Minimally Invasive Endometrial Ablation Device Complications and Use Outside of the Manufacturers' Instructions

Jill Brown, MD, MPH, and Ken Blank, MD

OBJECTIVE: To review the U.S. Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience database for reports describing serious adverse events and adverse events reports describing use outside of the manufacturers' labeled instructions for the five FDA-approved minimally invasive endometrial ablation devices.

METHODS: We queried the Manufacturer and User Facility Device Experience database for reports of device malfunction, patient injury, or death reported for each device from January 1, 2005 to December 31, 2011. We reviewed U.S. reports individually for annotations of patient injury or death and tabulated the reports by type of injury and device. We identified nine categories of serious injury (death, sepsis or bacteremia, intra-abdominal abscess, uterine rupture, thermal bowel injury, mechanical bowel injury, transmural uterine thermal injury, urologic injury, and lower genital tract or skin burns) and noted all reports citing device use outside of the manufacturers' labeled instructions. We also identified reports of hysterectomy or bowel resection attributable to an adverse event.

RESULTS: Serious adverse events, including bowel injury (n=128), sepsis or bacteremia (n=47), intra-abdominal abscess (n=18), urologic injury (n=2), and uterine rupture (n=1) were reported. Death was also reported (n=4). Eight percent (66 of 829) of serious adverse events reports cited use outside of the manufacturers' labeled instructions, as did 7.3% (6 of 82) of reports citing need for hysterectomy and 8.7% (9 of 103) of reports of bowel resection.

CONCLUSION: The findings from the Manufacturer and User Facility Device Experience database highlight the potential risk of serious complications related to endometrial ablation and underscore the importance of training in correct device use and familiarity with the manufacturer's labeled instructions.

(Obstet Gynecol 2012;120:865–70)
DOI: http://10.1097/AOG.0b013e31826af4fe

LEVEL OF EVIDENCE: III

Endometrial ablation was developed as a uterine-sparing procedure to treat heavy menstrual bleeding. Gynecologists originally used manual hysteroscopic techniques, including the ND:YAG laser, rollerball, or loop electrode, to coagulate the walls of the endometrium and thereby to decrease menstrual bleeding. Minimally invasive endometrial ablation devices were designed to make endometrial ablation technically less challenging and possibly safer (eg, by reducing the risk of fluid overload). Five endometrial ablation devices that use different mechanisms of action to accomplish endometrial destruction are commercially available in the United States. ThermaChoice (thermal balloon ablation) uses a heated fluid-filled intrauterine balloon, Her Option Cryoablator (cryoablation) uses cryotherapy, Hydro ThermAblator (hydrothermal endometrial ablation) uses circulating heated normal saline, Novasure (radiofrequency endometrial ablation) uses radiofrequency electrosurgical energy, and microwave endometrial ablation uses microwave energy. In 1997, thermal balloon ablation was the first minimally invasive endometrial ablation device to gain U.S. Food and Drug Administration (FDA) approval. Cryoablation, hydrother-

From the National Institute of Allergy and Infectious Diseases, Bethesda, Maryland; and the George Washington University School of Medicine, Washington, DC.

The authors thank Nancy Pressly for providing search results from the MAUDE database, and Dr. John Larsen for valuable editorial input.

The views expressed in this article reflect the opinions of the authors only and not the official policy of the Department of Health and Human Services.

Corresponding author: Jill Brown, MD, MPH, National Institutes of Health, NIAID/DMID/STDB, 6610 Rockledge Drive, Room 3106, Bethesda, MD 20892; e-mail: jill.brown@nih.gov.

Financial Disclosure
The authors did not report any potential conflicts of interest.

ISSN: 0029-7844/12

mal endometrial ablation, and radiofrequency endometrial ablation were all approved in 2001. Microwave endometrial ablation was the most recently approved (2003).

Because each device uses a different form of thermal energy, the ablation procedure for each device is unique. Particularly because all but hydrothermal endometrial ablations are not performed under direct visualization, nontarget thermal injury is one of the most important concerns with this class of devices. Each device has specific safeguards designed to ensure correct placement of the device within the uterus before performing ablation and, thus, to help prevent nontarget thermal injury. Again, because each technology is different, the safeguard mechanisms vary between devices.

The FDA Manufacturer and User Facility Device Experience database captures both voluntary and mandated reports of adverse events involving medical devices. Device manufacturers are required to report complaints they receive of device malfunctions, serious injuries, or deaths. User facilities are required to report device-related deaths to both the FDA and the device manufacturer, and to report serious injuries to the device manufacturer (although these events are widely under-reported). The general public, including providers and patients, may voluntarily report adverse events to the Manufacturer and User Facility Device Experience database via the FDA website. The FDA website also allows for the general public to search adverse events reported to the database.

After the introduction of commercial minimally invasive endometrial ablation devices, serious adverse events have been reported to the Manufacturer and User Facility Device Experience database, including bowel injury, necrotizing fasciitis, and death.[1] Gurtcheff and Sharp[2] describe endometrial ablation complications reported to the database in 2003, as do Baggish and Savells in 2007[3] and Della Badia et al also in 2007.[4] Baggish and Bhati[5] also reported three cases of bowel injury (one of which resulted in death) after endometrial ablation using radiofrequency endometrial ablation that were not reported to the database. We again reviewed the database for reports of adverse events associated with the five FDA-approved endometrial ablation devices and noted reported use outside of the manufacturer's labeled instructions. No other analysis of the database has focused on the contribution of use outside of the manufacturers' labeled instructions to reported adverse events.

MATERIALS AND METHODS

Information included in the FDA Manufacturer and User Facility Device Experience database is publically available and not individually identifiable; therefore, it is exempt from Institutional Review Board review. We searched the database by manufacturer, device name, and product code for the five FDA-approved endometrial ablation devices for reports of device malfunction, injury, and death. We included reports received from January 1, 2005 to December 31, 2011, to capture data not previously reported and excluded duplicate reports and reports specified as foreign. We reviewed reports individually for annotations of patient injury or death and tabulated by type of injury and device. Based on our assessment of events related to the procedure that could be life-threatening or life-altering, we identified the following categories of serious injury: death, sepsis or bacteremia, intra-abdominal abscess, uterine rupture, thermal bowel injury, mechanical bowel injury, transmural uterine thermal injury, urologic injury, and lower genital tract or skin burns. Mechanical bowel injury included reports of bowel injury that did not include a description of thermal injury. We also tracked injuries that resulted in the need for further surgery in the form of hysterectomy or bowel resection.

We then reviewed reports that cited use outside of the parameters included in the manufacturers' labeled instructions. These reports cited the following conditions of use: performing ablation on a patient with a condition in which weakness of the myometrium could exist; continuing treatment after suspected uterine perforation; allowing the sheath to rest on the patient; not supporting the device while in use; performing concomitant hysteroscopic sterilization; no pretreatment hysteroscopy (microwave endometrial ablation); no ultrasonography for myometrial thickness (microwave endometrial ablation); continuing after change in cavity length (microwave endometrial ablation); applicator re-inserted after previous treatment or partial treatment (microwave endometrial ablation); any previous endometrial ablation procedure (microwave endometrial ablation); poor ultrasound visualization (cryoablation); adding fluid during treatment cycle or using too much fluid (thermal balloon ablation); cycle length longer than prescribed (thermal balloon ablation); multiple therapy cycles (radiofrequency endometrial ablation); and removing the device before cooling or retracting active component (hydrothermal endometrial ablation, thermal balloon ablation, and radiofrequency endometrial ablation).

Table 1. Serious Adverse Events Per Device, 2005–2011

	Radiofrequency Endometrial Ablation	Thermal Balloon Ablation	Hydrothermal Endometrial Ablation	Cryoablation	Microwave Endometrial Ablation	Total
Death	2	1	0	1	0	4
Sepsis or bacteremia	43	1	2	1	0	47
Intra-abdominal abscess	16	0	2	0	0	18
Thermal bowel injury	64	3	8	0	18	93
Mechanical bowel injury	22	2	1	1	9	35
Transmural uterine thermal injury	76	1	3	0	9	89
Genital tract or skin burn	4	7	529	0	0	540
Uterine rupture	0	1	0	0	0	1
Urologic injury	0	0	0	0	2	2
Total	227	16	545	3	38	829

Data are n.

We recognize that the Manufacturer and User Facility Device Experience data have several limitations. The information and degree of detail contained within these reports are highly variable, making interpretation of the reports difficult and causality often uncertain. Vast under-reporting of adverse events also likely exists, resulting in unknown numerator data. This, in combination with lack of denominator data, makes the Manufacturer and User Facility Device Experience data unsuitable for determining adverse event rates. However, the data do provide a valuable resource for the types of adverse events that can occur.

RESULTS

Table 1 provides a summary of the number of serious adverse events reported for each device over this timeframe. Genital or skin burn associated with hydrothermal endometrial ablation was the most commonly reported adverse event to the Manufacturer and User Facility Device Experience database during this time period. Of note, the FDA issued a device recall for the hydrothermal endometrial ablation device in 2009 because of "cracked procedure sheaths, incorrect care or use of device, and console malfunctions" that could lead to fluid leaks and loss of a cervical seal causing burns.[6] The manufacturer also modified the procedure sheath in 2009 to reduce the likelihood of retrograde leakage of heated saline. The number of reported adverse events for hydrothermal endometrial ablation may be related to this recall and subsequent corrective action. Table 2 shows the number of genital or skin-burn reports for hydrothermal endometrial ablation from 2005 to 2011.

Thermal bowel injury was the most commonly reported life-threatening injury during this time period. Overall, our search produced 128 reports of bowel injury, 93 of which were specifically noted as thermal injuries. The numbers of bowel injuries per device were as follows: radiofrequency endometrial ablation (86), microwave endometrial ablation (27), hydrothermal endometrial ablation (9), thermal balloon ablation (5), and cryoablation (1). Eighty percent (103 of 128) of bowel injury reports noted a requirement for subsequent bowel resection. The majority of the serious adverse events reported for microwave endometrial ablation concerned thermal injury, including thermal bowel injury (18), thermal injury to the uterus (9), thermal injury to the bladder (2), or thermal injury to "adjacent tissue" (7 additional reports). The remaining serious adverse event reports for microwave endometrial ablation included nine reports of bowel injury, which did not specify thermal injury. Besides bowel injury, other life-threatening adverse events (or death) were reported for the following devices: radiofrequency endometrial ablation death (2), sepsis or bacteremia (43), and intra-abdominal abscess (16); thermal balloon ablation death (1) sepsis or bacteremia (1), and uterine rupture (1); cryoablation sepsis (1) death (1); hydrothermal endometrial ablation sepsis or bacteremia (2); and microwave endometrial ablation urologic injury (2).

The deaths reported after endometrial ablation with radiofrequency endometrial ablation were attrib-

Table 2. Hydrothermal Endometrial Ablation Genital or Skin-Burn Reports, 2005–2011

	2005	2006	2007	2008	2009	2010	2011
No. of reports	53	65	109	109	94	54	45

Table 3. Additional Surgery Associated With Endometrial Ablation Complications, 2005–2011

	Radiofrequency Endometrial Ablation	Thermal Balloon Ablation	Hydrothermal Endometrial Ablation	Cryoablation	Microwave Endometrial Ablation	Total
Hysterectomy	53	8	8	1	12	82
Unable to remove device	1	0	0	0	0	1
Uterine perforation	5	4	0	0	2	11
Endometritis, pyometra, or tubo-ovarian abscess	6	0	1	0	0	7
Abdominal pain	9	0	1	0	1	11
Transmural uterine thermal injury	8	0	0	0	4	12
With bowel resection	11	2	1	0	5	19
Hematometra	6	1	0	0	0	7
Postprocedure bleeding	1	0	1	1	0	3
Uterine rupture	0	1	0	0	0	1
Sepsis	5	0	0	0	0	5
Uterine necrosis	1	0	0	0	0	1
Bowel resection	66	5	6	1	25	103

Data are n.

utable to pulmonary embolism (one incident) and sepsis (one incident). The thermal balloon ablation death was attributable to bowel injury (one incident) and the cryoablation death was attributable to sepsis (one incident).

Table 3 lists the number of reports that noted a requirement for hysterectomy or bowel resection because of a complication from the procedure. For hysterectomy, Table 3 includes the type of complication that resulted in the need for hysterectomy. All of the cases of bowel resection were attributable to bowel injury occurring as a result of the endometrial ablation procedure.

Regarding use outside of the manufacturers' labeled instructions, the variability in information provided within the Manufacturer and User Facility Device Experience reports limits an accurate assessment of adverse events associated with this use. However, even with the data provided, a number of reports included description of use clearly contradictory to the respective device labeling. Of 829 total serious adverse events, 66 (8.0%) cited use outside of the manufacturers' labeled instructions. Of 82 reports citing requirement for hysterectomy, 6 (7.3%) occurred under conditions of use outside of the manufacturers' labeled instructions, as did 9 of 103 cases (8.7%) that cited subsequent bowel resection. Table 4 shows a summary of the reported serious adverse events associated with use outside of the manufacturers' labeled instructions for each device.

DISCUSSION

In the manufacturer-sponsored pivotal trials for these devices, intraoperative and postoperative complica-

Table 4. Serious Adverse Events Per Device Associated With Use Outside of the Manufacturers' Labeled Instructions, 2005–2011

	Radiofrequency Endometrial Ablation	Thermal Balloon Ablation	Hydrothermal Endometrial Ablation	Cryoablation	Microwave Endometrial Ablation	Total
Death	0	0	0	0	0	0
Sepsis or bacteremia	0	0	0	0	0	0
Intra-abdominal abscess	0	0	0	0	0	0
Thermal bowel injury	4	1	0	1	0	6
Mechanical bowel injury	2	0	0	0	2	4
Transmural uterine thermal injury	4	0	0	0	1	5
Genital tract or skin burn	0	2	49	0	0	51
Uterine rupture	0	0	0	0	0	0
Urologic injury	0	0	0	0	0	0
Total	10	3	49	1	3	66

tions were similar after using each endometrial ablation device compared with rollerball ablation, and few serious adverse events were seen.[7–12] The only nontarget thermal injury reported in the pivotal trials was thermal injury to an extremity, which was reported in 1% of women in the hydrothermal endometrial ablation trial. Other nontarget thermal injuries were not seen in these trials. Endometritis occurred in the thermal balloon ablation, hydrothermal endometrial ablation, radiofrequency endometrial ablation, and microwave endometrial ablation trials at rates of 2.4%, 1.1%, 1.1%, and 2.8%, respectively. Hematometra occurred in the hydrothermal endometrial ablation and radiofrequency endometrial ablation trials at rates of 1.1%. Pelvic inflammatory disease occurred at a rate of 1.1% in the radiofrequency endometrial ablation trial. Hemorrhage was reported in the radiofrequency endometrial ablation and cryoablation trials at rates of 0.6%. Death, sepsis or bacteremia, intra-abdominal abscess, uterine rupture, thermal bowel injury, mechanical bowel injury, transmural uterine thermal injury, and urologic injury were not reported in any of these trials.

Our updated review of the Manufacturer and User Facility Device Experience database demonstrates that serious adverse events after minimally invasive endometrial ablation continue to occur. Because numerator and denominator data are unknown, we cannot make conclusions about rates of adverse events associated with specific devices. However, a few trends emerge from the data that highlight aspects of specific devices surgeons should recognize. Despite improvements in the hydrothermal endometrial ablation device's cervical seal mechanism, retrograde leakage of heated saline remains a concern for hydrothermal endometrial ablation. False tracking may be a concern for the radiofrequency endometrial ablation device, as evidenced by the number of reports of transmural uterine thermal injury. The radiofrequency endometrial ablation device incorporates a CO_2 cavity integrity test that must be passed before beginning the ablation. In the setting of a false track that does not completely perforate the cavity, the cavity integrity test still may be passed and allow the procedure to continue. This may allow ablation to occur with the device partly through the uterine wall and in closer proximity to bowel than intended, thereby increasing the risk for nontarget thermal injury. Additionally, nontarget thermal injury appears disproportionate for the microwave endometrial ablation device. This also may be related to the potential for false tracking or perforation with the narrow microwave endometrial ablation probe or the amount of thermal energy released by the device.

Use outside of the manufacturers' labeled instructions contributes to the occurrence of serious adverse events associated with these devices. Because of their generally excellent safety records, physicians may underestimate the risk for serious adverse events and may become less vigilant over time in following the manufacturers' labeled instructions. Awareness among gynecologists of the potential for harm from these devices is essential. Given that the mechanism of action and procedural technique for each device is unique, knowledge of the use of one device does not confer knowledge of all endometrial ablation devices.

Because of the recent commercial introduction of these devices, many gynecologists in practice have learned to perform these procedures after completing residency training. Obtaining hospital privileges for endometrial ablation typically does not require proof of training with the individual devices; instead, hospitals require appropriate training in endometrial ablation in general. As a result, no standardized training program exists to ensure that gynecologists learn the nuances of each device. Dedicated training programs that focus on understanding each device's mechanism of thermal energy delivery and demonstrating procedural competency, including use of respective device safeguards, may help reduce the occurrence of serious adverse events associated with these devices. Such a program could be integrated into residency training programs and postgraduate training courses to ensure that all practicing gynecologists demonstrate competency in each device they intend to use on patients.

REFERENCES

1. Zarek S, Sharp HT. Global endometrial ablation devices. Clin Obstet Gynecol 2008;51:167–75.
2. Gurtcheff SE, Sharp HT. Complications associated with global endometrial ablation: the utility of the MAUDE database. Obstet Gynecol 2003;102:1278–82.
3. Baggish MS, Savells ST. Complications associated with minimally invasive, nonhysteroscopic endometrial ablation techniques. J oGynecol Surg 2007;23:7–12.
4. Della Badia C, Nyirjesy P, Atogho A. Endometrial ablation devices: review of a manufacturer and user facility device experience database. J Min Invas Gynecol 2007;14:436–41.
5. Baggish MS, Bhati A. Intestinal injuries associated with the Novasure bipolar device. J of Gynecol Surg 2009;25:73–8.
6. Food and Drug Administration. Medical and radiation emitting device recalls. Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=83991. Retrieved February 1, 2012.
7. Cooper J, Gimpelson RJ. Summary of safety and effectiveness data from FDA: a valuable source of information of the

performance of global endometrial ablation devices. J Reprod Med 2004;4:267–73.

8. Meyer WR, Walsh BW, Grainger DA, Peacock LM, Loffer FD, Steege JF. Thermal balloon and rollerball ablation to treat menorrhagia: a multicenter comparison. Obstet Gynecol 1998; 92:98–103.
9. Corson SL. A multicenter evaluation of endometrial ablation by Hydro ThermAblator and rollerball for treatment of menorrhagia. J Am Assoc Gynecol Laparosc, 2001;8:359–67.
10. Cooper J, Gimpelson R, Laberge P, Galen D, Garza-Leal JG, Scott J, et al. A randomized, multicenter trial of safety and efficacy of the NovaSure system in the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2002;9:418–28.
11. Duleba AJ, Heppard MC, Soderstrom RM, Townsend DE. A randomized study comparing endometrial cryoablation and rollerball electroablation for treatment of dysfunctional uterine bleeding. J Am Assoc Gynecol Laparosc 2003;10: 17–26.
12. Cooper JM, Anderson TL, Fortin CA, Jack SA, Plentl MB. Microwave endometrial ablation vs. rollerball electroablation for menorrhagia: a multicenter randomized trial. J Am Assoc Gynecol Laparosc 2004;11:394–403.