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Original article

Clinical practice and short-term efficacy of 2.45-GHz microwave endometrial ablation to treat menorrhagia

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ABSTRACT

Objective: To evaluate the clinical practice and short-term efficacy of microwave endometrial ablation (MEA) to treat menorrhagia, and to identify prognostic factors for optimal outcomes.
Methods: We performed MEA in 22 women with menorrhagia between October 2012 and December 2013. To evaluate efficacy, objective and subjective variables were measured using medical records and patients' pre- and postoperative responses to a written questionnaire with a visual analog scale (VAS) scored from 0 to 10 for each symptom. MEA outcome was evaluated 6 months after treatment. Patients with amelioration of menorrhagia and no anemia were defined as the effective group, and the others were defined as the noneffective group. Effective patients requiring no hormonal therapy were defined as the highly effective group. To identify prognostic factors, background factors were compared between the highly effective group and the other groups.
Results: Uterine fibroids and adenomyosis were diagnosed in 68% and 32% of patients, respectively. The median VAS score of postoperative pain was 1.0, and that of satisfaction was 8.1. Hemoglobin concentration, menstrual bleeding volume, menstrual duration, menstrual pain, vaginal discharge, and fatigue were ameliorated in the postoperative period. The effective group, the highly effective group, and the noneffective group included 95%, 84%, and 5% of patients, respectively. The uterine corpus cavity was significantly shorter in the highly effective group than in the other groups.
Conclusion: MEA was safe and effective. The short-term efficacy rate of MEA for alleviating menorrhagia symptoms was 95%. Optimal outcomes were correlated with a shorter uterine corpus cavity.

Introduction

Endometrial ablation is considered an important surgical option for the treatment of menorrhagia.[1] In Japan, microwave endometrial ablation (MEA) using a frequency of 2.45 GHz was described and developed as an original applicator for use by Kanaoka et al[2] in 2001. After the Japanese Ministry of Health, Labour, and Welfare authorized the use of MEA as an advanced medical therapy in 2009, MEA has been offered in a few approved institutions and facilities. In April 2012, MEA was approved by the national health insurance system in Japan as a covered treatment for menorrhagia. At that time, we began providing MEA in our hospital. Several researchers evaluated the efficacy of MEA based on the condition during 3–24 months after operations. Ishikawa et al[3] showed that no patient experienced recurrent menorrhagia for > 6 months after MEA. Therefore, the short-term postoperative condition was evaluated in 6 months in this research. The purposes of this research were to evaluate the clinical practice and short-term efficacy of 2.45-GHz MEA to treat menorrhagia and to identify the prognostic factors associated with optimal MEA outcomes.

Materials and methods

Patient selection

Patients with symptoms of menorrhagia who were no longer bearing children and with no uterine malignancy were initially

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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deemed eligible to receive MEA. After initial screening, eligibility to receive MEA was individually decided on the basis of preoperative assessment using ultrasonography and/or magnetic resonance imaging. In principle, patients whose menorrhagia was not easy to control by conservative therapy were deemed to be good candidates. Patients whose uterine cavity was too large or too complex in shape to appropriately and safely provide MEA were excluded. Patients who preferred hysterectomy, which would furnish a perfect effect for menorrhagia in exchange for the invasiveness, were excluded as well. Before undergoing MEA, patients received an iron supplement, pseudomenopausal therapy (subcutaneous leuprolide acetate), and an oral hormonal medication (dienogest or an estrogen–progestin combination) if necessary.

Ablation procedure

The microwave system used in this research was composed of a Microtaze device and a Sounding Applicator (Alfresa Pharma, Osaka, Japan). The former is a power generator of 2.45-GHz microwaves, and the latter is an intrauterine applicator that irradiates microwaves from its tip. The applicator is 4 mm in diameter and curved to access the endometrium easily, and it reaches to a maximum distance of 18 cm. MEA was performed according to the procedure guidelines described previously.[4] The microwave generator's output was set to 70 watts for 50 seconds for each irradiation. Transabdominal ultrasonography was used for intraoperative monitoring. Immediately before and after the procedure, as well as during the procedure if necessary, hysteroscopy was used to visualize the ablated area. Microwave irradiation was repeated until a sufficient area of the uterine corpus endometrium had been ablated. General anesthesia was used, and a nonsteroidal anti-inflammatory drug was administered intraoperatively.

Research design

We performed MEA in 22 women with menorrhagia between October 2012 and December 2013. To evaluate MEA efficacy, subjective and objective variables were measured. Objective variable data were drawn from patients' medical records, including their laboratory test results, and subjective variables were measured using patients' responses to a written questionnaire survey. Pre- and postoperative subjective symptom ratings of each patient were obtained using a questionnaire with a visual analog scale (VAS) scored from 0 to 10 for each symptom. The questionnaire survey was performed and MEA outcome was evaluated by each patient 6 months after treatment. At that time, patients with amelioration of menorrhagia and no anemia were defined as the effective group, and the others were defined as the noneffective group. Amelioration of menorrhagia was defined by self-report as mentioned in the patient's medical record 6 months after MEA, or by a subjective estimate of postoperative menstrual bleeding volume that was decreased to half or less than the preoperative volume in the patient. Moreover, the effective group was subdivided into two groups: those whose postoperative symptoms required no hormonal therapy comprised the highly effective group, whereas those who continued to use additional hormonal therapy in the postoperative period were classified as the fairly effective group.

To evaluate MEA efficacy in detail, each patient's pre- and postoperative variables were compared. To identify the prognostic factors associated with the optimal outcomes, background factors were compared between the highly effective group and the other groups. Correlation was measured between the length of the uterine corpus cavity (from the anatomical internal os to the upper edge of the endometrium) and the number of microwave irradiation sessions required.

This research was planned and performed on the basis of the approval of the research ethics committee in our hospital. Each patient's written informed consent to the research was obtained along with the responses to the questionnaire.

Data were analyzed using JMP version 8.0 (SAS Institute, Cary, NC, USA) and R version 2.13. Two-tailed p values were calculated using univariate methods including the Mann–Whitney U test, Wilcoxon signed rank test, McNemar test, Chi-square test, and Pearson product-moment correlation coefficient. A p value < 0.05 was considered significant.

Results

The characteristics of the 22 patients who received MEA are shown in Table 1. No patients received a diagnosis of functional menorrhagia; all patients had either uterine fibroids or adenomyosis. Summarized data concerning the MEA procedures are shown in Table 2. On the whole, MEA yielded high levels of patient satisfaction with minimal postoperative pain. The only clinically problematic adverse event occurred in a patient with a single intramural fibroid of 55 mm in diameter. The patient had a fever with purulent vaginal discharge 1 week after MEA. The condition was diagnosed as bacterial endometrisis, and she had to be briefly admitted to our hospital for intravenous antibiotics.

To evaluate MEA efficacy in detail, pre- and postoperative variables of each patient were compared. An iron supplement was administered to 81.8% and 5.3% of patients ($p < 0.001$ by McNemar test), pseudomenopausal therapy was administered to 68.2% and 10.5% ($p < 0.001$), and oral hormonal medication was administered to 5.3% and 10.5% ($p = 1.0$) of the 22 women in the pre- and postoperative periods, respectively. Changes in hemoglobin concentration and patients' subjective symptom ratings are presented in Figure 1. Hemoglobin concentration (median preoperative score, median postoperative score, and median variation were 8.6, 13.5, and +5.3, respectively), menstrual bleeding volume (10, 1.0, and −8.0, respectively), menstrual duration (7.0, 2.5, and −3.5, respectively), menstrual pain (7.5, 0.5, and −4.0, respectively), vaginal discharge (4.8, 1.6, and −2.4, respectively), and fatigue (7.5, 2.0, and −5.0, respectively) ameliorated in the postoperative period.

Table 1
Characteristics of the 22 patients who received microwave endometrial ablation to treat menorrhagia.

Factors	Median	Range	*n*	%
Age (y)	46.5	39–54		
Parity	2	0–4		
Previous cesarean delivery			6	27.3
Obesity (BMI ≥ 25)			4	18.2
Initial anemia[a]			18	81.8
Initial hemoglobin concentration (g/dL)	8.6	4.0–13.6		
Organic diagnosis causing menorrhagia				
Uterine fibroids			15	68.2
Multiple fibroids			9	60.0
Submucosal fibroids			8	53.3
Adenomyosis			7	31.8
Functional menorrhagia			0	0
Patient complaints				
Heavy menstrual bleeding			22	100
Prolonged menstruation			10	45.5
Painful menstruation			11	50.0
Uterine corpus cavity length (cm)	5.5	3.4–7.5		
Preoperative use of iron supplement			18	81.8
Preoperative pseudomenopausal therapy			15	68.2
Preoperative oral hormonal medication			1	4.5

BMI = body mass index.
[a] Initial hemoglobin concentration < 12.0 g/dL.

Table 2
Summarized data concerning microwave endometrial ablation procedures.

Variables	Median	Range	*n*	%
No. of microwave irradiation sessions per operation	7.0	5–12		
Operative time (min)[a]	18	10–43		
Postoperative use of painkiller on the operative day			6	27.3
Postoperative use of painkiller on and after the next day			4	18.2
VAS score of postoperative pain (points)[b]	1.0	0–10		
VAS score of satisfaction (points)[c]	8.1	2.5–10		

VAS = visual analog scale.
[a] The duration from starting the first irradiation to ascertaining necessary and sufficient ablation by hysteroscopy.
[b] A lower score indicates milder pain.
[c] A higher score indicates a higher level of satisfaction.

In the 19 patients whose postoperative conditions were obtained, amenorrhea was observed in 52.6% (10/19) in the postoperative period. Only one patient reported no improvement in the menstrual bleeding volume. She received a diagnosis of multiple uterine fibroids, including a 56-mm submucosal fibroid. Her uterine corpus cavity measured 7.5 cm, and the operator performed 12 microwave irradiation sessions during the patient's MEA procedure. Her pre- and postoperative ratings of menstrual bleeding volume were 10 and 10, respectively.

The MEA outcomes were largely positive: 94.7% (18/19) of patients were classified in the effective group, and 84.2% (16/19) also met the criteria for the highly effective group, whereas only 5.3% (1/19) of patients were classified into the noneffective group. Subsequent hysterectomies were performed in two patients, although these events occurred after the postoperative study period of 6 months. One case was the aforementioned patient who underwent hysterectomy 11 months after MEA. The second patient received a diagnosis of adenomyosis and pelvic endometriosis with severe anemia and dysmenorrhea. Although MEA reduced the patient's reported menstrual bleeding volume, her dysmenorrhea was not relieved and pelvic endometriosis was exacerbated. After MEA, she received pseudomenopausal therapy, which also did not produce sufficient improvement in her symptoms. Therefore, the patient underwent hysterectomy with affected-side salpingo-oophorectomy 1 year after MEA.

To identify the prognostic factors associated with the optimal outcomes, background factors were compared between the highly effective group and the other groups (Table 3). The mean uterine corpus cavity length was significantly shorter in the highly effective group than in the other groups, and no patients in this group had a cavity length greater than 7 cm.

The correlation between the uterine corpus cavity length and the number of microwave irradiation sessions required for treatment was analyzed (Figure 2), and a positive linear correlation was observed ($r = 0.54$, $p = 0.008$).

Discussion

MEA was safely and effectively provided in our hospital. The short-term efficacy rate of MEA for the treatment of menorrhagia was estimated to be 94.7%. The optimal MEA outcomes were associated with a shorter uterine corpus cavity. A positive linear correlation was

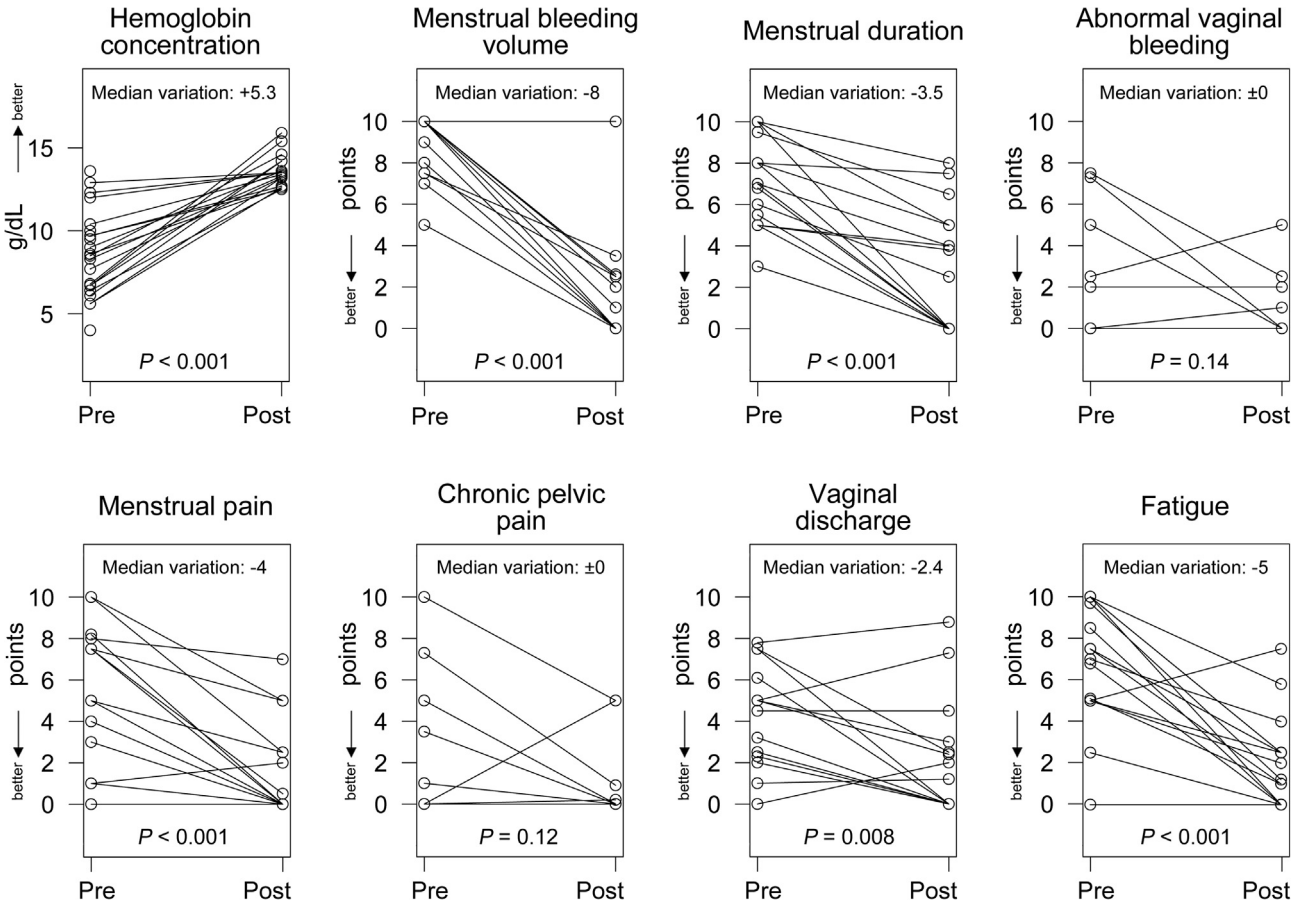

Figure 1. Changes in hemoglobin concentration and patients' subjective symptom ratings to evaluate the efficacy of microwave endometrial ablation in detail. The *p* values are calculated using Wilcoxon signed-rank tests.

Table 3
Comparison of background factors between the highly effective group and the other groups in the 19 patients whose postoperative ratings were obtained.

Factors	Highly effective group	Other groups	*p*
Age (y)	45.5	46	0.96
Parity	2	2	0.39
Previous cesarean delivery (%)	37.5	0	0.20
Obesity (BMI ≥ 25; %)	25.0	0	0.33
Initial hemoglobin concentration (g/dL)	8.4	9.7	0.91
Organic diagnosis causing menorrhagia (%)			
Uterine fibroids	68.8	33.3	0.25
Multiple fibroids	63.6	100	0.46
Submucosal fibroids	63.6	100	0.46
Adenomyosis	33.3	68.8	0.25
Patient complaints (%)			
Prolonged menstruation	43.8	33.3	0.74
Painful menstruation	50.0	100	0.11
Uterine corpus cavity length (cm)	5.5	7.2	0.010
VAS scores of patients' subjective preoperative conditions (points)			
Menstrual bleeding volume	10	7.5	0.18
Menstrual duration	7	5	0.19
Abnormal vaginal bleeding	0	5	0.068
Menstrual pain	5	8	0.21
Chronic pelvic pain	2.5	0	0.79
Vaginal discharge	5	2.4	0.27
Fatigue	7.5	5	0.28
Preoperative pseudomenopausal therapy (%)	68.8	66.7	0.95

Data are presented as the median or proportion in each group. The *p* values were calculated using Chi-square or Mann–Whitney *U* tests.
BMI = body mass index; VAS = visual analog scale.

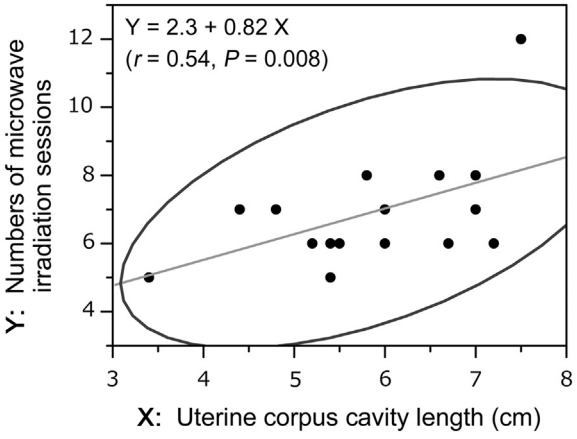

Figure 2. Correlation between the uterine corpus cavity length and the number of microwave irradiation sessions, measured using the Pearson product-moment correlation coefficient.

observed between the uterine corpus cavity length and the number of microwave irradiation sessions required for treatment.

To perform MEA safely, Kanaoka et al[4] presented guidelines for 2.45-GHz MEA procedures. Among the reported adverse events caused by MEA, the most severe outcomes are uterine perforation and heat damage to the extrauterine organs. To avoid the former event, ongoing ultrasonographic monitoring and hysteroscopic examination during the procedure are recommended to allow observation of the ablated endometrial area. To avoid the latter event, it is recommended that the myometrial layer of the area to be ablated should have a depth of at least 10 mm. This recommendation is based on the results of the original study, which showed that a single session of 2.45-GHz microwave irradiation with an output of 70 watts for 50 seconds formed a lemon-shaped necrotic area with a width of 16 mm and a length of 20 mm around the tip of the applicator.[4,5] Endometrial ablation, including MEA, has a higher latent risk in patients who underwent a previous cesarean delivery.[4,6] If the operator grasps the thinness on the previous cesarean scar properly, he or she can provide MEA and avoid irradiation sessions on the thin scar wall. In the current study, six patients with a history of cesarean delivery received MEA. They were safely treated with careful provision in consideration of the thinness around the previous cesarean scar. All of them obtained highly effective outcomes.

The short-term efficacy rate of MEA for the treatment of menorrhagia was estimated to be 94.7%. Moreover, a highly effective outcome was obtained in 84.2% of patients. Short-term efficacy of MEA reported in the recent literature is summarized in Table 4.[3,7–10] On the whole, the efficacy rate for reducing the menstrual bleeding volume is estimated to be ~90%, and the postoperative amenorrhea rate is 20–40%. The effectiveness for relieving concomitant menstrual pain is reportedly high as well. In the current study, similar results were observed.

The optimal MEA outcomes were associated with a shorter uterine corpus cavity. This result does not suggest that the factor had a robust influence on the highly effective outcome because the result was determined by univariate analysis. However, this prognostic factor may help clinicians determine the likelihood that MEA will produce positive outcomes in a particular patient. Women with a uterine corpus cavity length of < 7 cm may obtain better outcomes, whereas those with a longer uterine corpus cavity may be more likely to require subsequent hormonal therapy or hysterectomy postoperatively. A trend was observed that patients with lower preoperative levels of menstrual pain and abnormal vaginal bleeding may obtain better MEA outcomes, but this was not significant. Peeters et al[6] similarly reported that short uterine depth and no dysmenorrhea were prognostic factors for the success of endometrial ablation to treat menorrhagia. This information may help physicians plan individual therapeutic strategies in the management of menorrhagia.

A positive linear correlation was observed between the uterine corpus cavity length and the number of microwave irradiation

Table 4
Short-term efficacy of microwave endometrial ablation reported in the recent literature.

Year	Researchers	*n*	Period of assessment for therapeutic effect (mo after MEA)	Reduction in menstrual bleeding volume	Postoperative amenorrhea rate	Amelioration of menstrual pain	Subsequent hysterectomy rate
2009	Sambrook et al[7]	157	12	76	41		4
2012	Singh et al[8]	68	6–18	84	41	72	7
2012	Tsuda[9]	25	3	96	32		
2012	Ishikawa et al[3]	55	6–24	92	31	81	2
2014	Nakayama et al[10]	76	6	95	34	VAS score of 4.2 improved to 1.3	
2014	This research	19	6	95	53	VAS score of 7.5 improved to 0.5	9[a]

Data are presented as %, unless otherwise indicated.
VAS = visual analog scale.
[a] These were performed after the postoperative study period of 6 months.

sessions required for treatment. As a rough estimate, a uterine corpus cavity with a length of 5 cm generally required six microwave irradiation sessions, one of 6 cm needed seven sessions, and one of 7 cm required eight sessions. This guideline may assist MEA operators in selecting the number of microwave irradiation sessions, taking into account uterine size, uterine shape, organic diagnosis, and previous history of cesarean delivery.

Since the introduction of MEA for the treatment of menorrhagia in our hospital in 2012, the procedures have been shown to be both effective and safe. In our experiences, the cases that do not have very large cavities, protuberating submucosal myomas, and severe endometriosis outside the uterus are considered to be positive indications for MEA. Particularly for a case with large submucosal myomas, Kanaoka et al[11] developed and reported the system of transcervical microwave myolysis. It seems to have potency; however, it cannot be applied yet for approved treatment. We hope to continue contributing to improvements in the provision and research of this novel and useful therapy in Japan.

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