Original Research

Bipolar Radiofrequency Compared With Thermal Balloon Ablation in the Office

A Randomized Controlled Trial

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OBJECTIVE: To estimate the effectiveness of office-based bipolar radiofrequency ablation compared with thermal balloon ablation of the endometrium for the treatment of heavy menstrual bleeding at 5-year follow-up.

METHODS: A single blind randomized controlled trial was conducted in an office hysteroscopy clinic in a university teaching hospital. A total of 81 women were randomly allocated to either bipolar radiofrequency ablation or thermal balloon ablation in an office setting avoiding use of general anesthesia or conscious sedation. The primary outcome for the trial was amenorrhea at 6 months follow-up. In this planned secondary analysis, the main outcome measures were amenorrhea rates, patient satisfaction, health-related quality of life, and incidence of further uterine surgery at 5-year follow-up.

RESULTS: At 5-year follow-up, 59 (73%) women responded to postal questionnaires. Amenorrhea was reported in 60% of thermal balloon ablation and 62% of bipolar radiofrequency ablation (odds ratio [OR] 1.09 [0.38–3.11]) and satisfaction with treatment outcome in 96% of thermal balloon ablation and 96% of bipolar radiofrequency ablation (OR 0.92 [0.05–25.59]). Further surgical intervention was needed in three of 29 (10%) women treated with bipolar radiofrequency ablation compared with four of 30 (13%) of women treated with thermal balloon ablation (P=.7). There was no significant difference in either condition-specific or generic health-related quality-of-life measures.

CONCLUSION: There was no difference in the effectiveness of bipolar radiofrequency ablation and thermal balloon ablation performed in an office setting at 5-year follow-up.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, www.clinicaltrials.gov, NCT01124357.

(Obstet Gynecol 2014;124:219–25)

DOI: 10.1097/AOG.0000000000000395

LEVEL OF EVIDENCE: I

The safety, feasibility, acceptability, and short-term effectiveness of endometrial ablation for the treatment of heavy menstrual bleeding in an office setting has been demonstrated.[1,2] The results of longer-term follow-up are important so that women can be counseled properly about the results of the hysterectomy-sparing surgery on heavy menstrual bleeding. Although 5- and 10-year effectiveness data have recently been published for conventional inpatient endometrial ablation under general anesthesia,[3–6] there is a lack of any longer-term data for office-based endometrial ablation.

We previously have published the results of a randomized controlled trial (RCT) showing that office-based bipolar radiofrequency ablation (NovaSure) was significantly quicker and achieved a greater degree of endometrial destruction than the thermal balloon ablation (Thermachoice III), although there was no significant difference in amenorrhea rates at 6 months.[1] The aim of this article is to provide 5-year follow-up data for amenorrhea rate, patient satisfaction rate, health-related quality of life compared with baseline, and incidence of further uterine surgery, namely repeat endometrial ablation or hysterectomy.

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Supported by the BWH Foundation Trust. The administration costs of this research were supported by a research grant provided by Cytyc (now Hologic), which manufactures the NovaSure ablation system.

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Financial Disclosure
Dr. Clark has received research monies from Cytyc (now Hologic) for the administration costs of the thermal balloon compared with the bipolar radiofrequency ablation trial. In addition to this, he has received honoraria from Hologic and Gynecare to run training workshops in office hysteroscopy techniques. The other authors did not report any potential conflicts of interest.

ISSN: 0029-7844/14

MATERIALS AND METHODS

A single-blinded, parallel-group RCT comparing bipolar radiofrequency ablation with thermal balloon ablation for the treatment of heavy menstrual bleeding in the office setting was conducted at the Birmingham Women's Hospital Foundation Trust between May 2006 and October 2007. To be included in the trial, women needed to have heavy menstrual bleeding that affected their quality of life and opt for ablative treatment in the office setting. Women were excluded if they had pathology that distorted the uterine cavity, previous classical cesarean delivery or myomectomy, were younger than 25 years, were perimenopausal (defined as follicle-stimulating hormone level of 40 international unit/L or greater), or there was suspicion of genital tract infection. Endometrial sampling was performed before the procedure to rule malignant and premalignant causes for bleeding. All participating women gave written informed consent. This trial was registered on clinicaltrials.gov (identifier: NCT01124357). The National Research Ethics Service, UK, granted ethical approval (identifier: 06/q2709/34). Research and development approval was sought and granted at Birmingham Women's Hospital Community Trust.

Women were allocated in a one-to-one ratio to either of the interventions through a telephone-based system managed by the University of Birmingham Clinical Trials Unit. The randomization blocks were kept centrally in the Birmingham Clinical Trials Unit and block sizes varied so that the allocation could not be deduced prerandomization. Blocks were stratified by age (younger than 40 years or 40 years or older) and uterine cavity length (8 cm or less or greater than 8 cm) to ensure we achieved balance between groups for these variables. Uterine cavity length was chosen because it could influence the area ablated and age was chosen because of its association with an ensuing menopause. The allocated ablative technologies were performed according to the manufacturer's instructions using a standard departmental protocol for office endometrial ablation, which has been previously described.[1]

The primary outcome was the proportion of women with amenorrhea. This was assessed using the following Likert scale: "How would you describe your menstrual periods?": "no bleeding," "spotting or discharge only," "light bleeding," "moderate bleeding," or "heavy bleeding." Satisfaction with treatment was also measured using a Likert scale using the following response categories: "Compared with before treatment, would you say that your heavy menstrual bleeding is: 'much better,' 'a little better,' 'same,' or 'worse.'" Similar scales were using for dysmenorrhea and premenstrual syndrome.

General health-related quality of life was measured using the EuroQoL-5D scale (best possible score was 1 for utility and 100 for the health thermometer).[7,8] Sexual function was measured using the sexual activity questionnaire (on a scale from 0 to 18 for pleasure and 0 to 6 for discomfort)[9,10] with higher scores indicating more pleasure and less discomfort. Disease-specific quality of life was measured using the menorrhagia multiattribute utility assessment score (Shaw score)[11] and the menorrhagia outcomes questionnaire.[12] The menorrhagia multiattribute utility assessment score gives a maximum score of 100, which indicates no problems with the monthly cycle. For the menorrhagia outcomes questionnaire, the lower the score, the better; no baseline measurement was taken and the results were standardized to a mean of 50 as recommended by the author. Direct enquiry was made regarding further medical or surgical intervention for menstrual problems.

Data were collected using postal questionnaires, which were posted to women at 3, 6, 12, and 60 months follow-up. In cases in which there was no reply, a second questionnaire was sent. If there was still no reply, the women were phoned and a third questionnaire sent with their permission.

The sample size for this trial was originally chosen to give statistical power to detect a clinically important difference in the primary measure of amenorrhea at 6 months follow-up and has been previously described.[1] Analysis was performed by intention-to-treat. For the purpose of analysis, all women who had undergone hysterectomy were considered to have amenorrhea, although a sensitivity analysis was performed in which they were considered not to have amenorrhea. Furthermore, women with hysterectomies were excluded from the comparison of age between ablation groups because the relationship between age and menopause was no longer relevant. Logistic regression was used for the dichotomous outcomes amenorrhea, reduction in bleeding, dysmenorrhea, premenstrual syndrome, and further intervention rates. Odds ratios and 95% confidence intervals were derived with a χ^2 test used to assess statistical significance. Because data were not normally distributed, medians and interquartile ranges were calculated for the EuroQoL-5D, health thermometer, menorrhagia multiattribute utility assessment, menorrhagia outcomes questionnaire, and sexual activity questionnaire. A Mann–Whitney *U* test

was used to assess statistical significance. All analyses were carried out using SPSS 21.

RESULTS

Between May 2006 to October 2007, 39 women were randomized to thermal balloon ablation and 42 women were randomized to bipolar radiofrequency ablation (Fig. 1). At 5-year follow-up, 59 (73%) women responded to postal questionnaires. There were 29 (69%) women who responded in the bipolar radiofrequency group compared with 30 (77%) who responded in the thermal balloon ablation group. The baseline characteristics were comparable between the two groups, although there was a mean 2.2-year gap between those treated with thermal balloon ablation compared with bipolar radiofrequency ablation (49.2 compared with 47.0 years; Table 1). There was no significant difference in baseline characteristics between the women who returned the questionnaires compared with those who did not.

Over the 5-year follow-up there was an increase in rates of amenorrhea for both treatment groups (Table 2). At 3, 6, and 12 months follow-up, there were higher amenorrhea rates in the bipolar radiofrequency ablation group, but this was clinically significant only at the 12-month follow-up. However, this difference in amenorrhea rate did not persist at the 5-year follow-up (bipolar radiofrequency ablation 18 of 29 [62%] compared with thermal balloon ablation 18 of 30 [60%]; odds ratio [OR] 1.09, 95% confidence interval [CI] 0.38–3.11). Similarly, no difference in amenorrhea was observed when an adjusted OR was calculated to account for the age difference noted in respondents and the possible effects of menopause on the results (OR 1.39, 95% CI 0.42–4.62). Of the women who returned questionnaires at 12 months, 45 (90%) returned questionnaires at 5 years. A further sensitivity analysis was performed to check for a response bias by presuming that those who did not return the questionnaires at 5 years had the same symptoms as they did at 12 months (OR 1.21 [0.43–3.42]). For the purpose of these analyses, women who had hysterectomy were considered to be amenorrheic. A sensitivity analysis was performed in which those women with hysterectomy were considered not to have amenorrhea (OR 1.22 [0.44–3.40]; *P*=.7).

At 5-year follow-up, there were three of 29 (10%) women treated with bipolar radiofrequency ablation who had undergone hysterectomy compared with four of 30 (13.3%) women treated with thermal balloon ablation (*P*=.7). Two of the four women treated with thermal balloon ablation who ultimately had a hysterectomy had also undergone a repeat thermal balloon ablation procedure in the interim. Indications for hysterectomy in those who had thermal balloon ablation included complex hyperplasia (n=1) on biopsy and persistent heavy menstrual bleeding (n=3). Indications for

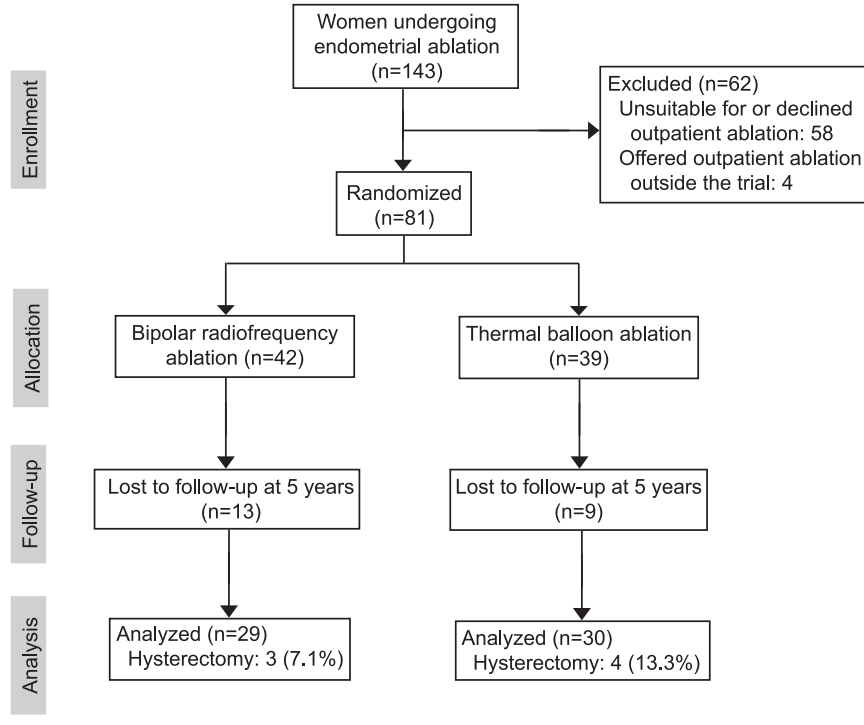

Fig. 1. A randomized controlled trial of office ablation techniques.
Smith. Office Endometrial Ablation Trial. Obstet Gynecol 2014.

Table 1. Baseline Characteristics of Those Followed Up for 5 Years

Characteristic	Thermal Balloon (n=30)	Bipolar Radiofrequency (n=29)	*P*
Age at 5-y follow-up*	49.2±4.6	47.0±4.4	NS
	41, 59	35, 55	
Parity	2.5±1.2	2.7±1.2	NS
	0, 6	1, 5	
Cesarean delivery	5 (17)	6 (21)	NS
BMI (kg/m^2)	29.3±6.6	29.7±5.9	NS
Follicle-stimulating hormone (international units/L)	7.2±6.4	5.7±5.0	NS
	2.1, 31.4	1.5, 26.4	
Uterine cavity length (cm)	8.6±1.2	8.1±0.6	NS
	6, 11	7, 9.5	
Uterine axis			
Anteflexed	22 (73)	23 (82)	NS
Retroflexed	8 (27)	5 (18)	NS
Axial	0	0	NS
Endometrium			
Proliferative	12 (40)	9 (32)	NS
Secretory	9 (30)	10 (35)	NS
Menstrual	8 (27)	9 (32)	NS
Atrophic	1 (3)	0 (0)	NS
Dysmenorrhea	25 (83)	21 (75)	NS
Premenstrual syndrome	21 (70)	22 (79)	NS

SD, standard deviation; NS, not significant; BMI, body mass index.
Data are mean±standard deviation, (minimum, maximum), or n (%) unless otherwise specified.
* Does not include the age of those who had hysterectomy ($P>.05$).

hysterectomy in those who had bipolar radiofrequency ablation included cyclical pelvic pain, offensive watery vaginal discharge, and persistent heavy menstrual bleeding (all n=1).

Significant improvement in heavy menstrual bleeding, premenstrual syndrome, and dysmenorrhea symptoms were observed after both treatments throughout the 5-year follow-up period, but there was no evidence of difference between the groups (Table 3). At 5-year follow-up there was no significant change from baseline for generic health-related quality of life or sexual activity scores for either technique. The disease-specific health-related quality of life (multiattribute utility score) was significantly higher at all time points compared with baseline for both techniques, but there was no significant difference between techniques (Table 4).

DISCUSSION

This secondary analysis of a RCT has shown that both bipolar radiofrequency ablation and thermal balloon ablation are equally effective at treating heavy menstrual bleeding, dysmenorrhea, and premenstrual syndrome and improving health-related quality of life 5 years after treatment. The 62% amenorrhea rate for bipolar radiofrequency ablation at 5 years reported in this trial is similar to longer-term follow-up rates previously reported for bipolar radiofrequency ablation performed under general anesthesia.[3,6] However, the 60% rate of amenorrhea for thermal balloon ablation was almost double that of other studies in which rates of 29–32% have been reported.[3,13] This improvement in thermal balloon ablation may be explained in part by our use of a newer model in contrast to earlier studies that have used the previous, now no longer available, model, which did not distribute heat so evenly throughout the balloon. The only other RCT comparing bipolar radiofrequency ablation and thermal balloon ablation was conducted under general anesthesia and used the older thermal balloon

Table 2. The Effect of Office Radiofrequency and Thermal Balloon Ablation of the Endometrium on Rates of Amenorrhea

Time Point	Thermal Balloon	Bipolar Radiofrequency	*P*	OR (95% CI)
Amenorrhea				
3 mo	7/36 (19)	12/36 (33)	.2	2.07 (0.71–6.09)
6 mo	7/34 (21)	11/28 (39)	.1	2.50 (0.81–7.69)
12 mo	6/26 (23)	14/25 (56)	.02	4.24 (1.27–14.18)
5 y	18/30 (60)	18/29 (62)	.9	1.09 (0.38–3.11)
			*.6	1.39 (0.42–4.62)
Amenorrhea+spotting				
3 mo	15/36 (42)	19/36 (53)	.3	1.56 (0.62–3.97)
6 mo	14/34 (41)	17/28 (61)	.1	2.21 (0.80–6.13)
12 mo	15/26 (58)	17/25 (68)	.4	1.56 (0.50–4.90)
5 y	22/30 (73)	23/29 (79)	.6	1.39 (0.42–4.67)

OR, odds ratio; CI, confidence interval.
Data are n/N (%) unless otherwise specified.
* Value at 5 years adjusted for age.

Table 3. The Effects of Office Radiofrequency and Thermal Balloon Ablation of the Endometrium on Menstruation, Dysmenorrhea, and Premenstrual Syndrome

Time Point	Thermal Balloon	Bipolar Radiofrequency	*P*	OR (95% CI)
Heavy bleeding now improved				
3 mo	33/36 (92)	34/36 (94)	.6	1.54 (0.24–9.85)
6 mo	30/33 (91)	28/28 (100)	.2	6.54 (0.32–132.29)*
12 mo	24/26 (92)	23/23 (100)	.3	4.80 (0.22–105.26)*
5 y	26/27 (96)	24/25 (96)	.9	0.92 (0.05–25.59)
Period pain now improved				
3 mo	22/29 (76)	23/30 (77)	.9	1.05 (0.32–3.47)
6 mo	21/29 (72)	20/24 (83)	.3	1.90 (0.50–7.33)
12 mo	12/21 (57)	16/21 (78)	.2	2.40 (0.64–9.03)
5 y	18/21 (86)	17/21 (81)	.7	0.71 (0.14–3.64)
Improvement in emotional symptoms of premenstrual syndrome				
3 mo	9/21 (43)	17/26 (65)	.1	2.52 (0.77–8.22)
6 mo	11/22 (50)	11/18 (61)	.7	1.57 (0.44–5.56)
12 mo	10/16 (63)	10/20 (50)	.5	0.60 (0.16–2.29)
5 y	13/21 (62)	14/22 (64)	.9	1.08 (0.31–3.71)
Improvement in physical symptoms of premenstrual syndrome				
3 mo	12/21 (57)	15/25 (60)	.8	1.13 (0.35–3.65)
6 mo	14/21 (67)	12/17 (71)	.8	1.20 (0.30–4.78)
12 mo	8/16 (50)	13/20 (65)	.4	1.86 (0.48–7.12)
5 y	14/22 (64)	15/21 (71)	.6	1.43 (0.40–5.16)

OR, odds ratio; CI, confidence interval.
Data are n/N (%) unless otherwise specified.
* For the purpose of working out, the odds ratio a value of 1 was used instead of 0.

ablation technology. Although the authors reported that bipolar radiofrequency ablation was superior to thermal balloon ablation at 5-year follow-up, this conclusion was not substantiated by their results that showed no significant differences in rates of amenorrhea (relative risk 1.6 [95% CI 0.93–2.6]).[3] This group have just reported their 10-year follow-up data and again identified no differences in longer-term rates of amenorrhea (relative risk 1.1 [95% CI, 0.83–1.5]).[4]

The strength of this trial includes its strict randomization and its originality comparing ablative technologies in the office setting. Although we achieved more complete follow-up at 5 years than at 12 months,[1] the 27% loss to follow-up may have affected the validity of our findings to an uncertain degree. However, there were no significant differences in baseline characteristics between responders and nonresponders to postal questionnaires at 5 years. In keeping with other RCTs evaluating endometrial ablation, our primary outcome was amenorrhea.[6,14,15] However, although this outcome is relatively objective, it may not be the most relevant clinical outcome when evaluating long-term successful treatment. This is because a proportion of women will enter menopause during follow-up, thereby increasing amenorrhea rates indirectly. The older mean age of the thermal balloon ablation group could explain the blunting of treatment effect seen at 5 years compared with that observed earlier at 12 months. However, an adjusted analysis using increasing age as a surrogate marker for menopause provided no evidence to support this contention. It should be noted that the mean ages of women in both treatment groups were younger than 51 years, the average age of female menopause.[16]

It was reassuring to note that other pertinent clinical outcomes supported the sustained and comparable effectiveness of bipolar radiofrequency ablation and thermal balloon ablation at 5 years; condition-specific health-related quality of life was substantially improved from baseline in both groups and nine in every 10 women treated avoided hysterectomy. Our surgical reintervention rates for heavy menstrual bleeding were consistent with rates reported in other trials of second-generation ablative technologies at 5 years.[3,5] Two of the four women in the thermal balloon ablation group who had a hysterectomy also had a preceding repeat thermal balloon ablation, suggesting that that there may not be any clinical benefit to this strategy. Office endometrial

Table 4. The Effects of Office Radiofrequency and Thermal Balloon Ablation of the Endometrium on Quality-of-Life Measures

Time Point	Thermal Balloon	Bipolar Radiofrequency	*P*
EuroQol change from baseline			
3 mo	0.07 (0.09; 36)	0. 03 (0.20; 35)	.9*
6 mo	−0.07 (0.13; 32)	−0.07 (0.15; 27)	.6*
12 mo	−0.07 (0.17; 24)	0.17 (0.22; 25)	.99*
5 y	0.00 (0.11; 28)	0.13 (0.25; 22)	.1*
Health thermometer change from baseline			
3 mo	5.0 (26.0; 32)	1.5 (30.0; 30)	.5*
6 mo	5.0 (22.5; 29)	2.5 (35.0; 26)	.4*
12 mo	7.5 (24.8; 21)	4.0 (40.0; 22)	.9*
5 y	7.5 (27.3; 26)	3.0 (32.5; 25)	.9*
Multiattribute utility score change from baseline			
3 mo	39.3 (37.5; 36)	45.5 (45.2; 35)	.7*
6 mo	44.3 (43.8; 33)	42.4 (32.5; 27)	.7*
12 mo	49.8 (34.7; 25)	46.2 (46.1; 26)	.99*
5 y	54.7 (29.5; 26)	47.6 (37.9; 24)	.4*
Menorrhagia Outcome Questionnaire†			
3 mo	49.6 (1.3; 36)	49.8 (1.2; 36)	.7*
6 mo	49.5 (1.0; 33)	49.9 (1.2; 28)	.2*
12 mo	49.7 (0.9; 25)	49.7 (0.4; 26)	.9*
5 y	49.6 (1.4; 28)	49.5 (1.0; 21)	.7*
Sexual Activity Questionnaire pleasure change from baseline			
3 mo	1.0 (4.0; 22)	0.0 (4.5; 15)	.2*
6 mo	2.0 (4.0; 18)	0.0 (3.0; 13)	.2*
12 mo	1.5 (4.5; 14)	−1.0 (5.5; 11)	.6*
5 y	−1.0 (6.8; 20)	0.0 (5.0; 13)	.9*
Sexual Activity Questionnaire discomfort change from baseline			
3 mo	0.0 (1.0; 23)	0.0; (2.0; 16)	.2*
6 mo	0.0 (1.0; 18)	0.0 (2.5; 12)	.9*
12 mo	0.0 (1.3; 15)	0.0 (1.0; 10)	.4*
5 y	0.0 (1.0; 20)	−1.0 (1.8; 12)	.3*
Sexual activity questionnaire increase in habit change from baseline‡			
3 mo	11/27 (41)	8/20 (40)	>.99§
6 mo	3/21 (14)	6/19 (32)	.2§
12 mo	7/17 (41)	5/17 (29)	.5§
5 y	10/21 (48)	4/13 (31)	.9§

Data are median (interquartile range; n) or n/N (%) unless otherwise specified.
* Derived from Mann–Whitney *U* test.
† Menorrhagia outcome questionnaire standardized to a mean of 50. Posttreatment scores only.
‡ "Much or somewhat more" compared with "the same or less." Data are n/N (%).
§ Derived from χ^2 test.

ablation may be convenient, but it is important that women are fully counseled about the longer-term effects of treatment. They should understand that clinical outcomes appear equivalent to data from inpatient procedures performed under general anesthesia and that approximately 10% of women will require subsequent hysterectomy within 5 years. Such information will facilitate clinical decision-making for women and their clinicians.

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