

First-generation endometrial ablation revisited: retrospective outcome study—a series of 218 patients with premenopausal dysfunctional bleeding

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Received: 6 February 2015 / Accepted: 15 June 2015 / Published online: 9 July 2015
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Abstract Premenopausal dysfunctional bleeding (PDB) is a common medical problem. Surgery is typically performed after the failure of a medical approach. Surgical options include endometrial ablation techniques or a hysterectomy. The aims of our study are to measure the outcome parameters of first-generation endometrial ablations (fgEA) and to identify patient-related prognostic factors. We included all fgEAs performed between September 2001 and December 2011 at the General Hospital of Turnhout, Belgium ($n=218$). The outcome was defined by the need for a postoperative therapy (group 1—no therapy; group 2—therapy, but no hysterectomy; group 3—hysterectomy). We also rated postoperative amenorrhea and patient satisfaction. The prognostic factors examined were associated dysmenorrhea, a history of cesarean section, preoperative duration of blood loss, age, parity, and a history of tubal ligation sterilization. We used Excel 2011, Version 14.0.0, and Statplus Mac LE 2009 for our statistical analysis. The hysterectomy rate post-fgEA was 10 % (22/218). The rate of amenorrhea (defined as cessation of bleeding from 3 months postprocedure until the moment the patient was interviewed) was 76 % (165/218). Ninety-two percent (202/218) of patients were either satisfied or very satisfied

with the procedure and outcome. The only significant prognostic factor was the age of the patient at the time of the fgEA ($p=0.0004$ for mean age at time of fgEA and $p=0.0433$ for comparison pre- versus perimenopausal age). The outcome of this fgEA technique is often underestimated and can still result in a high amenorrhea and satisfaction rate and low postoperative hysterectomy rate.

Keywords Premenopausal dysfunctional bleeding · Treatment · First-generation endometrial ablation · Hysterectomy rate · Amenorrhea rate · Patient satisfaction · Prognostic factors

Background

Premenopausal dysfunctional bleeding (PDB) is a very common reason for women to consult a general practitioner or gynecologist. Approximately one third of women will be affected by heavy or abnormal uterine bleeding at some point in their lives. While PDB significantly diminishes the quality of life, serious complications are rare [1].

Causes can be anatomical (uterine fibroids, adenomyosis, endometrial polyps, endometrial carcinoma, uterine vascular malformations, myometrial hypertrophy), systemic (coagulation disorders, hypothyroidism, chronic liver failure, systemic lupus erythematosus), functional (dysfunctional uterine bleeding), or involve a combination of these factors. We can distinguish between a medical and a surgical approach to dealing with PDB [2].

Medical solutions include the use of levonorgestrel intra-uterine systems (LNGIUS), non-steroidal anti-inflammatory drugs (NSAID), antifibrinolytic drugs (tranexamic acid), progesterones, oral contraceptives, and danazol.

Electronic supplementary material The online version of this article (doi:10.1007/s10397-015-0902-8) contains supplementary material, which is available to authorized users.

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Surgical approaches involve either a hysterectomy or less invasive endometrial resection/ablation procedures. With regard to the latter, two generations of techniques can be differentiated [3, 4]. First-generation techniques, the gold standard, involve hysteroscopy-dependent endometrial resection/ablation with resectoscopic electrosurgical instruments (rollerball, wire loop, vaporizing electrode) or with laser. Second-generation, non-resectoscopic endometrial ablation is performed with a disposable device, inserted into the uterine cavity, delivering energy to uniformly destroy the endometrial lining. This includes bipolar radiofrequency, hot liquid-filled balloon, cryotherapy, circulating hot water, and microwave techniques. These techniques demand less expertise and can sometimes be performed in an office setting, lowering the price of the procedure.

In general, in the first year after the procedure, surgery reduces menstrual bleeding to a greater extent than medical treatments, but LNGIUS appears to be equally beneficial to improving the quality of life and may control bleeding as effectively as conservative surgery over the long term. Oral medication only suits a minority of patients for a longer period [2].

When comparing different endometrial ablation generations/techniques, the 2013 Cochrane review of Lethaby et al. concludes that the existing evidence suggests comparable rates of success, satisfaction, and complications [5]. First-generation techniques have the disadvantage of higher risk of complications, such as perforation, water intoxication, and injury of the urogenital tract [6–8]. Second-generation techniques try to compensate for these weaknesses and have the advantages of being more rapid, safe, and easy to apply [3, 9–11].

Although these less invasive techniques have proven effective compared to a hysterectomy, there are still a proportion of patients for whom persisting symptoms necessitate a repeat ablation procedure or hysterectomy after a first ablation [12–14]. The 2013 Cochrane review of Fergusson and Lethaby states that both procedures are effective and that satisfaction rates are high. The advantage of a hysterectomy is the guarantee of permanent relief from bleeding. Endometrial resection/ablation is cheaper, but total costs are higher in the case of recurrence [15].

The aim of this retrospective study is to provide an overview of the outcome of first-generation endometrial ablation (fgEA) procedures performed on patients at the General Hospital of Turnhout, Belgium. We also assess possible prognostic patient-related factors, predicting the outcome of the ablation. El-Nashar et al. carried out a comparable study for second-generation endometrial ablation techniques. For a series of 816 patients, they noted an amenorrhea rate of 23 % (defined as cessation of bleeding immediately after ablation until at least 12 months after the procedure). Predictors of amenorrhea were age >45 years, uterine length <9 cm, endometrial thickness <4 mm, and use of radiofrequency ablation instead of thermal balloon ablation [16].

Methods

The study population consisted of patients undergoing an fgEA between September 2001 and December 2011 at the General Hospital of Turnhout, Belgium.

1. Satisfaction regarding the fgEA and the stay at daycare unit ?

Absolutely not satisfied	Not satisfied	Neutral opinion	Satisfied	Very satisfied
Score 1	Score 2	Score 3	Score 4	Score 5

2. Would you recommend the fgEA to friends/relatives with the same problem ?

Absolutely not	No	Neutral opinion	Yes	Absolutely
Score 1	Score 2	Score 3	Score 4	Score 5

3. Amenorrhea 3 months post-fgEA until now ?

No	Yes
Score 1	Score 2

4. What was the interval between the first bleeding symptoms and the fgEA ?

> 12 months	6 – 12 months	< 6 months
Score 1	Score 2	Score 3

5. Was any kind of therapy needed because of relapse AFTER the fgEA ? If so, please indicate the kind of therapy and the interval between the fgEA and the start of this new therapy (expressed in years).

Yes/No ? If yes: How many years after the procedure ? What kind of therapy ?

- 1) Hormonal medication combined estrogen-progesterone or progesterone only
- 2) Tranexamic acid
- 3) NSAID
- 4) LNGIUS
- 5) Hysterectomy
- 6) D and C
- 7) Another hysteroscopic ablation
- 8) Subdermal contraceptive implant

6. Was any kind of therapy applied BEFORE the fgEA ? If so, please indicate the kind of therapy and the interval between the start of this previous therapy and the fgEA (expressed in years).

Yes/No ? If yes: How many years before the procedure ? What kind of therapy ?

- 1) Hormonal medication combined estrogen-progesterone or progesterone only
- 2) Tranexamic acid
- 3) NSAID
- 4) LNGIUS
- 5) D and C
- 6) Subdermal contraceptive implant
- 7) Another hysteroscopic ablation

7. What kind of contraception was used since the procedure?

- 1) Copper-containing IUS
- 2) Condom
- 3) Sexual withdrawal peri-ovulatory
- 4) None
- 5) Patient had a sterilisation
- 6) Patient's partner had a sterilisation

8. The following questions apply to the moment the procedure was performed:

- 1) How many children did you have?
- 2) Did you have any twins or triplets ?
- 3) Can you tell me for every childbirth whether the way of delivery was vaginally or by caesarean section ?
- 4) Did you ever have a provoked abortion ?
- 5) Did you ever have a miscarriage ?

Fig. 1 Questionnaire

Until 2009, a unipolar loop technique was applied. After that, a bipolar loop mode was used. The procedures in our center were performed by two gynecologists, using the exact analogue method of transcervical resection of the endometrium. A radical resection of the endometrial lining over the total area of the cavity was applied. This was achieved using a technique developed and perfected over many years with resection up to the level of the myometrium over the anterior and posterior wall as well as the fundus, including the area of the ostia and the central part, up to the endocervical canal. Significant bleeding points were also coagulated. The minimum follow-up period was almost 2 years, as data collection started at the end of 2013.

A first inclusion criterion was a preoperative indication of PDB. All postoperative anatomopathological examinations were reviewed and cases of malignancies, myomas, polyps, and atypical hyperplasia were excluded. Postmenopausal patients were excluded as well. The preoperative bleeding patterns were menorrhagia or metrorrhagia, while intermenstrual blood loss was excluded. Patients who used hormonal contraception after the fgEA were excluded, as this could have been a confounding factor for the outcome.

By reviewing the patients' case notes and by contacting all patients by phone, we completed a questionnaire consisting of eight questions (Fig. 1). The first two questions emphasized on patient satisfaction. The third question estimated the amenorrhea rate. The fourth question determined how long the patient had suffered from PDB, before the procedure was applied. The next question concerned postoperative recurrence of the bleeding disorder. In the case of recurrence, we determined the timing of the associated intervention applied. Question six dealt with the therapeutic options used before the resection procedure and their timing related to the fgEA, while question seven investigated contraceptive methods used since the operation. The last question assessed the obstetric history of the patient. The remaining data was obtained by reviewing the patients' case notes.

Therapeutic options for PDB were defined as hormonal medication (combined estrogen-progesterone or progesterone only, applied in an oral or transdermal way or using ring application), LNGIUS, subdermal contraceptive implant, tranexamic acid, NSAID, hysterectomy, dilatation/curettage, and hysteroscopic ablation. Danazol was not included as it is no longer available in Belgium. Hormonal pretreatment before the fgEA is not a standard practice in our hospital.

Three categories of outcome were determined based on whether patients required additional therapy or not and on the type of intervention needed in case of failure. Group 1 involved patients who did not require therapy after the operation. Group 2 involved patients who required some kind of therapy after the operation, but not a hysterectomy. Group 3 involved patients who required a hysterectomy after primary ablation therapy.

We investigated the following prognostic parameters: dysmenorrhea versus no dysmenorrhea associated with the problem of PDB, a history of cesarean section, the duration of preoperative blood loss, age, and a parous compared to a nulliparous obstetric history. We also compared the outcome between premenopausal and perimenopausal women. Perimenopause was defined based on a minimum age of 47 years [17]. Finally, we emphasized on the influence of a history of tubal ligation sterilization.

Dysmenorrhea was examined because it can be a negative prognostic factor for patients still experiencing pain rather than problematic bleeding after the fgEA, thus necessitating further therapy. Parity could influence the volume of the uterus and, hence, also the operative technique and outcome. Also, in a uterus with a cesarean section scar, radical resection at the level of the anterior uterine isthmus could be limited due to risks of perforation.

Table 1 Patient characteristics

Age (mean) at the time of fgEA in years	43.81±5.1
Parity (mean) at the time of fgEA	2.12±0.98
History of cesarean section at the time of fgEA	41 (19 %)
Preoperative bleeding pattern	
Menorrhagia	202 (93 %)
Metrorrhagia	16 (7 %)
Dysmenorrhea associated with the problem of PDB	39 (18 %)
Duration of blood loss before the fgEA in months	
>12	160 (73 %)
6–12	45 (21 %)
<6	13 (6 %)
Therapy before the fgEA	119 (55 %)
Hormonal medication	85 (39 %)
Tranexamic acid	17 (8 %)
NSAID	7 (3 %)
LNGIUS	35 (16 %)
Dilation/curettage	20 (9 %)
Subdermal contraceptive implant	2 (1 %)
Another hysteroscopic ablation	1 (<1 %)
Therapy after the fgEA	36 (17 %)
Hormonal medication	9 (4 %)
Tranexamic acid	2 (1 %)
NSAID	0 (0 %)
LNGIUS	4 (2 %)
Hysterectomy	22 (10 %)
Dilation/curettage	2 (1 %)
Another hysteroscopic ablation	1 (<1 %)
Subdermal contraceptive implant	1 (<1 %)
Interval (mean) between previous therapy and the fhEA in years	2.94±3.75
Interval (mean) between the fhEA therapy after in years	1.38±1.42

Mean (±standard deviation) or fraction (a total of 218 patients)

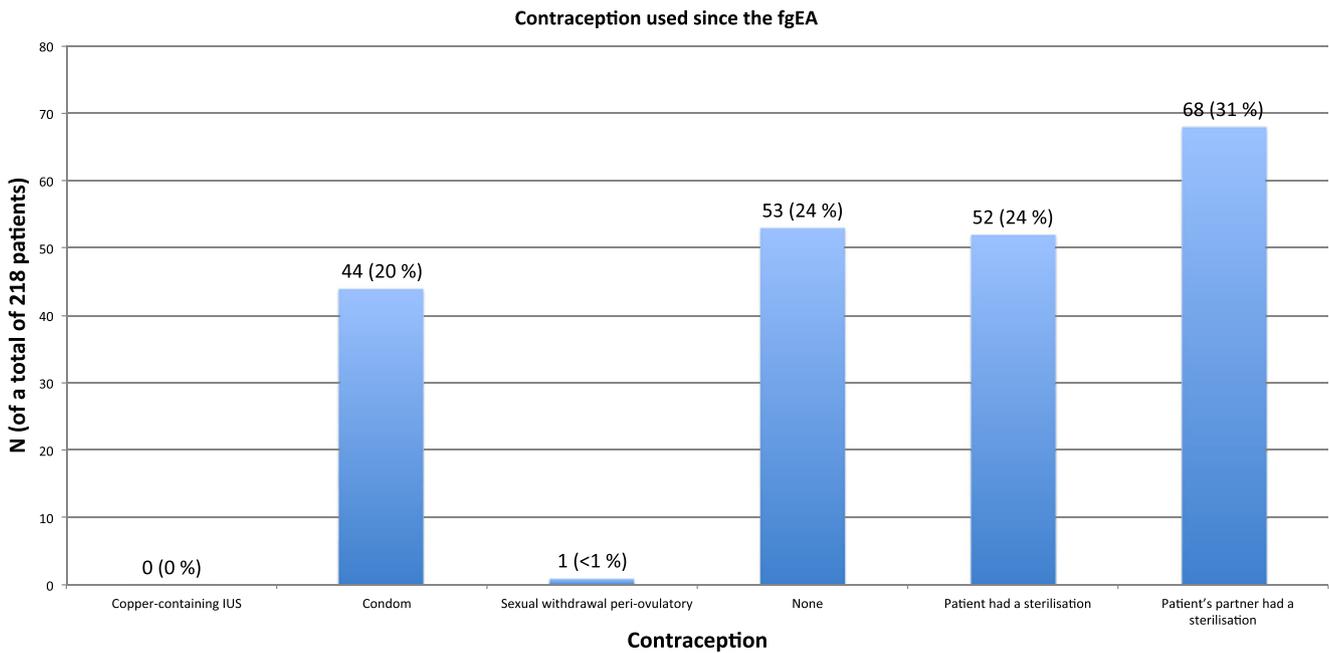


Fig. 2 Contraception used since the fgEA

Amenorrhea was defined as cessation of blood loss from 3 months post-fgEA until the moment the patient was contacted to complete the study questionnaire.

We used Excel 2011, Version 14.0.0, and Statplus Mac LE 2009, analysis of variance, and chi-square analysis for our statistical investigations. For all statistical analyses, a *p* value cutoff of <0.05 was considered significant.

Findings

A total of 363 patients were retained in the first phase, and eventually, 218 patients were included in our study. Patients were excluded if they did not fit the inclusion criteria (e.g., postoperative malignant pathological analysis, postmenopausal state, intermenstrual bleeding pattern).

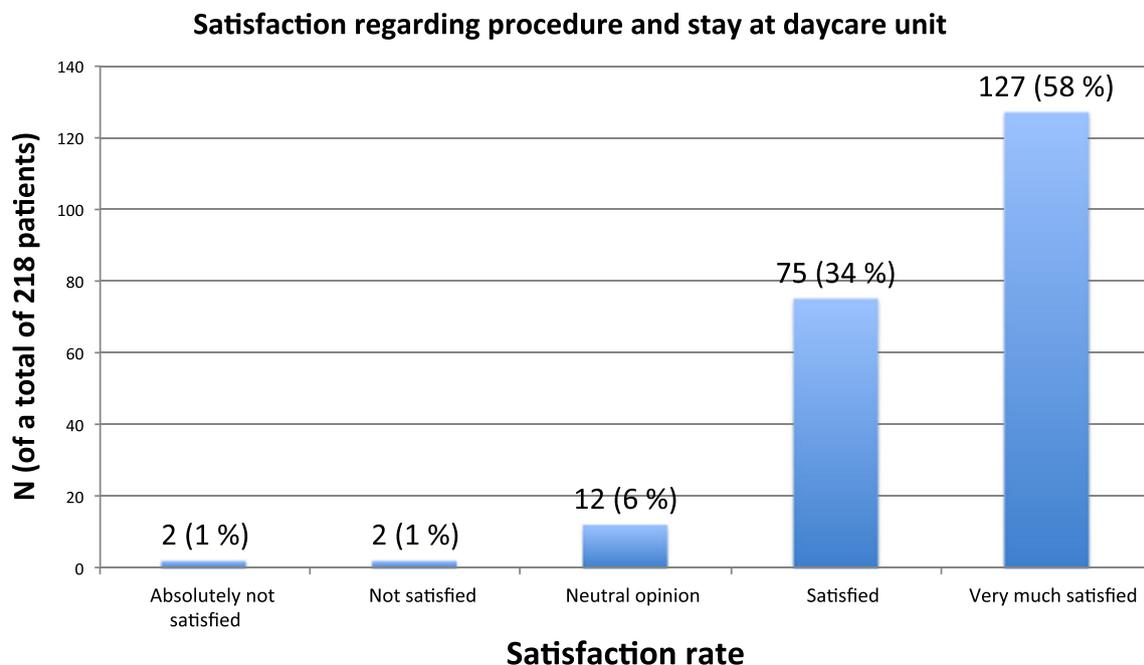


Fig. 3 Satisfaction regarding procedure and stay at daycare unit

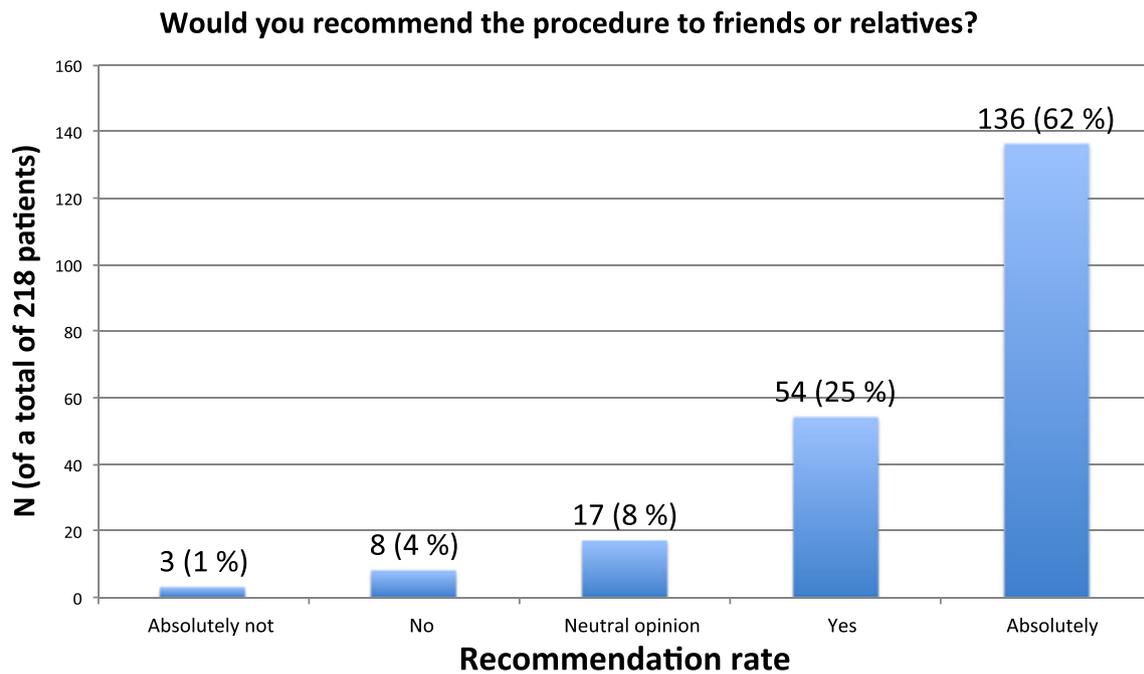


Fig. 4 Would you recommend the procedure to friends or relatives?

Table 1 gives an overview of patient characteristics. All percentages are calculated using the same denominator: 218, which is the total number of patients included. The age of included patients at the time of the fgEA ranged from 25 to

55 years. Parity ranged from 0 to 5. Since some people received multiple therapeutic options before the procedure, the absolute sum of pre-fgEA therapeutic approaches is higher than 119. The same applies to post-fgEA therapy. To calculate

Table 2 Statistical analysis on prognostic factors

Therapy after fgEA?	None Group 1	Yes, but no hysterectomy Group 2	Yes, but hysterectomy Group 3	<i>p</i> value	Statistical test
Dysmenorrhea associated?					
No (179 patients)	154 (71 %)	10 (5 %)	15 (7 %)	0.0921	Chi-square
Yes (39 patients)	28 (13 %)	4 (2 %)	7 (3 %)		
History of caesarian section					
No (177 patients)	148 (68 %)	11 (5 %)	18 (8 %)	0.9654	Chi-square
Yes (41 patients)	34 (16 %)	3 (1 %)	4 (2 %)		
Duration of preoperative blood loss					
>12 months (160 patients)	133 (46 %)	10 (3 %)	17 (6 %)	0.9935	Chi-square
6–12 months (45 patients)	38 (13 %)	3 (1 %)	4 (1 %)		
<6 months (13 patients)	11 (4 %)	1 (<1 %)	1 (1 %)		
Mean age at time of EA in years	42±4.88	43.64±5.98	39.77±5.28	0.0004	Analysis of variance
Pre-versus perimenopausal age at time of fgEA					
Premenopausal	121 (56 %)	8 (4 %)	20 (9 %)	0.0433	Chi-square
Perimenopausal	61 (28 %)	9 (3 %)	2 (1 %)		
Nulliparous versus parous					
Nullipara (13 patients)	10 (5 %)	1 (<1 %)	2 (1 %)	0.7828	Chi-square
Para (205 patients)	172 (79 %)	13 (6 %)	20 (9 %)		
History of sterilization?					
No (166 patients)	139 (64 %)	10 (5 %)	17 (8 %)	0.9084	Chi-square
Yes (52 patients)	43 (20 %)	4 (2 %)	5 (2 %)		

Mean (±standard deviation) or fraction (a total of 218 patients)

the mean interval between the fgEA and therapy (before or after), we noted all therapy intervals, divided by the total number of applied therapeutic options. The percentage of women who did not receive any kind of therapy after the fgEA (group 1) was 83 % (182/218). The proportion of women who needed therapy due to recurrence, but no hysterectomy (group 2), was 6 % (14/218). It turns out that the hysterectomy rate (group 3) after the fgEA was 10 % (22/218) of all cases. The amenorrhea rate was 76 % (165/218).

Figure 2 depicts an overview of contraception used after the fgEA. None of these options affect blood loss, since hormonal contraception was excluded.

Figures 3 and 4 describe patient satisfaction. For both question 1 (satisfaction regarding procedure and stay at daycare unit) and question 2 (recommendation of procedure to friends/relatives), the majority of women responded positively or very positively. For question 1, the proportion of positive and very positive responses was 92 % (34 % + 58 %), and for question 2, the proportion was 87 % (25 % + 62 %).

Table 2 is a synthesis of our findings on prognostic factors for the outcome of the fgEA. It turns out that only one of these is statistically significant: age at time of the fgEA ($p=0.0004$ for mean age at time of fgEA and $p=0.0433$ for comparison pre- versus perimenopausal age). No significant difference was seen for associated dysmenorrhea ($p=0.0921$), history of cesarean section ($p=0.9654$), or duration of preoperative blood loss ($p=0.9935$). Neither did there appear to be a significant difference in outcome when comparing parous versus nulliparous women ($p=0.7828$) or comparing patients with or without a history of tubal ligation sterilization ($p=0.9084$).

Conclusions

Table 1 shows that hormonal oral medication is still the first approach to the problem of PDB, followed by LNGIUS and dilatation/curettage. In the case of recurrence after fgEA, the most commonly chosen option is hysterectomy (partly explained by the fact that in most cases, the majority of conservative approaches have already been tried), followed by hormonal medication and LNGIUS. A consequence of radical ablation is impaired fertility or even total infertility. This explains why the procedure is only performed in those patients who do not plan to have (more) children in the future. Therefore, the mean age at fgEA is 43.81 ± 5.15 years.

The most common methods of contraception after the fgEA (Fig. 2) were a vasectomy, tubal ligation sterilization, and the use of condoms. A significant proportion of patients no longer used contraception, typically those of an advanced age, because they assumed no longer to be fertile. Others were not sexually active.

We defined amenorrhea as cessation of blood loss starting from 3 months postprocedure instead of immediately after the fgEA. The reason for this is that in the first postoperative

period, the healing reaction itself typically causes blood loss. There is also the possible expulsion of some retained resected tissue that could not be removed during the operation. We tried to quantify the amount of blood loss pre- versus postprocedure. However, since the operation had been performed at least 2 years before the time of our interviews, we found that patients were unable to recall exact details. This is why we used the simple approach of a postoperative amenorrhea versus no amenorrhea rate.

Figure 3 shows a very high satisfaction rate with respect to the procedure itself. Patients were highly motivated to recommend the procedure to others (Fig. 4).

The statistical analysis of prognostic factors in Table 2 shows that associated dysmenorrhea has a tendency to be a negative prognostic factor for the outcome. We notice a higher likelihood of a patient requiring extra therapy after the fgEA and a higher rate of post-fgEA hysterectomies. The same is true for a younger age at the time of the fgEA. It could be that the associated dysmenorrhea itself, regardless of the PDB, is sometimes the real indication for therapy afterwards. Concerning the differences based on age, one would expect that older patients would have a better long-term outcome, since some of them reach menopause in the first years after the fgEA.

A limitation of this study is its retrospective nature, restricting the possibility of examining additional possible prognostic factors, such as body mass index and hemoglobin. Another shortcoming of the retrospective approach is the difficulty some patients experience in recalling the details relevant to answering our questionnaire. This is why a quantification of pre- versus postoperative blood loss was impossible. This could be an interesting prognostic factor to examine in prospective studies.

We conclude that the fgEA technique is very effective in the treatment of PDB, particularly for perimenopausal patients. The results show a high satisfaction rate, a high percentage of postoperative amenorrhea, and a low number of hysterectomies required afterwards. Given these findings, the added value of less invasive (first-generation) endometrial ablation techniques should be reconsidered.

Authors' contributions Project development was accomplished by S. Van Calenbergh. Data collection and manuscript writing was performed by S. Knaepen.

Informed consent Informed consent was obtained from all individual participants included in the study. We received a signed approval from the local ethics committee as well.

Conflict of interest The authors declare that they have no competing interests.

Statement of responsibility I, Senne Knaepen, the corresponding author, declare that (a) every author allowed me to serve as the primary contact person, (b) I received consent for publication from every author, and (c) every author contributed sufficiently to the development of this manuscript.

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