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GENERAL GYNECOLOGY

Recurrence and prediction of abnormal uterine bleeding and re-intervention after initial hysteroscopic treatment: a retrospective cohort study

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Abstract

Purpose To estimate the incidence of recurrence of complaints and repeated interventions after hysteroscopic treatment for abnormal uterine bleeding in premenopausal women and to determine potential predictors for re-intervention.

Methods This is a retrospective cohort study in two secondary care centers in the Netherlands. We included 313 premenopausal women who underwent hysteroscopy for complaints of abnormal uterine bleeding and who had intrauterine pathology visualized at ultrasound. The intrauterine structure was hysteroscopically removed. These women were compared with women who had a hysteroscopy for abnormal uterine bleeding, but in whom hysteroscopy showed no abnormalities. We used Chi-squared test for categorical variables and independent-samples *T* test for continuous variables. *p* Values less than 0.05 were considered to indicate statistical significance.

Results In total, 262 women had intrauterine pathology removed at hysteroscopy; 136 (52%) women had recurrence of complaints, while 101 women (39%) underwent re-intervention. Heavy menstrual bleeding at baseline and multiparity were predictive factors for recurrence of abnormal uterine bleeding and re-intervention. In the 51 women with abnormal uterine bleeding in whom hysteroscopy showed no intrauterine abnormality, 29 women (60%) had recurrence of complaints and 12 (24%) a re-intervention.

Conclusion In premenopausal women with abnormal uterine bleeding, treatment of intrauterine pathology often does not reduce the complaints, thus questioning the effectiveness of hysteroscopic removal of these structures.

Keywords Abnormal uterine bleeding · Premenopausal · Intrauterine pathology · Therapeutic hysteroscopy · Recurrence

Introduction

Abnormal uterine bleeding (AUB), which is defined as menstrual flow outside of normal volume, duration, regularity, or frequency, accounts for a significant proportion of gynecologic complaints [1]. The International Federation of Gynecology and Obstetrics (FIGO) has developed a classification system for the causes of AUB, under the acronym PALM-COEIN (polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified) [2, 3]. When classified with the PALM-COEIN system, most women have structural benign uterine pathology (polyps, myoma). After malignancy has been excluded, the next step is often the removal of these structural pathologies by hysteroscopy [4, 5].

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Hysteroscopy has commonly been performed as an office procedure, for diagnostic purposes, since 1980 [6]. In recent years, therapeutic hysteroscopy in an office setting has become more prevalent [6]. The benefits of office hysteroscopy, such as no anesthesia, lower costs, and quicker revalidation, are widely known [7], which is why the incidence of the therapeutic office hysteroscopy has increased.

Although there is some evidence that removal of intrauterine structures is effective in reducing the women's complaints, its long-term effectiveness is not known, as most studies are limited to 3- or 6-month follow-up [8, 9]. The only study that followed women until four years after initial treatment showed that 60% of these women have persistent symptoms of AUB [10]. So, we questioned the effectiveness of hysteroscopic removal of intrauterine structures in women with AUB.

The aim of this study is to determine the incidence of recurrence of complaints and repeated interventions after initial hysteroscopic treatment for AUB in premenopausal women. We compared the results of women who underwent hysteroscopy for AUB with the results of women with AUB who were diagnosed without intrauterine pathology and thus did not require intervention. In addition, we determine potential predictive factors for recurrence of AUB and re-intervention in a prediction model.

Methods

We retrospectively studied women who underwent a hysteroscopy for AUB in two teaching hospitals in the Netherlands: Zuyderland Medical Center, Heerlen, and Máxima Medical Center, Veldhoven. Women were identified from electronic databases, and data were extracted from medical files. If information on follow-up was not available in the records of the institution, we contacted individual women.

We presented the study protocol to our institutional ethics committee, and they gave their approval that this study is not obliged to the rules of the Medical Research Involving Human Subjects Act (WMO in Dutch), because of the retrospective aspect of the study.

The data were not collected in the context of the study, so informed consent was waived.

We included all women who presented with AUB (subjectively) and who underwent a hysteroscopy between January 2005 and December 2010. AUB could be defined as heavy menstrual bleeding, metrorrhagia, or intermenstrual bleeding. Intrauterine pathology could be a polyp or myoma, and a diagnosis had to be made preoperatively by vaginal ultrasound, by saline infusion sonography, or by diagnostic hysteroscopy. Hysteroscopy could be performed in a therapeutic inpatient setting or in an office setting. Afterward, all biopsies were sent for histological assessment and were confirmed by a pathologist.

These women were compared with women from the same inclusion group in whom intrauterine pathology was suspected and who had a hysteroscopy for AUB, but where no intrauterine pathology was found. In these women, the vaginal ultrasound or saline infusion sonography had provided a false-positive diagnosis indicating intrauterine pathology. These women were either reassured that they had no pathology and received no further treatment, or they were treated with nonsteroidal anti-inflammatory drugs or oral contraceptives. The latter treatments were also prescribed frequently to women who had an intrauterine structure removed.

Intended was to exclude women if the removed pathology turned out to be malignant, but all polyps were benign. Women whose initial therapeutic hysteroscopy was combined with endometrial ablation or insertion of a levonorgestrel-releasing intrauterine device (LNG-IUD) were excluded from the study. Both interventions are also therapeutic treatment options for AUB.

We collected baseline characteristics including age, body mass index (BMI), parity, smoking, medication use (hormonal medication and anticoagulants), hemoglobin level, menstruation pattern, and duration of menstrual period. For the women who had intrauterine pathology and who underwent a therapeutic hysteroscopy, we collected the following additional data on the initial intervention: sort and size of intrauterine structure removed (polyps < 1 cm, polyps > 1 cm, myoma-type0 < 2 cm, myoma-type0 > 2 cm, myoma-type1 < 2 cm, or myoma-type1 > 2 cm); time of procedure; method of removal; and final diagnosis.

Main outcome measures were rate of recurrence of complaints of AUB and repeated interventions, and medical therapy for persistence or recurrence of AUB. Medical therapy included oral contraceptives, progestogens, NSAIDs, and LNG-IUDs. Repeated interventions included repeated therapeutic hysteroscopy, endometrial ablation, embolization, and hysterectomy. Secondary outcomes are the differences between the two groups of women regarding menstruation, namely the recurrence of heavy menstrual bleeding, metrorrhagia and days of period, and the differences between the two groups regarding the intervention, namely the type of structure removed (such as polyps or leiomyoma), size of the structural uterine pathology, relapsing time of symptoms, duration of procedure, and the removal method, such as mechanically (e.g., scissors or forceps) or electrosurgically.

For statistical analysis, we used the program R, version 3.3.3. We expressed continuous variables with a normal distribution as a mean with a standard deviation (SD) and 95% confidence intervals (CI). Skewed distributed continuous variables were expressed as a median and range. Differences in baseline characteristics or outcomes between intervention and nonintervention groups were tested with a Chi-squared

test for categorical variables and independent-samples T-test for continuous variables. *p* Values less than 0.05 were considered to indicate statistical significance.

Since missing data are often not missing completely at random, analyzing only completely observed subjects could result in bias and a severe loss of precision in the regression coefficient estimates. Therefore, we imputed these missing values using stochastic regression imputation. The imputation model included all the candidate predictors and the outcome, as is advocated in guidelines on imputation [11]. The imputation was performed on the total database after which only those women who underwent a therapeutic hysteroscopy were selected.

All candidate predictors for recurrence of AUB were included in the multivariable logistic regression model, after which a backward stepwise elimination was performed using a *p* value for deletion of 0.10. To prevent severe overfitting of the model to the data, an often used rule of thumb states that at least 10 recurrences are needed for each variable to be included in the model [12].

To assess its potential in future patients, we used standard bootstrapping techniques for internal validation of the model. A total of 1000 bootstrap samples were drawn from the original data. The results of the bootstrap validation were used to compute optimism-corrected indices of the model's performance and a shrinkage factor that can be used to adjust the regression coefficients in such a way that future predictions are less extreme.

The performance of the internally validated model was quantified by measures of overall fit, discrimination, and calibration. Overall fit was assessed by Nagelkerke's R square. Discrimination refers to the model's ability to separate women who will from those who will not develop recurrent bleeding, and is quantified by the area under the receiver operating characteristic (ROC) curve. Calibration, on the other hand, refers to the accuracy of the model's predictions. We assessed the model's calibration plot and computed Hosmer and Lemeshow (H–L) goodness-of-fit statistic. A nonsignificant H–L test indicates no evidence against good model fit.

Results

We included 313 women who underwent hysteroscopy for complaints of AUB. In 262 of these women, hysteroscopic removal of a polyp or myoma was performed (intervention group). We identified 51 women with AUB who underwent a hysteroscopy without findings of structural pathology (nonintervention group).

Baseline characteristics between the intervention group and the nonintervention group did not significantly differ (Table 1).

The majority (75%) of the women in the intervention group had heavy menstrual bleeding due to myoma. Polyps were found in 21% of the women with heavy menstrual

Table 1 Baseline clinical characteristics

Patient characteristics	Intervention group $N=262$	Nonintervention group $N=51$	*p*	Missing	
				IN	CO
Age	44.3 ± 5.7	42.5 ± 6.3	0.055	0	0
BMI	26.1 ± 5.9	25.6 ± 4.3	0.594	151	16
Smokers	37 (14.1%)	15 (29.4%)	0.696	152	12
Parity	1.4 ± 1.08	1.4 ± 0.99	0.917	42	6
P0	58 (22.1%)	10 (19.6%)	0.708		
P1	48 (18.3%)	12 (23.5%)	0.557		
P2	84 (32.1%)	19 (37.3%)	0.618		
P3	30 (11.5%)	4 (7.8%)	0.471		
Medication users	149 (56.9%)	26 (51.0%)	0.446	–	–
Hormonal	97 (37.0%)	6 (11.8%)	–		
Anticoagulants	6 (2.3%)	2 (3.9%)	–		
Ferrous fumarate	17 (6.5%)	1 (2.0%)	–		
Other	55 (21.0%)	20 (39.2%)	–		
Hemoglobin level	7.5 ± 1.2	7.6 ± 1.2	0.676	86	12
Duration of symptoms	10.3 ± 11.3	12.5 ± 12.3	0.475	172	34
Menstruation pattern:					
Metrorrhagia	76 (29.0%)	21 (41.2%)	0.098	–	–
Menorrhagia	142 (54.2%)	18 (35.3%)	0.015	–	–
Both	44 (16.8%)	12 (23.5%)	0.317	–	–
Days of period	8.6 ± 3.9	7.6 ± 2.6	0.305	160	34

bleeding. Of the women with metrorrhagia, however, 46% had polyps. All polyps were benign.

For the main outcome, the median follow-up time was seven years since initial hysteroscopy (maximum: 9.5 years, minimum: 4.5 years). Recurrence of complaints after initial therapy occurred in 136 (52%) women in the intervention group versus 29 (60%) in the nonintervention group ($p = .52$).

For the women in the intervention group and the nonintervention group, we compared the individual characteristics between recurrence and no recurrence (Table 2).

In the intervention group, there was a difference between recurrence and no recurrence in BMI (27.2 vs. 24.7, $p < .05$), parity 0 (16% vs. 29%, $p < .01$), parity 2 (40% vs. 24%, $p < .05$), metrorrhagia (24% vs. 35%, $p < .05$), heavy menstrual bleeding (63% vs. 44%, $p < .01$), and myoma-type0 smaller than 2 cm (9% vs. 18%, $p < .05$).

In the nonintervention group, there was no statistical difference between the individual characteristics in recurrence and no recurrence.

In the intervention group, we split the intrauterine pathologies into several groups, namely polyps < 1 cm (12%), polyps > 1 cm (23%), myoma-type0 < 2 cm (13%), myoma-type0 > 2 cm (14%), myoma-type1 < 2 cm (20%), myoma-type1 > 2 cm (15%). Between the different groups, there was no difference in recurrence except for myoma-type0 smaller than 2 cm, where there was less recurrence after removal.

Among women with recurrence of complaints, re-intervention occurred in 101 women of the initial group where an intracavitary structure was removed (74%) versus 12 (41%)

Table 2 Patient characteristics of recurrence group and no recurrence group

Patient characteristics	Intervention group $N = 262$			Nonintervention group $N = 51$		
	Recurrence $N = 136$	No recurrence $N = 126$	p	Recurrence $N = 29$	No recurrence $N = 22$	p
Age	43.8 ± 5.9	44.7 ± 5.5	0.226	41.6 ± 6.9	43.7 ± 5.3	0.241
BMI	27.2 ± 6.7	24.7 ± 4.2	0.030	26.2 ± 4.9	24.2 ± 2.1	0.226
Smokers	18 (13.2%)	19 (15.1%)	0.552	9 (31.0%)	6 (27.3%)	0.740
Parity	1.6 ± 1.0	1.2 ± 1.1	0.014	1.2 ± 0.93	1.7 ± 1.0	0.140
P0	22 (16.2%)	36 (28.6%)	0.003	8 (27.6%)	2 (9.1%)	0.272
P1	28 (20.6%)	20 (15.9%)	0.626	6 (20.7%)	6 (27.3%)	0.499
P2	54 (39.7%)	30 (23.8%)	0.036	12 (41.4%)	7 (31.8%)	0.766
P3+	17 (12.5%)	13 (10.3%)	0.502	1 (3.4%)	3 (13.6%)	0.286
Hemoglobin level	7.4 ± 1.2	7.6 ± 1.2	0.228	7.5 ± 1.2	7.7 ± 1.3	0.632
Hormonal medication	44 (32.4%)	53 (42.1%)	0.124	5 (17.2%)	1 (4.5%)	0.218
Duration of period	9.2 ± 4.2	7.6 ± 3.3	0.052	7.4 ± 2.0	7.8 ± 3.3	0.818
AUB						
Metrorrhagia	32 (23.5%)	44 (34.9%)	0.042	13 (44.8%)	8 (36.4%)	0.579
Menorrhagia	86 (63.2%)	56 (44.4%)	0.003	10 (34.5%)	8 (36.4%)	0.560
Both	18 (13.2%)	26 (20.6%)	0.137	6 (20.7%)	6 (27.3%)	0.741
Initial intervention[a]						
Polyp < 1 cm	17 (12.5%)	13 (10.3%)	0.699			
Polyp > 1 cm	31 (22.8%)	29 (23.0%)	0.541			
Myomata-type0 < 2 cm	12 (8.8%)	22 (17.5%)	0.044			
Myomata-type0 > 2 cm	17 (12.5%)	19 (15.1%)	0.593			
Myomata-type1 < 2 cm	29 (21.3%)	22 (17.5%)	0.440			
Myomata-type1 > 2 cm	24 (17.6%)	15 (11.9%)	0.225			
Polyp + Myomata	2 (2.0%)	3 (2.4%)	0.674			
Myomata-type0 + type1	–	1 (0.8%)	0.481			
Hysteroscopy + curettage	4 (2.9%)	1 (1.6%)	0.685	29 (100%)	22 (100%)	–
Final diagnosis						
Myomata	91 (66.9%)	84 (66.7%)	0.535			
Polyp	39 (28.7%)	37 (29.4%)	0.505			
Both	6 (4.4%)	5 (4.0%)	0.553			
No pathology	–	–	–	29 (100%)	22 (100%)	–

[a]Hysteroscopic removal of

in the group where hysteroscopy showed no abnormalities ($p = .01$).

In the intervention group, 26 women (10%) were treated with oral contraceptives and five women (2%) with NSAIDs compared to five women (10%) with oral contraceptives and one (2%) with NSAIDs in the nonintervention group ($p = .98$).

We also studied if there were significant differences between the two care centers for patient characteristics, incidence of recurrence, re-intervention, and medical treatment. There were no differences in any of these parameters.

The univariable analysis of predictors of women with and without recurrence in the intervention group is shown in Table 3.

Nulliparous women (OR 0.39 95% CI 0.21–0.72), metrorrhagia (OR 0.57, 95% CI 0.33–0.98), and myoma-type0 < 2 cm (OR 0.46 95% CI 0.21–0.97) were protective for recurrence in this cohort. Multiparous women with a parity of 2 (OR 1.9 95% CI 1.06–3.2) and heavy menstrual bleeding (OR 2.2 CI 1.3–3.5) were significantly related to recurrence of AUB after therapeutic hysteroscopy.

The prediction model resulting from the multivariable selection of predictors is shown in Table 4. The internally validated coefficients were penalized using the shrinkage factor (0.89) resulting from the bootstrap validation.

Nagelkerke's R square of the model was 18.8% (16.9% after correction for optimism). The discriminative ability of the model, expressed as the AUC (Fig. 1), was 71.5% (95% CI 65.3%–77.7%). After internal validation, the optimism-corrected AUC was 69.4%. Figure 2 shows the calibration plot. The smoothed line and the different groups of patients lie close to the ideal line of 45 degrees. This indicates good calibration. The formula that can be used to calculate an individual's probability of recurrence is presented in Table 4. The

Table 3 Distribution of and multivariable analysis between candidate predictors and recurrence of AUB in the intervention group

Candidate predictor	Recurrence $N = 136$	No recurrence $N = 126$	Univariate Logistic regression analysis			Multivariate Logistic regression analysis			
			OR	95% CI	*p*	*β*	OR	95%CI	*p*
Age	43.8 ± 5.9	44.7 ± 5.5	1.03	0.98–1.07	0.226	−0.038	0.96	0.92–1.01	0.108
BMI	27.2 ± 6.7	24.7 ± 4.2	0.92	0.85–.995	0.030	0.023	1.02	0.97–1.08	0.358
Parity									
P0	22 (16.2%)	36 (28.6%)	0.39	0.21–0.72	0.003	−0.705	0.49	0.25–0.97	0.04
P2	54 (39.7%)	30 (23.8%)	1.9	1.06–3.2	0.036	0.308	1.36	0.75–2.48	0.32
AUB									
Metrorrhagia	32 (23.5%)	44 (34.9%)	0.57	0.33–0.98	0.042	0.141	1.15	0.52–2.56	0.73
Menorrhagia	86 (63.2%)	56 (44.4%)	2.2	1.3–3.5	0.003	0.859	2.36	1.15–4.86	0.02
Myoma-type0 < 2 cm	12 (8.8%)	22 (17.5%)	0.46	0.26–0.98	0.044	−0.726	0.48	0.22–1.07	0.07
Duration of period	9.2 ± 4.2	7.6 ± 3.3	1.97	−0.11–3.18	0.052	0.067	1.07	1.00–1.14	0.04

Table 4 Prediction model for the recurrence of abnormal uterine bleeding

Variable	Regression	OR (95% CI)	Shrunk regression coefficient*
Intercept	−0.57		−0.48
Age (years)	−0.05	0.95 (0.91–1.00)	−0.04
BMI (kg/m^2)	0.07	1.07 (1.01–1.13)	0.06
Nulliparous (yes)	−1.08	0.34 (0.18–0.62)	−0.96
Menorrhagia (yes)	0.89	2.45 (1.43–4.19)	0.80
Myoma-type 0 < 2 cm (yes)	−0.72	0.48 (0.21–1.10)	−0.64
Duration of period (days)	0.11	1.12 (1.03–1.21)	0.10

The probability recurrence of abnormal uterine bleeding can be calculated as

p(recurrence) = 1/(1 + exp(− (Linear Predictor))), in which

Linear Predictor = −0.48 −.04*Age + 0.06*BMI − 0.96*Nulliparous + 0.80 * Menorrhagia − 0.64 * Myoma-type 0 < 2 cm + 0.10 * Duration of period

OR odds ratio, *CI* confidence interval, *BMI* body mass index

*Adjustment for overfitting by shrinkage (shrinkage factor = 0.89). The intercept was subsequently re-estimated

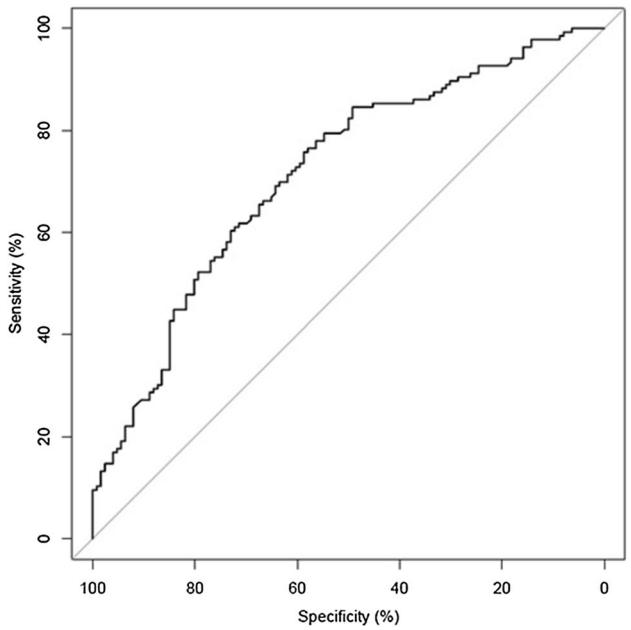

Fig. 1 The discriminative ability of the prediction model, expressed as the area under the curve (AUC)

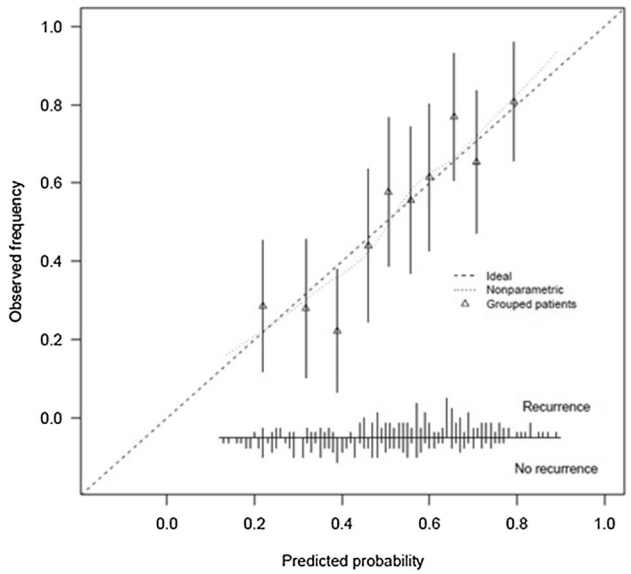

Fig. 2 Calibration plot of the prediction model

model may be used to calculate an individual's probability, or to classify patients into subgroups based on their risk (e.g., low risk, intermediate risk, and high risk).

Discussion

We found that over 50% of the women in the intervention group had recurrence of complaints of AUB after initial hysteroscopy. The risk of recurrence was not significantly smaller in the group without intrauterine abnormalities. This indicates that intrauterine pathology might not contribute to the cause of AUB and that hysteroscopic removal of these structures as treatment for AUB can be challenged. The sort of intrauterine pathology (myoma of polyps) is neither predicting recurrence. However, the sort of complaints of AUB, e.g., metrorrhagia or heavy menstrual bleeding, are predicting recurrence, with metrorrhagia being protective and HMB increasing the risk of recurrence.

The strengths of the present study include the reasonable cohort size, the long follow-up time, the inclusion of more than one hospital, and the presence of a control group without intrauterine pathology.

Limitations include the retrospective character of the study. This resulted in a lot of missing data regarding patient characteristics, which resulted in smaller subgroups. Moreover, the definition of recurrence was based solely on whether or not the patients returned with the same complaint. We did not have a questionnaire before and after the procedure to address women's menstrual complaints, and we did not have an objective blood loss assessment chart.

The prediction model indicated heavy menstrual bleeding and parity as predictive risk factors for recurrence.

Our prediction model can be used to calculate an individual probability of recurrence which can then be compared to the average risk of 52%. Nevertheless, even in the low risk of recurrence group, there is an incidence of recurrence of up to 40%. This suggests considering other treatments for women with AUB, like endometrial ablation or insertion of a levonorgestrel-releasing intrauterine device (LNG-IUD).

In our study, we found a high percentage of recurrence of complaints (52%). This is contrary to earlier studies, which found a satisfaction rate of at least 70% [8, 13]. This could be due to the objective recurrence rate used in our study, compared to the patient-reported satisfaction rate used in these earlier studies. However, the experience of recurrent or persistent AUB is always subjective, even in objective recurrence rates. Furthermore, in research of benign gynecology, subjective outcome measures are often used due to lack of objective cutoff points. In addition, this study has a much longer follow-up time compared to previous studies. As incidence of recurrence increases over time, this also explains our higher recurrence rates.

To our knowledge, this is the first study that compares the data of women undergoing hysteroscopic treatment for

AUB with data from a group undergoing hysteroscopy and suffering from the same complaints, but without intrauterine pathology. The only statistical difference between the intervention and the nonintervention groups is the risk of re-interventions among the women with recurrence (74% vs. 41%). An explanation for this might be that physicians assume that there is a recurrence of intrauterine pathology, which needs to be treated. In the nonintervention group, there was no explanation for the complaints, and therefore, a re-intervention would be useless. The evidence that the group without intrauterine pathology had a significantly higher risk of being treated with medication supports this.

In conclusion, the main finding of our study was the high recurrence rate and re-intervention rate of more than 50%. While in women with AUB without intracavitary abnormalities, treatment with Mirena or ablation results in a disappearance of complaints in 90% of the women, the rate of effectiveness of polypectomy and myomectomy was much lower. Thus, one could question whether hysteroscopic removal in women who suffer from AUB and have small intrauterine abnormalities is the best treatment. Whether these women might benefit from ablation or from a Mirena should be evaluated in new cohort studies or even randomized clinical trials.

Author contributions SFGS contributed to protocol development, data collection, data analysis, manuscript writing; JRJD took part in data collection, data analysis, manuscript writing; MYB involved in manuscript editing and critical revision of intellectual content; SMJK contributed to data analysis and manuscript writing; BWJM involved in protocol development, manuscript editing, critical revision of intellectual content; JL involved in protocol development, manuscript editing, critical revision of intellectual content.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Spencer CP, Whitehead MI (1999) Endometrial assessment revisited. Br J Obstet Gynaecol 106(7):623–632
2. Fraser IS, Critchley HO, Munro MG, Broder M (2007) Writing Group for this menstrual agreement. A process designed to lead to international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding. Fertil Steril 87(3):466–476
3. Munro MG, Critchley HO, Broder MS, Fraser IS (2011) Disorders FWGoM. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynaecol Obstet 113(1):3–13
4. Preutthipan S, Herabutya Y (2005) Hysteroscopic polypectomy in 240 premenopausal and postmenopausal women. Fertil Steril 83(3):705–709
5. Gimpelson RJ, Rappold HO (1988) A comparative study between panoramic hysteroscopy with directed biopsies and dilatation and curettage. A review of 276 cases. Am J Obstet Gynecol 158(3 Pt 1):489–492
6. Campo R, Van Belle Y, Rombauts L, Brosens I, Gordts S (1999) Office mini-hysteroscopy. Hum Reprod Update 5(1):73–81
7. Litta P, Cosmi E, Saccardi C, Esposito C, Rui R, Ambrosini G (2008) Outpatient operative polypectomy using a 5 mm-hysteroscope without anaesthesia and/or analgesia: advantages and limits. Eur J Obstet Gynecol Reprod Biol 139(2):210–214
8. Hamani Y, Eldar I, Sela HY, Voss E, Haimov-Kochman R (2013) The clinical significance of small endometrial polyps. Eur J Obstet Gynecol Reprod Biol 170(2):497–500
9. van Dongen H, Janssen CA, Smeets MJ, Emanuel MH, Jansen FW (2009) The clinical relevance of hysteroscopic polypectomy in premenopausal women with abnormal uterine bleeding. Br J Obstet Gynaecol 116(10):1387–1390
10. Henriquez DD, van Dongen H, Wolterbeek R, Jansen FW (2007) Polypectomy in premenopausal women with abnormal uterine bleeding: effectiveness of hysteroscopic removal. J Minim Invasive Gynecol 14(1):59–63
11. van Buuren S (2012) Flexible imputation of missing data. Taylor & Francis, Londn
12. Steyerberg E (2008) Clinical prediction models: a practical approach to development, validation, and updating. Springer, New York
13. Stamatellos I, Koutsougeras G, Karamanidis D, Stamatopoulos P, Timpanidis I, Bontis J (2007) Results after hysteroscopic management of premenopausal patients with dysfunctional uterine bleeding or intrauterine lesions. Clin Exp Obstet Gynecol 34(1):35–38