13	103 ± 8	106 ± 14	0.67
Diastolic blood pressure at the first pregnancy visit (mmHg)	62 ± 6	60 ± 5	62 ± 7	0.559
Heart rate at the first pregnancy visit (/minute)	74 ± 11	75 ± 11	74 ± 11	0.82
Echocardiography at time of DCM diagnosis	($n=21$)	($n=4$)	($n=17$)	
LVDd (mm)	55.0 ± 4.7	55.5 ± 1.3	55.0 ± 5.2	0.85
LVDs (mm)	42.8 ± 5.2	40.3 ± 3.0	43.4 ± 5.5	0.29
LVEF (%)	39.0 ± 7.8	41.6 ± 5.3	38.4 ± 8.3	0.47
Echocardiography before or during the first trimester				
LVDd (mm)	53.6 ± 5.1	55.9 ± 3.1	52.7 ± 5.6	0.13
LVDs (mm)	39.2 ± 5.7	41.6 ± 5.6	38.4 ± 5.7	0.16
LVEF (%)	46.4 ± 9.0	45.4 ± 6.2	48.6 ± 9.6	0.38
LVEF < 40%	6 (17.1%)	2 (25.0%)	4 (14.8%)	0.60
MR Moderate and severe	3 (8.5%)	1 (12.5%)	2 (7.4%)	0.55
TR Moderate and severe	3 (8.5%)	1 (12.5%)	2 (7.4%)	0.55
TMF E/A	2.1 ± 1.1	3.0 ± 2.0	1.8 ± 0.6	0.0008
TMF DcT (ms)	179 ± 44	154 ± 42	185 ± 43	0.08
TMF E/e'	7.8 ± 2.3	9.9 ± 2.8	7.4 ± 2.0	0.007
Values of BNP (pg/dl)[c]				
Before pregnancy	58.2 ± 64.7	135.6 ± 95.0	28.1 ± 20.2	0.0007
The third trimester	53.2 ± 79.5	149.8 ± 152.0	30.0 ± 26.7	0.0005
Within 1 week after delivery	89.9 ± 96.7	155.5 ± 111.5	71.9 ± 88.4	0.077
1 month after delivery	63.0 ± 94.2	187.8 ± 165.4	34.6 ± 35.1	0.0003
Medication before pregnancy	20 (57.1%)	6 (75.0%)	12 (44.4%)	0.22
ACE-I/ARB	7 (20.0%)	4 (50.0%)	3 (11.1%)	0.02
Beta-blockers	14 (40.0%)	5 (62.5%)	9 (33.3%)	0.22
Digoxin	3 (8.5%)	2 (25.0%)	1 (3.7%)	0.12
Diuretics	2 (5.7%)	2 (25.0%)	0	0.04
Anti-arrhythmic agents	5 (14.2%)	3 (37.5%)	2 (7.4%)	0.06
Medication during pregnancy	26 (74.2%)	7 (87.5%)	19 (70.3%)	0.64
ACE-I/ARB	0	0	0	
Beta-blockers	23 (65.7%)	5 (62.5%)	18 (66.6%)	0.99
Digoxin	2 (5.7%)	1 (12.5%)	1 (3.7%)	0.41
Diuretics	3 (8.5%)	3 (37.5%)	0	0.008
Anti-arrhythmic agents	6 (17.1%)	2 (25.0%)	4 (14.8%)	0.60

DCM, dilated cardiomyopathy; BMI, body mass index; PM, pacemaker; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; TR, tricuspid regurgitation; TMF, transmitral flow velocity pattern; E/A, early to late diastolic transmitral flow velocity; DcT, deceleration time; E/e', E to early diastolic mitral annular tissue velocity; BNP, brain natriuretic peptide; ACE-I/ARB, angiotensin-converting-enzyme inhibitor/angiotensin II receptor blocker.
[a] Between groups with and without cardiac events. Data are shown as means (± SD) or numbers (%).
[b] Percentage was calculated by the number of participants ($n=30$).
[c] Data were available in 29 pregnancies in 26 women (5 pregnancies in 5 women with cardiac events and 24 pregnancies in 21 women without cardiac events).

The mean LVEF prior to pregnancy; in the second trimester; the third trimester; within 1 week of delivery; at 1–3 months and 6–12 months after delivery were 47.1 ± 8.9%, 46.8 ± 8.8%, 44.7 ± 11.0%, 43.8 ± 12.2%, 45.6 ± 8.7%, and 46.4 ± 11.4%, respectively. The changes in LVEF were not significantly different at the different time points. Patients treated with beta-blockers had a significantly larger left ventricular diameter before pregnancy than those who were not: (LVDd: 54.5 ± 5.0 vs. 50.9 ± 5.1, $p = 0.04$; LVDs: 40.9 ± 5.5 vs. 35.0 ± 3.8, $p = 0.0007$). The LVEF prior to pregnancy in the beta-blocker group was also significantly lower than that in the group without beta-blockers ($p = 0.002$, Fig. 1). The change in LVEF in women treated with or without beta-blockers is shown in Fig. 1. No significant change of LVEF in each group was found at the different time points.

Obstetric outcomes

The mean gestational age at delivery was 36.2 ± 1.9 weeks. Five delivered vaginally, without induction. Of the 17 women who underwent induction of labor (cervical ripening and oxytocic agents, $n = 13$; oxytocic agents, $n = 4$), 10 delivered vaginally and 7 resulted in Cesarean section. Of the 22 women who tried to deliver vaginally, 15 (42.8%) had epidural anesthesia. Cesarean section was done for 20 (57.1%), and obstetric indications preceded half of them. The number who experienced obstetric complications was 16 (45.7%), including preterm deliveries before 37 weeks gestation in 15 (42.9%); before 34 weeks in 2 (5.7%), and SGA in 4 (11.4%). The number of obstetric complications was higher in women with larger LVDs (41.6 ± 6.3 vs. 37.3 ± 4.5, $p = 0.02$) and

Table 2
Details of women complicated with peripartum cardiac events.

Case	Age at DCM diagnosis (years)	Age at pregnancy (years)	NYHA class before pregnancy	LVEF before pregnancy[a]	ACE-I/ARB before pregnancy	Medication or device implantation at time of event	Gestational weeks at time of event	Perinatal cardiovascular events and clinical course
1	18	26	II	48%	–	Metoprolol ICD for primary prevention	29	VT (the first episode) → activated ICD → increased metoprolol
2	23	32	II	42%	–	Propranolol Heparin for PAF	31	Heart failure with LVEF 34% and pseudo VT → *termination at 31weeks of gestation* → started with ACE-I and switched from propranolol to carvedilol
3	26	38	I	48%	+	–	33	Heart failure with LVEF 25–30% → treated with diuretics → *termination at 34 weeks of gestation* → started with ACE-I and carvedilol
4	6	29	I	37%	–	Carvedilol, Spironolactone, Sotalol	32	Increased frequency of NSVT
							34	LVEF 25% → *termination at 34 weeks of gestation* → started with ARB
5	1	26	II	40%	+	Carvedilol, Digoxin, Furosemide, Spironolactone, Amiodarone, Mexiletine		A case with out-of-proportion PH and PAF
							34	Worsening PH (increased TRPG from 68 mmHg to 103 mmHg) → *termination at 34 weeks of gestation* → ICU treatment for 3days
6	36	39	II	53%	+	Carvedilol	12 34	Discontinuation of ARB right after conception and decreased LVEF35% at 12 weeks of gestation Heart failure with LVEF 44% → treated by diuretics → *induction at 37 weeks of gestation*
7	9	32	I	53%	–	–	37	Heart failure with LVEF 40–45% (increased TRPG from 24 mmHg to 43 mmHg) → *induction at 37 weeks of gestation* → treated with diuretics
8	34	36	II	45%	+	Heparin for chronic AF PM for SSS(III)	One day after delivery	Vaginal delivery at 37 weeks of gestation → congestive heart failure → treated with diuretics and catecholamine

DCM, dilated cardiomyopathy; NYHA, New York Heart Association; LVEF, left ventricular ejection function; ACE-I, angiotensin-conversion enzyme inhibitors; ARB, angiotensin receptor blocker; ICD, implantable cardioverter defibrillator; VT, ventricular tachycardia; PAF, paroxysmal atrial fibrillation; NSVT, non-sustained ventricular tachycardia; PH, pulmonary hypertension; TRPG, trans-tricuspid pressure gradient; ICU, intensive care unit; AF, atrial fibrillation; PM, pacemaker; SSS, sick sinus syndrome.
[a] LVEF at the first trimester of pregnancy is indicated if LVEF before pregnancy was unavailable.

LVEF < 40% (31.2% vs. 5.2%, $p = 0.04$) before pregnancy. The rate of SGA among women with beta-blockers during pregnancy was significantly greater than those without (17.4% vs 0%, $p = 0.03$). All neonates survived without major complications.

Long-term prognosis

The median follow-up period was 48 (2–183) months. At the final follow up, 17 (56.7%) patients were on medication, with 16 (53.3%) of these being on beta-blockers. The mean LVEF decreased from 47.1 ± 8.9% pre-pregnancy to 39.7 ± 8.6% at the last follow-up. Cardiovascular events occurred in 4 (13.3%) patients; 1 sudden cardiac death (22 months after delivery); 2 heart failures (at 4 months and 28 months after delivery, respectively) and 1 heart failure resulting in heart transplantation and cardiac death (at 24 and 84 months after delivery). All cases with cardiac events during the follow-up period were also complicated by peripartum cardiac events. Therefore, rates of long-term event-free survival were significantly worse in patients who experienced peripartum cardiovascular events than those who did not ($p < 0.0001$, log-rank test; Fig. 2).

Discussion

The pregnancy outcomes and the long-term prognoses of women diagnosed with DCM before pregnancy were analyzed. The

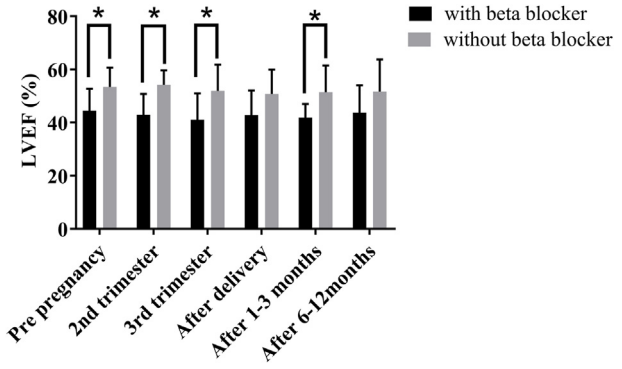

Fig. 1. LVEF changes in women with and without beta-blockers. The LVEF pre-pregnancy, in the second trimester, third trimester, within 1 week of delivery, and at 1–3 months and 6–12 months post-delivery, was significantly lower in the beta-blocker group than in the group without beta-blockers ($p = 0.02$, $p = 0.0006$, $p = 0.02$, $p = 0.01$, $p = 0.09$, and $p = 0.09$, respectively). No significant change in LVEF with or without beta-blockers was found at any of these time points. LVEF, left ventricular ejection function.

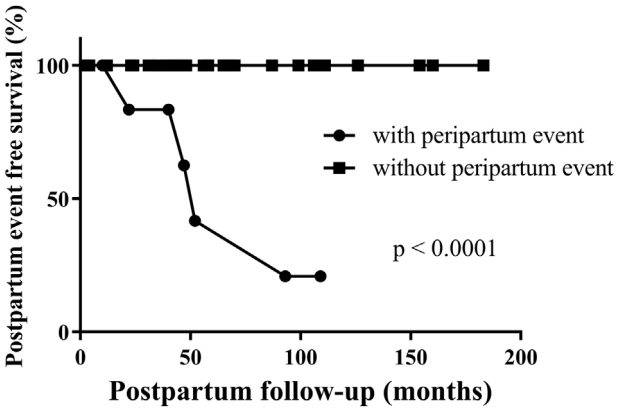

Fig. 2. Event-free survival rates in women with and without peripartum cardiac events. Event-free survival rates were worse for patients with adverse cardiovascular events during pregnancy ($p < 0.0001$). Follow-up period is defined as elapsed time from delivery to cardiovascular events and was analyzed using the Kaplan–Meier method with the log-rank test. Values with $p < 0.05$ are statistically significant.

study only included women with preexisting DCM and excluded women diagnosed with DCM-like cardiomyopathy during pregnancy such as PPCM. PPCM was defined as onset of cardiac failure in the last month of pregnancy or within 5 months of delivery without any an identifiable cause [11]. The outcomes of pregnancy in patients with preexisting DCM and in patients with PPCM are very different [12]. Moreover, Elkayam et al. defined 'pregnancy-associated cardiomyopathy' as a condition that was diagnosed during pregnancy (excluding in the last month) and reported similar clinical characteristics to those of PPCM [13]. The former study also showed that pregnancy outcomes were better among women with preexisting DCM than in those with 'pregnancy-associated cardiomyopathy' [6]. Thus, this study focused only on preexisting DCM.

All study participants displayed pre-pregnancy LVEF ≥30%, which were acceptable for pregnancy according to the guideline [4]. In such condition, most women tolerated pregnancy well. The incidence of peripartum cardiac events in our study was lower than in previous studies (23% compared to 39% [5] and 50% [14]). These previous studies included more severe patients, such as those with a LVEF <30–35% and NYHA ≥ class III, factors that are considered to confer higher risk during pregnancy. Other reports have found a similar cardiac event rate (25% [15]) or no cardiac events [7]. These studies, like ours, analyzed women with mild to moderate LV dysfunction. Generally, DCM women with mild to moderate LV dysfunction, such as LVEF ≥30–35%, seem to have preferable pregnancy outcomes.

Our study found that women with NYHA class II, as well as those who received ACE-I/ARB and/or diuretics before pregnancy, and diuretics during pregnancy, developed significantly more cardiac events than those without. NYHA classification has been one of the well-known risk factors of pregnancy in women with heart disease. Because ACE-I and ARB are known to cause fetal renal damage in pregnancy, these were discontinued before or right after conception among all women treated with them before pregnancy. All components of renin-angiotensin-aldosterone system are increased in pregnancy. Elevated renin activity has been demonstrated in patients with DCM and may lead to adverse effects, such as cardiac remodeling and sympathetic activation. Women with ACE-I/ARB should be informed about the pregnancy risk in preconception counseling and those women therefore need very careful monitoring after discontinuation of their ACE-I/ARB.

BNP levels before, during, and after pregnancy were significantly elevated in women with peripartum cardiac events. Due to the small number of study subjects, we did not analyze a cut-off value of BNP to predict peripartum cardiovascular events. The previous study of pregnancy with heart disease reported that a BNP >100 pg/ml during pregnancy was measured in all women with pregnancy-associated cardiac events, and a BNP ≤100 pg/ml had a negative predictive value of 100% [16]. In the study, all women who had a BNP >100 pg/ml before pregnancy were complicated with peripartum cardiac events. Therefore, 100 pg/ml of BNP may be a good index for a pregnancy risk, as well as other conditions or diseases.

Diastolic dysfunction, especially a restrictive pattern, by Doppler echocardiography was also one of the risk factors for peripartum cardiac events. Most cardiac events in the study were heart failure, and all instances of heart failure occurred after 31 weeks of gestation. This is compatible with the finding that heart failure during pregnancy among women with preexisting organic heart disease, appears to peak around the end of the second and the beginning of the third trimester, as plasma volume increases [14,17]. Two patients had heart failure with an almost preserved LVEF (Table 2, patients 6, 7). Excessive plasma volume and diastolic dysfunction (a restrictive condition) may explain that pathophysiology. Therefore, even the DCM women with mildly reduced LV contraction, but with more advanced diastolic dysfunction, are likely to be in need of careful follow-up during pregnancy.

Beta-blockers are well known to improve symptoms, cardiac function, and survival in DCM patients with congestive heart failure. Although the use of beta-blockers during pregnancy was previously reported to reduce adverse cardiac events in women with long QT syndrome [18] and Marfan syndrome [19], its efficacy in pregnant DCM women is unknown. In this study, patients treated with beta-blockers had significantly lower LVEF and a larger ventricular diameter before and during pregnancy than those without. That is, DCM patients with more severe disease tended to be treated with beta-blockers during pregnancy. However, no change in LVEF or rate of perinatal cardiac events was found between visits among women with or without beta-blockers during pregnancy. Previous studies have shown that moderate or severe left ventricular dysfunction was the main determinant of adverse maternal cardiac outcomes during pregnancy [17,20]. Considering these and our results, beta-blockers likely allow better outcomes for pregnant DCM patients with more severe disease.

The mean gestational age at delivery was 36.2 weeks, and half of the patients included in the study delivered preterm infants. The previously reported mean gestational ages at delivery are 38 and 34.0 weeks among women with preexisting DCM [5,12]. Thus our obstetric outcomes were similar to those that have been previously reported. There were several cases with SGA. We previously reported that beta-blocker use during pregnancy correlates with an elevated risk for SGA [21]. Wald et al. also reported that the risk factor for SGA among women with heart disease was conditions where cardiac output during pregnancy cannot be increased [22]. Fetal growth therefore needs to be carefully monitored in pregnant DCM women on beta-blockers and/or without reserve cardiac contractile capacity.

This study also examined the long-term prognosis of DCM women after pregnancy. The LVEF values of these patients however, decreased by almost 10% after the average 4-year post-delivery follow-up period. Women who experienced peripartum cardiac events, tended to experience repeat events within 3 years. One other study has investigated the prognosis of DCM patients after pregnancy. Although the follow-up period in that study is unclear, one of 8 patients was awaiting transplantation at 2 years after delivery [12]. Another report that discusses the prognosis post pregnancy, but only until 6 months postpartum, described that one of 36 patients developed heart failure at 16 weeks after delivery [5]. Our study found that the incidence of cardiovascular events during a median follow-up of 48 months was 13.3%. Although the exact reason for cardiac death remains unknown, death was sudden in one patient and was thought to be caused by an arrhythmia. It is therefore important to closely monitor not only cardiac dysfunction, but also to assess for arrhythmias. The development of cardiovascular events during pregnancy was a significant risk factor for future cardiovascular events within 3 years postpartum. One cohort study of women with congenital heart disease reported that adverse cardiac events during pregnancy are important and are associated with an increased risk of late cardiac events [23]. Our study found the same result in women with DCM. Pregnancy is often compared to a big stress test on maternal physical condition, including cardiovascular organs. Therefore, peripartum cardiac events may indicate reduced maternal cardiac reserve and/or high risk of arrhythmias. Therefore, patients with peripartum cardiac events should be closely monitored long-term post-delivery.

Study limitations

These findings should be interpreted as those of a relatively small, single-center study. The cases with LVEF $<$30% and NYHA $\geq$class III, factors considered to confer higher risk during pregnancy, were not included in this study. Because many of the study participants were not examined by a cardiopulmonary exercise test before pregnancy, their NYHA class was judged by their subjective symptoms. This is not an interventional study for medications, including beta-blockers. A large prospective study is therefore needed to clarify the long-term prognosis after delivery among women with DCM.

Conclusion

The incidences of peripartum cardiac and obstetrical events were 23% and 46%, respectively. Peripartum cardiovascular events occurred more often in women with NYHA class II, with more advanced diastolic dysfunction and those who received ACE-I/ARB and diuretics before pregnancy, as well as diuretics during pregnancy. The beta-blockers likely allowed better outcomes for pregnant DCM patients with more severe disease. The presence of cardiovascular events during pregnancy was associated with an increased risk of repeated cardiovascular events within 3 years of delivery. Close monitoring in later life is therefore required, particularly among women with peripartum cardiac events.

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Disclosures

The authors declare that there is no conflict of interest.

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