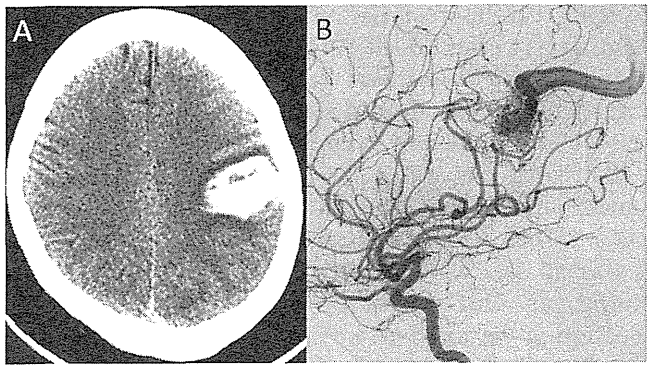

Fig. 1 Case 1: A: Computed tomography scan showing a left parietal intraparenchymal hematoma. B: Digital subtraction angiogram showing a grade 2 left parietal arteriovenous malformation.

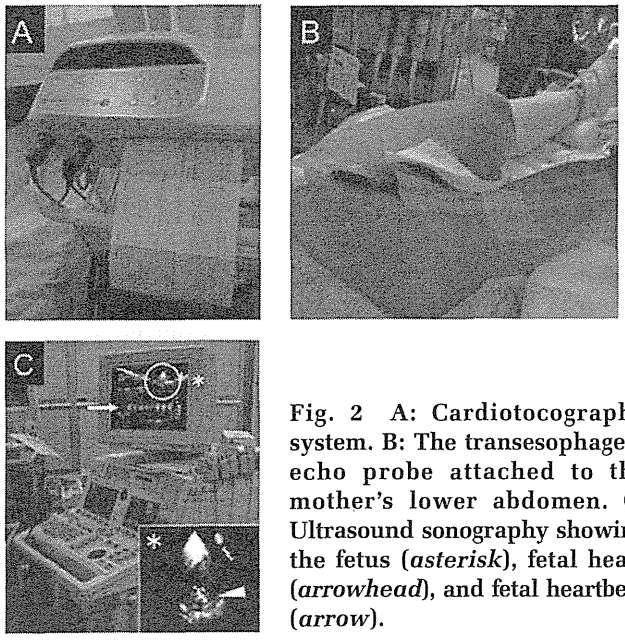

Fig. 2 A: Cardiotocography system. B: The transesophageal echo probe attached to the mother's lower abdomen. C: Ultrasound sonography showing the fetus (*asterisk*), fetal heart (*arrowhead*), and fetal heartbeat (*arrow*).

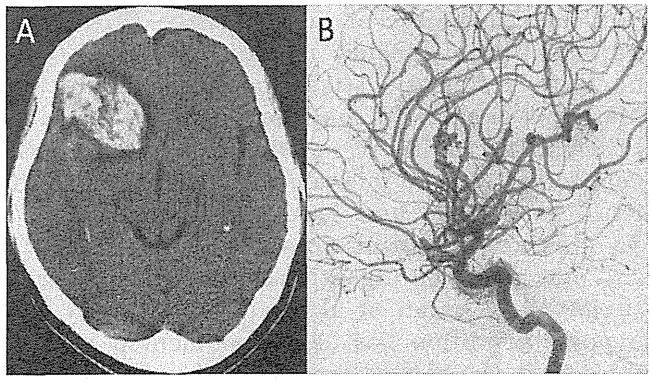

Fig. 3 Case 2: A: Computed tomography scan showing a right frontal intraparenchymal hematoma. B: Digital subtraction angiogram showing a grade 1 right frontal arteriovenous malformation.

in the same operating room. The patient's systolic blood pressure (SBP) was maintained between 90 and 100 mmHg during surgery, and the lowest SBP was 82 mmHg during the resection of the nidus by deliberate depression of maternal blood pressure. Her uterine contraction was restrained by anesthetic agents. The FHR remained between 130 and 140 beat per minute (bpm) and FHR variability decreased less than 6 bpm throughout the operation. The FHR decreased between 5 and 10 bpm under general anesthesia compared to pre-operative value. The surgery was completed without any problems. The amount of blood loss was 560 ml. The patient showed a slight right sensory disturbance, but the symptom improved rapidly. The remaining course of the pregnancy was favorable, and the patient successfully delivered via spontaneous vaginal delivery with epidural anesthesia in the 40th week of gestation.

II. Case 2

A 34-year-old woman (gravida 1, para 1) was admitted to our hospital in the 16th week of gestation because of sudden left hemiparesis. CT and MRI revealed an intracerebral hemorrhage in the right frontal lobe. Cerebral angiography showed a right frontal AVM of Spetzler and Martin grade 1 on the same day (Fig. 3A, B). The mother wished to continue the pregnancy and consented to the AVM resection. The surgery was performed in the 18th week of gestation. General anesthesia was induced with rocuronium 50 mg i.v., thiopental 250 mg i.v., fentanyl 0.2 mg i.v., and maintained with remifentanyl 0.20–0.25 μg/kg/min, and 1.0–1.5% sevoflurane in oxygen. During the procedure, FHR was directly monitored using ultrasonography, with a transesophageal echo probe attached to the mother's lower abdomen (Fig. 2B, C). The patient's SBP was maintained between 90 to 100 mmHg during surgery, and the lowest SBP was 84 mmHg during the resection of the nidus. Her oxygenation level was good and no fetal bradycardia occurred during surgery. The FHR remained between 150 and 160 bpm throughout the perioperative period. The surgery was completed without any problems. The amount of blood loss was only 200 ml. The mother complained of no new abnormal neurological symptom. The remaining course of the pregnancy was favorable, and a cesarean section was performed in the 40th week of pregnancy because of macrosomia and a history of cesarean section.

Discussion

The prevalence of AVM is estimated at 0.01–0.50%

of the population.[6,7] AVM is generally present in patients aged between 20 years and 40 years, and especially in those over 30 years, which is a childbearing age for women. AVM rupture during pregnancy is associated with maternal mortality of 28% and fetal mortality of 14%.[1] The implication of pregnancy in AVM rupture is controversial, but the bleeding rate appears to increase up to three-fold.[1–3,8] Although the rebleeding rate during the first year in the natural course of a ruptured AVM varied from 6% to 15.8%, the frequency of rebleeding during the same pregnancy could be as high as 27%.[3,9] Moreover, in a recent report by Gross and Du, the annual hemorrhage rate during pregnancy was 10.8%, the hemorrhage rate per pregnancy was 8.1%, and the hazard ratio for intracerebral hemorrhage during pregnancy was 7.91.[10] In view of these very high rates, cases of AVM in pregnant women should be treated with great care.

Here, we described the role of intraoperative FHR monitoring in two cases of elective surgery for AVM presenting with intracerebral hemorrhage at different stages of pregnancy. Although radical treatment for ruptured AVM tended to be performed after delivery in many case reports and case series, early surgical intervention for patients with an immature fetus before delivery would lead to improved maternal and fetal prognosis if the surgical risk is low.[3,11–13] The indication of surgery for AVM is determined primarily by the Spetzler-Martin grading scale.[14,15] The removal of AVM was supposed to be completed safely in our cases because the AVM grade was low. However, one of the anxieties for neurosurgeon is about fetal well-being during perioperative period. Although many cases of neurosurgery during pregnancy have been reported, the reference of intraoperative FHR monitoring was in few reports of brain tumor.[4,5] FHR monitoring is important for the assessment of reassuring fetal status in the antepartum as well as intrapartum stage.[16–18] Several reports have recommended continuous intraoperative FHR monitoring if non-obstetric surgery is performed after the 16th week of pregnancy.[19–22] Prolonged deceleration or bradycardia caused by maternal hypoperfusion, maternal hypoxia, compression of the umbilical cord, or the depression of the fetal cardiovascular system by anesthetic agents reflects a decreased uterine and placental circulation that can result in fetal asphyxia, acidosis, and death.[4,19] Loss of FHR variability does not always indicate fetal distress under general anesthesia because it may occur by the effect of anesthetic agents on the fetal autonomic nervous system.[19,23] Unexpected intraoperative bleeding or induced maternal hypotension would lead to the risk of mother and fetus during cerebrovascular surgery, especially in the timing as resection of AVM or clipping of cerebral aneurysm.[24,25] A mean arterial pressure of < 70 mmHg or a reduction in systolic arterial pressure of 25–30% is sufficient to reduce utero-placental blood flow.[23] We can adjust the maternal blood pressure, maternal oxygenation, and anesthetic agents as soon as possible if FHR abnormality occurs. Nevertheless, cesarean section is required unless the fetal distress improves. Our indication for emergency cesarean section is the incidence of prolonged deceleration or bradicardia with < 80 bpm for 2 minutes, based on the framework by Parer and Ikeda.[16] This value is correlated with the lower limit thresholds of pH 7.1 and base excess of −12 mEq/L in umbilical arterial blood, which indicates the fetal hypoxic damage. In these circumstances, FHR monitoring can be especially valuable for cerebrovascular surgery.

In the third trimester, CTG is widely used to monitor the FHR for fetal well-being. Being safe, easy, and quick, CTG has become very popular. In our case, the patient was in the supine position and her abdomen was left unobstructed so that emergent cesarean section could be performed if fetal asphyxia was suspected. In the second trimester, the transesophageal echo probe was useful because of the advantages of being flexible and easy to attach to the mother's lower abdomen comparing with the usual doppler ultrasound probe. Both these approaches allowed easy, stable, and successful FHR monitoring. The problem associated with FHR monitoring in the late stage of pregnancy is the movement of the fetus. The CTG sensor would have to be repositioned when the fetus moves. However, fetal movement tends to be reduced under general anesthesia as our first case.[26] The problem with FHR monitoring in the early stage of pregnancy is that the fetus cannot be rescued directly when non-reassuring fetal status is suspected. In addition, the usefulness of intraoperative FHR monitoring during pregnancy is controversial, because no large systematic study has been conducted. Maternal anesthesia may decrease the baseline FHR and variability.[19,23] Misinterpretation of FHR data could result in interventions that endanger the fetus, such as an unnecessary cesarean section.[27] So, a trained obstetrician team is needed to read it and prepare for an urgent cesarean delivery during surgery.[28] Horrigan et al. reviewed that no fetal hypoxic condition has been documented without the occurrence of a maternal hypoxic complication, whether FHR monitoring is used or not.[29] Balki and Manninen reported a successful craniotomy for suprasellar meningioma in a 28-week pregnant woman who suffered from rapidly deteriorating

vision, without FHR monitoring.[5] They did not use FHR monitoring because there was no preparation for emergency cesarean delivery with the mother's consent. The American College of Obstetrics and Gynecology Committee opinion on "Non-Obstetric surgery in Pregnancy" stated that "although there are no data to support specific recommendations regarding non-obstetric surgery and anesthesia in pregnancy, it is important for non-obstetric physicians to obtain obstetric consultation before performing non-obstetric surgery, and the decision to use fetal monitoring should be individualized and each case warrants a team approach for optimal safety of the woman and her baby."[28] FHR monitoring facilitates the best possible care for the fetus, especially when the mother wishes to continue the pregnancy or deliver the fetus if fetal asphyxia is suspected. In this line, we were able to operate safely, stably, and successfully for both mother and fetus under monitoring of FHR with the cooperation of obstetrician and anesthesiologist.

Conclusion

FHR monitoring is useful for AVM surgery during pregnancy. CTG is an appropriate method in the third trimester, whereas ultrasonography, using a transesophageal echo probe, can be used in the second trimester. These methods could have a wider application for cerebrovascular surgery during pregnancy.

Conflicts of Interest Disclosure

The authors declare no conflict of interest concerning the materials or methods used in this study or the findings specified in this article.

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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.

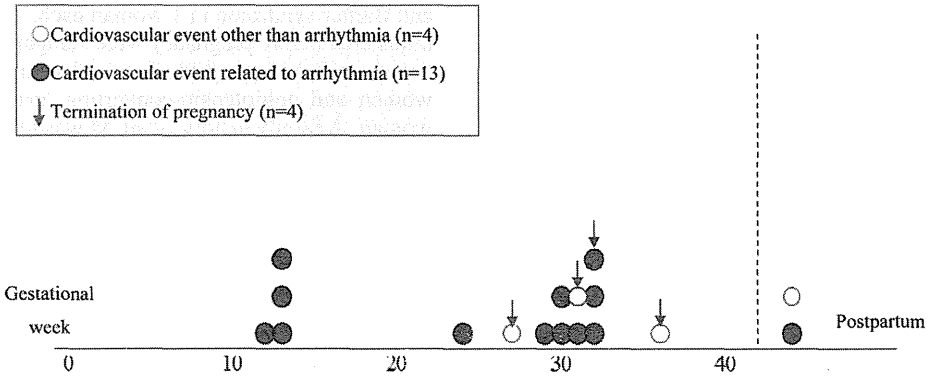

Figure. Cardiovascular events and gestational weeks (n=18).

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.

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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

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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.

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