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Hysteroscopic myomectomy for menorrhagia using VersascopeTM bipolar system: Efficacy and prognostic factors at a minimum of one year follow up

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ABSTRACT

Objective: To evaluate the effectiveness of hysteroscopic submucous myomectomy for women with heavy menstrual bleeding (HMB) over a minimum 1-year period and assess prognostic factors associated with treatment success

Study design: Prospective observational study set in a university teaching hospital in UK involving 92 women symptomatic of HMB with submucous myomas consecutively recruited between June 2003 and November 2006. Hysteroscopic myomectomy was performed under outpatient local anaesthetic (n = 35, 38%) or daycase general anaesthesia (n = 57, 62%) using Gynecare VersascopeTM bipolar system. The main outcome measures were: the need for secondary surgical or medical re-intervention, menstrual improvement and patient satisfaction. Other outcome measures include: successful completion of primary resection, type of secondary treatment.

Result: Mean follow up was 2.6 years (95% CI 2.3–2.9). Complete fibroid excision was achieved in 66%. Secondary surgical re-intervention was required in 27 (29%) of which 11 (12%) were repeat hysteroscopic myomectomy and 10 (11%) were hysterectomy procedures. Multiple uterine fibroids and adenomyosis were identified in 80% of hysterectomies. At follow up, improved menstrual symptoms and patient satisfaction were reported by 91% and 86%, respectively. Irregular cycle HMB and incomplete fibroid excision were associated with secondary retreatment. Size of the submucous fibroid resected, presence of intramural and subserosal fibroids, or LA vs. GA setting were unrelated to treatment success.

Conclusion: HMB with submucous myomas may be successfully treated by completely removing the intracavity myoma component, irrespective of co-existent intramural or subserosal fibroids or size of fibroid resected. This effect remains sustained over at least a 1–2 year period.

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1. Introduction

Uterine fibroids are present in 25–40% of women presenting with heavy menstrual bleeding (HMB) [1]. Although a direct cause–effect relationship has not been completely established, there are sufficient observational data to suggest that shrinkage or removal of any identified uterine fibroids is beneficial in alleviating menstrual bleeding abnormalities in most symptomatic women.

Hysteroscopic myomectomy is considered the first-line conservative surgical therapy for the management of symptomatic submucous fibroids [1–5]. Data, from mainly observational studies, have suggested beneficial effects in treating both menstrual abnormalities and infertility with this procedure. The few studies that

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have reported on long term outcomes for fibroid-related menstrual abnormalities, indicate that hysteroscopic myomectomy is associated with a 10–35% risk of surgical re-intervention, including repeat myomectomy, open myomectomy or hysterectomy [2,4,5]. However, such a high re-intervention rate may alter the cost effectiveness of hysteroscopic myomectomy compared to other uterus-conserving treatment options and hysterectomy.

Presently, there is insufficient evidence on reliable selection criteria, optimal surgical technique and long term outcomes for women with symptomatic intracavity fibroids who opt for hysteroscopic myomectomy [6]. This knowledge would be particularly important for preoperative counselling and appropriate patient selection. We therefore wished to evaluate long term efficacy of this treatment, and identify whether there were any adverse (e.g. coexistence of intramural or subserosal fibroids) or favourable (e.g. submucous myoma less than 5 cm size, completeness of lesion excision) peri-operative prognostic factors.

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 Table 1

 Classification system for submucous (intracavity) myomas.

Wamsteker [9] and ESGE (myometrial penetration)	Lasmar classification [10]		
Myometrial penetration	Size	Location	Myometrial penetration
Type 0 (no penetration, completely intracavity) Type 1 (<50% penetration within the myometrium) Type II (>50% penetration within the myometrium)	<2 cm 2 to 5 cm >5 cm	Upper Middle Fundus	≤1/3 >1/3 and <2/3 >2/3
	Higher correlation to completeness of the myomectomy, time spent in surgery, and fluid deficit		

2. Materials and methods

2.1. Patient population

Women symptomatic of abnormal uterine bleeding (i.e. mainly with heavy menstrual bleeding [HMB]), defined subjectively, were referred by primary care general practitioners (GPs) or secondary care to our "One Stop" "See and Treat" menstrual disorders clinic. All women underwent transvaginal pelvic sonography, outpatient hysteroscopy and endometrial Pipelle biopsy (Laboratoire C.C.D., Paris, France) investigations. Women who were considered suitable for hysteroscopic myomectomy were included in this study. Women were excluded from the study if an abnormally shaped uterine cavity (e.g. bicornuate uterus), endometrial hyperplasia, cancer or active pelvic infection were present.

2.2. Study design

Prospective consecutively recruited women who were deemed suitable for hysteroscopic myomectomy who presented to our unit between June 2003 and November 2006. Study participants were followed up to December 2007.

2.3. Intervention

All hysteroscopic myomectomies were performed using a rigid 3.5 mm fiberoptic minihysteroscope (VersascopeTM; Gynecare, Ethicon, Sommerville, NJ, USA) according to the manufacturer's recommended guidance and as previously reported by our group [7,8]. The Gynecare Versascope TM system is composed of a 1.8 mm diameter fiberoptic Zero degree hysteroscope that is housed within a 3.5 mm diameter disposable plastic sheath. The plastic sheath contains three channels: fluid input and output (achieving continuous flow) and an expandable (up to 2 mm diameter) working channel. A 5 Fr (1.6 mm diameter) Versapoint TM Spring Bipolar electrode, inserted into the 2 mm working channel, provided the coagulation/dessication energy for myomectomy. Illumination was provided by a 250-W Xenon light source. The hysteroscopic fibroid resection was under direct visualisation. A 3000 mL bag of normal saline, wrapped in pressure bag pumped up to approximately 100 mmHg, provided the uterine distension medium.

We defined a submucous intracavity fibroid at hysteroscopy as having characteristic appearances (sessile or pedunculated, superficial large blood vessels) and non-mobility with intrauterine fluid or gentle hysteroscopic tapping of the lesion. Histological analysis of the intracavity fibroid occurred after its excision; in all cases, our preoperative suspicion of intracavity fibroid was confirmed on subsequent histology. We chose to classify the fibroid cases in this study according to a modified version of the traditionally used Wamsteker [9] (European Society for Gynecological Endoscopy (ESGE)) and Lasmar classification systems [10] (Table 1). We devised a relatively easier to use classification system and recorded the size

of the intracavity fibroid component (<3 cm, 3–5 cm, >5 cm) and the synchronous presence of any other intramural or subserosal fibroids.

All women were offered the choice of having the intervention under local anaesthetic (LA) outpatient setting or general anaesthetic (GA) daycase setting. Factors that influenced the final decision included: patient preference for GA or LA, how she tolerated outpatient hysteroscopy, intrauterine location and size of intracavity fibroids (with large size or fundal fibroid location being factors that would favour GA rather than LA myomectomy option). Preoperative preparation with a 3-month course of GnRHa (11.25 mg Triptorelin acetate; *Decapeptyl* SR; Ipsen Ltd., Slough, UK) prior to myomectomy was deemed necessary in women with intracavity fibroids greater than 5 cm in size. A patient information leaflet was provided detailing the procedure, expected symptoms and analgesic advice post-hysteroscopic myomectomy.

2.4. LA hysteroscopic myomectomy

This was performed on a "See and Treat" basis with no fasting prior to the procedure and without antibiotic prophylaxis. Other elements of the treatment included:

- 1. *Local anaesthetic*: the cervix was directly injected in a circumferential manner with three 2 mL cartridges containing 3% prilocaine hydrochloride (30 mg/mL) and felypressin 0.03 unit/mL (Dentsply, UK) using a 27G dental syringe.
- 2. *Dedicated patient nurse:* a particular nurse was allocated to provide continuous supportive care to the patient during the procedure. The nurse engaged the patient in conversation ('distraction' analgesia effect termed "vocal local") and often held the patient's hand throughout the procedure.
- 3. Post-procedure analgesic regimen: all women received diclofenac 100 mg rectally and oral co-dydramol 10/500 (two tablets). All women were recovered in a dedicated patient waiting area and allowed home after a minimum 30 min stay. A strict protocol of post-procedure pain relief was adhered to.

2.5. GA hysteroscopic myomectomy

Women, fasted for at least 6 h, were admitted to hospital on the day of the procedure. In a minority of cases, women with high risk medical disorders (e.g. diabetes) were admitted the day before the planned procedure. Hysteroscopic myomectomy was carried out in gynaecology theatres after induction of general anaesthesia and without antibiotic prophylaxis. All women received diclofenac 100 mg and 1 g paracetamol rectally (or paracetamol alone if diclofenac was contraindicated) just prior to the procedure. Infiltration of the cervix with a local anaesthetic was not done in these women. The hysteroscopic myomectomy surgical procedure, post-procedure analgesia regimen and daycase bed stay for GA was identical to the LA hysteroscopic myomectomy procedure described above.

2.6. Complete excision, partial excision and devascularisation at hysteroscopic myomectomy

In all cases, a standardised technique was adopted in order to completely excise and remove the fibroid. The majority of resections were performed by one gynaecologist (JKG; n = 68), with the remainder performed by two other gynaecologists (RV, TJC; n = 24). The submucous fibroid was resected at the junction between the fibroid and uterine wall using a shearing technique. To facilitate this it was occasionally necessary to bisect, trisect or quadrisect the fibroid lesion to access this fibroid–uterine wall interface. Complete excision was achievable in most pedunculated (type 0) and in those superficially myometrially invading (type 1) intracavity fibroids. Occasionally, where the hysteroscopic view became obscured following commencement of the procedure, one of two modified procedures was performed:

- 1. Partial excision and removal of the fibroid was performed. The percentage of the fibroid removed relative to its entire intracavity size was estimated and recorded. The volume of the fibroid tissue extracted and the visual appearances of the fibroid lesion pre- and post-resection were used in deriving the estimate resection percentage.
- 2. Devascularisation of the intracavity without its excision. This entailed multiple scoring of the fibroid lesion (e.g. trisecting or quadrisecting the lesion) at or near its vascular attachment base. The percentage of the fibroid devascularised relative to the entire intracavity lesion was estimated by comparing visual appearances of the fibroid lesion pre- and post-resection.

2.7. Outcome measures

Initial baseline data recorded were: age, body mass index, parity, menstrual bleeding abnormality, ultrasound and hysteroscopy findings, and use of pre-procedure GnRHa. The size of the intracavity uterine fibroid resected was estimated using data from ultrasound and visual appearances at hysteroscopy. In relationship to hysteroscopic myomectomy procedure, the following data were recorded: LA or GA setting, completeness of excision and/or devascularisation, operation length, procedure related complications (e.g. vasovagal episodes) and duration of hospital stay.

After the procedure a postal questionnaire was sent to all women between June and December 2007, ensuring there was a minimum 12-month follow up period. Questionnaire response was maximised by re-contacting women (by phone and letter) with non-returned forms. Patient completed data recorded were: need for and nature of any secondary retreatment, improvement in their menstrual bleeding pattern and dysmenorrhoea (ordinal Likert scales), and patient satisfaction at that time (ordinal Likert scale). Secondary treatments were categorised according to medical (LNG-IUS, oral progestins, combined oral contraceptive, tranexamic acid) and surgical (repeat hysteroscopic myomectomy, open myomectomy, endometrial ablation, hysterectomy) interventions. Primary treatment success was defined as the absence of any type of medical or surgical secondary retreatment following the primary treatment of hysteroscopic myomectomy. The case records and histology results of all study participants were reviewed and recorded.

2.8. Statistical analysis

Dichotomous data were presented as simple proportions. SPSS version 13 was used to undertake multivariate regression analysis and to conduct Chi-square tests. P < 0.05 was considered statistically significant.

2.9. Ethics

A formal application to a Research Ethics Committee recommended that ethics approval was not required as the study was classified as service evaluation according to established Central Office for Research Ethics Committees (COREC) guidelines.

3. Results

Ninety-two women participated in the study and their baseline characteristics are depicted in Table 2. In all study participants, a single fibroid was either resected or devascularised at the index hysteroscopic resection procedure. None of the women were scheduled for an interval 'second-look' or 'second stage' hysteroscopic resection procedure. The characteristics associated with hysteroscopic myomectomy procedure are depicted in Table 3; complete excision was achieved in 61 (66%) cases. Of the 35 (38%) women undergoing LA procedure, none were admitted for overnight stay. Of the 57 (62%) women undergoing GA procedure, 20 (35%) were admitted for overnight stay. None of the study participants experienced uterine perforation or required a blood transfusion (Table 3).

In relation to menstrual symptom improvement and patient satisfaction outcomes, only 2 women (2%) failed to return their questionnaire, representing a 98% follow-up. Examination of the clinical case notes and contacting their GPs confirmed that neither of these two women had undergone secondary treatment following hysteroscopic myomectomy. The mean follow up was 2.6 years (95% CI 2.3–2.9; range 1–4.5 years; St Dev 1.5 years). Overall, greater than, or equal to, 12, 24 and 36 months outcome data were available for 90 (98%), 52 (57%) and 31 (34%) women.

The menstrual, dysmenorrhoea, patient satisfaction and secondary retreatment outcomes are depicted in Table 4.

Table 2Baseline characteristics for 92 women undergoing hysteroscopic myomectomy.

N = 57	N = 92
GA group	All study
Frequency	Frequency (percentage)
1	4 (4)
23	33 (36)
25	42 (46)
8	13 (14)
27.9	27.8
[25.8-30.0]	[26.3-29.4]
20-50	20-52
52	84 (91)
5	8 (9)
52	
[39]	62 (67)
[13]	22 (24)
5	8 (9)
21	34 (42)
27	43 (53)
2	4 (5)
7	11 (12)
	GA group Frequency 1 23 25 8 27.9 [25.8–30.0] 20–50 52 5 [39] [13] 5

^a Missing scan result data (n = 11).

Table 3Characteristics associated with hysteroscopic myomectomy procedure

Patient characteristics	N = 35	N = 57	N = 92
	LA group	GA group	All Study
	Frequency	Frequency	Frequency (percentage)
Preoperative GnRH analogue			
Yes	3	17	20 (22)
No	32	40	72 (78)
Length of operation			
<30 min	35	42	77 (84)
30-60 min	0	14	14 (16)
>60 min	0	1	1 (1)
Size of intracavity uterine fibroid (u/s and by clinical estimat	ion)		
<3cm	, 13	9	22 (24)
3–5 cm	21	32	53 (58)
>5 cm	1	16	17 (19)
Primary treatment performed			
Complete excision	45	22	40 (50) (64 (660))
Complete excision and removal	15	33	48 (52) (61 (66%))
Complete excision and endometrial ablation Complete excision and LNG-IUS (Mirena)	2 2	9 0	11 (12)
	2	U	2 (2)
Incomplete excision			
>50% excision and removal	4	8	12 (13) (31 (34%))
>50% devascularised and left in situ	12	7	19 (21)
Complications			
Bleeding requiring balloon tamponade	0	8	8 (9)
Cervical trauma	0	1	1 (1)
Blood transfusion	0	0	0 (0)
Uterine perforation	0	0	0 (0)
Length of hospital stay			
Daycase	35	37	72 (78)
Overnight	0	20	20 (22)

Surgical re-intervention was necessary in 27 (29%) women due to persistent heavy menstrual bleeding, and this involved hysterectomy in 10 cases and their characteristics are depicted in Table 5. Seven hysterectomies (70%) were performed by 12 months of the primary hysteroscopic myomectomy, and of these, 2 hysterectomies were performed for unexpectedly identified gynaecological pathology (one case complex hyperplasia, one case leiomyosarcoma). Adenomyosis and multiple fibroids were the commonest histological findings at hysterectomy (8/10 cases).

Multivariate analysis of prognostic factors identified incomplete compared to complete fibroid excision to be associated with an increased likelihood for secondary retreatment (OR 4.67; 95% CI 1.44–15.11) and secondary surgical re-intervention (OR 4.85; 95% CI 1.86–12.67] (Table 5). Whereas, regular cycle HMB compared to irregular cycle HMB was associated with a decreased likelihood for secondary retreatment (OR 0.12; 95% CI 0.03–0.49) and a trend towards decreased secondary surgical re-intervention (p = 0.09) (Table 6). Size of the resected fibroid, presence of intramural or subserosal fibroids, or LA vs. GA. setting were unrelated to treatment success (Table 6).

4. Discussion

Women with heavy menstrual bleeding (HMB) and submucous myomas may be successfully treated by completely excising the intracavity myoma component, irrespective of co-existent intramural or subserosal fibroids or size of the intracavity fibroid resected. The beneficial effects of hysteroscopic myomectomy persist long term (mean follow up around 2.5 years). Hysteroscopic myomectomy significantly reduces the likelihood of

women with HMB and fibroids requiring hysterectomy, with 11% requiring hysterectomy in this cohort study. The majority of women who underwent hysterectomy as secondary retreatment were identified to have adenomyosis and multiple uterine fibroids. Completeness of intracavity fibroid excision and presenting with regular cycle HMB rather than irregular cycle HMB are associated with treatment success.

To date, studies published on hysteroscopic myomectomy have utilised various technical approaches, been mainly performed under GA in daycase settings, have mixed retrospective and prospective observational designs, and have minimal data on long term follow up, particularly patient satisfaction and surgical re-intervention rates [7,11–19]. Our study adds to this published literature by exclusively utilising a modern VersascopeTM bipolar system, been successfully undertaken in both outpatient and daycase setting, has prospective design, has long term follow up incorporating patient satisfaction, has evaluated peri-operative features that may have prognostic value, and expands on our previously published work [7]. Our surgical re-intervention rate of 29% (over mean 2.5 years) was lower than that reported by previous study of 35% (over mean 5 years) [16]. This study has been pragmatic in design, ensuring our results our applicable to actual clinical practice.

We accept our study may have limitations that may make our conclusions less reliable. Our study sample size, although at 92 with a low dropout rate (2%), may be underpowered to identify all peri-operative prognostic factors. Because our follow up intervals varied between patients, there may be a tendency to overestimate or underestimate the beneficial effects of hysteroscopic myomectomy at the extremes of follow up. We made no adjustment for amenorrhoea achieved through the small

Table 4Outcomes after hysteroscopic myomectomy

Outcome measure	Entire study, n = 92	Excluding 10 women who had hysterectom (n = 82)
	Frequency (percentage)	Frequency (percentage)
Menstrual bleeding at enquiry		
Amenorrhoea	28 (30) [includes 10	18 (22)
Brown discharge	hysterectomies] 3 (3)	3 (4)
Much lighter	40 (43)	40 (49)
Marginally lighter	13 (14)	13 (16)
No change	4 (4)	4 (5)
Heavier	2 (2)	2 (3)
Unknown	2 (2)	2 (2)
Overall menstrual improvement	84 (91)	74 (90)
Dysmenorrhoea at enquiry		
None	50 (54) [includes 10 hysterectomies]	40 (49)
Less	26 (28)	26 (31)
No change	11 (12)	11 (13)
Worse	3 (3)	3 (4)
Unknown	2 (2)	2 (2)
Overall dysmenorrhoea improvement	76 (83)	66 (81)
Degree of satisfaction at enquiry		
Very satisfied	55 (60)	54 (66)
Satisfied	24 (26)	20 (24)
Dissatisfied	6 (7)	4 (5)
Very Dissatisfied Unknown	5 (5) 2 (2)	2 (2) 2 (2)
Overall satisfied	79 (86)	74 (90)
overall satisfied	75 (00)	71 (30)
Secondary retreatment		
Myomectomy (open) Thermal Balloon Endometrial Ablation	4 (4)	
LNG-IUS (Mirena)\$	2 (2) 7 (8)	
Hysterectomy	10 (11)	
Repeat resection	8 (9)	
Repeat resection and ablation	1 (1)	
Repeat resection and LNG-IUS (Mirena)\$	2 (2)	
Oral progestins	2 (2)	
No secondary retreatment	56/92 (61)	
Secondary retreatment (all types)	36/92 (39)	
No surgical re-intervention	65/92 (71)	
Overall repeat surgical treatment	27/92 (29)	

Missing questionnaire responses for menstrual (2) and dysmenorrhoea (2) characteristics and patient satisfaction (2). Case notes and GPs were contacted and no secondary treatments were undertaken in the 2 non-returned questionnaire responses. \$ LNG-IUS (Mirena) was used as treatment of menorrhagia and/or dysmenorrhoea.

proportion of women who became menopausal during follow up. The variation in follow up interval outcome data and relatively small numbers precluded our use of survival analysis techniques to assess both efficacy and durability of the hysteroscopic procedure. It is unclear why 20/57 GA daycases were admitted overnight, but this may reflect inherent differences in patient preferences and pain thresholds of women who opt for LA rather than GA type procedures.

Given the 29% risk of surgical re-intervention following submucous myomectomy, there is a need to identify significant peri-operative prognostic factors that could be usefully employed during preoperative counselling. Our study showed incompleteness of fibroid excision and irregular cycle HMB to

Table 5 Women (*n* = 10) undergoing hysterectomy following hysteroscopic myomectomy.

Characteristic	Value
Number of hysterectomies	10
Average time to hysterectomy	Mean 14.4 months
	(95% CI 4.5-24.3)
	Median 9.5 months;
	range 1-41 months;
	St Dev 13.9
Time from procedure and	By 6 months: 4/10
cumulative rate of hysterectomy	cases [one for
	leiomyosarcoma],
	By 12 months: 7/10
	cases [one for complex hyperplasia], By
	24 months: 8/10 cases,
	By 48 months: 10/10
	cases
Very satisfied	1
Satisfied	4
Dissatisfied	2
Very dissatisfied	3
Overall satisfied	5 (50%)
Overall dissatisfied	5 (50%)
Histology	
Adenomyosis and fibroids (multiple)	6
Fibroids (multiple)	2
Leiomyosarcoma	1 (identified on resection
	histology and reason for TAH)
Complex Hyperplasia	1 (identified at resection
	histology and reason for TAH)

adversely affect treatment outcome and showed no effect of the size of intracavity fibroid excised, presence of intramural or subserosal fibroids or LA vs. GA setting on treatment outcome. It is logical to assume that there is an inter-relationship between incompleteness of fibroid excision, size of intracavity fibroid and depth of its myometrial invasion, even though we did not explore the latter variable in this study. Our findings should be compared and contrasted with previous studies that have identified enlarged uterine size, three or more intracavity myomas, fibroid size >3 cm and increased depth of myometrial penetration to be adverse prognostic factors [15,16] (Table 1). Importantly, our study reinforces the widely held opinion that it is only the presence of the submucous fibroid itself that appears to be responsible for the HMB [4,5].

Our study showed that adenomyosis was frequently identified in those women who required hysterectomy as secondary treatment. It is plausible that the adenomyosis component may also be influential in adverse treatment outcome by contributing to both irregular cycle HMB and dysmenorrhoea in women with fibroid uteri. There is insufficient evidence on the ultrasonographic criteria that reliably predicts adenomyosis and whether adenomyosis should be routinely screened for in women with menstrual disorders [20,21].

Future studies are needed to identify the clinical efficacy, optimal patient selection and superior hysteroscopic resection technique for hysteroscopic myomectomy [6], and whether preoperative imaging suspicion of adenomyosis may be usefully employed in the treatment decision making process. More studies with long term follow up of hysteroscopic myomectomy patients are needed to provide data on surgical retreatment (particularly rates of hysterectomy) due to recurrence of fibroid pathology. Such studies would be useful in evaluating the long term cost effectiveness of hysteroscopic myomectomy compared to other treatment options and therefore be important for determining the optimal initial treatment decision.

Table 6Strength of association of prognostic factor with clinical outcome measure using multivariate analysis.

	· ·	
	p-Value for strength of association of prognostic factor to outcome Odds Ratio OR of prognostic factor if statistical significant association	
Prognostic factor	Likelihood for secondary retreatment (all types)	Likelihood for secondary surgical re-intervention
Regular cycle vs. irregular cycle HMB ^a	p = 0.003 ^a OR 0.12 [95% CI 0.03-0.49]	$p = 0.09^{a}$
Scan findings (submucous, intramural, subserosal fibroid presence)	p = 0.45	p = 0.86
Size of fibroid	p = 0.41	p = 0.84
LA vs. GA	p = 0.77	p = 0.92
Incomplete vs. complete excision	p = 0.010 OR 4.67 [95% CI 1.44–15.11]	p = 0.001 OR 4.85 [95% CI 1.86–12.67]

Multivariate regression corrected for the following confounding factors, including: age, BMI, menopausal status, type of menstrual bleeding abnormality, scan findings, preoperative GnRHa, size of uterine fibroid, completeness of excision at hysteroscopic myomectomy and LA vs. GA type of procedure. Binary logistic regression models for secondary treatment and secondary surgical re-intervention were statistically significant (p < 0.01).

a Irregular cycle HMB compared to regular cycle HMB was statistically significantly associated with secondary treatment. This prognostic factor showed a similar association with secondary surgical treatment which approached statistical significance (p = 0.09). Non-menstrual bleeding was not significantly associated to treatment outcome.

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