 Prague Medical Report / Vol. 109 (2008) No. 2–3, p. 166–174

Uterine Arteries Doppler Velocimetry Provides 3-years Follow up Endometrial Ablation Outcome

Kužel D.[1], Tóth D.[2], Fučíková Z.[1], Bartošová L.[1], Mára M.[1], Hrušková H.[1], Fanta M.[1], Žižka Z.[1], Sosna O.[1], Kubínová K.[1], A. Dohnalová[3]

[1]Charles University in Prague and the General Teaching Hospital, First Faculty of Medicine, Department of Gynaecology and Obstetrics, Prague, Czech Republic;
[2]Department of Obstetrics and Gynaecology, Clinique St. Germaine, Brive La Gaillarde, France;
[3]Charles University in Prague, First Faculty of Medicine, Institute of Physiology, Department of Cybernetics, Prague, Czech Republic

Received September 4, 2008; Accepted December 3, 2008.

Key words: Doppler velocimetry – Dysfunctional uterine bleeding – Endometrial ablation – Hysteroscopy – Uterine artery

This study was supported by the Grant Agency of Charles University in Prague No. 38108.

Mailing address: David Kužel, MD., PhD., Charles University in Prague and the General Teaching Hospital, First Faculty of Medicine, Department of Gynaecology and Obstetrics, Apolinářská 18, Prague 2, 128 51, Czech Republic;
Phone: +420 224 967 577; Fax: +420 224 922 545; e-mail: dkuzel@vfn.cz, kuzeld@centrum.cz

Abstract: The aim of this study was to assess whether uterine artery Doppler velocimetry [pulsatility index (PI) and resistance index (RI)] and thickness of the endometrium (TE) are able to predict 3-year clinical outcome after endometrial ablation (EA) for dysfunctional uterine bleeding (DUB). This was a prospective, observational study of 29 women of whom 22 were amenorrhoeic (A) and 7 eumenorrhoeic (E) at the end of the first postoperative year. The PI, RI and TE were measured prior to and 1, 6 and 12 months after EA. Statistical analyses were performed using BMDP statistical software, discriminant analysis, ANOVA and T test. Using the calculated classification function (CF) with the three parameters PI, RI and TE measured 12 months after FEAT, we were able to accurately (100%) specify which of the women will have A or E in 3 years. The predictive value of PI, RI and TE has been confirmed clinically in a minimum 3-year follow-up of outcome (ranging from 36 to 72 months [mean 55]). All A and E women have stayed in the same group (A or E) during the minimum of 3 years.

In conclusion we found that PI, RI and TE measured prior to EA cannot predict the outcome, however these measurements performed 1 year after FEAT can predict the duration of A or E in the 3-year follow up.

Introduction

Traditionally, medical therapy is the first line management of dysfunctional uterine bleeding (DUB). If contraindicated, associated with side effects or unsuccessful it is followed by surgical intervention. First-generation endometrial ablation techniques (FEAT), second-generation endometrial ablation techniques (SEAT), and hysterectomy represent the most common second line therapy [1, 2]. Worldwide experience has demonstrated a 75–95% success rate using hysteroscopic ablation [3, 4]. Safe and effective operative hysteroscopy requires highly specialised training, and serious complications, even death, may occur [5]. From this perspective, an individual prognosis of the EA outcome would be appreciated by both the patient and surgeon. In 1998, Bahceci et al. documented statistically different Doppler indices (PI and RI) in E, A and hypomenorrhoeic (H) women, one year after hysteroscopic rollerball endometrial ablation in menometrorrhagic patients [6]. In 2001 Järvalä et al. documented an increase in PI 6 months after thermal balloon endometrial ablation therapy [7]. Our aim was to evaluate the prognostic value of PI, RI and also TE measured before FEAT and during the first postoperative year (at 1, 6, 12 months) and comparing the results with the clinical outcome in a minimum 3-year follow-up.

Material and Methods

Between January 1997 and December 1999, 102 women were treated at our department for intractable DUB using FEAT. All patients had severe menorrhagia, regular cycles without intermenstrual bleeding, as evidenced by their Picturial Blood Loss Assessment Chart [8]. All had failed medical therapy with

medroxyprogesterone acetate 20–40 mg/day (6 in group A and 2 in group E) or oral contraceptives (8 in group A and 3 in group E), or were unwilling or unable to continue with therapy and were suitable candidates for either EA or hysterectomy. The study of 29 patients included 22 women with A and 7 women with E at the end of the first postoperative year. Women with H were excluded from the study because we wanted to compare the results of two clinically significantly different groups. Six women were indicated for hysterectomy after FEAT during the follow up (2 because of intractable bleeding, and 4 because of leiomyomas) and 1 woman died. The women were given detailed information prior to surgery.

DUB was a diagnosis of exclusion [9]. Prior to the procedure several screening examinations were performed. Each woman underwent a medical history (iatrogenic causes), physical examination and pelvic ultrasound (reproductive tract disease, benign pelvic lesions). A negative cervical smear from both the ectocervix and the endocervical canal was obtained within 6 months, hysteroscopy with endometrial biopsy within 2 months, and vaginal culture, as well as a pregnancy test were performed (to exclude cancer precursor, malignancy, infection, complication of pregnancy). All patients were screened for a coagulopathy with partial thromboplastin time (APTT) and had normal platelet count. All patients in the studied group had normal liver function tests and were euthyroid.

In all 29 women, the uterine cavity depths were not more than 9 cm and less than 8 cm, there were no previous EA nor a desire for preservation of fertility. Pre-treatment endometrial thinning regimens included follicular phase timing; no hormonal manipulation (gonadotrophin-releasing hormone agonists / GnRH, danazol) was used. General anaesthesia was used in all cases. For fluid hysteroscopy we used a mixture of mannitol, 0.54% and sorbitol 2.7%. We used the Olympus resectoscope system (Olympus Medical Systems, Tokyo, Japan). The endometrium of the fundus and cornua uteri was coagulated with "roller ball" and the remaining endometrium was resected with the loop close to the level of the internal os of the uterus. A mixed diathermy current of 100 W for cutting and 60 W for coagulation was used in most cases. All the women were discharged within 48 hours and were reviewed at 1, 6 and 12 months post-operatively, and again in the period between October and December 2002. No postoperative medical or surgical treatment was required.

The transvaginal ultrasound scan was performed with an Acuson 128 XP device (Mountain View, CA) using a 5–7 MHz curvilinear transvaginal transducer. The examinations were scheduled in the morning on days 5–8 of the menstrual cycle in E patients and in A patients in the absence of a developing follicle or corpus luteum. With an empty urinary bladder, the women were placed in the dorsal lithotomy position, and 15 minutes after lying on the table, the vaginal ultrasound probe was inserted and placed into the lateral fornix. The uterus and ovaries were visualized using B mode ultrasound. The uterine artery was identified using color Doppler at the level of the internal cervical os beside the cervix. The Doppler gate

was positioned on each uterine artery to detect the maximal signals. The waveforms were characterized by maximum systolic velocity (V_{max}), minimum systolic velocity (V_{min}), time-averaged maximum velocity (TAMX). The PI and RI were calculated by using the Acuson 128 XP machine's built in software. The RI and PI indices are reflectors of vascular impedance and were calculated according to the formula – (PI: systole – diastole / mean, RI: systole – diastole / systole). The same was then repeated for the contralateral uterine artery. Pulsatility and resistance index (PI, RI) were measured on five similar subsequent cycles.

BMDP statistical software was used for statistical analysis [10].

Statistical comparisons were made using t-test, ANOVA, and stepwise discriminant analysis. Stepwise discriminant analysis finds the combination of variables that predicts the group to which a woman belongs. The combination of predictor variables is called a classification function (CF). This function can then be used to classify a new patient whose group is unknown. The variables used in analysis were PI, RI, TE and age. The PI and RI were the mean values of the PI and RI measured in the left and right uterine arteries. The values of these three variables (PI, RI, TE) were measured in three periods after FEAT (1, 6 and 12 months).

Results

No serious complications occurred during the FEAT procedures and there were no serious postoperative consequences. Table 1 shows the age of the patients, duration of surgery, and length of follow-up. Women who were in group E 3 years after AE were statistically significantly younger ($p<0,05$) than women in group A. Table 2 shows the values of PI, RI and TE values in patients prior to FEAT. The means (PI, RI, and TE) of group A and E are not significantly different.

Table 3 shows the values of PI, RI, and TE at 1, 6 and 12 months after FEAT. The mean and standard deviation for each variable (PI, RI, TE) at each time and in each group are shown. The means of all 3 parameters (PI, RI, and TE) 12 months after EA are statistically significantly different in groups A and E. However, 6 months after ablation we did not demonstrate any significant difference in the 3 parameters between groups A and E.

Table 1 – Age of the patients, duration of surgery, and length of follow-up

Parameter	Group	Number	Mean	Range	p (t-test)
Age (years)	A	22	53.8	29–66	0.05
	E	7	42.6	31–51	
	A + E	29	49.2	29–66	
Operating time (minutes)	A + E	29	20	11–40	
Follow-up (months)	A + E	29	55	36–72	

Women who were in group E 3 years after AE were statistically significantly younger ($p<0,05$) than women in group A.

Graph 1 shows the values of PI 1, 6, and 12 months after FEAT. The means of PI are significantly greater for women in group A than in group E (p=0.01), the PI are significantly greater 12 months after FEAT than at 1 or 6 months after FEAT (p=0.0001). The PI growth in group A and group E significantly differs (p=0.05). Graph 2 shows the values of RI at 1, 6, and 12 months after FEAT. The means of RI are significantly greater for women in group A than in group E (p=0.01). The RI is significantly greater 12 months after FEAT than at 1 and 6 months after FEAT (p=0.0001 only in group A). The changes of RI in group A and group E significantly differs (p=0.0001).

Graph 3 shows thickness of the endometrium at 1, 6, and 12 months after FEAT.

The means of TE are significantly greater for women in group E than in group A (p=0.01). The TE differs significantly across the time (p=0.05) but not significantly for women in group A. The changes of TE in group A and group E significantly differ (only p=0.1).

Using the discriminant analysis with the variables measured twelve months after FEAT two classification functions were evaluated with significantly predicted variables RI 12, PI 12 and TE 12.

Table 2 – The values of PI, RI and TE values in patients prior to FEAT

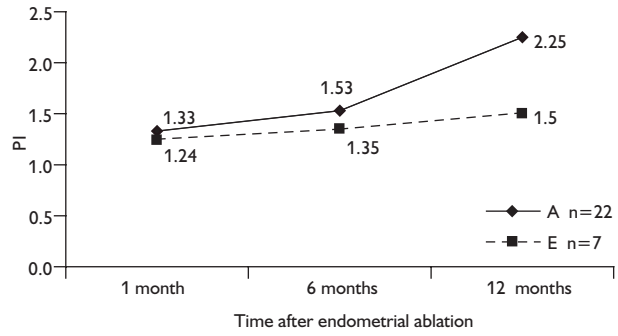
Parameter	Group	Number	Mean	SD	Range	p (t-test)
TE	A	22	5.78	1.92	1.80–9.00	0.8547 NS
(millimetres)	E	7	5.94	2.07	4.00–9.00	
PI	A	22	1.63	0.37	1.04–2.26	0.8537 NS
	E	7	1.62	0.37	1.18–2.12	
RI	A	22	0.80	0.08	0.63–0.95	0.2465 NS
	E	7	0.76	0.07	0.65–0.85	

The means (PI, RI, and TE) of group A and E are not significantly different.

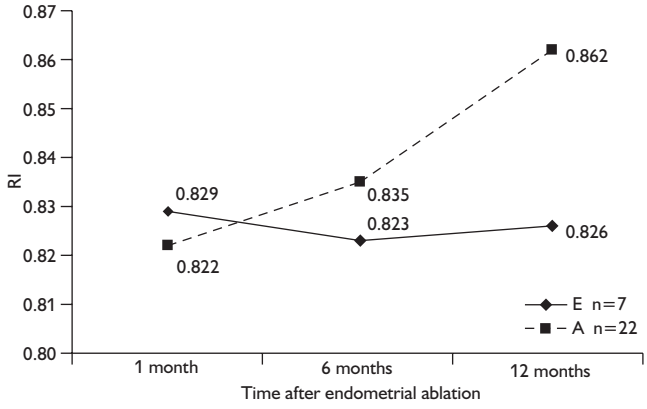
Table 3 – The values of PI, RI, and TE at 1, 6 and 12 months after FEAT

		1 month			6 months			12 months		
Parameter	Group	Mean	SD	p	Mean	SD	p	Mean	SD	p
PI	E	1.24	0.13	NS	1.35	0.18	NS	1.50	0.24	0.01
	A	1.33	0.19		1.53	0.53		2.25	0.56	
RI	E	0.83	0.01	NS	0.82	0.01	NS	0.83	0.01	0.0001
	A	0.82	0.01		0.84	0.02		0.86	0.02	
TE	E	6.86	3.39	0.01	3.71	3.90	NS	7.86	3.24	0.01
	A	3.16	2.92		3.45	2.94		3.73	3.01	

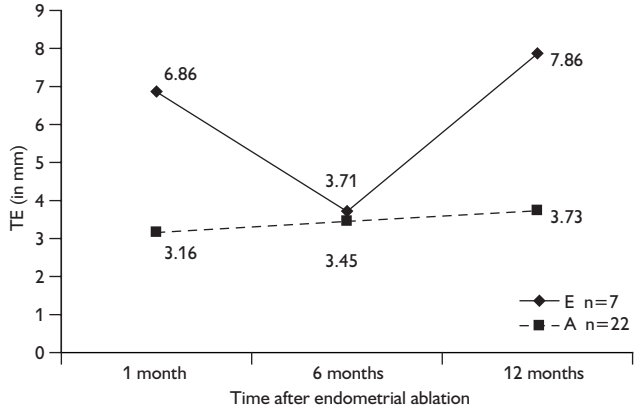
In Table 3 the mean and standard deviation for each variable (PI, RI, TE) at each time and in each group are shown. The means of all 3 parameters (PI, RI, and TE) 12 months after EA are statistically significantly different in groups A and E. However, 6 months after ablation we did not demonstrate any significant difference in the 3 parameters between groups A and E.



Graph 1 – Values of PI 1, 6, and 12 months after FEAT. E – eumenorrhoea, A – amenorrhoea, PI – pulsatility index, ANOVA – analysis of variance. The means of PI are significantly greater for women in group A than in group E (p=0,01), the PI are significantly greater 12 months after FEAT than at 1 or 6 months after FEAT (p=0,0001). The PI growth in group A and group E significantly differs (p=0,05).



Graph 2 – Values of RI at 1, 6, and 12 months after FEAT. E – eumenorrhoea, A – amenorrhoea, RI – resistance index, ANOVA – analysis of variance. The means of RI are significantly greater for women in group A than in group E (p=0,01). The RI is significantly greater 12 months after FEAT than at 1 and 6 months after FEAT (p=0,0001 only in group A). The changes of RI in group A and group E significantly differs (p=0,0001).



Graph 3 – Thickness of the endometrium at 1, 6, and 12 months after FEAT. E – eumenorrhoea A – amenorrhoea, TE – thickness of the endometrium, ANOVA – analysis of variance. The means of TE are significantly greater for women in group E than in group A (p=0,01). The TE differs significantly across the time (p=0,05) but not significantly for women in group A. The changes of TE in group A and group E significantly differ (only p=0,1).

$CF(E) = -1462.3 + 36.5 \times PI(12) + 3517.7 \times RI(12) - 4.62 \times TE(12)$

$CF(A) = -1645.2 + 42.4 \times PI(12) + 3727.7 \times RI(12) - 5.56 \times TE(12)$

The woman is assigned to the group for which the classification function has the largest value. These functions correctly (100%) classified all 29 women into each of group (A or E), they can also be used to classify new women. All A and E women have stayed in the same groups during the 3-year follow up.

Discussion

The invasiveness of the surgical approach decreases from abdominal to vaginal, laparoscopic to hysteroscopic as a minimally invasive procedure. For DUB we prefer EA (FEAT or still safer SEAT) as the first line surgical therapy. First-generation endometrial ablation techniques destroy the endometrium and superficial myometrium using laser energy [11] or electrical energy delivered via a roller-ball [12] or resector loop [13]. Worldwide experience has demonstrated a 75–95% success rate using hysteroscopic ablation [3, 4]. The success rates for the hysteroscopic treatment of DUB depend on the definition of success, length of follow up, preoperative preparation of endometrium, the length of the uterine cavity, experience of the surgeon, and of the energy modality or technique chosen [14]. On the other hand, according to Phillips et al. the age of the patient at ablation, dysmenorrhoea, premenstrual syndromes or the method of endometrial preparation do not appear to be predictive factors of success [15]. EA is a more cost effective and safer alternative to hysterectomy even when considering patients who will require repeat ablation or subsequent hysterectomy [16]. However, safe and effective operative hysteroscopy (FEAT) requires highly specialised training and complications may occur in 6–15% [5] or serious complications in 2–7% [17] including fluid overload, uterine perforation, infection, haemorrhage, thermal injuries, and even death.

Some women may also elect to have "a definitive procedure" even if it entails a longer recovery and the loss of an organ. From this point of view it would be valuable to predict individual long term outcome of conventional (hysteroscopic, FEAT) as well as global (nonhysteroscopic, SEAT) EA [18]. It would be ideal to individually predict the outcome of EA prior to the procedure. Prediction of the long-term outcome of EA in the early postoperative period provides information about the probability of repeated surgical intervention (endometrial re-ablation, hysterectomy).

Uterine artery Doppler velocimetry varies in relation to the phase of the menstrual cycle, circadian rhythm [19]. Body posture may also affect Doppler indices that influence clinical outcomes [20]. The Doppler measurements should therefore be performed within defined conditions to make valid comparisons. In 1998 Bahceci et al. documented that in patients with DUB, post-ablation treatment failures at the end of the first postoperative year are associated with decreases in the uterine artery Doppler indices. The increased uterine perfusion as reflected by decreased Doppler indices at the end of the first postoperative year is presumably

due to the increased activity of retained endometrial tissue after the ablation procedure. In well preserved endometrial tissue, downstream resistance to blood flow will be decreased due to the well developed endometrial vessels resulting in low PI and RI values in uterine arteries [6]. In 2001 Järvalä et al. documented an increase in PI 6 months after thermal balloon endometrial ablation therapy [7]. We suppose that the rise in impedance is due to the fibrosis in the uterine cavity walls which agrees with our results completed 12 months after the FEAT.

Conclusion

Measuring the PI, RI, and TE prior to FEAT cannot predict its outcome. On the contrary using the calculated classification function with three parameters RI, PI, and TE 12 months after ablation of the endometrium accurately (100%) specifies which of the women will have amenorrhoea or eumenorrhoea. At one or six months after ablation, only the thickness of endometrium 1 month after FEAT (TE 1) is a significantly predictive variable and classified women into each group A or E correctly in only 79.3%. The predictive value has been evaluated and was confirmed in clinical follow up outcomes ranging from 36 to 72 (mean 55) months.

References

1. ISAACSON K.: Endometrial ablation: Is one technique best? *Contemporary OB/GYN, Special Issue.* 246: 31–38, 2000.
2. ABBOTT J. S., GARRY R.: The surgical management of menorrhagia. *Hum. Reprod. Update*. 8: 68–78, 2002.
3. VILOS G. A., VILIS E. C., KING J. H.: Experience with 800 hysteroscopic endometrial ablations. *J. Am. Assoc. Gynecol. Laparosc*. 4: 33–38, 1996.
4. ROMER T.: Transcervical electrosurgical endometrial ablation: long-term results. *Geburtshilfe Frauenheilkd.* 59: 255–257, 1999.
5. O'CONNOR H., MAGOS A.: Endometrial resection for the treatment of menorrhagia. *N. Engl. J. Med*. 3: 151–156, 1996.
6. BAHCECI M., CEM DEMIREL L., AKSOY E., ISCAN S., YÜCEL R.: Doppler velocimetry of the uterine arteries after hysteroscopic rollerball endometrial ablation. *Hum. Reprod.* 13: 3456–3459, 1998.
7. JÄRVELÄ I., TEKAY M., SANTALA M., JOUPPILA P.: Thermal balloon endometrial ablation therapy induces a rise in uterine blood flow impedance: a randomized prospective color Doppler study. *Ultrasound Obstet. Gynecol*. 17: 65–70, 2001.
8. HIGHAM J. M., O'BRIEN P. M. S., SHAW R. W.: Assessment of menstrual blood loss using a picturial chart. *Br. J. Obstet. Gynaecol*. 97: 734–739, 1990.
9. BRENNER P. F.: DIFFERENTIAL DIAGNOSIS OF ABNORMAL UTERINE BLEEDING. *Am. J. Obstet. Gynecol*. 175: 766–769, 1996.
10. BMDP statistical software, University of California Press, W. J. Dixon, Chief Editor, 1990.
11. GOLDRATH M. H., FULLER T., SEGAL S.: Laser photovaporization of endometrium for the treatment of menorrhagia. *Am. J. Obstet. Gynecol.* 140: 14–18, 1981.
12. VANCAILLIE. T. G.: Electrocoagulatio of the endometrium with the ball-end resectoscope. *Obstet. Gynecol.* 61: 425–427, 1983.

13. DECHERNEY A., POLAN M. L.: Hysteroscopic management of intrauterine lesions and intractable uterine bleeding. *Obstet. Gynecol.* 61: 392–397, 1983.
14. BONGERS M. Y., MOL B. W., BROLMANN H. A.: Prognostic factors for the success of thermal balloon ablation in the treatment of menorrhagia. *Obstet. Gynecol.*; 99: 1060–1066, 2002.
15. PHILLIPS G., CHIEN P., GARRY R.: Risk of hysterectomy after 1000 consecutive laser ablations. *Br. J. Obstet. Gynaecol.* 105: 897–903, 1998.
16. BRUMSTEAD J. R., BLACKMAN J. A., BADGER G. J., RIDDICK. D. H.: Hysteroscopy versus hysterectomy for the treatment of abnormal uterine bleeding: a comparison of cost. *Fertil. Steril.* 65: 310–316, 1996.
17. OVERTON C., MARESH M. J. A.: Audit of currently available endometrial ablative techniques. *Baillieres Clin. Obstet. Gynaecol.* 9: 357–372, 1995.
18. SHAMONKI M. I., ZIEGLER W. F., BADGER G. J., SITES C. K.: Prediction of endometrial ablation success according to perioperative findings. *Am. J. Obstet. Gynecol.* 182: 1005–1007, 2000.
19. ZAIDI J., JURKOVIC D., CAMPBELL S., POTTROF R., MCGREGOR A., TAN S. L.: Description of circadian rhythm in uterine artery blood flow during the peri-ovulatory period. *Hum. Reprod.* 10: 1642–1646, 1995.
20. DICKEY R. P., HOWER J. F., MATULICH E. M., BROWN G. T.: Effect of standing on non-pregnant uterine blood flow. *Ultrasound Obstet. Gynecol.* 4: 480–487, 1994.