22) Macarthur A: Craniotomy for suprasellar meningioma during pregnancy: role of fetal monitoring. *Can J Anaesth* 51: 535–538, 2004
23) Reitman E, Flood P: Anaesthetic considerations for non-obstetric surgery during pregnancy. *Br J Anaesth* 107(Suppl 1): i72–78, 2011
24) Minielly R, Yuzpe AA, Drake CG: Subarachnoid hemorrhage secondary to ruptured cerebral aneurysm in pregnancy. *Obstet Gynecol* 53: 64–70, 1979
25) Newman B, Lam AM: Induced hypotension for clipping of a cerebral aneurysm during pregnancy: a case report and brief review. *Anesth Analg* 65: 675–678, 1986
26) Ito T, Toyoshima N, Takahashi H, Ozasa A, Nakajima K, Tatsumura M, Teragawa N, Nobuhara H, Iwanaga M: [Study by fetal movement meter of effects of general anesthesia on fetal movement and fetal cardiac rate]. *Obstetrical and Gynecological Practice* 39: 1115–1118, 1990 (Japanese)
27) Immer-Bansi A, Immer FF, Henle S, Spörri S, Petersen-Felix S: Unnecessary emergency caesarean section due to silent CTG during anaesthesia? *Br J Anaesth* 87: 791–793, 2001
28) ACOG Committee on Obstetric Practice: ACOG Committee Opinion Number 284, August 2003: Nonobstetric surgery in pregnancy. *Obstet Gynecol* 102: 431, 2003
29) Horrigan TJ, Villarreal R, Weinstein L: Are obstetrical personnel required for intraoperative fetal monitoring during nonobstetric surgery? *J Perinatol* 19: 124–126, 1999

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ORIGINAL ARTICLE
Myocardial Disease

Cardiovascular Events in Pregnancy With Hypertrophic Cardiomyopathy

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Background: The influence of the physiological circulatory changes during pregnancy on hypertrophic cardiomyopathy (HCM) is unclear. There have been no comprehensive studies of pregnant women with HCM in the Japanese population.

Methods and Results: A total of 27 pregnancies (23 women with HCM) were retrospectively reviewed. A total of 18 cardiovascular events occurred in 13 of the 27 pregnancies (48%), and 13 of these events (76%) were related to arrhythmia. The cardiovascular events tended to occur in the early stage of pregnancy (≈30 gestational weeks) or postpartum. The events related to arrhythmia mainly occurred in the early stage of pregnancy or at approximately 30 gestational weeks. Four pregnancies were terminated because of cardiovascular events. Cardiovascular events occurred in 8 of 9 pregnancies in women on medication before pregnancy (88%), 7 of 10 pregnancies with high CARPREG score (70%), and in 9 of 12 pregnancies with high ZAHARA score (75%).

Conclusions: Cardiovascular events occurred in more than half of the pregnant women complicated with HCM, and the arrhythmia is the most common cardiovascular event. Medication in the pre-pregnancy period, and CARPREG or ZAHARA score ≥1 were identified as risk factors of cardiac events during pregnancy or postpartum. (*Circ J* 2014; **78:** 2501–2506)

Key Words: Arrhythmia; CARPREG score; Hypertrophic cardiomyopathy; Pregnancy; ZAHARA score

Hypertrophic cardiomyopathy (HCM) is a disease that presents as cardiac muscle dilation with asymmetric diversity. The complications of HCM include arrhythmia, left ventricular outflow obstruction, and diastolic and partial systolic dysfunction because of the myocardial thickening. HCM may result in heart failure, thrombosis, atrial and ventricular arrhythmias, and sudden death, but is often asymptomatic. HCM is thought of as a rare disease, but a recent investigation showed a prevalence of approximately 1.8% in Japan, corresponding to an estimated 21,900 patients with HCM in Japan.[1,2] Therefore, HCM may be more common than previously thought, and this is a matter of concern in the context of pregnancy.

Editorial p2386

There are few reports on pregnancy in women with exacerbated cardiomyopathy, and the perinatal prognosis of this condition is unclear. The available reports include 7 studies of pregnancy with HCM.[3–9] In the first of these studies, which examined 13 pregnancies with HCM, Turner et al found that vaginal birth was not possible in 2 cases because of worsening angina and in 1 because of breathing difficulties.[3] Autore et al identified 98 survivors and 2 deaths during pregnancy among 100 women with HCM (199 pregnancies),[5] giving a maternal mortality of 10 in 1,000 live births (95% confidence interval 1.1–36.2/1,000), which is higher than that in normal pregnancy. An investigation of the morbidity rate in 40 pregnancies with HCM showed deterioration in New York Heart Association cardiac performance (NYHA class) in 1 of 28 women who were asymptomatic before pregnancy, and in 5 of 12 women who were symptomatic, thus indicating that the perinatal prognosis is excellent in patients who are asymptomatic before becoming pregnant.[5] In a comparison of nonpregnant and pregnant (n=23) women with HCM, the incidence of arrhythmia was higher in those who were pregnant (33.3% vs. 13.4%), but

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Table 1. Background of the 27 Pregnancies in 23 Women With HCM

Case no.	Age (years)	Parity	Complication	HOCM	D-HCM	Medication pre-pregnancy	NYHA class (pre-pregnancy)
1	25	0	TOF	–	–	–	1
2	25	0	No	+	–	Metoprolol, Verapamil	1
3	31	0	ITP	–	–	–	1
4	33	1	ITP	–	–	–	1
5	33	1	–	–	–	–	1
6	32	2	–	–	–	–	1
7	21	0	Bartter syndrome	–	–	–	1
8	32	0	–	+	–	Verapamil	1
9	39	0	–	+	–	–	1
10	30	0	–	+	–	Diltiazem	2
11	33	1	–	–	–	–	1
12	25	0	–	+	–	Mexiletine, Metoprolol	1
13	30	1	–	+	–	Mexiletine, Metoprolol	1
14	33	0	–	–	–	–	1
15	32	0	–	–	–	–	1
16	34	1	–	–	–	–	1
17	32	0	–	–	–	Propranolol	1
18	32	0	–	+	–	–	1
19	33	0	–	–	–	Diltiazem, Enalapril	1
20	34	1	–	–	–	–	1
21	29	0	–	–	–	–	1
22	33	1	–	–	–	–	1
23	31	1	–	–	–	–	1
24	27	0	–	–	–	–	1
25	33	0	–	–	–	Propranolol	1
26	35	1	–	–	–	–	1
27	28	0	–	–	–	Propranolol, Verapamil	1

D-DCM, dilated phase of hypertrophic cardiomyopathy (HCM); HOCM, hypertrophic obstructive cardiomyopathy; LADs, atrial diameter in endsystole; LVEF, left ventricular ejection fraction; LVOTO, left ventricular outflow tract obstruction; MR, mitral regurgitation; NYHA, New York Heart Association.

(**Table 1** continued the next page.)

heart failure and cardiac infarction rates did not differ significantly.[6] There were no deaths in either group, and pregnancy was assumed to have had no influence on the natural course of HCM. Cardiovascular events that required hospitalization increased when there was a family history (71.4% vs. 25.0%), which indicates the need to obtain a family medical history in the case of pregnancy with HCM.[6]

Pregnancy increases the circulating blood volume and cardiac output because of increases in the ventricular rate and stroke volume, while the peripheral vascular resistance decreases. The circulating blood volume increases more rapidly after 20 gestational weeks and reaches a plateau at 32 gestational weeks of 40–45% of the nonpregnant volume.[10,11] In HCM, the preload increase, afterload decrease and increase in cardiac contraction are precipitating factors because the ventricular blood volume decreases and left ventricular outflow obstruction deteriorates. The influence of these pregnancy-related physiologic changes on the circulation in HCM is not well understood. Therefore, in this the first study of this condition in Japan, we investigated the cardiovascular events that occurred during pregnancy with HCM.

Methods

We examined the outcomes of 27 pregnancies (23 women with HCM) between 1995 and 2013 at the Department of Perinatology, National Cerebral and Cardiovascular Center, Japan. HCM was diagnosed using the definition and type classification of cardiomyopathy published by the World Health Organization/International Society and Federation of Cardiology Joint Committee in 1995, by a cardiovascular physician based on medical history, physical findings, ECG, chest X-rays, an echocardiogram, and Doppler ultrasound. Radionuclide scans, computed tomography, magnetic resonance imaging, a cardiac catheter test, coronary arteriography, myocardial biopsy, and genetic diagnosis were performed when necessary. HCM was subcategorized into hypertrophic nonobstructive cardiomyopathy (HNCM), hypertrophic obstructive cardiomyopathy (HOCM), and dilated phase of HCM (D-HCM) with systolic dysfunction such as left ventricular ejection fraction (LVEF) <50%.

Information on maternal background was collected, including age, parity, complications, medications before pregnancy, NYHA class before pregnancy, family history of HCM, echocardiographic parameters; maximum wall thickness, LVEF, left atrial diameter in endsystole (LADs), mitral regurgitation (MR), and the pressure gradient (PG) of the left ventricular outflow tract obstruction (LVOTO), CARPREG score[12] and ZAHARA score[13] were retrospectively calculated. The CARPREG score is a contemporary assessment of maternal and neonatal risks

Case no.	LVEF <50%	Family history	LADs >50 mm	MR ≥moderate	LVOTO >50 mmHg	Maximau wall thickness >30 mm	ZAHARA score	CARPREG score
1	–	–	–	–	–	–	0	0
2	–	–	–	–	–	–	1.5	0
3	–	+	–	–	–	–	0	0
4	–	+	–	–	–	–	0	0
5	–	+	–	–	–	–	0	0
6	–	+	–	–	–	–	0	0
7	–	–	–	–	–	–	1.5	0
8	–	–	–	–	–	–	3	1
9	–	–	–	–	–	–	0	0
10	–	+	+	+	+	+	4.75	1
11	–	–	–	–	–	–	0	0
12	–	–	–	–	–	–	3	1
13	–	–	–	–	–	–	3	2
14	–	–	–	–	–	–	0	0
15	–	+	–	–	–	–	0	0
16	–	+	–	–	–	–	0	0
17	–	–	–	–	–	–	3	1
18	–	+	–	–	–	–	0	0
19	–	–	–	–	–	–	3	1
20	–	–	–	–	–	–	0	0
21	–	–	–	–	–	–	0	0
22	–	–	–	–	–	–	0	0
23	–	–	–	–	–	–	0	0
24	–	–	–	–	–	–	1.5	1
25	–	–	–	–	–	–	3	1.5
26	–	–	–	–	–	–	1.5	1
27	–	–	–	–	–	–	3	1.5

associated with pregnancy in women with heart disease who are receiving comprehensive prenatal care. Frequency of maternal primary cardiac events, as predicted by the risk index and observed in the derivation and validation groups, is expressed as a function of the number of cardiac predictors or points. The ZAHARA score is a modified risk score for cardiac complications during completed pregnancies in women with congenital heart disease.

Maternal and neonatal outcomes were examined, including cardiovascular events, NYHA class during pregnancy, NYHA class postpartum, gestational age, delivery mode, indication for cesarian section, birth weight, pH of the umbilical artery, and Apgar score at 5 min. Cardiovascular events were defined as new onset or worsening of arrhythmia, heart failure, endocarditis, or thromboembolic events that required medication, hospitalization, or termination of pregnancy. The gestational week of the occurrence of all cardiovascular events was recorded. Cardiovascular events were also classified as those related to arrhythmia or other than arrhythmia. The type of arrhythmia, gestational week of occurrence, and the detection method were recorded for each cardiovascular event related to arrhythmia.

Statistical Analysis

Univariate analysis by chi-squared test and the Cochran-Armitage trend test was used for statistical analysis. $P<0.05$ was considered significant.

Results

Maternal Background

Maternal background data for the 27 pregnancies (23 women) with HCM are shown in **Table 1**. The median age was 32 years (21–39 years). The mother was nulliparous in 17 pregnancies (63%) and multiparous in 10 (48%). Cases 3 and 4, 12 and 13, 15 and 16, and 21 and 22 relate to the same woman in each pair of cases (4 women). There were 17 women with HNCM, 6 with HOCM, and none D-HCM. One woman was complicated with tetralogy of Fallot after repair. Other maternal complicating diseases were idiopathic thrombocytopenic purpura and Bartter syndrome in 1 woman each. The medications administered before pregnancy were verapamil in 3 women, diltiazem in 2 women, β-blocker in 6 women, mexiletine in 2 women and angiotensin-converting enzyme inhibitor in 1 woman. A family history of HCM was identified in 6 women (26%). The NYHA class before pregnancy was I in all except 1 woman in class II (case 10) and that woman had LADs >50 mm, moderate MR, and a PG of LVOTO >50 mmHg. Among the other women with HOCM, the PG of LVOTO before pregnancy or in early pregnancy was between 15 and 35 mmHg. Therefore, all of the patients, except for the woman in case 10, were in good general condition.

Pregnancy Outcomes

Maternal and neonatal outcomes for the 27 pregnancies (23 women) with HCM are shown in **Tables 2,3**. A total of 17 cardiovascular events occurred in 13 pregnancies (48%), includ-

Table 2. Outcomes of the 27 Pregnancies in 23 Women With HCM

Case no.	Cardiovascular event	Gestational week	NYHA class (pregnancy)	NYHA class (postpartum)	Gestational age (weeks)	Delivery mode	Indication of CS	Birth weight (g)	UA pH	APS (5 min)
1	No		1	1	36	VD		2,690	7.36	9
2	Yes	30	1	1	38	VD		2,822	7.33	9
3	Yes	30	1	1	38	CS	NRFS	2,286	7.28	9
4	Yes	13	1	1	37	CS	Previous CS	2,940	7.35	9
5	Yes	32	1	1	40	VD		3,190	7.32	9
6	No		1	1	38	VD		2,724	7.25	9
7	Yes	32	1	1	36	VD		2,426	7.31	9
8	Yes	12, 31	1	1	31	CS	Heart	1,512	7.25	6
9	No		1	1	40	VD		3,016	7.32	9
10	Yes	13, 27	3	2	27	CS	Heart	850	7.29	5
11	Yes	32, 36	3	1	36	CS	Heart	2,250	7.21	7
12	Yes	13, 29	1	1	29	CS	Heart	1,013	7.33	3
13	Yes	Postpartum	1	1	37	CS	Previous CS	2,070	7.35	8
14	No		1	1	37	VD		2,326	7.24	10
15	No		1	1	39	VD		2,562	7.25	9
16	No		1	1	38	VD		3,124	7.38	10
17	Yes	31	1	1	39	VD		2,250	7.306	9
18	No		1	1	37	VD		2,874	7.201	8
19	Yes	Postpartum	1	1	37	VD		2,533	7.26	9
20	No		1	1	37	VD		3,364	7.35	9
21	No		1	1	38	VD		2,858	7.27	8
22	No		1	1	40	VD		3,054	7.29	8
23	No		1	1	39	CS	Previous CS	3,008	7.28	9
24	No		1	1	34	VD		2,434	7.35	10
25	Yes	24	1	1	39	CS	CPD	3,994	7.34	9
26	No		1	1	37	VD		2,674	7.29	10
27	Yes	Postpartum	1	1	38	VD		2,646	7.27	8

CPD, cephalopelvic disproportion; CS, cesarean section; NRFS, non-reassuring fetal status; UA, umbilical artery; VD, vaginal delivery. Other abbreviations as in Table 1.

Table 3. Summary of Maternal Outcomes of 27 Pregnancies With HCM

Cardiovascular event	14/27 (52%)
Termination of pregnancy because of cardiovascular event	4/27 (15%)
Worsening of NYHA class during pregnancy	2/27 (7%)
Preterm birth	7/27 (26%)

Abbreviations as in Table 1.

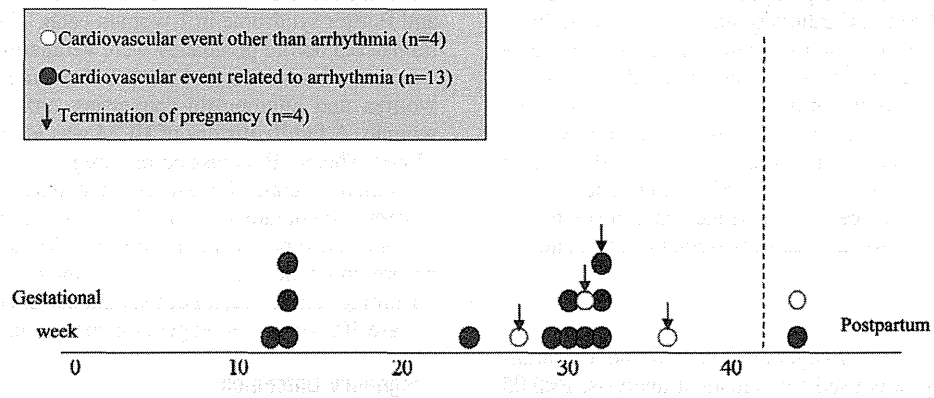

Figure. Cardiovascular events and gestational weeks (n=18).

Table 4. Arrhythmic Cardiovascular Events (n=13) During 27 Pregnancies in 23 Women With HCM

Case no.	Type of arrhythmia	Period (week)	Correspondence	Antiarrhythmic drug	Dose (mg)
2	PVC	30	Antiarrhythmic drug started	Metoprolol	30
3	NSVT	30	Antiarrhythmic drug started	Metoprolol	60
4	NSVT	13	Antiarrhythmic drug started	Propranolol	60
5	NSVT	32	Antiarrhythmic drug started	Metoprolol	40
7	PVC, PAC	32	Antiarrhythmic drug started	Metoprolol	40
8	PVC	12	Antiarrhythmic drug started	Bisoprolol	2.5
10	PVC	13	Antiarrhythmic drug started	Propranolol	60
11	NSVT	32	Antiarrhythmic drug started	Atenolol	25
12	NSVT	13	Antiarrhythmic drug increased	Metoprolol	40→60
12	NSVT	29	CS	–	–
17	PVC	31	Antiarrhythmic drug started	Propranolol	20
25	VT	24	Antiarrhythmic drug started	Carvedilol	10
27	PVC	Postpartum	Antiarrhythmic drug increased	Propranolol	60→80

NSVT, nonsustained ventricular tachycardia (VT); PAC, premature atrial contraction; PVC, premature ventricular contraction. Other abbreviations as in Tables 1,2.

ing 13 events (76%) related to arrhythmia (**Table 4**). Arrhythmia was the most common cardiovascular event. The cardiovascular events occurred in the early stage of pregnancy at approximately 30 gestational weeks, or postpartum (**Figure**). The events related to arrhythmia mainly occurred in the early stage of pregnancy or at approximately 30 gestational weeks. A total of 4 pregnancies were terminated because of a cardiovascular event (cases 8, 10, 11, 12). In case 8, the pregnancy was terminated at 31 gestational weeks because the mother was developing pulmonary hypertension and the PG of LVOTO had increased rapidly (peak PG 57 mmHg). Postpartum, the PG returned to the pre-pregnancy value. In cases 10 and 11, pregnancy was terminated at 27 and 36 gestational weeks, respectively, because in both cases there was an increased PG of LVOTO resulting from increased preload, and the mothers developed lung edema. After termination, the lung edema improved in both cases. In case 12, the pregnancy was terminated because nonsustained ventricular tachycardia (NSVT) could not be controlled with drug therapy. Thus, 3 of the 4 pregnancies (75%) were terminated because of a cardiovascular event in the mother who had started or increased her dose of antiarrhythmic drugs.

Premature delivery occurred in 7 of the 27 pregnancies (26%) because of cardiovascular events in 4 cases (57%) and obstetric complications (threatened premature labor) in 3 cases.

When comparing the pregnancies complicated by cardiovascular events with those unaffected by such events, the NYHA class before pregnancy, and echocardiographic parameters (LVEF, LADs, MR, LVOTO, maximum wall thickness) could not be analyzed because of the small number of positive findings. HOCM or family history of HCM were not risk factors (P=0.22, P=0.90). In the current study, medication in the pre-pregnancy period and CARPREG or ZAHARA score ≥1 or more were identified as risk factors of cardiac events during pregnancy or postpartum (**Table 5**).

Table 5. Relation of Cardiovascular Event and ZAHARA/CARPERG Score and Pre-Pregnancy Medication in 23 Women With HCM

	Cardiovascular events	P value
HCM		
No	8/20 (40%)	NS
Yes	5/7 (71%)	
D-HCM		
No	13/27 (48%)	NS
Yes	0/0 (0%)	
Medication (pre-pregnancy)		
No	5/18 (28%)	<0.05
Yes	8/9 (88%)	
NYHA class (pre-pregnancy)		
1	12/26 (46%)	NS
≥2	1/1 (100%)	
LVEF <50%		
No	13/27 (48%)	NS
Yes	0/0 (0%)	
Family history		
No	9/19 (33%)	NS
Yes	4/8 (50%)	
LADs >50 mm		
No	12/26 (46%)	NS
Yes	1/1 (100%)	
MR ≥ moderate		
No	12/26 (46%)	NS
Yes	1/1 (100%)	
LVOTO >50 mmHg		
No	12/26 (46%)	NS
Yes	1/1 (100%)	
Maximum wall thickness >30 mm		
No	12/26 (46%)	NS
Yes	1/1 (100%)	
High CARPREG score		
0	6/17 (35%)	<0.05
≥1	7/10 (70%)	
High ZAHARA score		
0	4/15 (26%)	<0.05
≥1	9/12 (75%)	

NS, not significant. Other abbreviations as in Table 1.

Discussion

A cardiovascular event related to HCM occurred in 13 of 27 pregnancies. Cardiovascular events showed 3 peak times of occurrence: early pregnancy, approximately 30 gestational weeks, and postpartum. In previous similar studies,[3–8] women who were symptomatic before pregnancy and who had a family history were at risk of cardiovascular events during their

pregnancies. Our new findings are that risk factors of cardiovascular events were medication before pregnancy and higher CARPREG or ZAHARA score.

The frequency of cardiovascular events (48%) is similar to the 28–73% reported in previous studies.[3–9] Collectively the findings show there is a high frequency of cardiovascular events in pregnancy for women with HCM. In the present study, 13 of the 18 events were related to arrhythmia, indicating that many of the cardiovascular events in pregnancy with HCM involve arrhythmia. Mostly, it was ventricular arrhythmias, including premature ventricular contraction and NSVT, and in some cases they were not controllable by medication, which is unusual. These findings indicate the importance of recognizing arrhythmia as a probable cardiovascular event in a pregnant woman with HCM.

Cardiovascular events occurred most frequently at approximately 30 gestational weeks. The increase in the circulating blood volume at 32 gestational weeks reaches 40–45% of the nonpregnant level, and it is notable that the most frequent period of cardiovascular events coincided approximately with the period of peak circulating blood volume during pregnancy. In 3 of the 4 pregnancies terminated because of a cardiovascular event, the event occurred during this period, which suggests that such cases require strict management and medication in the early stage of pregnancy.

Medication before pregnancy and higher CARPREG or ZAHARA score were risk factors for experiencing a cardiovascular event during pregnancy. However, further accumulation of cases and a study of multiple factors are required. These additional factors should include the general condition of the HCM patient, which appeared to influence the outcome in this study, and the observations from previous studies, which include an excellent perinatal prognosis in patients who are asymptomatic before pregnancy,[5] family history,[8] the apparent lack of influence of pregnancy on the natural course of HCM, and the tendency for a good prognosis when no symptoms are present before pregnancy.[7] Consideration of the timing of cardiovascular events may also be included in this analysis, given our finding of a high frequency of cardiovascular events in the early stage of pregnancy, at approximately 30 gestational weeks, and postpartum. Medication in the pre-pregnancy period, and CARPREG or ZAHARA score ≥1 were identified as risk factors of cardiac events during pregnancy or postpartum. However, this study was a retrospective analysis with the limitations of a small number of patients and the rarity of the condition.

Conclusions

If a pregnant woman with HCM has such factors as medication in the pre-pregnancy period or CARPREG or ZAHARA score ≥1, careful observation for cardiovascular events is required, especially at approximately 12 and 30 weeks' gestation and also postpartum.

References

1. Miura K, Nakagawa H, Morikawa Y, Nishikawa T, Yamamoto E, Ohki H, et al. Epidemiology of idiopathic cardiomyopathy in Japan: Results from a nationwide survey. *Heart* 2002; **87:** 126–130.
2. Matsumori A, Furukawa Y, Hasegawa K, Sato Y, Nakagawa H, Morikawa Y, et al. Epidemiology and clinical characteristics of cardiomyopathies in Japan: Results from nationwide surveys. *Circ J* 2002; **66:** 323–336.
3. Turner GM, Oakley CM, Dixon HG. Management of pregnancy complicated by hypertrophic obstructive cardiomyopathy. *BMJ* 1968; **4:** 281–284.
4. Oakley GD, McGarry K, Limb DG, Oakley CM. Management of pregnancy in patients with hypertrophic cardiomyopathy. *BMJ* 1979; **1:** 1749–1750.
5. Autore C, Conte MR, Piccininno M, Bernabò P, Bonfiglio G, Bruzzi P, et al. Risk associated with pregnancy in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002; **40:** 1864–1869.
6. Avila WS, Rossi EG, Ramires JA, Grinberg M, Bortolotto MR, Zugaib M, et al. Pregnancy in patients with heart disease: Experience with 1,000 cases. *Clin Cardiol* 2003; **26:** 135–142.
7. Thaman R, Varnava A, Hamid MS, Firoozi S, Sachdev B, Condon M, et al. Pregnancy-related complications in women with hypertrophic cardiomyopathy. *Heart* 2003; **89:** 752–756.
8. Avila WS, Amaral FM, Ramires JA, Rossi EG, Grinberg M, Bortolotto MR, et al. Influence of pregnancy on clinical course and fetal outcome of women with hypertrophic cardiomyopathy. *Arq Bras Cardiol* 2007; **88:** 480–485.
9. Siu SC, Sermer M, Colman JM, Alvarez AN, Mercier LA, Morton BC, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation* 2001; **104:** 515–521.
10. Katsuragi S. Maternal outcome in pregnancy complicated with pulmonary arterial hypertension. *Circ J* 2012; **76:** 2249–2254.
11. Kamiya CA. Outcome of pregnancy and effects on the right heart in women with repaired tetralogy of Fallot. *Circ J* 2012; **76:** 957–963.
12. Siu SC, Sermer M, Colman JM. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation* 2001; **104:** 515–521.
13. Drenthen W, Boersma E, Balci A. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J* 2010; **31:** 2124–2132.

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CLINICAL ARTICLE

Safety of induced abortions at less than 12 weeks of pregnancy in Japan

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Vacuum aspiration

ABSTRACT

Objective: To assess the safety of various methods of induced abortion when used before 12 weeks of pregnancy in Japan. *Methods:* A retrospective study was undertaken of induced abortions conducted between January 1 and December 31, 2012. Questionnaires were sent to 4154 institutions that employed doctors who were licensed to conduct induced abortions. Information was obtained about the numbers of induced abortions performed before 12 weeks, methods, complications, and routine management. *Results:* Completed questionnaires from 2434 institutions showed that 100 851 induced abortions had been performed. Vacuum aspiration (VA) was used in 20 458 (20.3%) abortions, VA with sharp curettage in 47 148 (46.8%), dilatation and curettage (D&C) in 32 958 (32.7%), and medical abortion in 287 (0.3%). Overall, 358 complications were reported (355.0 per 100 000 procedures). The rate of complications was significantly higher after D&C than after VA and after VA with sharp curettage ($P < 0.001$ for both). However, incomplete abortion requiring repeat procedures was the only complication that was significantly associated with D&C ($P < 0.001$). *Conclusion:* D&C can be safely used for induced abortion before 12 weeks of pregnancy, but changing from D&C to VA could reduce incomplete abortions and improve the safety of induced abortions before 12 weeks of pregnancy in Japan.

1. Introduction

After evaluation of several proposed methods for induced abortion during the first trimester, WHO has recommended the adoption of vacuum aspiration (VA) or medical methods using mifepristone and misoprostol to ensure procedures are both safe and effective [1,2]. The organization also stated that dilatation and curettage (D&C) should be replaced by VA to improve safety and quality of care for women [2]. The rationale for this guidance was based on previous studies in which D&C was found to be less safe [3], substantially slower, and associated with more blood loss [4] than was VA. Furthermore, rates of major complications are higher with D&C than VA [5].

The potential risks of D&C have been known since the 1970s [3–5]. Nevertheless, some support exists for the clinical acceptability of this procedure. Kulier et al. [6] conducted a systematic review of randomized controlled trials of different surgical methods for induced abortion during the first trimester and concluded that the incidences of complications were not markedly different between D&C and VA. The only difference observed between these two methods was the operation time, which was lower for VA than D&C. A study conducted by Niinimäki et al. [7] analyzed 42 619 induced first trimester abortions in Finland, and showed that medical abortions were more likely to be associated with bleeding and re-evacuation than were surgical methods of induced abortion, including VA and D&C. Although surgical abortions led to injury more often than did medical abortions, the overall incidence of such injuries was rare [7]. Consequently, Niinimäki et al. concluded that both VA and D&C could be considered generally safe and clinically acceptable methods for induced abortion.

In the USA, 80% of induced abortions were performed by surgical methods in 2010 [8]; furthermore, most of the procedures since 1995 have involved VA [3]. In England and Wales in 2012, sharp curettage was no longer used, although 50% of abortions were performed by surgical methods [9]. However, D&C still remains one of the most frequently used procedures for induced abortion in Japan [10], with medical abortions using mifepristone or misoprostol not yet legally accepted. The aim of the present study was, therefore, to elucidate the safety of various methods of induced abortion used before 12 weeks of pregnancy in Japan.

2. Materials and methods

A retrospective study was undertaken of induced abortions performed before 12 weeks of pregnancy between January 1 and December 31, 2012. The Japan Association of Obstetricians and Gynecologists provided a list of hospitals that employed doctors licensed to perform induced abortions, and questionnaires were mailed on September 5, 2013, to the Departments of Obstetrics and Gynecology of 4154

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Japanese institutions (1171 hospitals and 2983 clinics). Managers of the departments were asked to complete the questionnaire. Completion and return of the study questionnaire was considered as consent to participate in the present study. Approval was obtained from the ethics committees of the coordinating center (Tama Nagayama Hospital, Nippon Medical School, Tokyo) and the Japan Association of Obstetricians and Gynecologists. The present study conformed to the principles of the Declaration of Helsinki.

The questionnaire obtained information about the number of induced abortions performed before 12 weeks of pregnancy, methods used, complications, and routine management approaches before and during the procedure. Complications were subdivided into uterine perforation, cervical injury, gross bleeding, pelvic infection requiring hospital admission, thromboembolism, anaphylaxis, incomplete abortion requiring repeat procedures, and other types of complication. Routine management approaches included preoperative examination, cervical preparation, monitoring and treatment during the procedure, and use of anesthetics. Responses were confidential and data that might reveal the identity of the patients were not requested.

Data were analyzed using SPSS version 17.0 (SPSS Inc, Chicago, IL, USA). Categorical variables were evaluated using χ^2 or Fisher exact tests with Bonferroni correction. $P < 0.05$ was considered statistically significant.

3. Results

Completed questionnaires were received from 2434 (58.6%) of the 4154 institutions, including 738 (63.0%) of the 1171 hospitals and 1696 (56.9%) of the 2983 clinics. A total of 100 851 induced abortions were performed before 12 weeks of pregnancy, of which 15 946 (15.8%) were performed in hospitals and 84 905 (84.2%) in clinics. Induced abortions had been performed at 1963 institutions, of which 543 (27.7%) were hospitals and 1420 (72.3%) clinics.

The most frequently used method to induce abortion was VA with sharp curettage, whereas medical methods were used rarely (Table 1). Blood cell count, blood group typing, and screening for infection were the most frequently performed preoperative tests (Table 2). Cervical preparation using an osmotic dilator was conducted at 1288 institutions (65.6%). Cervical preparation was performed at 445 (82.0%) hospitals and 843 (59.4%) clinics. Intravenous infusion, oxygen saturation monitoring, and automatic blood pressure monitoring were used during procedures at many institutions (Table 2). The most frequently used anesthetics were thiamylal or thiopental (Table 2).

Overall, 358 (0.4%) of the induced abortions had complications, equivalent to a total complication rate of 355.0 per 100 000 induced abortions. Among the 358 complications, 295 (82.4%) were incomplete abortions, 19 (5.3%) uterine perforations, 17 (4.7%) gross bleeding, 12 (3.4%) anaphylaxis, 3 (0.8%) pelvic infections requiring hospitalization, 2 (0.6%) cervical injuries, and 10 (2.8%) other (Table 3). No instances of thromboembolism or maternal death were recorded.

Rates of complications, and specifically incomplete abortions, were significantly higher after D&C than after VA and after VA with sharp curettage ($P < 0.001$ for all) (Table 3). The rates of complications and incomplete abortions were also higher for VA with sharp curettage than for VA alone ($P < 0.001$ for both) (Table 3). The rates of uterine perforation and gross bleeding were not significantly different among the three surgical methods (Table 3). The rates of uterine perforation and gross bleeding were significantly lower after VA (1 in 20 458 and 2 in 20 458, respectively) than after medical abortion (0 in 287 for both; $P < 0.001$ and $P = 0.004$, respectively).

Cervical preparation was associated with increased rates of total complications and incomplete abortions (Table 4). By contrast, the use of ultrasonography during surgical abortion did not influence the rates of complications (Table 4).

Table 1
Methods used for induced abortion before 12 weeks of pregnancy (n = 100 851).

Method	No. (%)
Vacuum aspiration	20 458 (20.3)
Vacuum aspiration with sharp curettage	47 148 (46.8)
Dilatation and curettage	32 958 (32.7)
Medical abortion	287 (0.3)

Table 2
Routine management of women undergoing induced abortion before 12 weeks of pregnancy within the 1963 participating institutions.

Management approach	No. (%)
Preoperative examination	
Blood cell count	889 (45.3)
Blood group typing	839 (42.7)
Screening for infection	733 (37.3)
Laboratory test[a]	366 (18.6)
Electrocardiograph	300 (15.3)
Blood coagulation test	192 (9.8)
Irregular antibody screening	125 (6.4)
Chest radiograph	35 (1.8)
Cervical preparation	
Yes	1288 (65.6)
No	675 (34.4)
Monitoring and treatments during the procedure	
Intravenous infusion	1770 (90.2)
Oxygen saturation monitoring	1615 (82.3)
Automatic blood pressure monitoring	1508 (76.8)
Electrocardiogram monitoring	1110 (56.5)
Ultrasound-guided procedure	777 (39.6)
Use of anesthetic	
Thiamylal or thiopental	937 (47.7)
Pentazocine	882 (44.9)
Diazepam	715 (36.4)
Ketamine	538 (27.4)
Propofol	420 (21.4)

[a] Measurements of aspartate transaminase, alanine transaminase, lactate dehydrogenase, blood urea nitrogen, and creatinine.

4. Discussion

The present study found that sharp curettage (either as D&C or with VA) was used in 79.5% of induced abortions performed before 12 weeks of pregnancy in Japan. Nevertheless, the rates of complications were increased when this method was used, either as part of D&C or with VA. The most frequent complication overall was incomplete abortion. By contrast, other complications, including uterine perforation and gross bleeding, were rarely reported and no maternal deaths occurred.

A report published in 2007 by the Society of Family Planning [11] showed that the incidences of major complications, uterine perforation, and cervical injury associated with surgical abortion performed during the first trimester in the USA were less than 1000, 10–400, and 10–1000 per 100 000 induced abortions, respectively. The Royal College of Obstetricians and Gynaecologists in the UK investigated complications following either medical or surgical abortion during the first trimester [5]. For medical abortion, rates of uterine rupture and severe bleeding requiring transfusion were both less than 100 per 100 000 induced abortions. For surgical abortion, the rates of uterine perforation and cervical injury were 100–400 and less than 1000 per 100 000 induced abortions, respectively. Failure to end pregnancy was the most frequent complication reported overall (1000 per 100 000 induced abortions) [5,7,9,12]. Consequently, the findings of the present study regarding rates of complications were similar to previous reports.

Nonetheless, the observed rates of total complications and incomplete abortions in the present study differed according to the method of induced abortion used. The use of VA alone seemed to be associated with the lowest incidence of incomplete abortion. The reason why this method was advantageous is unclear. It is possible that clinicians

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Table 3
Complications associated with each method of induced abortion.

Method	Number of procedures in which method used	Total complications			Incomplete abortion			Uterine perforation			Gross bleeding		
		No. (%)	Rate[a]	*P* value[b]	No. (%)	Rate[a]	*P* value[b]	No. (%)	Rate[a]	*P* value[b]	No. (%)	Rate[a]	*P* value[b]
Vacuum aspiration	20 458	23 (0.1)	112.4	NA	20 (0.1)	97.8	NA	1 (<0.1)	4.9	NA	2 (<0.1)	9.8	NA
Vacuum aspiration with sharp curettage	47 148	139 (0.3)	294.8	<0.001[c]	107 (0.2)	226.9	<0.001[c]	6 (<0.1)	12.7	0.611[c]	9 (<0.1)	19.1	0.586[c]
Dilatation and curettage	32 958	194 (0.6)	588.6	<0.001[c] <0.001[d]	166 (0.5)	503.7	<0.001[c] <0.001[d]	12 (<0.1)	36.4	0.047[c] 0.028[d]	6 (<0.1)	18.2	0.682[c] 0.863[d]
Medical abortion	287	2 (0.7)	696.9	0.048[c] 0.482[d] 0.882[e]	2 (0.7)	696.9	0.029[c] 0.299[d] 0.967[e]	0	0.0	<0.001[c] 0.015[d] 0.216[e]	0	0.0	0.004[c] 0.055[d] 0.048[e]
Total	100 851	358 (0.4)	355.0	NA	295 (0.3)	292.5	NA	19 (<0.1)	18.8	NA	17 (<0.1)	16.9	NA

Abbreviation: NA, not applicable.
[a] Per 100 000 induced abortions performed by that method.
[b] For comparisons of rates.
[c] Versus vacuum aspiration.
[d] Versus vacuum aspiration with sharp curettage.
[e] Versus dilatation and curettage.

might tend to use sharp curettage in combination with VA for the management of technically difficult abortions, in which complications are likely irrespective of the use of sharp curettage.

Cervical preparation has been recommended when using surgical methods [5] or for high-risk patients with cervical injury and uterine perforation [2]. Both mechanical and medical cervical dilatations can shorten induced abortion procedures; however, the optimum gestational period at which cervical preparation should be performed has not yet been identified [13]. In the present study, routine cervical preparation was performed in 65.6% of all institutions. Nevertheless, use of this treatment was unexpectedly related to a high incidence of incomplete abortion. This result could reflect the fact that cervical preparation was more frequently performed in hospitals than in clinics, and women referred to hospitals from clinics could be at increased risk of incomplete abortion.

Ultrasound-guided procedures have been recommended for D&C performed after 14 weeks of pregnancy [5], but the effect of this approach during the first trimester is unclear [2]. In the present study, the routine use of ultrasonography during induced abortions conducted before 12 weeks of pregnancy did not decrease the rates of complications. Although ultrasound-guided procedures are not routinely required during the first trimester in Japan, they could be effective for some patients, such as women with multiple uterine myoma, a uterine anomaly, or a history of uterine surgery.

The use of anesthesia during surgical abortions remains controversial. Although no difference was reported in the incidences of complications between general and local anesthesia in one study [14], it has been suggested that paracervical block [2] and non-steroidal anti-inflammatory drugs [5] should be used instead of general anesthesia during routine procedures because of quick recovery and low cost. In the present study, general anesthesia was widely used for first trimester abortions. However, intravenous infusion, electrocardiogram monitoring, automatic blood pressure monitoring, and oxygen saturation monitoring were also frequently used during surgical methods preformed under general anesthesia. These treatments and monitoring methods are postulated to have effectively prevented adverse effects related to general anesthesia.

The main limitations of the present study were the retrospective design and the fact that the data were collected using questionnaires, which were completed by only 58.6% of the institutions that were invited to participate. Furthermore, the effects of cervical dilatation and ultrasound-guided procedures on prevention of complications were not analyzed for each patient because individual medical records were not obtained.

Furthermore, the legal and social context of induced abortion differs among countries. Mifepristone and misoprostol are not currently available for induced abortion in Japan; however, surgical procedures can be provided with general anesthesia and sufficient monitoring of vital signs. A total of 287 medical abortions were reported in the present study, but the medication used was not asked. In regions where medical abortion using mifepristone and misoprostol is available, it is possible that this method has advantages over surgical abortion in terms of accessibility, safety, and cost-effectiveness.

In conclusion, although D&C was used in almost one-third of induced abortions conducted at less than 12 weeks of gestation in Japan, the incidence of total complications was comparable to that in other high-income countries that predominantly use VA and medical methods. However, use of VA rather than D&C could decrease the incidence of incomplete abortions, the need for repeat procedures, and further improve the safety of early abortions.

Table 4
Association between complications of induced abortion and routine management.[a]

Management approach	Institutions (n = 1963)	Induced abortions (n = 100 851)	Total complications (n = 358)			Incomplete abortion (n = 295)			Uterine perforation (n = 19)			Gross bleeding (n = 17)		
			No. (%)	Rate[b]	*P* value[c]	No.	Rate[b]	*P* value[c]	No. (%)	Rate[b]	*P* value[c]	No. (%)	Rate[b]	*P* value[c]
Cervical preparation														
Yes	1288 (65.6)	58 321 (57.8)	238 (66.5)	408.1	<0.001	189 (64.1)	324.1	0.032	15 (78.9)	25.7	0.103	13 (76.5)	22.3	0.19
No	675 (34.4)	42 530 (42.2)	120 (33.5)	282.2		106 (35.9)	249.2		4 (21.1)	9.4		4 (23.5)	9.4	
Ultrasound-guided procedure														
Yes	777 (39.6)	42 930 (42.6)	140 (39.1)	326.1	0.185	116 (39.3)	270.2	0.246	7 (36.8)	16.3	0.614	8 (47.1)	18.6	0.90
No	1186 (60.4)	57 921 (57.4)	218 (60.9)	376.4		179 (60.7)	309.0		12 (63.2)	20.7		9 (52.9)	15.5	

[a] Values given as number (percentage) unless indicated otherwise.
[b] Per 100 000 induced abortions with that management approach.
[c] For comparisons of rates.

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Conflict of interest

The authors have no conflicts of interest.

References

[1] World Health Organization. Safe abortion: technical and policy guidance for health systems. http://whqlibdoc.who.int/publications/2003/9241590343.pdf. Published 2003. Accessed November 24, 2014.
[2] World Health Organization. Safe abortion: technical and policy guidance for health systems. Second edition. http://apps.who.int/iris/bitstream/10665/70914/1/9789241548434_eng.pdf?ua=1. Published 2012. Accessed November 24, 2014.
[3] Cates W, Grimes DA, Schulz KF. Abortion surveillance at CDC: creating public health light out of political heat. Am J Prev Med 2000;19(1 Suppl.):12–7.
[4] Lean TH, Vengadasalam D, Pachauri S, Miller ER. A comparison of D & C and vacuum aspiration for performing first trimester abortion. Int J Gynecol Obstet 1976;14(6):481–6.
[5] Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting Induced Abortion: Evidence-based Clinical Guideline Number 7. https://www.rcog.org.uk/globalassets/documents/guidelines/abortion-guideline_web_1.pdf. Published September 2004. Accessed November 24, 2014.
[6] Kulier R, Fekih A, Hofmeyr GJ, Campana A. Surgical methods for first trimester termination of pregnancy. Cochrane Database Syst Rev 2001;4:CD002900.
[7] Niinimäki M, Pouta A, Bloigu A, Gissler M, Hemminki E, Suhonen S, et al. Immediate complications after medical compared with surgical termination of pregnancy. Obstet Gynecol 2009;114(4):795–804.
[8] Pazol K, Creanga AA, Burley KD, Hayes B, Jamieson DJ. Centers for Disease Control and Prevention (CDC). Abortion surveillance - United States, 2010. MMWR Surveill Summ 2013;62(8):1–44.
[9] Abortion Statistics, Department of Health. Abortion Statistics, England and Wales: 2012. Summary information from the abortion notification forms returned to the Chief Medical Officers of England and Wales. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/307650/Abortion_statistics__England_and_Wales.pdf. Published April 2014. Accessed November 24, 2014.
[10] Adachi T. Prevention of repeated induced abortions in Japan: survey of induced abortions in Japan. Annual report of research on children and families (in Japanese). Tokyo: Japanese Ministry of Health, Labour and Welfare; 2008.
[11] Allen RH, Goldberg AB. Board of Society of Family Planning. Cervical dilation before first-trimester surgical abortion (<14 weeks' gestation). SFP Guideline 20071. Contraception 2007;76(2):139–56.
[12] UK Department of Health. Abortion statistics, England and Wales: 2009. Statistical Bulletin 2010/1. London: Department of Health; 2010.
[13] Kapp N, Lohr PA, Ngo TD, Hayes JL. Cervical preparation for first trimester surgical abortion. Cochrane Database Syst Rev 2010;2:CD007207.
[14] Peterson HB, Grimes DA, Cates Jr W, Rubin GL. Comparative risk of death from induced abortion at less than or equal to 12 weeks' gestation performed with local versus general anesthesia. Am J Obstet Gynecol 1981;141(7):763–8.

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LETTER TO THE EDITOR

Cases of death due to serious group A streptococcal toxic shock syndrome in pregnant females in Japan

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Serious group A streptococcal (GAS) infections and its toxic shock syndrome (TSS) are associated with early onset and rapid progression, often resulting in death [1, 2]. The initial symptoms of a high fever and abdominal or chest pain are characteristics and are attributable to a common cold syndrome or viral infection [1]. The incidence rate is extremely low, with rates largely between 2 and 4 per 1,00,000 [3]. However, GAS-TSS is still one of the causes of maternal death.

The perinatal and infant mortality rates in Japan are lowest worldwide (3:1,000). On the other hand, the maternal mortality rate is relatively high (4:1,00,000) [4]. Therefore, the Japan Association of Obstetricians and Gynecologists (JAOG) established a registration system for maternal death in 2010. If maternal death occurs, detailed reports are to be submitted to the JAOG. The individual data are analyzed by the Maternal Death Exploratory Committee (Chairman: Ikeda, T.). This committee consists of 15 obstetricians, four anesthesiologists, two pathologists, an emergency physician and some specialists who attend review sessions every month, in order to make recommendations for reducing the maternal mortality every year. The present study was performed as part of a series which analyzed maternal deaths in Japan by this committee.

Report forms regarding the maternal death cases where a female patient died during pregnancy or within a year after delivery are submitted to this registration system. The 12 pages of the report form contain approximately 100 questions, and elicit detailed information about the clinical history of each death, the facility characteristics and which personnel participated in the patient's care. All of the anonymized reports were analyzed for factors associated with the maternal mortality and the circumstances of death. A total of 155 reports of maternal death were completely analyzed by the Maternal Death Exploratory Committee between 2010 and 2012, while 128 cases of maternal death that occurred during pregnancy or within 42 days after delivery were reported by the Ministry of Health, Labour and Welfare, Japan [4].

Because GAS-TSS is still one of the causes of maternal death, though number of maternal death is decreasing in Japan, we thought it was necessary to clarify the clinical course and features of maternal death due to serious GAS infection in order to reduce the maternal mortality rate.

In the analyzed reports of maternal deaths between 2010 and 2013, the clinical features in the pregnant patients who died due to serious GAS-TSS were reviewed in the present study. Cases were enrolled when the diagnosis of GAS-TSS based upon the previously published criteria [5] was made, and when culture findings were positive or the GAS toxin was detected.

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Table 1 Maternal and neonatal clinical features in maternal death due to serious group A streptococcal toxic shock syndrome

Case	Age	O.H	Month at occurrence	Initial symptom(s)			Interval between initial symptom(s) and fulmination	Fulminant symptom(s)			Fetal outcome	Evidence of GAS	Autopsy	Interval between fulmination and death
				Gestational age	Symptoms	Treatment		Gestational age	Symptoms	Treatment				
1	38	1G1P (1CS)	March	34 weeks	Abdominal pain, common cold, diarrhea (at home)	ABPC/MCIPC, CLDM, anti-DIC	Same time	34 weeks	Abdominal pain, common cold, diarrhea (at home)	ABPC/MCIPC, CLDM, anti-DIC, CPR	IUFD (at initial fulminant symptom) > spontaneous still birth	Culture (vagina, maternal blood, umbilical cord blood)	Mother (pneumonia, MOF, sepsis), infant (MOF, sepsis, cerebral bleeding)	31 days
2	35	1G1P (1CS)	May	18 weeks	Fever, sore throat (at home)	CTRX, CFPN-PI	3 days	18 weeks	Abdominal pain, hematuria (at home)	ABPC, anti-DIC, CPR	IUFD (after visiting hospital due to fulminant symptoms)	Culture (maternal blood, sputum)	Mother (MOF, sepsis), Infant (no remarkable findings)	18 h
3	36	2G2P	February	35 weeks	Fever (at home)	acetaminophen	2 days	36 weeks	Fever, shock (at the hospital)	ABPC/MCIPC, steroid, CPR	IUFD (after initial symptoms before fulminant symptoms)	GAS toxin, Culture (negative)	Performed but not available	7 h
4	40	3G1P 1SA1KA	April	10 weeks	Fever (at home)	NSAIDs	10 h	10 weeks (IUFD)	Fever, abdominal pain, shock (at home)	CPR	IUFD (3 days before initial symptom) > D&C (after fulminant symptoms)	Culture (maternal blood, uterus)	Mother (fungus ball in uterine and ovarian vessels)	8 h
5	26	0G	November	1 day after delivery (39 weeks)	Epigastralgia (at the hospital)	observe	1 day	2 days after delivery (39 weeks)	Epigastralgia, shock (at the hospital)	Laparotomy due to diagnosis of panperitonitis, PIPC, CLDM, IPM/CS, globulin	Live birth	Culture (vagina, maternal blood, ascites)	Not performed	3 days
6	32	3G3P	May	15 weeks	Cough (at home)	anti-tussive	4 days	15 weeks	Abdominal pain, genital bleeding, shock, impaired consciousness (at home)	EM, SBT/ABPC, CLDM, VCM, anti-DIC, globulin	IUFD (at fulminant symptom) > spontaneous abortion	Culture (nasal cavity, placenta, vagina), genetic test (emm type: *emm1*)	Not performed	10 h
7	35	1G1P (1CS)	August	37 weeks	Fever (at home), rapid diagnostic test for GAS was negative	admission, CS, CMZ	2 days	2 days after CS (37 weeks)	Fever, abdominal pain, dyspnea, shock, DIC (at the hospital)	ABPC, MEPM, CLDM, anti-DIC, hemodialysis	Live birth	Culture (maternal blood)	Mother (MOF, DIC, necrosis in pharynx and uterus)	31 h

GAS group A streptococcus, *O.H* obstetric history, *SA* spontaneous abortion, *AA* artificial abortion, *CS* cesarean section

ABPC ampicillin, *MCIPC* cloxacillin, *CLDM* clindamycin, *CTRX* ceftriaxone, *CFPN-PI* cefcapene pivoxil, *CMZ* cefmetazole

PIPC piperacillin, *IPM/CS* imipenem/cilastatin, *EM* erythromycin, *SBT* sulbactam, *MEPM* meropenem, *NSAIDs* nonsteroidal antiinflammatory drugs

DIC disseminated intravascular coagulation, *MOF* multiple organ failure, *IUFD* intrauterine fetal death, *D&C* dilatation of curettage, *CPR* cardiopulmonary resuscitation

Among the 190 maternal deaths reported over the 4-year period, seven maternal deaths due to serious GAS-TSS (3.7 % of all maternal deaths) were reported. The maternal and neonatal clinical features in maternal death due to serious GAS-TSS are shown in Table 1. Most of the cases occurred in the winter and spring (71 %), with initial symptoms similar to those of the common cold or influenza. This is similar to a previous study which suggested that GAS could be related to upper respiratory tract infections [6]. In fact, none of the cases was diagnosed as GAS based on the initial symptoms, and only symptomatic treatments for the common cold were prescribed upon the occurrence of the initial symptoms.

All mothers developed fulminant disease within 4 days after the initial symptoms developed. Severe abdominal pain and vital shock were the most common symptom of fulminant disease. Intrauterine fetal death occurred in all cases, regardless of the gestational age at the onset of fulmination, which resulted in spontaneous delivery. GAS was detected in the cultures and sensitivity test of various fluids and tissues, including the upper airway and reproductive organs. One case was diagnosed by the GAS toxin instead of the culture result and sensitivity test. According to the analysis of the clinical course and autopsy findings, sepsis and disseminated intravascular coagulation seemed to be final causes of maternal death. Four of the seven cases of in our series (57 %) resulted in maternal death within a day after the development of fulminant symptoms.

It has been suspected that, after invading the myometrium through the throat, skin or vagina, large amounts of GAS become disseminated into the systemic circulation of the mother by the active uterine contractions caused by purulent myometritis [6, 7], although the primary site was not identified in most cases [7]. Intrauterine fetal death was observed at the time of fulminant symptoms in all of the present cases, because massive inflammation led to maternal hypercytokinemia and multi-organ failure, and then insufficiency of the fetomaternal circulation due to maternal hypotension [6]. Otherwise, strong uterine contractions caused by GAS infection in the uterine myometrium may result in spontaneous delivery. The majority (86 %) of our cases were multiparous patients, similar to the previous report [6].

Unfortunately, most of our analyzed cases resulted in death rapidly after the development of fulminant symptoms. So far, it is also unclear usefulness of rapid diagnostic test for GAS. Maternal death might have already been unpreventable when fulminant symptom due to GAS is revealed. Although, it is still unknown that the early detection and treatment of GAS-TSS could contribute to a reduction in maternal mortality, all one can say that rapid intensive care with antibiotics is required in suspicious cases of GAS infection regardless of obtaining result of culture and sensitivity test. Since postpartum females have a 20-fold increased incidence of GAS, compared with non-pregnant females [8], administration of antibiotics for pregnant women might be recommended even at the initial symptoms such as a high fever, abdominal and chest pain. Zimbelman et al. [9] suggested that clindamycin in combination with beta-lactam antibiotic was the most effective treatment for invasive GAS infection. GAS infection also should be suspected when spontaneous abortion and strong uterine contractions associated with infections are noted.

In conclusion, the clinical suspicion followed by quick optimal antibiotic treatment might help in reducing mortality rate due to GAS. We believe that widespread recognition of GAS could improve the maternal mortality rate in Japan.

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Ethical standard This study was approved by the ethics board of the Japan Association of Obstetricians and Gynecologists.

References

1. Sugiyama T, Kobayashi T, Nagao K, Hatada T, Wada H, Sagawa N (2010) Group A streptococcal toxic shock syndrome with extremely aggressive course in the third trimester. J Obstet Gynaecol Res 36:852–855
2. Schuitemaker N, van Roosmalen J, Dekker G, van Dongen P, van Geijn H, Gravenhorst JB (1998) Increased maternal mortality in the Netherlands from group A streptococcal infections. Eur J Obstet Gynecol Reprod Biol 76:61–64
3. Steer AC, Lamagni T, Curtis N, Carapetis JR (2012) Invasive group A streptococcal disease: epidemiology, pathogenesis and management. Drugs 72:1213–1227
4. Kaneda I (2013) (ed Maternal and child health statistics in japan. ed. Mothers' and Children's Health and Welfare Association. Tokyo
5. (1993) Defining the group A streptococcal toxic shock syndrome. Rationale and consensus definition. The working group on severe streptococcal infections. JAMA : J Am Med Assoc 269:390–391
6. Udagawa H, Oshio Y, Shimizu Y (1999) Serious group A streptococcal infection around delivery. Obstet Gynecol 94:153–157
7. Stevens DL (1992) Invasive group A streptococcus infections. Clin Infect Dis 14:2–11
8. Deutscher M, Lewis M, Zell ER, Taylor TH Jr, Van Beneden C, Schrag S, Active Bacterial Core Surveillance T (2011) Incidence and severity of invasive *Streptococcus pneumoniae*, group A streptococcus, and group B streptococcus infections among pregnant and postpartum women. Clin Infect Dis 53:114–123
9. Zimbelman J, Palmer A, Todd J (1999) Improved outcome of clindamycin compared with beta-lactam antibiotic treatment for invasive *Streptococcus pyogenes* infection. Pediatr Infect Dis J 18:1096–1100

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CLINICAL ARTICLE

Safety of induced abortions at less than 12 weeks of pregnancy in Japan

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ABSTRACT

Objective: To assess the safety of various methods of induced abortion when used before 12 weeks of pregnancy in Japan. *Methods:* A retrospective study was undertaken of induced abortions conducted between January 1 and December 31, 2012. Questionnaires were sent to 4154 institutions that employed doctors who were licensed to conduct induced abortions. Information was obtained about the numbers of induced abortions performed before 12 weeks, methods, complications, and routine management. *Results:* Completed questionnaires from 2434 institutions showed that 100 851 induced abortions had been performed. Vacuum aspiration (VA) was used in 20 458 (20.3%) abortions, VA with sharp curettage in 47 148 (46.8%), dilatation and curettage (D&C) in 32 958 (32.7%), and medical abortion in 287 (0.3%). Overall, 358 complications were reported (355.0 per 100 000 procedures). The rate of complications was significantly higher after D&C than after VA and after VA with sharp curettage ($P < 0.001$ for both). However, incomplete abortion requiring repeat procedures was the only complication that was significantly associated with D&C ($P < 0.001$). *Conclusion:* D&C can be safely used for induced abortion before 12 weeks of pregnancy, but changing from D&C to VA could reduce incomplete abortions and improve the safety of induced abortions before 12 weeks of pregnancy in Japan.

1. Introduction

After evaluation of several proposed methods for induced abortion during the first trimester, WHO has recommended the adoption of vacuum aspiration (VA) or medical methods using mifepristone and misoprostol to ensure procedures are both safe and effective [1,2]. The organization also stated that dilatation and curettage (D&C) should be replaced by VA to improve safety and quality of care for women [2]. The rationale for this guidance was based on previous studies in which D&C was found to be less safe [3], substantially slower, and associated with more blood loss [4] than was VA. Furthermore, rates of major complications are higher with D&C than VA [5].

The potential risks of D&C have been known since the 1970s [3–5]. Nevertheless, some support exists for the clinical acceptability of this procedure. Kulier et al. [6] conducted a systematic review of randomized controlled trials of different surgical methods for induced abortion during the first trimester and concluded that the incidences of complications were not markedly different between D&C and VA. The only difference observed between these two methods was the operation time, which was lower for VA than D&C. A study conducted by Niinimäki et al. [7] analyzed 42 619 induced first trimester abortions in Finland, and showed that medical abortions were more likely to be associated with bleeding and re-evacuation than were surgical methods of induced abortion, including VA and D&C. Although surgical abortions led to injury more often than did medical abortions, the overall incidence of such injuries was rare [7]. Consequently, Niinimäki et al. concluded that both VA and D&C could be considered generally safe and clinically acceptable methods for induced abortion.

In the USA, 80% of induced abortions were performed by surgical methods in 2010 [8]; furthermore, most of the procedures since 1995 have involved VA [3]. In England and Wales in 2012, sharp curettage was no longer used, although 50% of abortions were performed by surgical methods [9]. However, D&C still remains one of the most frequently used procedures for induced abortion in Japan [10], with medical abortions using mifepristone or misoprostol not yet legally accepted. The aim of the present study was, therefore, to elucidate the safety of various methods of induced abortion used before 12 weeks of pregnancy in Japan.

2. Materials and methods

A retrospective study was undertaken of induced abortions performed before 12 weeks of pregnancy between January 1 and December 31, 2012. The Japan Association of Obstetricians and Gynecologists provided a list of hospitals that employed doctors licensed to perform induced abortions, and questionnaires were mailed on September 5, 2013, to the Departments of Obstetrics and Gynecology of 4154

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Japanese institutions (1171 hospitals and 2983 clinics). Managers of the departments were asked to complete the questionnaire. Completion and return of the study questionnaire was considered as consent to participate in the present study. Approval was obtained from the ethics committees of the coordinating center (Tama Nagayama Hospital, Nippon Medical School, Tokyo) and the Japan Association of Obstetricians and Gynecologists. The present study conformed to the principles of the Declaration of Helsinki.

The questionnaire obtained information about the number of induced abortions performed before 12 weeks of pregnancy, methods used, complications, and routine management approaches before and during the procedure. Complications were subdivided into uterine perforation, cervical injury, gross bleeding, pelvic infection requiring hospital admission, thromboembolism, anaphylaxis, incomplete abortion requiring repeat procedures, and other types of complication. Routine management approaches included preoperative examination, cervical preparation, monitoring and treatment during the procedure, and use of anesthetics. Responses were confidential and data that might reveal the identity of the patients were not requested.

Data were analyzed using SPSS version 17.0 (SPSS Inc, Chicago, IL, USA). Categorical variables were evaluated using χ^2 or Fisher exact tests with Bonferroni correction. $P < 0.05$ was considered statistically significant.

3. Results

Completed questionnaires were received from 2434 (58.6%) of the 4154 institutions, including 738 (63.0%) of the 1171 hospitals and 1696 (56.9%) of the 2983 clinics. A total of 100 851 induced abortions were performed before 12 weeks of pregnancy, of which 15 946 (15.8%) were performed in hospitals and 84 905 (84.2%) in clinics. Induced abortions had been performed at 1963 institutions, of which 543 (27.7%) were hospitals and 1420 (72.3%) clinics.

The most frequently used method to induce abortion was VA with sharp curettage, whereas medical methods were used rarely (Table 1). Blood cell count, blood group typing, and screening for infection were the most frequently performed preoperative tests (Table 2). Cervical preparation using an osmotic dilator was conducted at 1288 institutions (65.6%). Cervical preparation was performed at 445 (82.0%) hospitals and 843 (59.4%) clinics. Intravenous infusion, oxygen saturation monitoring, and automatic blood pressure monitoring were used during procedures at many institutions (Table 2). The most frequently used anesthetics were thiamylal or thiopental (Table 2).

Overall, 358 (0.4%) of the induced abortions had complications, equivalent to a total complication rate of 355.0 per 100 000 induced abortions. Among the 358 complications, 295 (82.4%) were incomplete abortions, 19 (5.3%) uterine perforations, 17 (4.7%) gross bleeding, 12 (3.4%) anaphylaxis, 3 (0.8%) pelvic infections requiring hospitalization, 2 (0.6%) cervical injuries, and 10 (2.8%) other (Table 3). No instances of thromboembolism or maternal death were recorded.

Rates of complications, and specifically incomplete abortions, were significantly higher after D&C than after VA and after VA with sharp curettage ($P < 0.001$ for all) (Table 3). The rates of complications and incomplete abortions were also higher for VA with sharp curettage than for VA alone ($P < 0.001$ for both) (Table 3). The rates of uterine perforation and gross bleeding were not significantly different among the three surgical methods (Table 3). The rates of uterine perforation and gross bleeding were significantly lower after VA (1 in 20 458 and 2 in 20 458, respectively) than after medical abortion (0 in 287 for both; $P < 0.001$ and $P = 0.004$, respectively).

Cervical preparation was associated with increased rates of total complications and incomplete abortions (Table 4). By contrast, the use of ultrasonography during surgical abortion did not influence the rates of complications (Table 4).

Table 1
Methods used for induced abortion before 12 weeks of pregnancy (n = 100 851).

Method	No. (%)
Vacuum aspiration	20 458 (20.3)
Vacuum aspiration with sharp curettage	47 148 (46.8)
Dilatation and curettage	32 958 (32.7)
Medical abortion	287 (0.3)

Table 2
Routine management of women undergoing induced abortion before 12 weeks of pregnancy within the 1963 participating institutions.

Management approach	No. (%)
Preoperative examination	
Blood cell count	889 (45.3)
Blood group typing	839 (42.7)
Screening for infection	733 (37.3)
Laboratory test[a]	366 (18.6)
Electrocardiograph	300 (15.3)
Blood coagulation test	192 (9.8)
Irregular antibody screening	125 (6.4)
Chest radiograph	35 (1.8)
Cervical preparation	
Yes	1288 (65.6)
No	675 (34.4)
Monitoring and treatments during the procedure	
Intravenous infusion	1770 (90.2)
Oxygen saturation monitoring	1615 (82.3)
Automatic blood pressure monitoring	1508 (76.8)
Electrocardiogram monitoring	1110 (56.5)
Ultrasound-guided procedure	777 (39.6)
Use of anesthetic	
Thiamylal or thiopental	937 (47.7)
Pentazocine	882 (44.9)
Diazepam	715 (36.4)
Ketamine	538 (27.4)
Propofol	420 (21.4)

[a] Measurements of aspartate transaminase, alanine transaminase, lactate dehydrogenase, blood urea nitrogen, and creatinine.

4. Discussion

The present study found that sharp curettage (either as D&C or with VA) was used in 79.5% of induced abortions performed before 12 weeks of pregnancy in Japan. Nevertheless, the rates of complications were increased when this method was used, either as part of D&C or with VA. The most frequent complication overall was incomplete abortion. By contrast, other complications, including uterine perforation and gross bleeding, were rarely reported and no maternal deaths occurred.

A report published in 2007 by the Society of Family Planning [11] showed that the incidences of major complications, uterine perforation, and cervical injury associated with surgical abortion performed during the first trimester in the USA were less than 1000, 10–400, and 10–1000 per 100 000 induced abortions, respectively. The Royal College of Obstetricians and Gynaecologists in the UK investigated complications following either medical or surgical abortion during the first trimester [5]. For medical abortion, rates of uterine rupture and severe bleeding requiring transfusion were both less than 100 per 100 000 induced abortions. For surgical abortion, the rates of uterine perforation and cervical injury were 100–400 and less than 1000 per 100 000 induced abortions, respectively. Failure to end pregnancy was the most frequent complication reported overall (1000 per 100 000 induced abortions) [5,7,9,12]. Consequently, the findings of the present study regarding rates of complications were similar to previous reports.

Nonetheless, the observed rates of total complications and incomplete abortions in the present study differed according to the method of induced abortion used. The use of VA alone seemed to be associated with the lowest incidence of incomplete abortion. The reason why this method was advantageous is unclear. It is possible that clinicians

Table 3
Complications associated with each method of induced abortion.

Method	Number of procedures in which method used	Total complications			Incomplete abortion			Uterine perforation			Gross bleeding		
		No. (%)	Rate[a]	P value[b]	No. (%)	Rate[a]	P value[b]	No. (%)	Rate[a]	P value[b]	No. (%)	Rate[a]	P value[b]
Vacuum aspiration	20 458	23 (0.1)	112.4	NA	20 (0.1)	97.8	NA	1 (<0.1)	4.9	NA	2 (<0.1)	9.8	NA
Vacuum aspiration with sharp curettage	47 148	139 (0.3)	294.8	<0.001[c]	107 (0.2)	226.9	<0.001[c]	6 (<0.1)	12.7	0.611[c]	9 (<0.1)	19.1	0.586[c]
Dilatation and curettage	32 958	194 (0.6)	588.6	<0.001[c] <0.001[d]	166 (0.5)	503.7	<0.001[c] <0.001[d]	12 (<0.1)	36.4	0.047[c] 0.028[d]	6 (<0.1)	18.2	0.682[c] 0.863[d]
Medical abortion	287	2 (0.7)	696.9	0.048[c] 0.482[d] 0.882[e]	2 (0.7)	696.9	0.029[c] 0.299[d] 0.967[e]	0	0.0	<0.001[c] 0.015[d] 0.216[e]	0	0.0	0.004[c] 0.055[d] 0.048[e]
Total	100 851	358 (0.4)	355.0	NA	295 (0.3)	292.5	NA	19 (<0.1)	18.8	NA	17 (<0.1)	16.9	NA

Abbreviation: NA, not applicable.
[a] Per 100 000 induced abortions performed by that method.
[b] For comparisons of rates.
[c] Versus vacuum aspiration.
[d] Versus vacuum aspiration with sharp curettage.
[e] Versus dilatation and curettage.

might tend to use sharp curettage in combination with VA for the management of technically difficult abortions, in which complications are likely irrespective of the use of sharp curettage.

Cervical preparation has been recommended when using surgical methods [5] or for high-risk patients with cervical injury and uterine perforation [2]. Both mechanical and medical cervical dilatations can shorten induced abortion procedures; however, the optimum gestational period at which cervical preparation should be performed has not yet been identified [13]. In the present study, routine cervical preparation was performed in 65.6% of all institutions. Nevertheless, use of this treatment was unexpectedly related to a high incidence of incomplete abortion. This result could reflect the fact that cervical preparation was more frequently performed in hospitals than in clinics, and women referred to hospitals from clinics could be at increased risk of incomplete abortion.

Ultrasound-guided procedures have been recommended for D&C performed after 14 weeks of pregnancy [5], but the effect of this approach during the first trimester is unclear [2]. In the present study, the routine use of ultrasonography during induced abortions conducted before 12 weeks of pregnancy did not decrease the rates of complications. Although ultrasound-guided procedures are not routinely required during the first trimester in Japan, they could be effective for some patients, such as women with multiple uterine myoma, a uterine anomaly, or a history of uterine surgery.

The use of anesthesia during surgical abortions remains controversial. Although no difference was reported in the incidences of complications between general and local anesthesia in one study [14], it has been suggested that paracervical block [2] and non-steroidal anti-inflammatory drugs [5] should be used instead of general anesthesia during routine procedures because of quick recovery and low cost. In the present study, general anesthesia was widely used for first trimester abortions. However, intravenous infusion, electrocardiogram monitoring, automatic blood pressure monitoring, and oxygen saturation monitoring were also frequently used during surgical methods preformed under general anesthesia. These treatments and monitoring methods are postulated to have effectively prevented adverse effects related to general anesthesia.

The main limitations of the present study were the retrospective design and the fact that the data were collected using questionnaires, which were completed by only 58.6% of the institutions that were invited to participate. Furthermore, the effects of cervical dilatation and ultrasound-guided procedures on prevention of complications were not analyzed for each patient because individual medical records were not obtained.

Furthermore, the legal and social context of induced abortion differs among countries. Mifepristone and misoprostol are not currently available for induced abortion in Japan; however, surgical procedures can be provided with general anesthesia and sufficient monitoring of vital signs. A total of 287 medical abortions were reported in the present study, but the medication used was not asked. In regions where medical abortion using mifepristone and misoprostol is available, it is possible that this method has advantages over surgical abortion in terms of accessibility, safety, and cost-effectiveness.

In conclusion, although D&C was used in almost one-third of induced abortions conducted at less than 12 weeks of gestation in Japan, the incidence of total complications was comparable to that in other high-income countries that predominantly use VA and medical methods. However, use of VA rather than D&C could decrease the incidence of incomplete abortions, the need for repeat procedures, and further improve the safety of early abortions.

Table 4
Association between complications of induced abortion and routine management.[a]

Management approach	Institutions (n = 1963)	Induced abortions (n = 100 851)	Total complications (n = 358)			Incomplete abortion (n = 295)			Uterine perforation (n = 19)			Gross bleeding (n = 17)		
			No. (%)	Rate[b]	P value[c]	No.	Rate[b]	P value[c]	No. (%)	Rate[b]	P value[c]	No. (%)	Rate[b]	P value[c]
Cervical preparation														
Yes	1288 (65.6)	58 321 (57.8)	238 (66.5)	408.1	<0.001	189 (64.1)	324.1	0.032	15 (78.9)	25.7	0.103	13 (76.5)	22.3	0.19
No	675 (34.4)	42 530 (42.2)	120 (33.5)	282.2		106 (35.9)	249.2		4 (21.1)	9.4		4 (23.5)	9.4	
Ultrasound-guided procedure														
Yes	777 (39.6)	42 930 (42.6)	140 (39.1)	326.1	0.185	116 (39.3)	270.2	0.246	7 (36.8)	16.3	0.614	8 (47.1)	18.6	0.90
No	1186 (60.4)	57 921 (57.4)	218 (60.9)	376.4		179 (60.7)	309.0		12 (63.2)	20.7		9 (52.9)	15.5	

[a] Values given as number (percentage) unless indicated otherwise.
[b] Per 100 000 induced abortions with that management approach.
[c] For comparisons of rates.

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Conflict of interest

The authors have no conflicts of interest.

References

[1] World Health Organization. Safe abortion: technical and policy guidance for health systems. http://whqlibdoc.who.int/publications/2003/9241590343.pdf. Published 2003. Accessed November 24, 2014.
[2] World Health Organization. Safe abortion: technical and policy guidance for health systems. Second edition. http://apps.who.int/iris/bitstream/10665/70914/1/9789241548434_eng.pdf?ua=1. Published 2012. Accessed November 24, 2014.
[3] Cates W, Grimes DA, Schulz KF. Abortion surveillance at CDC: creating public health light out of political heat. Am J Prev Med 2000;19(1 Suppl.):12–7.
[4] Lean TH, Vengadasalam D, Pachauri S, Miller ER. A comparison of D & C and vacuum aspiration for performing first trimester abortion. Int J Gynecol Obstet 1976;14(6):481–6.
[5] Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting Induced Abortion: Evidence-based Clinical Guideline Number 7. https://www.rcog.org.uk/globalassets/documents/guidelines/abortion-guideline_web_1.pdf. Published September 2004. Accessed November 24, 2014.
[6] Kulier R, Fekih A, Hofmeyr GJ, Campana A. Surgical methods for first trimester termination of pregnancy. Cochrane Database Syst Rev 2001;4:CD002900.
[7] Niinimäki M, Pouta A, Bloigu A, Gissler M, Hemminki E, Suhonen S, et al. Immediate complications after medical compared with surgical termination of pregnancy. Obstet Gynecol 2009;114(4):795–804.
[8] Pazol K, Creanga AA, Burley KD, Hayes B, Jamieson DJ. Centers for Disease Control and Prevention (CDC). Abortion surveillance - United States, 2010. MMWR Surveill Summ 2013;62(8):1–44.
[9] Abortion Statistics, Department of Health. Abortion Statistics, England and Wales: 2012. Summary information from the abortion notification forms returned to the Chief Medical Officers of England and Wales. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/307650/Abortion_statistics__England_and_Wales.pdf. Published April 2014. Accessed November 24, 2014.
[10] Adachi T. Prevention of repeated induced abortions in Japan: survey of induced abortions in Japan. Annual report of research on children and families (in Japanese). Tokyo: Japanese Ministry of Health, Labour and Welfare; 2008.
[11] Allen RH, Goldberg AB, Board of Society of Family Planning. Cervical dilation before first-trimester surgical abortion (<14 weeks' gestation). SFP Guideline 20071. Contraception 2007;76(2):139–56.
[12] UK Department of Health. Abortion statistics, England and Wales: 2009. Statistical Bulletin 2010/1. London: Department of Health; 2010.
[13] Kapp N, Lohr PA, Ngo TD, Hayes JL. Cervical preparation for first trimester surgical abortion. Cochrane Database Syst Rev 2010;2:CD007207.
[14] Peterson HB, Grimes DA, Cates Jr W, Rubin GL. Comparative risk of death from induced abortion at less than or equal to 12 weeks' gestation performed with local versus general anesthesia. Am J Obstet Gynecol 1981;141(7):763–8.

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Vaginal delivery in pregnancy with Moyamoya disease: Experience at a single institute

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Abstract

Aim: Cesarean section is commonly selected in pregnancy with Moyamoya disease. We consider vaginal delivery with epidural anesthesia a viable alternative in such cases.

Methods: Mode of delivery and outcomes were examined in 27 pregnancies in 19 women with Moyamoya disease treated at the Department of Perinatology, National Cardiovascular Center, Japan, from 1983 to 2013. Of these 27 pregnancies, 20 were delivered vaginally with epidural anesthesia. The cerebral circulation, mode of delivery, maternal outcome (presence of symptoms due to Moyamoya disease intrapartum) and neonatal outcome (gestational week, birthweight, Apgar score at 5 min and pH of umbilical artery) were investigated.

Results: The cerebral circulation was judged to be good in all pregnancies. No symptoms due to Moyamoya disease intrapartum were seen in the vaginal delivery cases.

Conclusion: Our findings indicate that vaginal delivery is viable in pregnancy with Moyamoya disease and that unnecessary cesarean section may be avoided. These findings are limited by the retrospective nature of the study.

Key words: delivery mode, Moyamoya disease, pregnancy.

Introduction

Results from cerebral angiography were first described in 1957, and Moyamoya disease was established as a disease thereafter.[1] Moyamoya disease causes progressive stricture in the bilateral internal carotid artery and formation of abnormal vessels (moyamoya vessels) at the base of the brain as collateral circulation. In Japanese, 'moyamoya' indicates the shrouding of a view by smoke or steam.[2] The disease results in ischemia due to stricture (ischemic type) and hemorrhage due to the failure of blood vessels (hemorrhagic type). The primary symptoms overlap, though at different frequencies, with those of the ischemic type and include (in order of frequency) impaired consciousness, headache, movement disorder, speech disorder and disturbance of sensations, while those in the hemorrhagic type include movement disorder, speech disorder, disturbance of sensations, headaches and impaired consciousness.

Moyamoya disease is common in Japan and Asia.[3] The incidence is highest at the age of less than 10 years and decreases after the age of 30 years. Therefore, pregnancy in women with Moyamoya disease is often experienced in Japan, but there is no consensus on the best way to manage such cases. Cerebral ischemia due to spasm of cerebral blood vessels may occur in preeclampsia and leakage from blood vessels may cause

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Table 1 Maternal characteristics in 27 pregnancies with Moyamoya disease

Case no.	Age	Parity	Age of diagnosis	Bypass surgery	Complication	Epilepsy	Symptoms in pregnancy	
1	34	0	31	Yes	Hyperthyroidism	No	Yes	Headache
2	37	1	31	Yes	Hyperthyroidism	No	No	
3	31	1	5	No	Hyperthyroidism	Yes	Yes	TIA
4	26	0	23	Yes	No	No	Yes	Headache
5	28	1	23	Yes	No	No	Yes	Headache
6	32	2	23	Yes	No	No	No	
7	22	0	18	Yes	No	No	Yes	Headache
8	21	1	18	Yes	No	No	No	
9	30	0	22	Yes	No	No	No	
10	34	0	12	No	No	No	No	
11	30	1	26	Yes	No	No	No	
12	32	2	26	Yes	No	No	No	
13	21	0	12	No	No	No	No	
14	24	1	12	No	No	No	No	
15	21	0	8	No	No	No	Yes	Headache
16	23	1	8	No	No	No	No	
17	29	0	27	Yes	No	No	No	
18	32	1	27	Yes	No	No	No	
19	26	0	3	Yes	No	No	Yes	Headache
20	34	0	21	Yes	Hypertension	No	No	
21	37	0	10	Yes	No	No	No	
22	35	0	20	No	Hypertension	Yes	Yes	Headache
23	32	0	10	Yes	Hypothyroidism	No	No	
24	38	0	15	Yes	No	No	No	
25	23	0	20	Yes	No	No	Yes	TIA
26	27	1	11	No	No	No	No	
27	40	0	2	Yes	No	No	Yes	Headache

TIA, transient ischemic attack.

Two women had epilepsy, but this was well controlled in both cases. Symptoms due to Moyamoya disease occurred in 10 pregnancies: headache in eight and TIA in two. No incidence of cerebral infarction, intracranial hemorrhage or epilepsy was observed. SPECT was performed in eight cases (42%) before pregnancy, and cerebral blood flow was good in these cases (Table 2). No cases had frequent symptoms due to Moyamoya disease within 1 year before pregnancy. Therefore, cerebral circulation was judged to be good in all pregnancies. Obstetric complications were pre-eclampsia, hypertension, threatened premature delivery and fetal growth restriction in two, two and one pregnancy, respectively.

The mode of delivery was vaginal delivery in 20 pregnancies (74%) and cesarean section in seven (26%). Delivery mode for the 27 pregnancies (19 women) with Moyamoya disease is shown in Figure 1. The cerebral circulation was judged to be good in all pregnancies. The indications for cesarean section were pregnancy-induced hypertension, fetal disorder, previous cesarean section, breech presentation and previous myomectomy in two, two, one, one and one pregnancies, respectively. All mothers survived, and no symptoms due to Moyamoya disease intrapartum or post-partum complications occurred in either the vaginal delivery or cesarean section groups. The only significant obstetric event was preterm birth, and these incidents were not related to Moyamoya disease.

Table 2 Evaluation of cerebral circulation before pregnancy in 27 pregnancies in women with Moyamoya disease

	$n = 19$
SPECT showed good cerebral circulation	8 (42%)
No frequent symptoms due to Moyamoya disease observed within 1 year before pregnancy	19 (100%)

SPECT, single photon emission computed tomography.

Birthweight, Apgar score at 5 min and pH of umbilical artery were excellent (Table 3). All newborn infants survived.

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